UNIVERSITY OF SOUTHAMPTON

Identifying New Health Care Technologies

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ABSTRACT

FACULTY OF MEDICINE, HEALTH AND BIOLOGICAL SCIENCES

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IDENTIFYING NEW HEALTH CARE TECHNOLOGIES

Glenn Brian Robert

The introduction of new health care technologies can have enormous consequences, both desirable and undesirable, for health services and patients. Early identification of technologies prior to their widespread adoption can enable timely cost-effectiveness evaluations to be undertaken, as well as fulfilling a number of other objectives. This thesis has two aims: (a) to explore the most useful sources for identifying new health care technologies prior to their widespread adoption by the National Health Service (NHS), and (b) to recommend how to establish and operate an early warning system (EWS) in the United Kingdom (UK). Within this context an assessment is made of the likely 'payback' from the operation of an EWS.

Four methods are used: a systematic review of the literature on the methodology of predicting the future of health care; a semi-structured telephone enquiry of EWS coordinators from around the world; an international Delphi study to identify preferred sources for identifying new health care technologies; and retrospective case studies to illustrate how specific innovations could have been identified prior to their introduction and the payback to the NHS of such early identification.

A combination of the following information sources (many of which can now be accessed via the Internet) is recommended:

- scanning of 'specialist' medical journals, key medical journals, Food & Drug Administration licensing applications in the US, key pharmaceutical journals and conference abstracts, and liaison with pharmaceutical & biotechnology companies to produce a database of potential technologies, and
- regular meetings and/or surveys involving sentinel groups of expert health professionals.

The exact form of an EWS will ultimately depend upon the purposes for which the EWS is to be used and the policy environment within which it is expected to operate. Important general aspects of the operation of an EWS are:

- continuity, so that the important monitoring function of an EWS can be performed on those technologies which have a long development phase;
- that only a relatively small core staffing is required as long as there is access to experts either through formal committee structures or regular surveys;
- the need for collaboration with existing national and international programmes with the aim of ensuring adequate coverage of all types of technologies and providing sufficient early warning; and
- that an EWS should be part of a national HTA programme in order to allow health technology assessment (HTA) research to be commissioned or run in parallel alongside early clinical trials.

The overall value of an EWS for HTA purposes should be judged by the extent to which it facilitates timely research-based evidence on new technologies. The assessment of the likely 'payback' to the NHS from EWS-instigated research on the nine case-studies suggests a number of important potential benefits. Suggestions for realising and increasing the value of an EWS in the context of recent policy developments in the UK are presented.

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PUBLICATIONS

Robert G, Stevens A, Gabbay J. Identifying new health care technologies. In: Fitzpatrick R, Black N, Stevens A (eds.) *Methodology for Health Technology Assessment.* London; Sage Publications, 2000 (in press)

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"Trends and issues in Science and Technology forward to 2015", *International Society of Technology Assessment in Health Care,* Edinburgh, 1999 (poster)

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"Three case studies of predicting future expenditure implications of new/emerging health care technologies: a drug, a setting and an intervention", *European Public Health Association Annual Meeting,* London, 1996

"New and Emerging Technologies in the UK - A 'Horizon' scanning exercise for the National Standing Group on Health Technology", *International Society of Technology Assessment in Health Care,* San Francisco, 1996

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ABBREVIATIONS USED IN THE TEXT

ANAES:	L'Agence Nationale d'Accréditation et d'Evaluation en Santé (France)
BPA:	British Paediatric Association
CCOHTA:	Canadian Coordinating Office for Health Technology Assessment
CF:	cystic fibrosis
CMP:	Changing Medical Practice group (of the Standing Medical Advisory Committee)
CRD:	Centre for Reviews & Dissemination (UK)
CT:	computed tomography
DEC:	Development & Evaluation Committee
DH:	Department of Health (UK)
DHSS:	Department of Health & Social Security (UK)
DIPG:	Drug Information Pharmacists Group (UK)
DIS:	Drug Information Services
DSI:	Danish Institute for Health Services Research & Development
EC:	European Community
ECMO:	extra corporeal membrance oxygenation
EL:	executive letter
ESWL:	exta corporeal shockwave lithtripsy
EWS:	early warning system
FDA:	Food and Drug Administration
FinOHTA:	Finnish Office of Health Technology Assessment
HTA:	health technology assessment
IDE:	investigational device exemption
IDDM:	insulin dependent diabetes mellitus
IFN-β:	beta interferon
IHFN:	International Health Futures Network
INAHTA:	International Network of Agencies for Health Technology Assessment
IND:	investigational new drug
ISTAHC:	International Society of Technology Assessment in Health Care
LVAD:	left ventricular assist device
MDA:	Medical Devices Agency
MRC:	Medical Research Council
MS:	multiple sclerosis
NHS:	National Health Service
NICE:	National Institute for Clinical Excellence
NPC:	National Prescribing Centre
NRR:	National Research Register
NSCAG:	National Specialist Commissioning Advisory Group
OST:	Office of Science & Technology (UK)
OTA:	Office of Technology Assessment (US)
PET:	positron emission tomography
PIC:	paediatric intensive care
PICU:	Paediatric Intensive Care Unit
PLA:	product licensing application
PTCA:	percutaneous transluminal coronary angiography
QALY:	quality adjusted life year
R & D:	research and development
RCT:	randomised controlled trial
SBU:	Swedish Council on Technology Assessment in Health Care
SDAT:	senile dementia of the Alzheimer's type
SERNIP:	Safety and Efficacy Register of New Interventional Procedures
SMAC:	Standing Medical Advisory Committee (UK)
STG:	Steering Committee on Future Health Scenarios (The Netherlands)
UK:	United Kingdom
US:	United States
YSI:	Yellow Springs Instruments
WHO:	World Health Organisation

SUMMARY

AIMS

This thesis aims to:

(i) explore the most useful sources for identifying new health care technologies prior to their widespread adoption by the National Health Service (NHS), and

(ii) make recommendations regarding the establishment and operation of an early warning system (EWS) in the United Kingdom (UK).

Within this context the thesis also examines the likely 'payback' to the NHS from the operation of an EWS.

BACKGROUND

The introduction of new health care technologies (whether drugs, devices, procedures or innovative ways of delivering services) can have enormous consequences, both desirable and undesirable, for health services and patients. Often new technologies are introduced in a haphazard and uncontrolled manner causing unnecessary confusion or expense. Early identification of impending technologies can help to ensure that the maximum benefits and/or minimal costs are realised for the health care system (either through the adoption or non-adoption of the technology), and can also help to fulfill a number of other objectives. Futures studies in health care can broadly operate within the short (up to five years) or long term (more than five years). An EWS for health technology assessment (HTA) is concerned with the short-term.

An important recent policy development in the UK has been the establishment of the National Institute of Clinical Excellence (NICE) which is using the intelligence from an EWS to help inform its selection of technologies for national appraisal. This thesis determines which sources might best be used to provide such intelligence, considers how an EWS should operate, and discusses the likely benefits that could be realised by its operation.

METHODS

The methods used comprise:

(i) a systematic review of the literature on the methodology of predicting the future of health care,

(ii) a semi-structured telephone enquiry of EWS coordinators from around the world,

(iii) an international Delphi study about preferred sources for identifying new health care technologies, and

(iv) retrospective case studies to learn how specific technologies could have been identified prior to their introduction to the NHS and to estimate the likely 'payback' to the NHS from EWS-instigated research on these technologies.

RESULTS

The literature review might have been expected to reveal four types of literature related to studies of the future of health care:

- type I: methodological papers which assessed the processes and information sources by which health care technologies could be identified with a short-term perspective, whether set in the context of a national EWS or not,
- type II: scientific attempts at identifying new health care technologies using formal and empirical methods but which did not assess those methods,
- type III: editorials or polemics relating to future technological developments in health care but without any explicit description of their empirical methods or sources of information, and
- type IV: Delphi studies or scenario analyses of future trends in health or health care which were concerned not with likely technologies but with preferable 'futures' and/or related to a longer term perspective than that with which this thesis is concerned.

No type I papers were found that had as their main objective the systematic assessment of various sources of information for identifying new health care technologies or methods for accessing such information. However, five type II studies were identified. Although most used several sources of information, the only source that was common to all the studies was consultation with experts. There was no agreed or proven method of identifying new health care technologies.

The telephone enquiry of existing EWS also suggested that liaison with experts is a *sine qua non*. Such an approach allows access to the informal networks in a particular field that communicate research findings by personal contact before they are known by publication. Contemporary sources, such as the Safety & Efficacy Register of New Interventional Procedures (SERNIP) in the UK, also have an important contribution to make.

The literature review and telephone enquiry showed that the establishment of an EWS is a recent concept for virtually all countries. An EWS has been in operation in the Netherlands since 1988 and five other national organisations are currently beginning to establish such systems (Canada, Denmark, France, Sweden, United Kingdom). These are often principally aimed at establishing research priorities for HTA but may also seek to inform professional groups and other interested parties of imminent technologies. Existing EWS seek to identify all types of health care technologies likely to emerge within five years. They generally have a staff of no more than five whole-time equivalents (WTE) and use a variety of methods for accessing expert opinion (although there is as yet no empirical evidence to suggest the 'best' way of doing so). On average, information on ten to twelve technologies is disseminated each year by existing EWS via a wide range of mechanisms and products. Close collaboration with HTA programmes, as well as with other national and international early warning initiatives, is recommended. The overall aim of any EWS is as an aid to policy-making and to the rational introduction of new technologies. Within this remit early warnings can be used for a variety of policy purposes. In general, EWS seek to help control and rationalise the complex patterns of adoption and diffusion of technologies which result from the promotion of technologies by the health care industry and professional opinion-leaders.

Participants in the Delphi study ranked the timeliness and the efficiency of searching the sources as being the most important criteria by which their value to an EWS should be judged. On this basis they recommended using a combination of the following information sources: key pharmaceutical journals, pharmaceutical & biotechnology companies, specialist medical journals (i.e. those containing early case reports, case series and uncontrolled studies), principal medical journals, medical engineering companies, private health care providers, newsletters & bulletins from other national & regional HTA agencies and sentinel groups of expert health professionals.

The case studies suggest that, in addition to liaising with experts, particularly important documentary sources include key pharmaceutical journals, specialist medical journals

and Food & Drug Administration (FDA) licensing applications in the United States (US). Conference reports can also be useful. The payback analyses of the retrospective case-studies suggest that the operation of an EWS in the UK has the potential to:

- assist in the development of timely guidelines for health care professionals,
- assist early monitoring of new technologies through registers in recognised centres,
- enable 'watchful waiting' where appropriate,
- allow longer term effectiveness information on new technologies to be available sooner,
- lengthen methodological lead time to, for example, assist in the development of appropriate outcome measures, and
- assist in commissioning research with realisable payback.

DISCUSSION

Four separate methods were adopted as there is no definitive way of establishing the best information sources for identifying new health care technologies. This approach allowed comparison between the results from each of the methods: a review of the published literature, a survey of existing systems, a Delphi study and nine case studies.

From the results of the four methods a three-fold classification of potential sources for identifying new health care technologies was developed: *primary* (the manufacturer or innovator), *secondary* (knowledge or expertise intended for other purposes) *and tertiary* (other agencies' efforts to identify technologies). *Primary* information sources are likely to provide earlier warning but are uncertain indicators of the likely adoption of a new technology. They often provide little detail on the potential new technology. *Secondary* and *tertiary* sources, on the other hand, will provide later warning, perhaps in some cases only after the introduction of the technology, but greater detail and more accurate predictions of its likely impact. There is some overlap between these categories (for example experts at the cutting edge may also act as *primary* information sources) but the classification highlights the important trade-off between earlier warning and greater accuracy.

The relative importance of potential sources for identifying new health care technologies varies under different circumstances; it will depend upon the type of innovation under

consideration and the audience at which the early warning is aimed. Clearly, some types of technology (for example, pharmaceuticals) are easier to identify than others.

Of the many information sources identified by the various methods adopted, each has its own particular advantages and disadvantages. There were some discrepancies between the sources recommended by the literature review, telephone enquiry, Delphi study and case studies but widespread consensus that key pharmaceutical journals and liaison with experts are important components of an EWS. In addition, 'specialist' medical journals, key medical journals, FDA licensing applications, conferences and liaison with pharmaceutical and biotechnology companies were highlighted, with reservations, as being potentially useful, additional information sources. The iteration between the use of documentary sources and the involvement of experts appears to be vital to any EWS. A number of the information sources (for example, the Internet and patient special interest groups) are becoming more prominent; their potential value to an EWS will need to be monitored.

There are a number of factors which may limit the success of an EWS. In particular, there is a need to design and implement new routes to incorporate the results of research in guidelines or policy mechanisms, and, by doing so, improve the relationship between knowledge, evidence, and policy- and decision-making.

CONCLUSIONS

A combination of the following information sources (many of which can now be accessed via the Internet) is recommended and is based on all four of the methods adopted:

- scanning of 'specialist' medical journals, key medical journals, FDA licensing applications, key pharmaceutical journals and conference abstracts and liaison with pharmaceutical & biotechnology companies, to produce a database of potential technologies, and
- regular meetings and/or surveys involving sentinel groups of expert health professionals.

The exact form and operation of the EWS (and the sensitivity and specificity, level of detail and timeliness which will be required from the chosen information sources) will ultimately depend upon the health care system of which it is a part and the purposes to which the EWS are to be applied. Important aspects of the operation of an EWS are:

- continuity, so that the important monitoring function of an EWS can be performed on those technologies which have a long development phase;
- that only a relatively small core staffing is required as long as there is access to experts either through formal committee structures and/or regular surveys;
- the need for collaboration with existing national and international programmes (for example, in the UK collaboration with regional DIS, SERNIP, SMAC-CMP, NSCAG and NICE) with the aim of ensuring adequate coverage of all types of technologies and providing sufficient early warning; and
- that the EWS should be part of a national programme to allow HTA research to be commissioned or run in parallel alongside early clinical trials.

Applications of early warning should help to minimise unnecessary costs, health disbenefits and policy confusion. A national EWS, for example, could help to inform the preparation of guidelines by NICE for commissioners of health care (whether health authorities or general practitioner consortia) in advance of the introduction of new innovations and establish national priorities for researching cost-effectiveness. Such an EWS should be prospectively evaluated. Its value in the HTA context should be judged firstly by the extent to which it facilitates timely research-based evidence on important new technologies and ultimately by how the resulting research evidence informs and influences health care professionals behaviour.

1 AIMS

The overall aim of this research is to develop a robust method for identifying new health care technologies in order to help a national HTA programme provide timely information to decision-makers in the NHS. It sets out to achieve this by cataloguing and assessing, through a variety of methods, potential information sources for identifying new health care technologies. As part of this overall aim the potential 'payback' of such an initiative is assessed.

The *a priori* hypothesis (based on the findings of the Scenario Commission on Future Health Scenarios in the Netherlands[1]) was that the best source of information on future health care technologies would be regular liaison with sentinel groups of experts. The Commission recommended that individuals with an interest in future technology (such as applied researchers and inventors, and clinicians who keep up with developments in their specialised fields) are ideal as experts.

Specific objectives were to:

1. make recommendations on the most useful sources for identifying new health care technologies,
2. make recommendations on the establishment and operation of an EWS in the UK as part of a national HTA system, and
3. to consider the likely value of such an EWS to the NHS.

2 TIMELINESS OF THIS THESIS

The rapid speed with which new health care technologies can diffuse through the NHS, their potential impact and their increasing numbers mean that there is an urgent need to develop and operate an approach which singles out those technologies which might have a significant impact on the NHS in the near future. At the national level such an approach can be used[a]:

- to develop and prioritise a HTA research programme (given the limited resources available for research and development[2] (R & D)),
- to assist with issuing guidance to service commissioners,
- to estimate future cost implications,
- to consider the implications for planning the configuration of health care, and
- to encourage professional bodies to develop any necessary guidance and to assess implications for standards and training.

Success in these objectives will be in part determined by the selection of the information sources used to identify new technologies and by the methods adopted to evaluate them. It will also depend on understanding the complex process of adoption and diffusion that underpins the development and use of new technologies in the NHS, with the aim of enabling more timely provision of HTA information for decision-making[3].

Many of these objectives are central to the recent establishment in the UK, in April 1999, of NICE[b]. In recent evidence to the Select Committee on Health the Chairman of NICE commented that '. .over the past few years with new technologies, new devices, new pharmaceuticals . . . appraisal has been undertaken by district health authorities each acting independently with little warning, no horizon scanning, but suddenly presented with a new technology'[4]. This thesis aims to determine the method for operating an EWS in the context of the UK's HTA programme and NICE, and builds on previous work carried out on behalf of the UK's National Standing Group on Health Technology[5].

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[a] Source: Smee C. *The need for early warning in health policy making and planning*. European Workshop: Scanning the Horizon for Emerging Health Technologies, Copenhagen, 1997

[b] the policy documents relating to the establishment of NICE are available from http://www.nice.org.uk

3 DEFINITIONS

INTRODUCTION

The following are brief descriptions of the key concepts that are central to this area of study and examined in this thesis. Appendix 1 provides fuller discussion on these concepts.

3.1 HEALTH CARE TECHNOLOGY

Health care technology 'encompasses all methods used by health professionals to promote health, prevent and treat disease, and improve rehabilitation and long-term care. It includes the activities of the full range of health care professionals, and the use of equipment, pharmaceutical and health care procedures generally'[6].

3.2 NEW HEALTH CARE TECHNOLOGIES

New health care technologies are those that have been relatively unevaluated and are only just about to be introduced, or have only recently been introduced, to clinical practice[7]. They are distinct from 'emerging' technologies which are not yet fully developed[8]. Thus new technologies comprise those in the applied research stage, about the time of initial clinical testing, and those past the stage of clinical trials but not yet in widespread use[9]. They may also be technologies localised to only a few centres, and for the purposes of this thesis may be new applications of existing technologies.

3.3 HEALTH TECHNOLOGY ASSESSMENT (HTA) IN THE UK

The concept of HTA began formally in the mid-1960s in the Committee on Science and Astronautics of the United States (US) House of Representatives with the recognition that scientific and technological developments present potential social consequences. It is not within the scope of this thesis to detail the subsequent history of the development of HTA in the UK and elsewhere. This development can be traced through a number of key publications[9,10,11,12,13,14,15,16,17] and a brief review is already available[18].

Contemporary HTA considers the effectiveness, appropriateness and cost of technologies. It does this by asking four fundamental questions[a]: does the technology

[a] Source: UK HTA programme home page, http://www.soton.ac.uk/~hta

work, for whom, at what cost, and how does it compare with alternatives? A comprehensive HTA strategy should include the following strands[3]:

- the systematic identification and prioritisation of health care technology requiring assessment,
- the synthesis of existing research findings and production of overviews or meta-analyses,
- the co-ordination of empirical studies where research evidence is lacking, and
- dissemination of HTA findings and implementation.

The current HTA programme in the UK was established in 1993 and is a national programme of commissioned research. The aim of the HTA programme is 'to ensure that high quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage and work in the NHS'[8]. From 1999 onwards the HTA programme will also provide key inputs to the work of NICE which is aiming to perform appraisals on 30-50 technologies each year once it has become fully established.

3.4 FUTURES STUDIES AND FUTUROLOGY

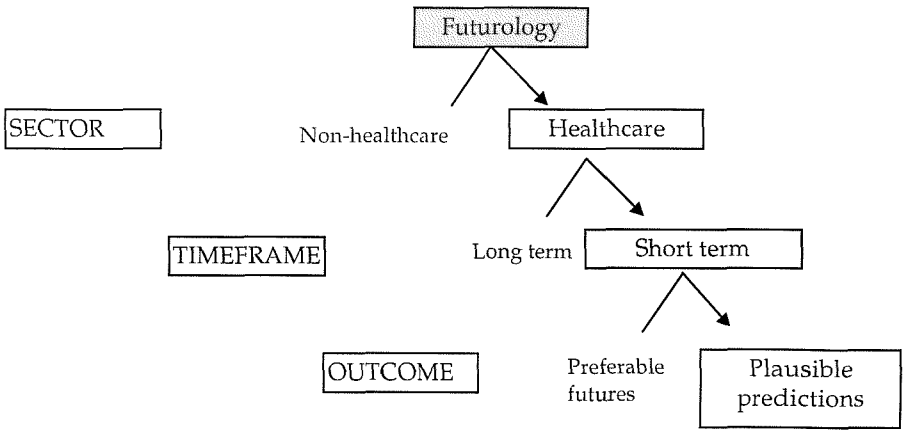
'Futures' is an extremely wide field, and futures studies fulfill many, and quite different, purposes[19,20]. Bezold[21] suggests that the futures field involves:

- the systematic consideration of what might happen (exploring plausible futures),
- the identification of what we want to create (visions or preferable futures), and
- assisting in the development of strategies and tactics directed towards achieving the vision, in the light of plausible environments faced.

There is a strong division between plausible and preferable futures[21]. Work on plausible futures identifies and forecasts the potential trajectories in key aspects of health care (for example, health care technologies) whilst 'vision' work in health explores preferred futures. Futurologists often employ a combination of projection, extrapolation and pure guessology to create 'visions' of technology and society in the decades ahead[22]. Generally, the accuracy of forecasts, or of scenarios[23,24], is secondary to whether the work either aids in wiser decision making or results in actions which create the futures we would prefer.

Figure 1 sets the scope of this thesis in the context of the discipline of futurology. It is concerned with new health care technologies (sector) in the short-term (timeframe) and making plausible predictions (outcome) as to which are likely to be important upon their introduction into the NHS:

Figure 1 *Focus of this thesis within the context of 'futures' research: plausible, short term predictions in the health care sector*



3.5 INNOVATION AND DIFFUSION

An *innovation* is an idea, practice or object that is perceived as new by an individual or other unit of adoption[25]. Technological innovation in medicine covers the wide range of events that includes the discovery or invention, development and dissemination of a new health care technology[26].

Diffusion is the process, whether planned or spontaneous, by which an innovation is communicated through certain channels over time among the members of a 'social system' (health care system)[25]. The study of diffusion is concerned with three phenomena[27]:

- the speed of diffusion,
- its extent (what percentage of potential adopters ever adopt the innovation), and
- patterns of diffusion (including the shape of the time path of diffusion, patterns of geographic spread, and patterns of diffusion among members of the health care system).

3.6 EARLY WARNING SYSTEMS (EWS)

A system for identifying future health care technologies can act as a mechanism to allow early communication between policy makers and experts, and is an integral part of a complete system for HTA[1]. Identification of technologies might occur, for instance, at the point in their development when they are tested on a human being for the very first time. The aim of an EWS in the health care sector is to identify potential health care technologies expected to diffuse into that sector in the years to follow. An early technology assessment can then be performed if needed.

Activities which form an integral part of an EWS and which seek to provide a list of potential new health care technologies are, for example, scanning particular key medical journals or liaising with pharmaceutical companies. Early warning activities are sometimes referred to as 'horizon scanning'. These terms are interchangeable as illustrated in the context of NICE: '. . very early on in the life of a product we will be undertaking what we call horizon scanning . . . as to what are the most significant technologies that might be coming over the horizon over the next few years so that we have some advance intelligence'[28].

4 BACKGROUND AND RATIONALE FOR THE STUDY

Chapter Summary

The introduction of new health care technologies (whether drugs, devices, procedures or innovative ways of delivering services) can have enormous consequences, both desirable and undesirable, for health services and patients. Often new technologies are introduced in a haphazard and uncontrolled manner causing unnecessary confusion or expense. Early identification of impending technologies can help to ensure that the maximum benefits and/or minimal costs are realised for the health care system (either through the adoption or non-adoption of the technology), and can also help to fulfill a number of other objectives.

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INTRODUCTION

This chapter sets the context for this research by outlining the need for an EWS (section 4.1), describing the state of the art of early warning (section 4.2) and, finally, by discussing two potential problems relating to the development of methods for operating an EWS (section 4.3).

4.1 THE NEED FOR AN EARLY WARNING SYSTEM

New health care technologies have led to significant social benefits. Nevertheless they have been increasingly questioned during the last 25 years, reflecting a growing concern with the role of technology in society[10,29,30,31,32,33,34,35,36,37]. Concerns are not only about effectiveness but also the impact of the costs of new technologies in a fixed-budget, publicly funded health care system such as the NHS. Often the focus is on expensive health care technology. A technology can fall into this category by involving expensive capital equipment (for example, a whole body scanner), by requiring substantial time of highly skilled persons to operate it (for example, renal dialysis) or by its high usage (for example, certain diagnostic tests or drugs).

While the overall effect of technology applied to health care has unquestionably increased health gain, rising health expenditures have led economists to examine the

impact of new technology on health care costs[38,39,40,41,42,43,44,45,46,47,48]. The economic impact may take a number of forms:

- new technologies may substitute for existing technology but at higher cost (including the cost of the technology itself and required supportive resources),
- the new technology may replace existing ones, thereby reducing use of some resources, but by complementing existing technologies it may increase the intensity of their use, and thus the cost per patient,
- the introduction of new technologies may enable the treatment of previously untreatable patients or may lower the treatment threshold for others,
- if the technology has clinical side effects, there may be induced resource use, and
- there may be non-medical costs associated with receiving the health care, effects on employment, and other unanticipated resource effects.

However, the positive effects on health outcomes may balance part or all of these higher costs[49,50,51,52].

Other sectors such as electronics, aviation[53] and agriculture, have undertaken extensive studies of technological innovation and diffusion[25]. It is in health care where major shortcomings in managing technological change have been identified, possibly because of the unusual way in which health technologies diffuse. The entry of some types of new technologies into the NHS, such as drugs, certain ethically and legally complex innovations (for example, infertility treatment and xenotransplantation[62]) and a limited number of highly specialised services (designated as such by the National Specialist Commissioning Group (NSCAG)), are to some extent controlled. Generally, however, the NHS has tended to introduce technologies haphazardly before their effectiveness and appropriateness have been proven[a] [54,55,56,57,58,59]. Stocking[55] suggests that the problem is two-fold:

- firstly, many innovations diffuse before they are shown to be effective, the trials are not done or are done very late in the process; and

[a] Rawlins cites coronary artery bypass grafting as an example of a technology which was widely adopted by the NHS with 'absolutely no evidence that there was any benefit whatsoever' and where early RCTs would have provided the necessary evidence (Source: Select Committee on Health. Minutes of Evidence for Thursday 4 February 1999. National Institute for Clinical Excellence: Professor Sir Michael Rawlins; Dr Gina Radford and Dr Timothy Riley (question 30)

- secondly, even if some evidence is available, it often comes from the national product champions' own units or districts, precisely the places where the innovation is most likely to work. The results, especially for organizational innovations, may not apply more generally.

For example, while there are currently 62 replacement hip joints (manufactured by 19 different companies) available in the UK, there is usually no evidence in peer-reviewed journals supporting the use of these different prostheses over other alternatives and there are large geographical variations in use[60a]. In early 1998 the UK Medical Devices Agency (MDA) issued a hazard warning[61] about one of these products which may lead to up to 5,000 patients who have undergone hip replacement surgery having to be recalled and possibly having repeat operations (at a cost of £5,000 per operation). Such devices are not required to undergo long-term clinical trials before being introduced and their longer-term outcomes are not subject to monitoring via national registries as has been suggested by some commentators[62]. In contrast, in Sweden there is a national register of hip replacement operations, which allows problems with a new device or material to be spotted early. When a new cement called *Boneloc* was discovered to have a high failure rate in Sweden it had been used on only 15 patients, but in Britain it had already been used on 1,800 patients[b].

Such concerns about the introduction of new health care technologies has led, in line with developments such as the NHS R & D strategy[56] and evidence-based medicine[63], to increasing interest in improved NHS evaluation and control of technology. New technologies must be shown, by rigorous evaluation, to be more cost-effective than the technologies they may replace. This interest has culminated in the newly established NICE whose 'fundamental objective is to improve standards of patient care, and to reduce inequities in access to innovative treatment'[64]. Part of the NICE process will include identifying[64]:

> "those new treatments and products which are likely to have a significant impact on the NHS, or which for other reasons would

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[a] One of the first technologies to be appraised by NICE in the UK will be hip prostheses as two recent studies in the HTA programme concluded that there was no evidence of additional benefit from using more expensive prostheses. NICE will advise the NHS on obtaining best value for money for patients without reducing the quality of patient care (Source: NICE press release 6th August 1999)

[b] Source: '5,000 hip operations may have to be repeated', *The Independent* (February 19, 1998). Such failures have led to calls for the establishment of a registry of hip implants (Source: Riordan P et al. Lessons of a hip failure. *BMJ*, 1998, 316: 1985). Similar pleas have been made with regard to other health care technologies, such as neurological implants (Source: Miles J. National registry is also needed for neurological implants. *BMJ*, 1998, 317: 1658-9)

> benefit from the issue of national guidance at an *early stage* (italics added)".

Similarly, the introduction of a new drug treatment for multiple sclerosis (MS), beta interferon (IFN-β), led to the observation that[65]:

> "[commissioners] will need *early information* (italics added) about future developments in drug treatment and their likely impact on benefits, costs, extent of use, and other aspects of NHS services. This information is often not publicly available and the only source is the pharmaceutical company".

A wide range of organisations are interested in the assessment of new technologies (including manufacturers, health care institutions and policy making agencies[8]) but the responsibility for the adoption of new technologies by the NHS, and for handling these consequences, falls to commissioners of health care (whether health authorities or general practice consortia). A key problem with HTA is the paucity of published scientific literature which is available when commissioning decisions are made about new technologies[66]. This causes decision-makers and clinicians to rely on other forms of information, such as manufacturers guidance and anecdotal information.

Examples of health care technologies that have diffused without having been fully evaluated and/or without adequate consideration of their expenditure and policy implications demonstrate the need for an EWS. Dornase alfa (trade name *Pulmozyme*), a drug for cystic fibrosis (CF), was first marketed to the NHS in December 1993. It was developed with unprecedented speed, moving from initial cloning to product licensing application (PLA) in less than five years. Analysts have speculated that *Pulmozyme* could bring its manufacturers Genentech $100 to $500 million worldwide[67]. In December 1994 it was reported that dornase alfa had been refused reimbursement in Australia by the Pharmaceutical Benefits Advisory Committee (which is required to consider both effectiveness and costs in making its recommendations). PHARMAC, the New Zealand drugs subsidy agency, came to the same conclusion. The long term benefits and side effects of another drug, IFN-β for patients with MS, which was launched in the UK in December 1995, remain unknown. The expenditure and broader policy implications of these two drugs continue to be enormous. In one district health authority IFN-β was estimated to have cost somewhere in the range of £1-3 million in 1996[68]. However, the development and likely introduction of dornase alfa into the NHS could have been

predicted in January 1993, perhaps as early as February 1991, and the development of IFN-β could have been identified in April 1993, or even as early as November 1981 (see case studies, chapter 8). The introductions of other types of health care technologies that have had large implications for the NHS have also been uncontrolled. Examples include laparoscopic surgery in the early 1990s (which has been termed the 'biggest unaudited free-for-all in the history of surgery'[69]).

It is particularly important to identify technologies early where there is likely to be only a brief opportunity for evaluation before ethical constraints set in, or where they are likely to substantially increase or decrease costs or to have a major impact on the organisation and delivery of NHS care. Generally, the diffusion of pharmaceutical and equipment-related technologies is quicker than that for organizational changes or procedures as dissemination of the idea is often performed by industrial representatives. Although pharmaceutical patents are temporary monopolies, other industrial products may have shorter life-spans of perhaps only one to two years and it is necessary for companies to recoup their costs during this short period[70]. In contrast, there are usually no sales representatives for organizational change other than those health care professionals who take it upon themselves to 'sell' an idea[71] and the diffusion of procedures demanding a high level of skill may be held back to some extent by delays in training appropriate personnel[72].

The need to prioritise important new technologies for evaluation has been recognised by NICE[73]:

> "We are not going to be appraising every single new incoming technology, the numbers are so great that it would be impractical."

Similarly, a study of the diffusion of three types of technologies in Europe concluded that[74]:

> "what seems to be necessary is for governments to be clearer about which technologies are emerging, which of them will require attention and which can be left to be 'managed' within the medical profession".

If important technologies are evaluated early in their diffusion, their future uptake might more easily be discouraged, encouraged or left alone. Whilst early evaluations often fail to compare new and existing interventions, and may focus on physiological or biochemical outcomes rather than changes in clinical condition or quality of life, they

can provide limited information on effectiveness which can be used to guide initial decisions on adoption and use[7]. Economic evaluation of new technologies should, therefore, be viewed as a continuous process over time, progressing from early 'indicative' studies to rigorous comparative analysis[75]. The hypothesis is that an EWS, by providing early information as part of a HTA system, can help to minimise unnecessary costs, health disbenefits and policy confusion within the NHS[76,77].

However, it is not easy to assess the effectiveness and costs of a technology before its introduction and diffusion[78,79,80]. Early assessments may not reflect potential capabilities or lower costs, and therefore will be of little interest either for the researchers or policy makers. Later assessments risk being only 'obituaries for already widely diffused procedures' and of little use for decision-makers[81]. Notwithstanding the Buxton Paradox[82] that 'it's always too early *(to evaluate a new technology)* until, unfortunately it's suddenly too late', early identification of new technologies may enable a more controlled approach to evaluation and economic analysis[17,83,84,85].

However, it can be particularly difficult to determine at an early stage which new technologies are likely to be important for a health care system and when. For example, the attrition rate of pharmaceuticals in the second half of the 1970s was such that of roughly each 10,000 compounds synthesized, 1,000 underwent animal testing, ten were selected for human testing, and ultimately only one would enter the health care market[16] (although more recent data suggest that the success rate of this last stage is now nearer to one in five). Similarly, medical research at the purely scientific end of the spectrum is too uncertain to allow cost consequences and other features to be clearly foreseen.

Furthermore, the antecedents of major innovations typically occur over a long period and across a variety of technical fields[86]. For example, progress in five different biomedical research programmes (X-ray, tomographic techniques, instrumentation, mathematics and computers) were required in order to develop computed tomography (CT) head scanners and subsequently CT body scanners (see chapter 8). Some of the key components can directly be traced back to the 1940s with the development of the first electronic on-line computer, scintillation counters and transistors. In addition, different categories of health technologies show different patterns of development[a]; a high percentage of new medical devices (for example, lasers, ultrasound, magnetic resonance

[a] For example, in the medical device field, as opposed to pharmaceuticals, innovation is usually based on engineering problem solving by individuals or small firms, is often incremental rather than radical, seldom depends on the result of long-term research in basic sciences and generally does not reflect recent generation of fundamental new knowledge

spectroscopy and computers) have emerged not out of biomedical research, but through transfer of technologies that were developed elsewhere.

Even in the early adoption stage of a technology's diffusion, many uncertainties remain over the eventual patient group, precise indication, or both. The population of potential adopters has often turned out to be a moving target (for example, intravascular three-dimensional imaging increasing the use of stents) which can continue to change long after initial adoption. It is misleading, therefore, to presume the existence of a fixed population of potential patients for new health care technologies, as the technology may itself create new categories of patients by virtue of new indications[a]. In addition, new health care technologies often interact with other technologies in unexpected ways. These interactions frequently cannot be anticipated for the simple reason that a complementary technology may not yet have been invented (for example, day surgery and anaesthetics). Fineberg likens attempts at assessment ". . . in this complex of evolution in science, disease, technology and society to standing on shifting ground and aiming at a moving target that is also changing shape"[87].

Often these uncertainties surrounding the innovation and diffusion of new health care technologies make it very difficult to select the technologies most likely to have a large impact on a health care system[b]. Treasure[88] illustrates this uncertainty by comparing what happened to two pioneering cardiac surgery operations from the 1940s. Thoracolumbar sympathectomy was a dramatic and effective operation which relieved hypertension but which vanished without trace. Valvotomy to relieve mitral stenosis was regarded in contemporary textbooks as reckless and without basis in science. From valvotomy, however, heart surgery developed to modern practice, in which virtually no structural or mechanical problem is regarded as inoperable. The fate of thoracolumbar sympathectomy illustrates what Treasure terms the 'research cul-de-sac'.

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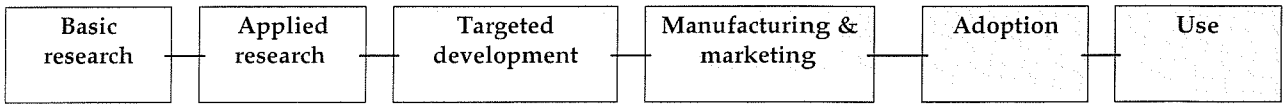
[a] Two examples are: (1) the application of beta-blocking drugs to new uses, and (2) the lengthy evolution of lasers. Beta-blocking compounds were originally introduced for the treatment of two cardiovascular indications (arrhythmia and angina pectoris) but today they are used in the treatment of more than twenty diverse conditions. Lasers were originally intended for ophthalmic and dermatological purposes the laser is now being used or evaluated for a wide variety of indications in gynaecology, gastroenterology, oncology, thoracic surgery and numerous other specialties (Source: Gelijns AC, Rosenberg N. The dynamics of technological change in medicine. *Health Affairs*, 1994, 28-46)

[b] Rogers[25] defined five characteristics of innovation as being most influential in adoption: relative advantage, compatability, complexity, observability and trialability (whether they can be tested out). An attempt to predict the likely adoption of new health care technologies by means of a mathematical model has been made. However, this only related to durable equipment and, only then, when annual unit sales data can be established for the period immediately after market entry (Source: Sillup GP. Forecasting the adoption of new medical technology using the Bass model. *J Health Care Market*, 1992, 12(4):42-51).

From the 1970s onwards, studies of biomedical innovation, and of the diffusion of health care technology, have become more frequent, and slowly a base of knowledge is emerging[89] but the basic mechanisms underlying medical research and development remain largely unknown[90]. Peckham bemoans the fact that '. . . development and innovation are concepts and functions that have had a remarkably low profile in the NHS' and argues that '. . . the affordable exploitation of new opportunities should have the highest priority'[91].

The evolution of a new biomedical technology was initially thought of as a series of technical events, which is usually described as linear-sequential[92,93] or the 'science-push' model (figure 2). However, in the 1980s the validity of the linear-sequential model was questioned. Its basic limitation was its implication that innovation is much more systematic than it really is, whereas not only research but also the broader environment (as expressed through market forces) influences each stage of the development process[94].

Figure 2 *A Linear Model of Biomedical Innovation: too simplistic and systematic*



[Source: Gelijns A, Rosenberg N. The dynamics of technological change in medicine. *Health Affairs*, 1994: 28-46]

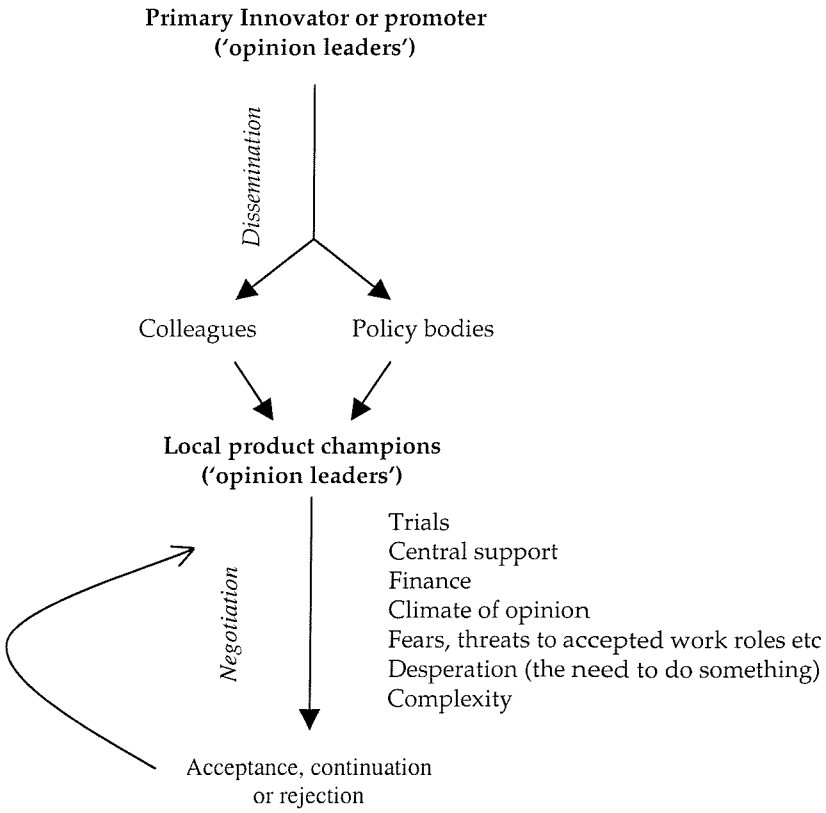
In health, as in industry, innovation involves the interaction of the providers and users of research in a complex iterative process[95,96,97]. Bower[98] cites the major study by Sneader[99] that traced the discovery and development of over 100 drugs brought into use between the earliest period of scientific drug development in the mid-nineteenth century and the early 1980s, as evidence of the complex inter-relations of innovation and diffusion. Sneader revealed very intense interaction between medical practitioners, scientists in universities and medical schools, and scientists in companies in nearly all the cases examined. He concluded that pharmaceutical innovation projects require management of an increasingly complex interplay of skills and resources from different individuals working in different organisations in both the public and private sectors.

Another drawback to the linear model is that it implies that one can make a neat distinction between R & D on the one hand and adoption on the other, with all of the uncertainty inherent in innovation attached to the former. However, most innovations are relatively crude and inefficient at the date when they are first recognised as

constituting an innovation. It is thus a misconception to think that all important uncertainties have been ironed out by the time a new technology has finally been introduced into clinical practice; for example, technological innovation in percutaneous transluminal coronary angiography (PTCA) continued long after diffusion into practice. Thus, much uncertainty associated with a new technology can be resolved only after extensive use in practice[100]. In the context of surgical procedures in particular, technological diffusion is mediated over time by the experience that results from the performance of the procedure on many different patients in different settings with different long and short-term results[101]. Innovative activity is a gradual process of accretion, an accumulation of minor improvements, modifications and economies, a sequence of events where, in general, continuities are much more important than discontinuities (i.e. sharp and dramatic departures from the past). As a consequence, Spilker[102] suggests that most predictions of revolutionary change in medicine are 'pure hype' and it is impossible to predict which ones will occur and when they will occur.

Diffusion research in the health care sector has focused on the role of opinion leaders and communication channels[25]. Opinion leaders have been defined as 'people who are able to influence informally other individuals' attitudes or overt behaviour in a desired way with relative frequency'[25]. Stocking found that in 22 innovations that she studied there was one central person who had the idea, developed it, and was central in promoting it[103](figure 3). In the majority of the innovations the person with the original idea or who first took up the idea in the UK, was a doctor.

Figure 3 Diffusion of innovations: role of opinion leaders



[Source: Stocking B. *Initiative and Inertia. Case studies in the NHS*. London; Nuffield Provisional Hospitals Trust, 1985]

Experience seems to suggest that when new technologies become available enthusiasm is often so great that careful considered planning of the introduction of the drug or device may be impossible[a], whereas other valuable technologies have sometimes diffused only slowly, delaying either health care benefits or financial savings or both.

Gelijns and Rosenberg[92] therefore suggest that the linear model reflects only part of the reality, particularly with regard to non-pharmaceutical technologies. Rather the development of new technologies is influenced not only by advances in scientific and engineering knowledge but also by the potential demand and support for particular innovations. However, the fact remains that there is no accepted, generalisable predictive model of the likely adoption and diffusion of new health care technologies[7,104].

Many high cost, high profile technologies have diffused rapidly, not always appropriately nor in a controlled way[105]. Their diffusion, evaluated or not, is

[a] Source: Blume S. *Early warning in the light of theories of technological change*. European Workshop: Scanning the horizon for emerging health technologies, Copenhagen, 1997

disorganised and occurs at varying rates[a], depending on the strength of various influences[25,106,107], such as clinical enthusiasm for a new surgical technique[108] and the tendency for clinicians to interpret and act upon early studies on the basis of their 'invisible colleges' and social networks[7]. Thus the development and uptake of an innovation is unpredictable and cannot be described in terms of standard processes[109]. This is not surprising given that the key features of the market for health care technology include a lack of information, and the separation of technology provision from its financial ramifications[110].

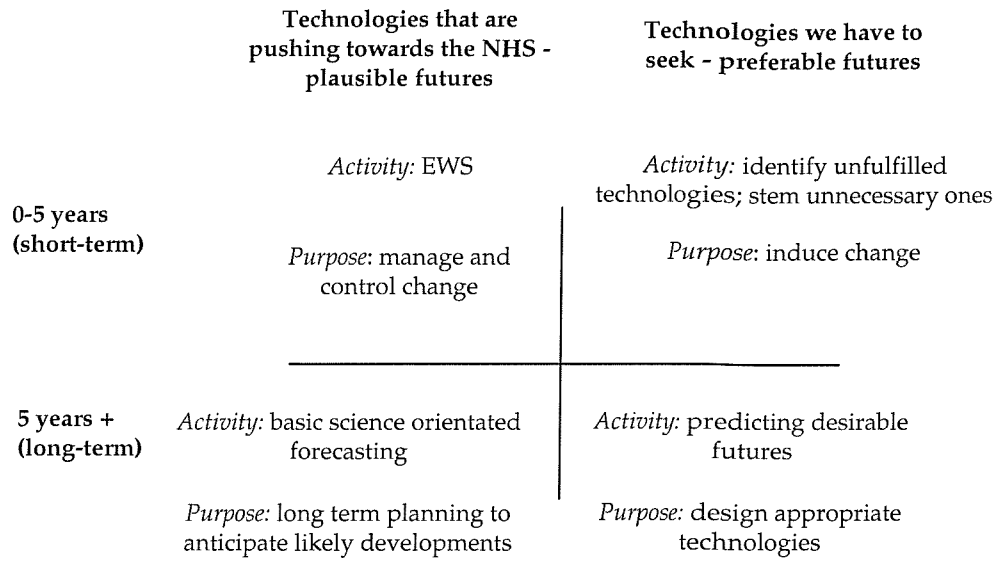
In summary, there are several factors which have led to an increased interest in timely HTA information. These include the increasingly rapid diffusion of technologies, shortened life-cycles, expanding indications for use and the active promotion of new innovations by manufacturers and opinion-leaders[3].

4.2 STATE OF THE ART OF EARLY WARNING

Early warnings may be used for different purposes. The most important function of an EWS as part of a national HTA system is to identify the relatively small number of new technologies that have potentially large implications for a health service. Appropriate research can then be commissioned to determine the desirability or otherwise of the technology. Figure 4 illustrates this point as well as the different time-frames that determine the purposes and methods of an EWS:

[a] may be 'creeping diffusion' (e.g. in only a few local centres) or 'big bang' diffusion (very rapidly and occurring everywhere at the same time)

Figure 4 *Different timescales and purposes of an EWS*



[Source: Stevens A, Robert G. *Early warning of new health care technologies in the United Kingdom.* European Workshop on Scanning the Horizon for Emerging Medical Technologies, Copenhagen, 1997]

An EWS intending to help set priorities for HTA research lies in the upper-left quadrant. It aims to help control and rationalise the adoption and diffusion of technologies that are being promoted by the health care industry and professional opinion-leaders[111]. Other than for HTA, an EWS with a short-term perspective may be used by others needing early information on emerging technologies, such as health professionals and commissioners of health care, though they often find the available information inadequate. Occasionally, for example in the Netherlands, the EWS is also used for identifying broader health problems. The dissemination of early warnings to such audiences can be purely advisory, as in Sweden, or can be set in a regulatory context, as in the Netherlands.

Futures studies may also take a longer term perspective and comprise a more cooperative approach with industry (bottom-left and bottom-right quadrants). For example, futurologists and researchers brought together by British Telecommunications have tried to look into the future by combing the literature and talking to leading practitioners. They produced a timetable for major medical and scientific developments over the period 1998-2030[112]. Such initiatives may often be part of national attempts at technology forecasting. In the UK the Department of Health (DH) is establishing a group whose remit is to help develop new and emerging 'orphan' technologies. Adopting a longer-term approach and collaborating with the health care industry in

order to develop technologies desirable to the NHS is an important task but beyond the remit of an EWS for HTA purposes.

Therefore, although EWSs serve various purposes, and their outputs may be aimed at different audiences, the rationale for their existence is the same: 'managed entry'. Their aim is either to help prevent the undesirable consequences of the irrational and haphazard introduction of new health care technologies or to promote the adoption of beneficial and cost-effective technologies[113]. NICE envisages being involved in such promotion which should be greatly assisted by the availability of early warning well in advance of the new technology being launched or introduced to the NHS:

> "Where a new intervention has been shown to be clinically and cost-effective then NICE would wish to engage with the sponsor in ensuring its more rapid up-take"[114].

Examples of interventions for which unacceptable delays have occurred before their implementation include the detection and management of hypertension, the eradication of helicobacter pylori in patients with duodenal ulcers and the use of thrombolytic therapy in patients with myocardial infarction[115]. An important corollary to promoting the adoption of beneficial and cost-effective technologies is to ensure the elimination of outdated and unnecessary technologies. One study of the introduction of CT scanning in the US reported that '..the less informative screening procedure of conventional brain scanning continued to be utilised as an additive pattern for approximately two years after CTs introduction'[116].

Prediction strategies that could be used to inform the operation of an EWS vary: some are quite broad and long-range, looking at futures in terms of societal, technical and demographic change[117] (bottom left quadrant of figure 4), perhaps using scenario analysis[23], and examples include industry (Shell[118]) and the Office of Science and Technology's (OST) Technology Foresight Programme[119]. More focused examples include the PRISM report on cardiovascular research[120] and the UK's Standing Group on Health Technology's own forecasting exercise[5] and other local initiatives[121]. Some are technology, and/or specialty, specific such as those undertaken by pharmaceutical companies or *ad hoc* expert panels. An example is the Genetics Advisory Group to the NHS's Research & Development Programme. Their report in 1995[122] is the first of a series of NHS appraisals of scientific growth areas that aim at a clearer view of the likely implications of major research discoveries for the NHS over a ten-year period.

There are many existing programmes in the UK which can contribute to an EWS but they have not all been formally brought together to perform such a function. Information on new health care technologies can be obtained from sources such as the MDA, regional Drug Information Services (DIS), the National Research Register (NRR), the Medical Research Council (MRC) and the Changing Medical Practice (CMP) group of the Standing Medical Advisory Committee (SMAC). In 1994 the Senate of the Royal Surgical Colleges of Great Britain proposed a system for controlling the introduction of new surgical procedures. The proposed scheme, which led to the establishment of SERNIP, began with the 'detection' of new techniques through the literature, communications, and conference reviews[123]. Few of these initiatives have identified critical technologies that could have a major impact on health services, outcomes or cost. Indeed, studies attempting to forecast emerging health care technologies are infrequent and, if done at all, are often undertaken 'in-house' and therefore rarely published[124].

In the US, the need for surveillance of technologies is evident but no process of gathering the primary data is currently established for technologies other than drugs, which are a responsibility of the FDA[125]. The National Institutes of Health carries out a yearly study of its clinical trials and publishes a catalogue of those trials it supports. Other agencies such as the Veterans Administration have similar catalogues or lists and, as stated, the FDA[a], through its pre-market approval process, gathers information on drugs and devices that are being developed. However, no existing system adequately identifies all types of developing health care technologies that will require evaluation.

The Netherlands was one of the first countries after the US to identify the potential benefits of HTA[126]. Since 1979 the minister of health in the Netherlands has taken explicit control over some expensive hospital technologies under the Hospital Provisions Act. Article 18 of this Act enables the minister to restrict hospital technologies that need planning nationally because they are expensive or demand special skills to certain hospitals on the advice of the Dutch Health Council. Throughout the 1980s the Dutch government maintained the Dutch Steering Committee on Future Health Scenarios (STG). This was an ongoing futures service to the health system and policy makers, recognising the need to anticipate future technological developments in (long-term) health planning[1]. In 1985 the STG started a project on future health care technologies, in collaboration with the European office of the World Health Organisation (WHO/EURO). The results of that project were first presented in Rotterdam in May

[a] In 1981 the FDA prepared a list of emerging medical devices and drugs (see chapter 6 for further details)

1987. The report recommended the following process for identifying new health care technologies[1]:

Figure 5 *Process for identifying new health care technologies as recommended by the STG in 1987*

Step 1	periodical updating through written surveys (open ended questions in a general letter; future surveys can be more specific; international collaboration is desirable)
Step 2	work with key informants from different scientific and technological areas of medicine to be sure that technological changes have been identified accurately
Step 3	general screening of the medical literature, and focused literature reviews when a specific subject is identified

[Source: Scenario Commission on Future Health Care Technology. *Anticipating and assessing health care technology. Volume 1: General Considerations and Policy Considerations.* The Netherlands; Martinus Nijhoff publishers, 1987]

The STG organised the first International Health Futures Network (IHFN) meeting in 1991 in response to a request from the European Community and WHO/EURO. The IHFN, comprising professionals in both health and futures, aims to promote health futures work.

Few other countries have established programmes for identifying, and monitoring the diffusion of, new and emerging health care technologies. In 1993 Jorgenson attempted unsuccessfully to establish a European system for early identification of emerging health care technologies[a]. The main objective of the proposed system was to make health authorities, policy makers and planners aware of a number of specific technological developments, thereby enhancing their anticipatory power in decision making. This would enable them to take these expected changes into consideration when developing national health services. Jorgenson noted that there were nationally fragmented attempts to perform continuous systematic early identification[b]. However, national HTA agencies have very limited resources which restricts their ability to perform continuous early identification of emerging health care technologies. Coordination, he argued, would bring together these limited efforts, and whilst comprehensive medical

[a] Source: personal communication, T Jorgenson, based on submission to EC, December 1993

[b] Those cited were the studies carried out by the STG in the Netherlands, the Norwegian Medical Research Council and the Welsh NHS Office. In addition, reference was made to studies in 1990 and 1991 of the future of some medical technologies carried out under the auspices of the Commission of the European Communities FAST research programme. The bid suggested that the UKs SGHT and Sweden would soon be initiating continuous processes for early identification of new medical technologies

technology assessments must be performed on a national or regional basis, early identification (including a pre-assessment) could be done internationally.

Despite this failure to establish a formal European EWS in 1993, there is collaboration between countries and national agencies in the development of EWS for new technologies. In September 1997 the Danish Institute for Health Services Research and Development (DSI) and the Swedish Council on Health Technology Assessment in Health Care (SBU), in collaboration with the European Commission, held a 'European Workshop[a] on Scanning the Horizon for Emerging Medical Technologies' in Copenhagen. The main objectives of the workshop were:

- to specify and assess the need for and use of early warnings in health policy planning;
- to discuss methodological issues related to (a) identification of emerging medical technologies, (b) assessment performed early in the life cycle of the technology, and (c) dissemination of results;
- to discuss how early warnings can influence the development and diffusion of medical technology;
- to assess the development of national EWS; and
- to discuss and assess the feasibility of a European network of EWS.

I made a presentation at this workshop, and the overall conclusions[127] and resulting collaboration have helped to inform my thinking and recommendations.

Many of the technologies in regular use today would have been hard to predict 25 years ago[128] but there is widespread recognition that a long-term perspective is useful in all aspects of national policy-making. Nevertheless, formal analysis of the future remains a low priority for most national decision-makers[129], including those in the health sector[1,130]. However, whatever the method adopted there are uncertainties inherent in all applications of futures work and forms of forecasting[b] [102,131,132]. None of the small number of existing studies has been evaluated and, with the exception of the STG in the

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[a] the Canadian Coordinating Office for HTA also participated

[b] Spilker[102] suggests that in the field of pharmaceuticals, many predictions from the 1950s and 1960s have been wrong. New medicines and techniques which have been predicted to be 'right-around-the-corner' for more than 25 years that had not, by 1991, achieved their predicted degree of success include: liposomes as a common delivery vehicle for new and old medicines; non-addictive strong analgesics; major breakthroughs in the use of medicines for treating patients with schizophrenia; cognition-enhancing medicines; medicines implanted under the skin to treat a large variety of diseases; and delivery systems to bring cytotoxic chemicals to only carcinogenic cells and tissues

Netherlands[1], no on-going, iterative process has resulted. There is, therefore, no agreed or empirically proven method of identifying and predicting the likely future impact of new health care technologies.

4.3 SOME PROBLEMS IN DEVELOPING METHODS IN EWS

Mowatt et al[133] suggest that all systems for detecting new technologies require value judgments by experts about what is 'new' and whether it is likely to give rise to health technologies that are safer or cheaper or more effective than existing treatments. Given that many of these judgments would have to be made by experts who have vested interests and an 'insider' perspective, they question whether systems would be effective or dispassionate enough to justify the amount of resources they would consume: "Would they detect all emerging health care technologies? Would they correctly assess their potential? Would voluntary systems work?". Some commentators support these suppositions, suggesting that attempts by 'experts' to predict the future results in the identification of developments that are known to be possible, whereas the real developments arise from the things we do not yet know and hence are unpredictable[134]. Others, whilst reiterating these concerns, recognise that '. . . people in general, and decision-makers in particular, actually do put weight on the uncertain opinion of experts', and that '. . . informed conjecture is useful if it alerts us to opportunities, threats and choices that we might not otherwise have thought about'[135].

A good EWS will be explicit about its aims and the trade-offs between timeliness and level of accuracy of information, and between sensitivity and specificity.

Timing of early warning and level of accuracy

The primary objective of the EWS will determine the required length of early warning. Stocking suggests that the important time to assess a new technology is 'at the point when opinion-leaders become interested in it' which is at a very early stage, often before clinical trials data are available. Other commentators suggest that the technology must be developed adequately to reflect a level of efficiency close to its optimal performance[136]. As a rule of thumb, an EWS intended to help HTA research prioritisation will require at least three years early warning. An EWS operating in the health policy context may require much less warning, perhaps six months for commissioners of health care services. For new technologies under development ('emerging' technologies as defined in this thesis) NICE is expecting to provide

manufacturers or sponsors with two years or longer advance warning that their technologies are likely to be the subject of referral[a]. For new technologies formal notice of referral will usually occur one year before anticipated use by the NHS. However, the length of early warning required will also depend on:

- the type of technology requiring evaluation (for example, the opportunity for trials of new surgical techniques to be conducted is particularly limited by the tendency for them to spread rapidly into clinical practice: for example, laparoscopic cholecystectomy (see chapter 8) and heart transplantation[b]), and
- on the type of research (for example, more for a randomised controlled trial (RCT) than for a review or modeling exercise).

Although, interventions for evaluation are to be referred to NICE by the DH twelve months before the point at which its guidance is to be ready for dissemination, a shorter notice period may be invoked when a technology is changing rapidly or when new evidence radically alters the perception of an existing technology.

Inevitably earlier warning will not be able to provide as precise and detailed information as warnings which come much nearer to the technology's uptake into the NHS. This trade-off between level of accuracy and earlier warning may be pertinent when selecting which information sources are to be used as part of an EWS; different sources may be better suited to the different potential purposes of an EWS.

Sensitivity and specificity

Often, a further trade-off between sensitivity and specificity has to be made. For prioritising a HTA research programme a major challenge is to forecast which technologies are likely to generate the most policy interest once they are widely used. Sources that provide high sensitivity will ensure that no important technologies are missed but the appraisal of such sources will require more resources, most of which will be expended on technologies that come to nothing. Such an approach will also need the development of criteria for selecting the technologies most likely to have a large impact. Alternatively, sources with a high specificity will require less appraisal in order to select the most important technologies but run the risk of omitting from the research

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[a] Source: *Appraisal of health technologies* (appendix G), NICE Board Meeting, 21 July 1999 (http://www.nice.org.uk/updates/2107/app_g.htn)

[b] Problems experienced by Buxton et al when evaluating heart transplants suggest that delaying a trial until the technology has stabilised and a steady state has been reached (in terms of skills and patient throughput) may be desirable, but this risks allowing widespread diffusion before an evaluation is conducted[82]

prioritisation exercise technologies which turn out to have large implications for the health service. A report from the existing EWS in the UK, using lubeluzole as an example, suggests that 'the problem of devoting time to new drugs . . . that are subsequently withdrawn is a recognised hazard for all early identification systems[137].' However, the report suggests that spending time investigating advances that are subsequently halted is preferable to missing the window of opportunity for important topics.

5 METHODS

Chapter Summary

The methods used comprise: (i) a systematic review of the literature on the methodology of predicting the future of health care, (ii) a semi-structured telephone enquiry of EWS coordinators from around the world, (iii) an international Delphi study about preferred sources for identifying new health care technologies, and (iv) retrospective case studies to learn how specific technologies could have been identified prior to their introduction to the NHS, and to estimate the likely 'payback' from EWS-instigated research on these technologies.

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INTRODUCTION

This chapter describes in detail the methods that were used to undertake the research. The original intention was to undertake a systematic review of the literature to identify previous and existing examples of EWS, to assess their effectiveness and to heed any lessons which had been learnt from their operation (section 5.1). However, it quickly became clear that there were weaknesses in the existing literature. Not only did there appear to be relatively few published reports of EWS but those that did exist appeared not to have been evaluated in any systematic fashion. Due to these weaknesses supplementary methods were adopted (sections 5.2 to 5.4), in addition to the literature review, in order to achieve the stated aims of the research. The four methods were:

1. A systematic review of the literature on health futures and forecasting in the UK and from health care systems overseas to assess information sources which have previously been used to identify new health care technologies
2. A telephone enquiry of coordinators of existing EWS in six countries to identify which sources are currently being used and to inform recommendations on the establishment and operation of an EWS in the UK as part of a national HTA system,
3. A Delphi study, involving international experts, to identify and assess potential sources for identifying new health care technologies, and

4. Retrospective case studies of exemplar technologies to identify (with hindsight) information sources for providing 'early warning' and the likely 'payback' to the NHS from EWS-instigated research on these technologies.

Table 1 summarises where the results of the four methods that informed the two primary objectives appear in this thesis:

Table 1 Structure of thesis: location of results of the four methods

Method	Objective 1: Most useful sources	Objective 2: Establishment & operation of an EWS
Literature review	47	-
Telephone enquiry	63	65
Delphi study	78	-
Case studies	90-149 (both objectives)	

The results from each of the four methods are drawn together in the synthesis chapter (chapter 9) which includes an evaluation of the likely value of an EWS to the NHS. Conclusions and recommendations are made in the final chapter (chapter 10).

5.1 SYSTEMATIC REVIEW OF THE LITERATURE ON HEALTH FUTURES AND FORECASTING EXERCISES

The purpose of the systematic review was to assess information sources that have previously been used to identify new health care technologies. The search strategies and results are presented on page 48. The databases used are described in appendix 2. The title and abstracts (where available) of all the references were scanned. All those which related to methods adopted in health futures studies which focused on health care technologies, or forecasting methods (related to health care technologies) or strategies for identifying new health care technologies were retrieved. In order to analyse the accuracy of published initiatives, their results were presented to experts in particular fields who were asked to give their retrospective opinions on a sample of the predictions that were made. Studies that related to the more general area of the application of futures methodology in health care were also retrieved.

As a supplement to the published literature an e-mail survey of members of the International Society of Technology Assessment in Health Care (ISTAHC) was carried out. Ninety-two members of the Society whose e-mail addresses were published in the

1997 members' directory were contacted, representing twenty-four countries[a] and a wide range of disciplines and organisations. They were asked for brief details of any EWS that had sought to identify new technologies either in one particular area, or across the wide spectrum, of health care. The responses were also used to help identify interviewees for the telephone enquiry.

5.2 TELEPHONE ENQUIRY OF CO-ORDINATORS OF EWS

In order to inform all aspects of the establishment and operation of an EWS a semi-structured, telephone enquiry of coordinators of all the existing EWS (in the Netherlands, Denmark, France, Canada, Sweden and the UK) was carried out. Participants were identified either from the published literature, the responses to the e-mail survey or from my network of informal contacts. The questionnaire focused on the aims, methods and level of financial support of each of the EWS. The *pro forma* for the questionnaire is at appendix 5.

5.3 A DELPHI STUDY TO ASSESS POTENTIAL SOURCES FOR IDENTIFYING NEW HEALTHCARE TECHNOLOGIES

A Delphi study was used to devise and develop a classification of health care technologies and a list of the potential sources for identifying each type. This method was used because of the lack of documented evidence[138] on the use of information sources in an EWS and because it allowed consensus development over a wide geographical area[139]. The Delphi study involved 37 participants who were identified through informal networks and a cascade to other nominated individuals. It became clear during the early phase of the study that no one individual or institution could claim to have insight into all the components needed in order to develop an EWS in the UK which would be able to identify all types of new health care technologies. The individuals were selected because they could claim expertise either on:

- particular information sources for identifying new health care technologies (for example, the pharmaceutical literature), or
- specific types of health care technologies (for example, medical devices) or
- operating or planning EWS in other countries.

[a] The countries were US, Argentina, Sweden, Japan, Australia, Canada, Israel, France, Germany, Brazil, United Kingdom, Denmark, The Netherlands, Greece, Spain, Portugal, Italy, Hong Kong, South Africa, Finland, Ireland, Mexico, New Zealand and Switzerland

Reservations about the use of Delphi studies, including the selection of experts, are presented in appendix 1.

Copies of the questionnaires used in all the stages of the Delphi study are reproduced in appendix 3. An initial list of potential information sources was formulated and sent to all Delphi participants, together with a suggested set of criteria for assessing the ease with which the sources could be used for extracting and assessing information. A basic classification of health care technologies was proposed (drugs, devices, procedures, settings, and information technology).

In round 1 participants were asked:

- to rank how important they thought each of the potential sources was
- to indicate which were the most important criteria with which to assess the sources
- to suggest additional potential sources of which they were aware, and
- to give their views on the proposed classification of health care technologies.

The responses were summarised and included in round 2 of the survey, when participants were asked to use the criteria to assess information sources for each agreed type of technology. They were asked to suggest which information sources were most likely to answer each of the following five questions for each type of technology:

- 'how much?' (the unit/total cost of the technology),
- 'for whom?' (the patient group to which the technology will be applied),
- 'in place of what?' (the displacement effects of adopting the new technology),
- 'when?' (the timing of the introduction of the technology) and
- 'how good?' (the effectiveness of the technology)

In round 3 participants were asked to express their level of agreement with the results, and to change, if they wished, their recommended sources in view of the group's response. Specific questions that had arisen from the earlier rounds and which would benefit from further elaboration and discussion were addressed. The final results of the Delphi study were fedback to the participants.

5.4 RETROSPECTIVE CASE STUDIES OF EXEMPLAR TECHNOLOGIES (INCLUDING 'PAYBACK' ANALYSES)

Given the lack of empirical evidence with which to assess the results of the Delphi study nine retrospective case studies (table 2) were carried out to assess the ability of potential sources to identify new and important health care technologies. In an exploratory study of this type, case studies are well suited[140] for answering questions such as how and when an EWS using the information sources recommended by the Delphi study might have identified certain health care technologies and illustrate why there could be differences between the various types of health care technology. A further benefit of using a case study approach is that they can use various forms and sources of data[140]. The sources of data for these case studies were from the literature (books, journals, articles, informal and formal documents) and discussions with key persons in the relevant industry and within the NHS. The databases and search strategies that were used are shown in appendix 4.

Whilst case studies are recognised as useful research tools in other disciplines, such an approach has been relatively underused in HTA and health services research. A particular criticism that can be leveled at the use of case studies is, if they are selected at random, any hypotheses or explanations are unlikely to be widely generalisable. As it is impossible to know what the total population of innovations was over any particular time period, these particular case studies were chosen in order to ensure examples of each of the broad types of health care technology (drugs, devices, settings and procedures). In addition, not all of the case studies are currently emerging examples; using old and contemporary examples provides an opportunity to reflect on the actual diffusion of some of the technologies into the NHS and the benefits that might derive from the operation of an EWS.

Table 2 Selection of case studies determined by type and time of introduction to the NHS

Technology	Type	Timing of introduction to NHS
Beta Interferon	Drug	Contemporary
Dornase alfa	Drug	Contemporary
Donepezil	Drug	Emerging
MediSense ExacTech pen	Device	Emerging
Left ventricular assist devices	Device	Emerging
Telemedicine	Device	Emerging
Computed tomography scanners	Device	Old
Paediatric Intensive Care Units	Setting	Contemporary
Laparoscopic cholecystectomy	Procedure	Old

Each case study aims to present a comprehensive list of all the sources by which each of the nine technologies could have been identified prior to their launch or initial adoption within the NHS. However, in retrospective studies such as these it is difficult to assess how non-documentary sources might have assisted an EWS. This issue is discussed in chapter 9.

The thesis also examines the likely value or 'payback' to the NHS from EWS-instigated research, by applying an existing theoretical model to the nine case studies. The value of research can be defined purely in terms of the provision of improved information for decision-making from undertaking a given assessment[2]. However, Buxton and Hanney use five main categories to encompass the concept of assessing 'payback' from research[141]:

Figure 6 Buxton and Hanney's five categories of payback from research

1. knowledge
2. benefits to future research and research use
3. political and administrative benefits
4. health sector benefits, and
5. broader economic benefits

[Source: Buxton M, Hanney S. How can payback from health services research be assessed? *Journal of Health Services Research & Policy*, 1995, 10-18]

It is important, however, to recognise that it would be quite unreasonable to expect most discrete projects to produce payback in all the categories suggested in this model[141].

The analyses involve predicting the behaviour of the NHS with respect to each of the case studies if the likely effectiveness and cost-effectiveness of the technologies had been widely known at the time of their introduction. The primary method for assessing the payback from the nine case studies was to estimate the likely impact that timely research findings might have been likely to have on the technology's diffusion. This requires an examination of:

- whether the lengths of early warning regarding each technology as reported in chapter 8 would have provided sufficient time to allow a HTA to be performed *and* for the results to potentially influence the adoption of the technology,
- the likelihood that adoption decisions and the actual diffusion of the technology would have been influenced even if timely HTA results had been available,

- the costs of operating an EWS and performing appropriate HTAs, and
- the duration of benefits (both in terms of knowledge generation and health sector benefits) resulting from the research, and the determinants of this duration.

6 LITERATURE REVIEW AND TELEPHONE ENQUIRY

Chapter Summary

The literature review did not find any studies that had as their main objective the systematic assessment of various sources of information for identifying new health care technologies or methods for accessing such information. However, five scientific attempts at identifying new technologies across a broad spectrum of health care were identified. Although most used several sources of information, the only source that was common to all the studies was consultation with experts. There was no agreed or proven method of identifying new health care technologies.

The telephone enquiry of existing EWS also suggested that liaison with experts is a *sine qua non*. Such an approach allows access to the informal networks in a particular field that communicate research findings by personal contact before they are known by publication. Contemporary sources, such as SERNIP, also have an important contribution to make.

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INTRODUCTION

This chapter presents the results of the systematic literature review (section 6.1) and the results of the telephone enquiry into sources and methods used in existing HTA EWS (section 6.2).

6.1 RESULTS OF LITERATURE REVIEW

The retrieval from the literature review was:

Table 3 Results of literature review by database

Database	Years	Search strategy	Retrieved
OVID MedLine	1966-9/98*	[exp FORECASTING\] and [(TECHNOLOGY\ or technology.ti.ab.rw.sh) or (exp TECHNOLOGY\)]	1,214
OVID Core Biomedical Collection	1993-7/98*	[future.ti.ab.tx,ct] and [technology.ti.ab.tx.ct]	2,186
HealthStar	1975-8/98**	[forecasting (mh) or future (tw) or future (kw)] and [explode technology or technology (tw) or technology (kw)]	815
HTAIS (ECRI - US)	1990-96***	'Methods for identifying new health care technologies'	31

*Final electronic search was carried out on September 1, 1998
** Final electronic search was carried out on September 1, 1998 and results exclude MedLine references
***Search was carried out on March 11, 1996 by ECRI

In total, after extraction of duplicates, there were 4,160 references. Only references which specifically addressed either (a) the methods adopted in health futures studies which sought to identify new health care technologies or (b) were scientific attempts at identifying new health care technologie were of interest. However, the scanning and subsequent appraisal of a sample of the references enabled a four-way classification to be developed.

The four types of papers were:

- type I: methodological papers which assessed the processes and information sources by which health care technologies could be identified with a short-term perspective, whether set in the context of a national EWS or not,
- type II: scientific attempts at identifying new technologies across a broad spectrum of health care, i.e. using formal and empirical methods (but which did not assess those methods),
- type III: discursive pieces (often editorials or polemics) relating to future technological developments in health care but without any explicit description of their empirical methods or sources of information, and
- type IV: Delphi studies or scenario analyses of future trends in health or health care which were concerned not with likely technologies but with preferable 'futures' and/or related to a longer term perspective than that with which this research is concerned.

Although ideally it was the type I literature which would have been of most interest, no such studies were identified by the literature search. However, table 4 gives the bibliographic details of the five studies[1,5,142,143,144] which adopted formal and empirical methods to identify future health care technologies across the broad spectrum of health care; for example, a systematic review of the literature or some form of opinion gathering (the type II literature). These five studies are reviewed on page 50 onwards and in some cases did provide some limited methodological analysis, albeit not in a systematic manner. Only two national initiatives have been reported on in the peer-reviewed literature (the EWS in the Netherlands[1] and UK[5]).

Table 4 *Bibliographic details of the five scientific attempts at identifying new health care technologies (the type II literature)*

Bibliographic details
Food & Drug Administration. *Forecast of emerging technologies.* US Dept of Health & Human Services, June 1981
Banta HD, Gelijns AC (eds.). *Anticipating and assessing health care technology. Volume I: General considerations and policy conclusions.* Report of the Scenario Commission on Future Health Care Technology. Dordrecht; Martinus Nijhoff Publishers, 1987[a]
Spiby J. Advances in medical technology over the next 20 years. *Community Medicine,*1988, 10(4): 273-78
Technology Foresight Programme. *Notes on the Delphi survey. Companion paper B to the Health & Life Sciences panel report,* Office of Science & Technology, London; HMSO, 1995
Stevens A, Robert G. Gabbay J. (1997) Identifying new health care technologies in the United Kingdom. *International Journal of Technology Assessment in Health Care,* 1997, **13**(1); 59-67

The third category comprised the vast majority of papers; those that were discursive pieces, often editorials, about future developments in particular areas of health care (for example in one specialty or concerning one particular technology). These papers were often written from a single commentator's perspective in his or her particular area of expertise. Such papers are not reviewed here but they are a potential information source for identifying likely future developments and, in this context, are discussed further in chapter 9.

The final category of papers were those that used a method common to health futures (such as a Delphi study or scenario analysis) to predict trends in health or health care

[a] summarised in: Banta HD, Gelijns AC, Griffioen J, Graaff PJ. An inquiry concerning future health care technology: methods and general results. *Health Policy,* 1987, **8**: 251-64; and Banta HD, Gelijns AC. The future and health care technology: implications of a system for early identification. *Wld hlth statist. Quart.,* 1994, **47**: 140-48. Both these citations relate to the same project undertaken in the mid 1980s

but which were not focused on identifying new health care technologies and often took a longer-term perspective. There are numerous examples of the application of futures methodologies to health care but these have often taken a very broad approach, examining demographic and scientific trends as opposed to specific technologies[145]. Bibliographic details of exemplar papers which together provide an introduction to this area are provided in appendix 1 for readers who may be interested in the wider application of futures methodologies in health care.

In summary, a small number of empirical studies have sought to identify new health care technologies in a particular specialty or across health care as a whole but only three initiatives[1,142, 143] provide any critique of the various sources which might be adopted for the purposes of an EWS.

Scientific attempts at identifying new health care technologies

This section reviews the studies in table 4 (the type II literature) and aims to:

- evaluate any methodological findings regarding the best sources to use;
- discuss the appropriateness of the methods adopted in terms of establishing an EWS for identifying new health care technologies; and
- retrospectively analyse their accuracy.

Methodological findings

It is important to note that none of the studies is either a systematic review of all potential sources of information for identifying new health care technologies or used empirical data to justify any suggestions that they have made. No evidence could be found that any retrospective analyses has been carried out on any of the initiatives[a]. Three of the studies[1,142,143] did provide some discussion around methodological issues such as which sources to use and how to use them. However, the authors comments are their subjective views based on experience during their own particular study. All of the five studies used experts but only one was part of an ongoing process[1].

The FDA[142] analysed their study results by comparing the views of the FDA and outside experts. The comparison of experts views was intended to enable the FDA to determine if its mechanisms for keeping appraised of new technologies (for example, monitoring

[a] personal communications, Professor D Banta and Dr J Spiby, April 1998. Banta noted that the predictions in the STG report, whilst being 'globally' accurate, would have 'problems with timing and focus', citing that the study did not pick up minimally invasive surgery, although endoscopes and microsurgery were mentioned

scientific meetings and publications) were working adequately. In general the FDA and outside experts saw the same technologies on 'the horizon': every one of the 20 most frequently identified technologies in the survey were cited by inside and outside experts alike.

The STG study in the Netherlands suggested that a key problem is how to identify experts who are particularly concerned about future health care technology, and to find experts who will respond to surveys with helpful information[1]. One lesson which the authors drew from the project is that the task of identifying future technology cannot be *ad hoc* and that it needs:

- expertise and experience,
- a system of contacts with experts,
- consistent methods for updating information, and a
- commitment to improving these methods.

Spiby[143] reported that a Delphi study was relatively easy to administer but had several sources of bias: the choice and number of experts used, the potential effect of the non-responders, the difficulties in producing a questionnaire that all panelists would interpret in the same way, providing useful feedback and the implementation of an arbitrary endpoint. In a related report Spiby very briefly reviewed other methods that could have been adopted to identify new health care technologies (for example, trend extrapolation, econometric methods and scenarios)[124]. She concluded that 'the method used and the experts involved in a technology forecasting study are no more important than when the study is carried out'.

Methods adopted

The criteria to assess the methods adopted in the five studies and how useful they might be in relation to the establishment and operation of a national EWS for HTA purposes were:

- was an empirical approach adopted?
- was more than one method suggested: i.e. was there any 'triangulation'?
- did they suggest an explicit sampling approach when selecting participants to provide 'expert' views?

- are their results generalisable; i.e. would all five substantial advisory panels to the UK's Standing Group on Health Technology[a] have been informed by the findings?
- did they take an international perspective or not?
- did they focus on an appropriate (short to medium term) timeframe; ideally, technologies likely to be introduced within five years?
- did they incorporate any 'checkback' methods?

Table 5 summarises the extent to which each of the five studies fulfilled these criteria. The following pages provide further details of the methods adopted by each of the five studies.

Table 5 Usefulness of earlier studies to inform establishment and operation of a national EWS for HTA purposes

Study	Empirical	Triangul.	Expl. Sample	Generalisable	Int'l.	Time (years)	Check back
FDA	✓	x	✓	✓	x	1-10	x
STG	✓	✓	?	✓	✓	4-15	x
Spiby J	✓	x	✓	✓	x	up to 20	x
Technology Foresight Programme	✓	x	✓	✓	x	20+	x
Stevens A et al	✓	✓	✓	✓	x	up to 5	x

The FDA[142] forecast of emerging technologies, initiated in 1980 and published in 1981, is the earliest scientific study of emerging technologies across the broad spectrum of health care that was identified. This study used scientific experts inside and outside the FDA to identify emerging health care technologies. A total of 190 individuals participated in the study (156 FDA professionals; 24 scientists, administrators and health professionals from a variety of public and private sector organizations; and 10 science advisors to the FDA). Participants were sent a questionnaire and asked to:

1. briefly identify and describe each technology,
2. estimate its year of arrival, and

[a] the five panels are: acute sector, primary & community care, diagnostics & imaging, screening and pharmaceuticals

3. identify any major factors which might affect when it would first arrive on the market or reach FDA (for example, technical feasibility, health risk, cost or public acceptance).

In total 429 individual citations were condensed into 168 distinct technologies. The FDA's major program areas were used to categorise the technologies: biologics, medical devices, radiological health, human drugs, animal drugs and feeds, foods and agency-wide technologies. As Spiby notes the study did not attempt to produce any consensus opinion among the participants, except indirectly by indicating how many citations were made for each technology, and the citations received no peer group review[124]. The timeframe adopted was somewhat longer than that anticipated for HTA prioritisation (up to fifteen years as opposed to less than five). However, the eight most frequently mentioned new technologies were predicted to arrive within five years.

Banta et al[146] is the first publication relating to a large-scale analysis of future health care technology, initiated by the government of the Netherlands, and carried out formally from 1985 to 1988. The study was formulated by the STG and aimed to develop an EWS for health care technology. It involved both the early identification of future developments in health care technology and prospective assessments of a number of high-priority technologies[a]. An eight-volume report of this study is available[1]. Volume I provides conclusions on the need to develop a national program or system of health care technology assessment, as the Commission recognised that a system for identifying future health care technology would be of limited benefit on its own. Later volumes looked at specific future technologies.

The project identified the following problems when analyzing future health care technologies:

- the lack of urgency of long-range issues has meant that the future has often received less attention than present, day-to-day policy issues;
- individuals or groups doing forecasting have quite often been subject to political pressures, which has led to forecasts more consistent with the policy wishes of one powerful group;
- policy makers have sometimes expected forecasts to give ready answers or lead to clear decisions; and that

[a] Assessments were reported in the following areas: (1) developments in the regeneration, repair & reorganization of nervous tissue (2) lasers (3) developments in genetic screening (4) the new

- some forecasting groups have not been successful because they have not been part of the decision making process.

This project depended very much on experts (including Delphi techniques and less structured surveys of expert opinion) whilst noting that some identification of technologies is carried out routinely (for example, drug registration). A variety of other sources were considered such as the published literature, news services, biomedical and bioengineering conference proceedings, and others (for example, 'Scrip'). For drugs and devices, additional sources were patent and licensing applications, investigational drug exemption (IND) and investigational device exemption (IDE) documents released by the FDA in the US and commercial databases on pharmaceuticals in the development phase. However, given a limited budget and the need for a quick start the primary method used was to consult, through several surveys, US and European experts in industry and government R & D laboratories, those working in various areas of clinical medicine and health care, and specialist societies. This material was supplemented with literature syntheses and in-depth interviews with selected experts as necessary.

The Office of Technology Assessment (OTA) carried out a survey of experts in late 1984 as part of the STG project. An informal survey letter was sent to approximately 400 experts in various areas of health care technology in the US. Participants were not selected on any statistically significant basis; nor were they asked to provide any probabilities. The survey consisted of a letter inviting ideas about coming applications of health care technology that would be significant in terms of clinical outcomes, institutional effects, economic effects, social or ethical implications, or otherwise. The letter requested that responses be divided into two time periods: 4 to 6 years and 7 to 15 years. 100 usable responses were received and the resulting list was organized into 17 categories. A later paper summarised the methods used in the STG study and made recommendations as to the establishment of an EWS for HTA purposes[81]. This paper recommended that achieving an early identification system that remains both relevant to operations and to policy will require a permanent structure for early identification, which would update the information collected periodically and correct mistakes in entries into the system. It was recommended that the most efficient way of establishing such a system would be to build a network consisting of groups of two or three experts in various clinical and biomedical research areas. The justification given for this approach was that such a system would tap into the informal networks of top experts in

biotechnology: vaccines (5) computer-assisted medical imaging, and (6) home care technology

a particular field that communicate research findings by personal contact before they are known by publication.

Spiby reports on a similar study which comprised 210 people, derived from 66 people selected according to their professional post who were then asked to nominate up to a further five people each[143]. They were asked to identify what they saw as the three most significant changes likely to occur in medical technology that would be available for clinical practice in the UK within the next 20 years. Approximately 90 people responded to each stage of this Delphi study. The results of the study, plus those of similar studies and the published opinions of various experts, suggested a number of possible impacts of technological change on the NHS.

The British government's technology foresight exercise was a key policy initiative announced in the White Paper on Science, Engineering and Technology. The purpose was to bring together industrialists and scientists to identify opportunities in markets and technologies likely to emerge during the next 10-20 years, and the investments and actions which will be needed to exploit them[119]. Foresight panels worked in 15 sectors including one on Health & Life Sciences[a]. The panel began its work by developing ideas on the trends and driving forces that will effect major, long-term changes in technologies, products and services over the next 10 to 20 years. A series of 'hypotheses' were developed to explore the possible implications of separate, narrow, groups of related trends and the degree of uncertainty involved. A major postal consultation exercise was carried out in parallel with a Delphi study and workshop programme. The Delphi survey of 142 respondents (a response rate of 32% from the 464 individuals invited to participate) was carried out between September and November 1994. Time periods for which predictions were made were 1995-99, 2000-2004, 2005-2009, 2010-2014, 2015+ and 'never'. Overall respondents seemed to assume a rapid rate of progress, and chose 'realisation dates' in the early part of the range offered for 80 topics. For 13 of the 80 topics responses were widely spread indicating uncertainty amongst the 'experts' in the Delphi. This approach aimed not only to test panel ideas and refine views, but also to promote debate and general exchange of ideas among the academic, business and health care communities.

[a] the other sectors were: agriculture, natural resources & environment; chemicals; communications; construction; defence & aerospace; energy; financial services; food & drink; IT/electronics; leisure & learning; manufacturing, production & business processes; materials; retail & distribution; and transport

Stevens et al report on one years work in the UK to identify new health care technologies likely to have an impact within the time period 1996-2001[5]. Three main strategies were used:

- scanning of medical, pharmaceutical and scientific journals for an eighteen month period beginning in 1994 and a 'watching brief' on pharmaceuticals going through clinical trials,
- evidence from other initiatives in the UK (for example, the CMP group) and Europe (for example, Health Council of the Netherlands), and
- a national postal survey of approximately 3,500 individuals.

From these sources 1,099 new and emerging health care technologies were identified. There were 652 replies (19%) to the survey. Common to the most frequently mentioned technologies is that they were well defined, rapidly diffusing at the time of the survey and predicted to make their impact by 1998-2000. 66% of the technologies were predicted to make their impact in 1996/97 but only 8% in 2001, making clear that many respondents' horizons were very close. Drugs and devices (41.4% and 37.8% respectively) were more commonly mentioned than procedures and settings (12.0% and 8.7%, respectively). The survey results have been used to help determine national HTA research priorities in the UK.

Accuracy of predictions

The authors of the studies have noted that it is inevitable that some of their predictions will prove to be wrong, as have other commentators on the application of futures studies. Furthermore, the validity of the results of any forecasting are difficult to assess as no control group can be used[124]. Previous retrospective analyses of earlier studies have revealed relatively poor accuracy of predictions but it is not clear if this reflects the failure of the method used, the way in which a specific study has been carried out or forecasting in general. Spiby analysed the results of a Delphi study carried out on behalf of Smith Kline and French in the 1960's[124]. Of 21 predictions forecast to occur within the 1970-80s only 2 (a drug for dissolving gall stones and a device for visualising soft organs of the body) were reported to be available, and the former had not yet proven to be very effective.

Retrospective analyses of the results of previous initiatives may provide lessons as to the likely predictive value of their methods and the sources that they used. All the studies that (a) provide likely dates with their predictions (or some indication of time period)

prior to 1998, and (b) make predictions across the broad spectrum of health care (as an EWS for HTA would be expected to do) are assessed below.

Of the technologies identified by the FDA survey 25% were related to the areas of genetic engineering or advances in CT. Table 6 shows the eight most frequently mentioned new technologies in the complete survey:

Table 6 *Most frequently mentioned new technologies in FDA survey (1980-81)*

Technology	Time of predicted arrival
Hybridoma technology (e.g. monoclonal antibodies)	1983-84
Nuclear magnetic resonance imaging	1983-84
DNA-produced Interferon/antigen	1983-84
Risk assessment	1985-86
Computerized instrumentation	1985-86
Computed tomography	1985-86
Immunoassays	1980-82
Chromotography/mass spectrometry	1985-86

Of the 168 distinct new technologies that were identified, 38 were related to the Human Drugs Program (approximately 25%). As three of the case studies in chapter 8 are pharmaceuticals this particular area of the FDA survey will be focused on here. The ten technologies in this program which were the subjects of three or more separate citations are shown in table 7. Retrospective analysis by one practicing clinician in this field[a] reveals that two of the ten predictions have not yet occurred and still seem a long way off ('using DNA to produce antibiotics' and 'artificial blood') despite their having been predicted to occur in 1980-82 and 1983-84 respectively. Five of the predictions were correct but of the remaining three, one occurred several years later than predicted ('microencapsulation of drugs') and two others were broadly correct but differed in the detail of the predictions made in 1981 ('mind-altering drugs' and 'computerized drug analysis and testing').

[a] Professor Tom Walley, Prescribing Research Group, The University of Liverpool

Table 7 Accuracy of FDA predictions relating to new technologies in human drugs program

No. citations	Technology	Time of predicted arrival	Retrospective analysis
9	Using DNA to produce insulin	1980-82	Correct; date may have been a little early
6	Computerized drug analysis and testing	1983-84	Correct; in clinical setting is available but of limited use
6	Using DNA to produce new pharmaceuticals	1983-84	Correct
5	Computerized drug manufacturing and process control	1980-82	Correct
5	Microencapsulation of drugs	1983-84	Came later in 1990-91
4	Mind-altering drugs, e.g. endorphin-releasing drugs	1987-88	As a line of research this seems to have been largely abandoned. Prediction of types of drugs and their indications was reasonably accurate; just not endorphin-related
4	Using DNA to produce antibiotics	1980-82	Has not happened yet and seems long way off still
3	Artificial blood	1983-84	Still several years away from being a practical proposition
3	Identifying particulates and detecting trace chemical contaminants in drugs	1983-84	Correct
3	New synthetic hormones from DNA technology	1980-82	Correct; dates vary for different drugs

In volume II of the STG report, eighteen chapters examine technological capabilities in specific areas of health care. Rather than provide a superficial examination of each of these eighteen areas the predictions made in just two are assessed: 'medical imaging and other diagnostic technologies' and 'artificial and transplanted organs'. The STG's analyses of technological capabilities in these two areas, again chosen because of their relevance to the case studies in chapter 8, were made during the period 1985-87. The aim of these area-specific chapters was to anticipate future health care technologies and to provide information on their importance.

In the area of medical imaging and other diagnostic technologies the STG identified five specific areas of technological development:

Table 8 Technological developments in medical imaging & other diagnostic technologies (1988 onwards) as predicted by STG

Technological development	Comments
Magnetic resonance imaging	Metabolic data will be integrated into the image to give functional, as well as anatomical, information. This development is being actively pursued and could result in clinical technology within 10 years. Another important development is developing faster imaging systems that could be applied in heart and blood flow studies
Positron emission tomography (PET)	PET scanning, although still considered primarily a research tool, is beginning to be used for routine clinical diagnosis in the US and Japan, although the technology is still at an early stage of development. With development of cyclotrons, PET scanning may become more widely available
Digitalization	Perhaps 20% of diagnostic imaging is now done with digital data; this will increase. In the foreseeable future, film could disappear from imaging departments with computers directing the diagnostic procedure, processing the data and producing the image. It may be possible that the computer will directly interpret the diagnostic study. The use of video techniques and image storage will probably increase and so will the distribution of images to many places within and outside of hospitals.
Biosensors	The first biosensor to become widely available clinically may be one to measure blood glucose, allowing more effective control of blood sugar in people with diabetes. It could also allow a closed-loop system, in which the biosensor would continuously monitor the infusion of insulin by a pump. This technology seems possible within five years or so, but some experts are sceptical that it will ever become completely operational.
Other diagnostic technologies	- endoscopy using fibreoptics - flow cytometer (with monoclonal antibodies) - two-dimensional gel electrophoresis (with monoclonal antibodies) - automated genetic diagnosis

Generally, these predictions are correct but the majority of them do not say anything about timing. This would have limited their usefulness in terms of establishing priorities for HTA.

In the area of artificial and transplanted organs and tissues, two specific areas of technological development were identified:

Table 9 Artificial and transplanted organs and tissues (1988 onwards) as predicted by STG

Technological development	Comments
Transplanted organs and tissues	- with advances in the field of immunosuppressive drugs and with growing understanding of immune system functioning, such organs and tissues as pancreas, small bowel, and endocrine organs could be transplanted successfully - cloning of skin and growth of retinal tissue and corneal endothelium could be achieved - organ and tissue replacements will more often combine living tissue with some artificial components
Artificial organs and tissues	- the artificial heart, artificial pancreas and shoulder joint replacement might become commonplace

The predictions related to 'artificial and transplanted organs and tissues' seem to have been made with a longer time-frame in mind than five years and, again, the lack of suggested dates as to when the technologies are likely to be introduced prevents any meaningful analysis of their accuracy to be undertaken. Broadly, however, the areas mentioned are ones in which initial clinical experience has been reported or research is underway.

The Delphi study undertaken by Spiby in 1987 identified ten main health care technologies as major development areas:

- the use of monoclonal antibodies
- genetic engineering and gene probes
- biosensors
- implantable mechanisms including drug delivery devices
- laser and endoscopic surgery
- transplantation procedures
- imaging devices
- non-invasive techniques, and
- information technology.

The study predicted the likely availability of advances within 10 years, i.e. 1997 (see table 10). Retrospective analysis of these predictions by a practicing clinician[a] reveals that 11 of the 23 predictions were correct. Of the remaining predictions it appears that, particularly in the area of developments in surgical techniques, innovations have not been developed as quickly as respondents believed they would be in 1987.

[a] Professor Duncan Colin-Jones, Consultant Physician, Queen Alexandra Hospital, Portsmouth

Table 10 Innovations predicted to occur during the period 1987-1997 by Spiby

Innovations predicted to occur during the period 1987-1997 by Spiby survey	Accuracy of prediction
DIAGNOSTIC INNOVATIONS	
Monoclonal antibodies will be used in:	
• histopathological techniques	Correct
• biochemical techniques	Correct
• in-vivo diagnostic techniques	Correct
Gene probes will be used to screen for potentially deleterious genes	Correct (if refers to 'screening' individuals, for example colorectal cancer; if population screening then probably not yet available)
Imaging techniques will be in widespread use and less hazardous use including:	
• ultrasound	Correct
• Doppler measurement	Correct
• CT scanning	Correct
• Nuclear magnetic resonance scanning	Correct
• Nuclear medicine and positron detection	Still research based
THERAPEUTIC INTERVENTIONS	
Dug therapy will be enhanced by genetic engineering	Correct
More effective treatment will be available for:	
• viral infections	Correct
• heart failure (better drugs)	Much promised; little achieved
• arthritic joints (more biocompatible prosthetic materials and a wider range of joint replacements)	Not convinced
• incontinence (stimulation via implantable electrodes)	Not for faecal incontinence
• disability (wider range of low technology aids)	
• tropical parasitic disease (vaccines)	No
Surgical techniques which will have developed include:	
• laser microsurgery	No
• laser endoscopic surgery	No
• laser angioplasty and angiography	No
• lithotripsy	No
• transplantation will be enhanced by better techniques enabling long term in vitro organ preservation	
• bone marrow transplantation with purified stem cells	Correct
• contraception: improved techniques for detecting ovulation will enhance natural family planning	No
INFORMATION TECHNOLOGY	
Expert interrogation will be possible due to data centralization	No
Optical disc storage and communication will be used with X-rays and other diagnostic images	Not yet

The survey also suggested several advances (inter-species organ transplantation, the development of vaccines for the common cold, cure of cancer or multiple sclerosis, the successful treatment of mental handicap, the control of the elastin aging process, and the production of a safe cigarette) that would not be realised by 1997. All of these predictions were correct.

In the Technology Foresight exercise undertaken by the OST, the following four predictions were made for the period 1995-99 based on respondents who rated their expertise on each particular topic as 'familiar', 'knowledgeable' or 'expert':

Table 11 Predictions likely to occur between 1995-1999 as reported by Technology Foresight exercise

Practical use of technologies for routine, accurate and sensitive carbohydrate sequencing
Practical use of technologies for directly visualising molecular structure at an atomic level (e.g. ultra microscopy)
Major programmes are initiated to carry out research in integrated biological sciences (i.e. integrating molecular and cell biology, biochemistry and physiology)
First practical use of therapies based on purpose-designed nonpeptide molecules which mimic the activity of peptides

In the postal survey undertaken by Stevens et al, of the forty-eight most frequently mentioned new or emerging technologies that were identified as being likely to have an impact on the NHS within the next five years (table 12), 23 were predicted to make their impact during 1995 and a further 13 were predicted to make their impact during the period 1996-97:

Table 12 Technologies predicted to have impact on NHS during the period 1995-97 by Stevens et al

1995	1996-97
Magnetic resonance imaging	Implantable vascular stents
Minimally invasive surgery	Dornase alfa for cystic fibrosis
Drugs for treatment refractory schizophrenia	Near patient testing
Peripheral blood stem cells	Paclitaxels for ovarian and breast cancer
Doppler measurement studies	Nitric oxide for neonates
Laser treatment of benign prostatic hyperplasia	New anaesthetic vapours
Interventional radiology	Drugs for Alzheimer's
Angioplasty	Alendronate for osteoporosis
Interferon for chronic granulocytic leukemia and hepatitis C in haemophilia patients	Fludarabine in lymphoma and chronic leukemia
Lasers for dermatology	Combined therapy for HIV/AIDS
Ultrasound	ICSI
Revision of joint replacements	Computed Tomography advances
Helicobactor pylori eradication	Ventricular assist device technology
Phacoemulsification	
Cochlear implants	
Bone densitometry screening	
Anticoagulants for atrial fibrillation	
Continuous positive airways pressure	
Expanding metal stents for oesophageal cancer	
Community placements for severe mental illness	
Intra arterial metallic stents	
Epilepsy surgery	
Lipid lowering drugs for raised cholesterol	

These predictions seem very accurate but given the closeness of the timing of the survey and the timeframe for the predictions this is perhaps not surprising.

6.2 RESULTS OF TELEPHONE ENQUIRY OF SOURCES AND METHODS USED IN HTA EARLY WARNING SYSTEMS

Building on the results of the literature review the following section details the sources used by existing EWS and describes the aims, and lessons that can be learnt from EWS that have been established for the purposes of HTA.

The EWS were identified from the systematic literature review and the e-mail survey of ISTAHC members. There were 14 respondents (two from the UK, two from Finland, three from the US, three from the Netherlands and one each from, Germany, Sweden, Argentina, and Spain) to the e-mail message sent to ISTAHC members which provided details on specific EWS.

Norway and Finland were not included in the telephone survey. In 1985 Norway carried out a study to identify future technologies and undertake economic analyses in selected technological areas, using groups of medical specialists as well as examining special research areas (for example, biotechnology and immunology). In 1995 Finland also aimed to identify different health technologies that need assessment by means of a postal questionnaire to all hospital districts, specialist associations and other parties.

Sources

All the systems use expert consultation in some form: sometimes through meetings (Netherlands and Sweden) but mostly through telephone contact (Netherlands, Sweden, UK and Canada). Commonly a small number of experts are used to provide advice on each technology but in some systems formal committee structures have been established as an integral part of the EWS (the Netherlands, Sweden). In the Netherlands the EWS incorporates the expertise of the 170 members of the Health Council, as well as the nine standing advisory boards of the Council each of which have approximately 10 members. The current initiative in Sweden uses a scientific board (with members representing radiology, nursing, physiotherapy, gene technology, oncology, general surgery, general medicine, pharmacology and pharmaco-epidemiology) and standing committees in certain fields. In Canada, experts, who are nominated by provincial government advisors or otherwise identified through MRC excellence awards and publications, are used via postal surveys and telephone interviews both to identify technologies initially

advisors or otherwise identified through MRC excellence awards and publications, are used via postal surveys and telephone interviews both to identify technologies initially and to comment on technologies identified by other sources (usually three to five experts are consulted per technology).

Scanning documentary sources is also widely adopted by existing EWS (table 13). All of the systems scan medical journals with the majority also scanning conference and meeting abstracts, scientific journals and pharmaceutical journals. Two systems specifically mentioned the Internet as a source of information (Denmark, Canada): appendix 8 details the Internet sites which the Canadian Coordinating Office for HTA (CCOHTA) has identified[a]. Links with other agencies through bulletins and newsletters have also been used (Sweden). Efforts in Canada have focused on sources which are available free of charge and sources to which CCOHTA already have access to through its library collection.

Only the UK seems to have specifically maintained a 'watching brief' on drugs going through clinical trials, via formal links with another organisation, although the EWS in the Netherlands has close links both with the Sick Fund Council and the Investigational Medicine programme.

Table 13 Documentary sources used by existing EWS: results of telephone survey

Country	Medical journals	Scientific journals	Pharm. journals	Market. journals	Internet	Conf. abstracts	HTA reports	Other pharm.	News papers
The Netherlands	✓	✓	✓			✓			
Sweden	✓					✓	✓		✓
United Kingdom	✓	✓						✓	
Denmark	✓	✓	✓		✓				
France	✓	✓		✓		✓			
Canada	✓	✓	✓		✓	✓			

The DSI undertook a small feasibility study of information sources and potential informants in 1997 (table 14). The informants were members of the DSI, scientific medical societies, drug & equipment suppliers, test agencies, science journalists and opinion leaders known to have special interests in the field. The study aimed to identify and evaluate important sources of information, identify potential informants and their incentives for participating, to identify potential users of the system (i.e. decision-

[a] Source: *A preliminary list of information sources for emerging health technologies.* CCOHTA. Prepared for the European Workshop on Scanning the Horizon for Emerging Medical Technologies, Copenhagen, 1997

who received a postal questionnaire, indicated that principal medical journals and key scientific journals monthly or more often contain information on new technology of relevance to the Danish health service. The quality of each source of information for an EWS was assessed by the respondents on three parameters: the significance, the 'hit rate' (specificity) and the objectivity of the information:

Table 14 Quality of Information sources - Danish feasibility study (1997)

Significance*	Hit Rate*	Objectivity*
Principal medical journals	Scientific medical societies	National medical journals
Conferences & meetings	Expert & research networks	Principal medical journals
Scientific medical societies	National medical journals	Key scientific journals
Expert & research networks	Press releases from manufacturers	Other journals

*(top four in descending order)

Establishment and operation of an EWS

National HTA organisations have tried to establish an EWS (or at least to systematically identify new health care technologies at a given time) and table 15 summarises the aims and involvement of experts in the six organisations which are currently operating an EWS. Although the US does not operate a national HTA system as such, there are, or have been, a number of projects undertaken in the US which are similar in scope to an EWS (although not necessarily for the explicit purposes of HTA). Initiatives similar to the EWS in Europe and Canada are undertaken at both the Federal level and within the private sector in the US by organisations with an interest in the evaluation of health care technologies.

Some earlier initiatives (for example in Norway and Finland) have not been continual but have looked at future technologies at one particular time. Norway initiated a study on future health care technology in early 1985, sponsored by the Council for Medical Research[a]. The project sought to identify future technologies with the help of groups of medical specialists as well as examining special research areas such as biotechnology and immunology. There is no established system of 'early warning' in Finland but at the beginning of 1995 the Finnish Office of HTA (FinOHTA) sent a questionnaire to all Finnish hospital districts, specialist associations and other parties[b]. The respondents were asked to identify different health technologies that needed assessment and place

[a] Source: Gjone E. *Presentation at the meeting on future health scenarios.* WHO, Copenhagen, 1985 as cited in Scenario Commission on Future Health Care Technology, 1987

[b] Source: personal communications, Kristian Lampe, Medical Office, IT and Communications, FinOHTA, August 1997, and Harri Sintonen, September 1997

them in four categories. A total of 1,005 technologies were identified but the results have not been formally published and are only available in Finnish.

The most striking aspect of all these initiatives is, with the exception of the Netherlands, how recently they have been established. It remains to be seen how well established some of the latest initiatives will become.

Table 15 Current national HTA programmes as reported in telephone survey

Country: organisation & start date	Main purpose	Time horizon	Role of experts	Outputs
The Netherlands: Health Council of the Netherlands, 1988	Both national HTA prioritisation and health policy planning	1-2 years before adoption	5-10 experts are used, via postal survey, telephone and meetings, to comment on identified technologies. In addition, nine standing committees (10 members each) are part of the routine operation of the EWS.	50-100 technologies are identified each year, 20 are considered in detail and 10 have reports written or are prioritised for R & D. The results are used to advise the Dutch government on the current level of knowledge and also disseminated to parliament, professional groups and the media. The government uses the results to inform regulatory measures, research decisions and the introduction and adjustment of legislation.
Sweden: 'ALERT': SBU, 1997	Health policy planning	<5 years before adoption	A scientific board of 8 members and standing committees in certain fields are used (by telephone and meetings) both to identify technologies initially and to comment on technologies identified by other sources. 1 or 2 experts are used to advise on each specific technology.	80 technologies are identified each year, 40 are considered in detail and brief reports of 5-6 pages are written on 30 of these. The reports are published in a database available on the Internet, and in the SBU newsletter.
United Kingdom: Univ. of Southampton (1995-96); Univ. of Birmingham (1997-)	National HTA prioritisation & health policy planning.	<5 years before adoption	2 or 3 experts used to check on each technology identified by other sources (by telephone)	The EWS directly informs the UK's Standing Group on Health Technology, and thus the NHS R & D, of important new health care technologies
Denmark: DIHTA, 1997	National HTA prioritisation and health policy planning	1-2 years before adoption	Experts are used both to identify technologies initially and to check on technologies identified by other sources.	Results are fed in to the R & D programme, the health service and industry.
France: ANAES, 1997	National HTA prioritisation and health policy planning	Adoption phase	Use 5-8 experts, who are generally proposed by scientific societies, to check on each technology identified by other sources.	Reports are written on less than 10 technologies each year. The results are disseminated to health policy makers (French Ministry of Health and insurers) and scientific societies, to inform coverage decisions and planning

Country: organisation & start date	Main purpose	Time horizon	Role of experts	Outputs
Canada: CCOHTA, 1997	Ongoing 1 year pilot project for purpose of health policy planning (planning, budgeting and prioritizing for provincial review)	1-2 years before adoption	Use postal surveys & telephone to access experts both to identify technologies initially and to check on technologies identified by other sources. Experts are either nominated by provincial government advisors, or chosen as they are holders of MRC excellence awards or on the basis of their publications. 3-5 experts are used to advise on each specific technology	Identify over 1,000 technologies each year, consider 6-12 in detail and write reports on 6-10. Results are published in 'Issues in Emerging Health Technologies' newsletter and on Internet. Selective communications are also sent to provincial decision-makers on 'hot' topics.

In the longest established EWS (the Netherlands) the identification and selection of technologies that need to be assessed are routine activities of the Health Council[a]. This EWS combines the following stages:

- scanning (collecting information from the scientific, medical and pharmaceutical literature, conference and meeting abstracts, individual expert health professionals and international networking with other HTA agencies),
- identification and selection (each technologies importance is weighed by disease burden, speed of diffusion, cost, quality of care and policy relevance) by 16 staff members with specific tasks,
- priority setting (to disseminate warning or monitor for future possible action),
- dissemination (bulletins, advisory board), and
- follow-up.

All of the current EWS assist health policy planning and four (the Netherlands, UK, Denmark and France) also assist in setting HTA research priorities. In the Netherlands the outputs of this EWS serve various policy functions. The annual advisory reports suggest technologies that may qualify for application of specific legislation (for example, the Hospital Provisions Act or the Population Screening Act). They also list suggestions for technologies (new and old) to be studied within a HTA-research programme or to be addressed in a quality assurance programme of the professionals concerned. In Sweden the explicit purpose of the EWS is not to give prognoses, but to use information distribution and consequence analyses to facilitate the efficient introduction of the selected technologies (i.e. to assist health policy planning by initiating public debate). It is not the SBU's role to speculate on what new technologies may appear in the future. In Canada the one-year pilot project was initiated in June 1997 with support from regional government with the tasks of:

- identifying key sources to scan for relevant information,
- preparing information on four topics of importance in emerging health technologies,
- presenting these topics in a number of different formats to a target audience of policymakers,

[a] Source: G ten Velden. *Identification of new health care technologies by the Health Council of the Netherlands.* European Workshop; Scanning the horizon for emerging health technologies, Copenhagen, 1997

- and conducting follow-up surveys to determine if the information was both relevant to their needs and, also, to find which format was most suitable.

As Stevens et al indicate there are a number of organisations and initiatives that either explicitly or implicitly have a role in providing early warning of health care technologies in the UK[147]. As well as the Forecasting Secretariat to the national Standing Group on Health Technology[a], which was established in 1995, there are various activities for clinical early warning, such as SERNIP and the CMP subcommittee of the Government's SMAC, which aim to allow time for the preparation of guidelines, or to act as a brake on unjustified expenditure. In addition, there is a well-established network of pharmacists that provides information on new drugs on a regional and national basis, via the DIS and the National Prescribing Centre (NPC). Further details on these additional contemporary sources in the UK are given in appendix 6.

All of the EWS are mainly concerned with relatively short time horizons, commonly less than two years before a technology is likely to be adopted, with the exception of Sweden and the UK, where a slightly longer horizon was cited. In the DSI feasibility study, 47 of the 52 potential users indicated that it would be of great importance to have the information 0-2 years before introduction of the technology. Only five respondents suggested that it would be of great importance to have the information as early as 5-10 years in advance. Each of the EWS commonly produces reports on approximately ten technologies per year (with the exception of Sweden, which produces brief reports on 30 technologies) but the number of technologies actually identified by the EWS varies from 80 to 1,000. In terms of staffing an EWS for HTA, table 16 details the current staff employed on each of the six existing EWS:

Table 16 Permanent staff of existing EWS as reported in telephone survey

Country	Staff (full-time: f/t, whole time equivalent: wte)
The Netherlands	Lecturer f/t; research assistant (0.5wte); 2 library staff (0.25 wte); secretary; and 20 scientific staff (0.1 wte)
Sweden	Director/researcher - health economist (0.5 wte); Coordinator - policy analyst (0.75 wte); administrative assistant (0.5 wte); and 10 members of scientific board (10 days per annum)
United Kingdom	Director (0.2 wte); project manager f/t; horizon analyst f/t; health economist f/t; and information scientist f/t
Canada	Information scientist (0.5 wte); 2 medical/pharmaceutical researchers (part-time); and health economist (part-time)
France	Researcher f/t; librarian (part-time)
Denmark	Researcher (part-time); librarian (part-time); and secretary (part-time)

[a] now the National Horizon Scanning Centre based at the University of Birmingham

7 DELPHI STUDY: INFORMATION SOURCES FOR IDENTIFYING NEW HEALTH CARE TECHNOLOGIES

Chapter Summary

Participants in the Delphi study ranked the timeliness and the efficiency of searching the sources as being the most important criteria by which their value to an EWS should be judged. On this basis they recommended using a combination of the following information sources: key pharmaceutical journals, pharmaceutical & biotechnology companies, specialist medical journals (i.e. those containing early case reports, case series and uncontrolled studies), principal medical journals, medical engineering companies, private health care providers, newsletters & other bulletins from other national & regional HTA agencies and sentinel groups of expert health professionals.

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INTRODUCTION

This chapter catalogues potential information sources that might be used by an EWS (section 7.1), details the design of the Delphi survey (section 7.2), reports which of the sources were recommended by the survey (section 7.3) and discusses further a number of issues including how feasible it is to use the recommended sources in an EWS (section 7.4). Section 7.5 presents some concluding thoughts.

7.1 POTENTIAL INFORMATION SOURCES

Sources used by HTA agencies

The sources that other national HTA programmes have adopted are:

(a) the published literature (scientific, pharmaceutical, medical) using scanning and focused searching [Netherlands, Canada, UK, Sweden, Denmark, France]

(b) expert opinion by way of either (i) written surveys either focused (Norway) or general (UK, Denmark, Canada, Finland) or (ii) in depth interviews [Netherlands, Norway, Sweden, Finland, Canada, France]

(c) newsletters; links with other agencies; other EWS [Netherlands, Canada, UK, Sweden]

(d) conferences [Netherlands, UK, Sweden, France, Canada]

(e) patents [Netherlands - STG]

(f) Licensing applications [Netherlands - STG]

(g) News services; financial press [Sweden, Netherlands - STG]

(h) IND/IDE documents [Netherlands - STG]

(i) Internet [Denmark, Canada]

(j) Marketing journals [France]

Other potential sources

In addition, further sources have been included as they have been used by other 'futures' orientated health care exercises that have been reported in the literature:

(a) financial markets

(b) specialist registers (SERNIP, MDA, DIS, SMAC)

(c) research funding sources (NRR, MRC)

(d) regulatory organizations (European Community regulations)

(e) pharmaceutical, biotechnology and medical engineering companies

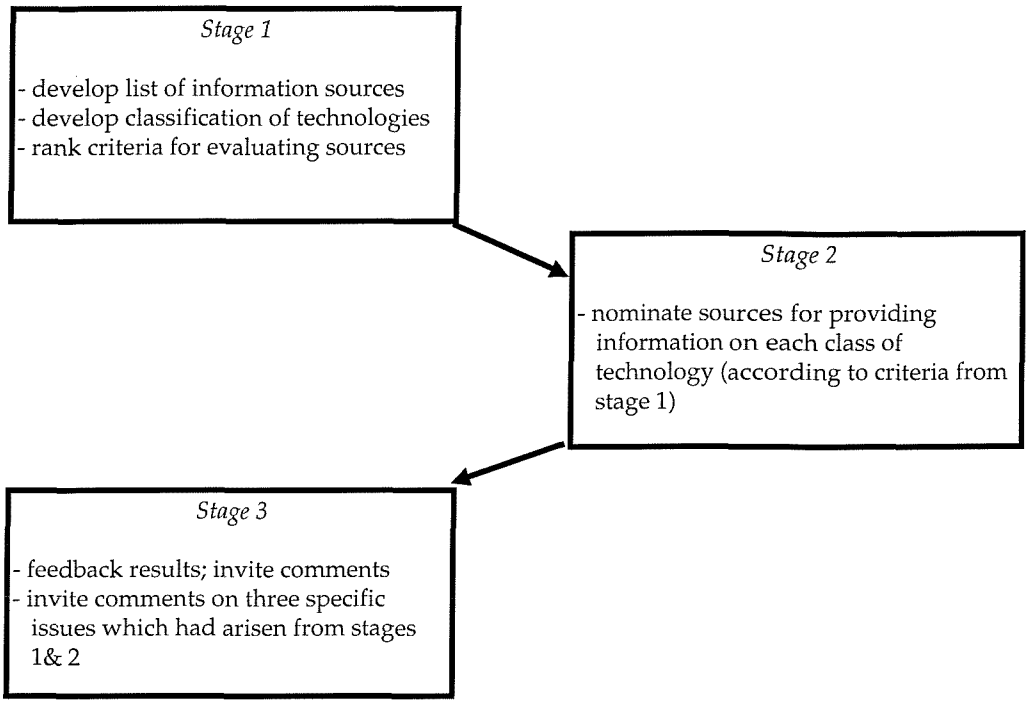
(f) private health care providers

(g) patient special interest groups

7.2 INTERNATIONAL DELPHI STUDY

The contents of the three stages of the Delphi study are described in detail in chapter 4 and summarised in figure 7:

Figure 7 Content of three-stage Delphi study undertaken by the author



Classification of health care technologies

Because each type of health care technology must be expected to draw on somewhat different information sources, an initial classification of health care technologies was suggested to the 37 participants in round 1 of the Delphi study. Thirty-one responses (84%) were received and there was a wide divergence in views as to the best classification to use and the basis on which the classification should be developed. One Delphi respondent suggested that it might be useful to go on from our original classification and characterise emerging technologies by whether they were 'product enhancing' (improving characteristics of treatment for an existing patient group), 'product diversifying' (offering new possibilities of treatment) or 'cost saving' (no change in characteristics from perspective of beneficiary but changed input mix)[148]. Another suggestion focused on the need to take account of technological convergence and the substitution of technologies, using a classification that comprised cognitive, biological, informational and mechanical technologies. Finally, one respondent stated that such classifications were not necessarily helpful and that there was a need to ensure that 'pigeon-holing does not let emergent technologies slip through'.

In the light of the responses technologies were separated by the sectors from which they are most likely to originate. For example, pharmaceuticals from the pharmaceutical sector, other medical and assistive devices from medical engineering and procedures

from clinical experience. This would be most likely to highlight specific sources for identifying technologies at an early stage of their development. The final classification of health care technologies is shown in table 17.

Table 17 Classification of health care technologies as determined by the author

Type of technology
Pharmaceuticals
Diagnostic strategies
Procedures
Procedural devices
Other medical & assistive devices
Health care settings or treatment delivery systems
Information technology
New professions

Baseline list of sources

A list of potential information sources for identifying new health care technologies was compiled from existing or previous EWS and other similar initiatives:

Table 18 Baseline list of information sources on new health care technologies compiled from existing EWS

	Sources
1	Key medical journals (i.e. British Medical Journal, New England Journal of Medicine, The Lancet)
2	Key pharmaceutical journals (i.e. PharmaProjects, Scrip, InPharma)
3	Key scientific journals (i.e. New Scientist, Nature)
4	The financial press and press cuttings generally
5	Patent literature
6	Pharmaceutical companies
7	Private health care providers
8	Biotechnology companies
9	Medical engineering companies
10	Sentinel groups of expert health professionals
11	Patient special interest groups
12	Conference/meeting abstracts
13	The results of other countries' horizon scanning exercises (e.g. the Netherlands)

Participants were invited to comment on this baseline list. Ten participants replied that no single source will identify most or all new health care technologies and that a composite approach was required rather than relying on just one of the information sources shown in table 18. Three participants highlighted that few, or any, of the sources explicitly aimed to provide early warning of new health care technologies; the information from the sources is produced for other reasons and it is the role of an EWS to interpret the available information.

On the specific sources, many respondents commented that, whilst 'key medical journals' do provide a broad coverage, by the time reports of technologies are appearing in such journals an EWS should already have identified them. Two respondents highlighted the usefulness of the news sections in such journals, (for example, the medical progress section in the *New England Journal of Medicine).* 'Scientific journals' were seen as a good source but one with a long lead-time before the application of the new technology. They could be particularly helpful when innovations or ideas were being transferred from other sectors and into health services. One respondent felt that 'private health care providers' and 'patient special interest groups' were more suited to identifying needs for new technology as opposed to predicting which technologies are likely to have an important impact.

Additional sources

In the first round of the Delphi survey, the participants were also asked to nominate any additional sources of information for identifying new health care technologies. Table 19 shows the additional suggestions from the 31 participants who replied:

Table 19 Additional information sources on new health care technologies as suggested by Delphi participants

	Sources
14	Internet (suggested by 3 respondents)
15	Funding proposals and trial registers in other countries (suggested by 2 respondents)[a]
16	Stock market analysts/venture capitalists (suggested by 2 respondents)
17	Newsletters and bulletins from other HTA organisations (suggested by 2 respondents)
18	Specialist industry sector journals (suggested by 2 respondents)
19	FDA licensing applications[b]
20	Department of Health Industrial division
21	Science fiction literature
22	Legal cases; product liability/failures
23	Research programme papers
24	Specialist medical journals (defined as those journals which contain early case series/case reports/uncontrolled studies which strongly influence early adopters but do not make it into the 'big' journals)
25	Ethical committee applications
26	Drug Information Services

[a] the Institute for Scientific Information (Philadelphia, US) which ranks (using criteria such as number of people currently researching issue, number of recent papers and research funds allocated) the following ten research areas as the main sources of current biomedical interest as of 1998: genetic predisposition towards obesity; genetic causes of cell death; BRCA1 gene in breast cancer; co-factors involved in HIV infection; ICE protein involved in coronary disease and cell death; Karposi's sarcoma (Aids-related); mechanisms triggering proteins to programme cells; blood-clotting mechanisms; testing for prostate cancer; and how cells transmit signals

[b] FDA Drug Approvals List (updated weekly) http://www.fda.gov/cder/da/da.htm

Classification of information sources

From both the baseline list and the additional sources suggested by the participants it seemed that there was a clear classification of information sources:

Table 20 Threefold classification of information sources developed by author

Types	Description	Examples
Primary:	Applications by manufacturers to have technologies 'recognised'/'legitimised'	patents, FDA licensing applications, companies
Secondary:	Drawing on clinical 'knowledge' or expertise designed for other purposes	published literature, conference abstracts, sentinel groups of experts, patient special interest groups, financial press, private health care providers, drug information services
Tertiary:	Drawing on other agencies' efforts to identify new health care technologies	other EWS or 'horizon' scanning initiatives

There is some overlap between these categories (for example experts at the cutting edge of research may also act as 'primary' information sources) but the classification highlights the trade-off between earlier warning and greater accuracy. 'Primary' information sources are likely to provide earlier warning but may not be very certain indicators of the likely adoption of a new technology, nor be able to provide much detail on the potential new technology. 'Secondary' and 'tertiary' sources, on the other hand, will provide later warning, perhaps in some cases only after the introduction of the technology, but greater detail and more accurate predictions of the technology's likely impact.

Assessment criteria

The costs of collecting information from the various sources must be weighed against the value of the additional information for the specific users[81]. In round 1 of the Delphi study a suggested list of criteria by which each of the potential information sources could be judged was presented and participants were asked to comment on it. In round 2 participants ranked the criteria in terms of their importance for assessing the potential information sources (1 least important - 5 most important). The scores that the 18 respondents (58% of round 1 participants) gave to each of the suggested criteria for assessing the value of the various possible information sources are presented in table 21:

Table 21 Criteria for assessing information sources as assessed by Delphi participants

Criteria	Median scores	Mode scores
Timeliness	5	5
Time efficiency	4	4
Correlation with other sources	3	4
Objectiveness	3	4
Sensitivity of source	3	3
Depth of source	3	3
Specificity of source	3	3
Elucidation of likely knock-on effects	3	2
Explicitness of limitations	2	3

It is essential that any source should identify technologies sufficiently early in order for the technology to be evaluated before its widespread diffusion, so 'timeliness' is a vital criterion for any source to meet. This was reflected in the participants' ranking. It is also important that the sources should not be inefficiently labour intensive to search (as with handsearching key medical journals), given that only limited resources will be available for this aspect of the identification stage of the HTA process. As highlighted by the responses to the baseline list of sources provided in stage 1 of the survey, participants did not believe that any one source would be able to identify all the different types of new technologies. Consequently, 'correlation with other sources' ranked highly, as did the 'objectiveness' of the source, reflecting the desire for a more 'credible evidence base' (see below).

Clearly it is important not to miss any items that are likely to have a large expenditure impact on a health care system or are likely to diffuse quickly so sources need to a have a high sensitivity. In the Delphi survey participants ranked specificity as being equally important as sensitivity. Comments showed that participants recognised that any source is likely to identify a large number of false-positives and this would have resource implications for an EWS. In short, the Delphi participants preferred to deal with these false-positives rather than miss something important.

In round 2 of the Delphi study participants were asked to suggest, whilst remembering these criteria, which information sources were most likely to answer each of the following five questions for each of the eight types of health care technology:

- 'how much?' (the unit/total cost of the technology),
- 'for whom?' (the patient group to which the technology will be applied),
- 'in place of what?' (the displacement effects of the adopting the new technology),

- 'when?' (the timing of the introduction and adoption of the technology) and
- 'how good?' (the effectiveness of the technology).

7.3 RESULTS

Table 22 presents the results after the 18 respondents had applied the chosen criteria to the 26 potential information sources across the eight types of technology. The table shows the most frequently recommended source for each type of technology and each piece of information (where two or more sources were equally recommended all the sources are included).

Participants seemed able to identify particular sources as being more effective at answering the five specific questions for some of the types of technology but not others. Taking emerging pharmaceuticals as an example, pharmaceutical & biotechnology companies were clearly seen as being the most effective source for answering the 'how much' and 'for whom' questions; key medical journals were recommended for answering 'how good' and 'in place of what'; and key pharmaceutical journals were recommended for identifying 'when' an emerging pharmaceutical might be introduced. These differentiation's were less clearly marked for other types of technology (e.g. new professions and information technology) for which participants seemed less certain as to the best sources to use. 'Best' here means they provide timely 'early warning'; are sensitive enough to ensure no important technologies are missed; and specific enough to ensure that the selection of the most important technologies is not too complex.

Table 22 Results of stage 2 of Delphi survey[a]

Type of technology	'How much': the unit/total cost of the technology	'For whom': the patient group to which the technology will be applied	'In place of what': the displacement effects of the adopting the new technology	'When': the timing of the introduction and adoption of the technology	'How good': the effectiveness of the technology
Pharmaceuticals	Pharmaceutical & biotechnology companies	Pharmaceutical & biotechnology companies	Principal medical journals	Key pharmaceutical journals	Principal medical journals
Diagnostic strategies	**Specialist medical journals** Pharmaceutical & biotechnology companies	Principal medical journals	Newsletters & bulletins from other national/regional HTA agencies	**Specialist medical journals** FDA licensing applications in the US	Principal medical journals
Procedures	Specialist medical journals	**Specialist medical journals Principal medical journals**	**Specialist medical journals Principal medical journals**	Specialist medical journals	Principal medical journals
Procedural devices	**Medical engineering companies Specialist medical journals**	**Medical engineering companies Specialist medical journals** Principal medical journals	Medical engineering companies	Medical engineering companies	Principal medical journals
Other medical & assistive devices	Specialist medical journals	**Specialist medical journals Newsletters & bulletins from other national/regional HTA agencies**	Newsletters & bulletins from other national/regional HTA agencies	Specialist medical journals	**Newsletters & bulletins from other national/regional HTA agencies** Patient special interest groups
Health care settings/treatment delivery systems	Private health care providers	**Patient special interest groups** Conference & meeting abstracts	Private health care providers	Sentinel groups of expert health professionals	Principal medical journals

[a] where there is more than one entry, bold entries indicate that that source was the most commonly recommended for that particular technology and type of information. Where two or more sources are in bold they received the same number of recommendations.

Type of technology	'How much': the unit/total cost of the technology	'For whom': the patient group to which the technology will be applied	'In place of what': the displacement effects of the adopting the new technology	'When': the timing of the introduction and adoption of the technology	'How good': the effectiveness of the technology
Information technology	**Specialist medical journals** Newsletters & bulletins from other national/regional HTA agencies Private health care providers	**The Internet** Newsletters & bulletins from other national/regional HTA agencies	Specialist medical journals	The Internet	
New professions	Specialist medical journals	Specialist medical journals	Conferences Newsletters & bulletins from other national/regional HTA agencies	Newsletters & bulletins from other national/regional HTA agencies Private health care providers Sentinel groups of expert health professionals	Sentinel groups of expert health professionals Newsletters & bulletins from other national/regional HTA agencies

Respondents were most prepared to suggest likely information sources for identifying 'pharmaceuticals' and 'diagnostic strategies'; few were able to recommend particular sources for 'other medical & assistive devices' and 'new professions'.

From the responses received, eight information sources could be recommended as forming the minimum of any comprehensive EWS for identifying new health care technologies:

- key pharmaceutical journals,
- pharmaceutical & biotechnology companies,
- 'specialist' medical journals,
- principal medical journals,
- medical engineering companies,
- private health care providers,
- newsletters & bulletins from other national & regional HTA agencies, and
- sentinel groups of expert health professionals.

The relative usefulness of the many available sources of information about new health care technologies depends on the particular types of technology under consideration. Additionally, each source has its advantages and disadvantages, and some provide earlier (and often, as a consequence, less certain) warning of new technologies than others. Each will also provide information about different aspects of a technology and its likely impact and some sources will provide more detail than others. It is important to note that each of the recommended sources can be accessed or searched in a number of ways and each has its own disadvantages:

Table 23 Disadvantages of recommended sources as perceived by author drawing on comments from Delphi respondents

Information source	Comments
Key pharmaceutical journals	May generate high proportion of 'false-negatives' from drugs whose development ends after phase I or phase II trials.
Pharmaceutical & biotechnology companies	Problems with extent and timing of disclosure. Information specific to a certain drug may be overoptimistic as to the clinical effect and other immediate benefits, and underestimate the cost.
'Specialist' medical journals,	Problems of bias (editorial filtering and professional interests) and timing.
Principal medical journals	Many technologies will already have begun to diffuse.
Medical engineering companies	Similar to pharmaceutical companies: problems with extent and timing of disclosure. However, the less regulated approval procedures makes them a more important source of information than drug companies
Private health care providers	Only limited range of potential technologies will be of interest to private providers. May be difficult to access
Newsletters & bulletins from other national & regional HTA agencies	Short horizon; more useful for identifying current technologies already undergoing assessment rather than 'the one to watch'.
Sentinel groups of expert health professionals	Time consuming and need careful management.

The results of the study were fedback to participants. Some respondents felt that 'too much faith' had been put in the scope and accuracy of information that may emerge from companies, due to 'bias and vested interest' and that 'greater emphasis should be placed on a credible evidence base'. Another respondent was surprised at the emphasis on the published literature ('so often retrospective and delayed in publication') and 'would emphasize the personal contact implied in 'companies', 'providers' and 'sentinel groups'.'

Several respondents drew an interesting distinction between discovery and application. For example, the first reports of the discovery of a new technology may appear in specialist journals of scientific journals (for example, *New Scientist, Nature*) whilst speculative applications derived from the basic discoveries would probably appear in the more populist journals (for example, *New England Journal of Medicine*) before the applications become generally accepted. This distinction suggests that whilst specialist medical journals may be best placed to provide early warning of new discoveries or technologies they are not so helpful at monitoring technology diffusion activities. In

relation to new pharmaceuticals, one respondent commented that 'discovery is more open, application is usually covert and commercially sensitive'.

In stage 1 of the study one respondent had suggested that the scanning of specialist medical journals would have 'spotted' the rapid increase in the number of papers on excimer lasers in ophthalmology journals or on positron emission tomography scanners in nuclear medicine, cardiology and oncology journals. When this comment was fedback in stage 3, another participant felt that these two examples highlighted the 'risks' ('massive bias and timing problems') of using such a source, suggesting that papers on excimer lasers mostly appeared well after the technology had diffused and that nuclear medicine journals have 'been advocating a positron emission tomography (PET) scanner on every corner ... for 10-15 years'.

One respondent was surprised that news services available electronically via the Internet were not the primary source for all the types of technology. One respondent did not feel that any of the sources covered information technology very well.

7.4 ISSUES ON WHICH FURTHER COMMENTS AND ELUCIDATION WERE SOUGHT

In round 3 of the study participants were asked to respond to prompts concerning issues which had arisen out of the earlier rounds and which deserved further exploration. Sixteen responses (89% of round 2 respondents) were received and are summarised below.

Use of sentinel groups of expert health professionals

In previously reported EWS and other health futures studies sentinel groups of expert health professionals have commonly been used as the main source of information[5,81]. It was clear from open comments received from participants that this source would have to be a key aspect of any EWS. However, in the round 2 responses the use of such groups was only commonly mentioned in relation to identifying new 'health care settings and delivery systems' and 'new professions'. Further clarification was sought from participants with the following prompt:

Your views as to the value of using such groups would be welcomed. What form should such groups take - focus groups, postal surveys, Delphi studies? On what basis should members of such groups be selected? What incentives should or could be used to ensure that invited experts participate in such exercises? Should

expert groups be used as an initial source of information on new health care technologies or as a filter for information obtained from other sources or both?

Responses were very positive, with comments such as 'expert panels are essential', 'potentially very fruitful', 'very important source', 'invaluable (expert review group)', 'value++', and 'important sources of information'. However, some problems or disadvantages were also noted: 'not easy to persuade good people to find the time to participate', 'is there such a thing as an honest broker under these circumstances?', and 'focus groups=labour intensive++ for what value?'.

Generally the respondents felt that there would have to be two stages to a process which involved experts: the identification of potential new health care technologies (stage 1) and then the filtering and refining of the technologies that had been identified (stage 2). Participants felt that stage 1 could be achieved by a number of methods (for example, brief two-round Delphi survey, e-mail discussion group, or periodic telephone calls) but that some form of focus group would be required to filter and refine the topics (stage 2). The justifications given for this approach were:

- surveys and Delphi studies are useful for consultations and can supplement focus groups which are difficult and expensive;
- 'seeding' the group with external scientific sources (for example, the results of a Delphi study of peers) would add excitement to discussions;
- the judgment of a single individual is error prone;
- personal contact is important, at least initially to gain an awareness of the project and establish contact with experts; and
- the interaction and challenging of judgments is essential.

Some participants felt that different experts would be required for the two stages (i.e. different experts to act as, firstly, a source of information for identifying new health care technologies and, secondly, as evaluators of the information generated in stage 1) whereas other participants believed that the two tasks could be carried out by the same experts (but with stage 2 requiring a much tighter remit). If different experts were to be used for each stage, researchers at the forefront of their specialty should be used to identify new potential technologies and to review early information, and generalists should be used a filter for information obtained from other sources.

The method of selection of experts drew some comments. One participant suggested that US-pan European representation is essential and that experts should each represent a key therapeutic area (for example cardio-renal, oncology, etc.), another recommended co-nomination of members as had been used in by the OST in their recent Technology Foresight exercise[119]. Others believed that 'known experts' from academia or industry and the professions (from university teaching hospitals) were required.

Other countries' horizon scanning exercises - scope for collaboration

Participants did not identify the results of other countries' horizon scanning exercises as a particularly useful source of information although some commented that this might be a useful starting point or cross-check. There does seem to be some grounds for collaboration as the majority of new health care technologies are international in their likely impact. This suggests the possibility of sharing specific tasks between agencies within a group of countries. Each could specialise in particular areas (for example, pharmaceuticals) or sources (for example, medical journals). Participants were asked to:

Please give your views on the scope for international collaboration with relation to early warning systems for new health care technologies.

Participants responses contained many positive comments, such as: 'must be a large opportunity to collaborate', 'think we have to move in this direction', 'potentially very fruitful', 'good networking possibilities exist', 'collaboration needed', 'good idea', 'provide a focus for 'futures' orientated teams, 'bit of scope for this collaboration' and 'could and should be shared amongst us'.

As far as how to collaborate was concerned a number of participants recommended that it should occur within the framework of the European Union (perhaps building on existing European programmes on research and development, such as EUR-ASSESS). The potential for involvement of other English-language countries (US, Canada, Australia) was also highlighted. One respondent saw a potential role for INAHTA. Two participants also suggested that as well as collaboration between national HTA agencies there might also be scope to improve links with the private sector, such as device manufacturers.

Tasks on which agencies could collaborate were:

- identifying and scanning sources of information;
- sharing the information produced by other agencies; and

- maintaining a register of sources of information.

Whilst such collaboration would avoid duplication, economic and organisational consequences may differ from one health service to another, and the social, ethical and legal implications of a new technology might also differ from one country or culture to another. Nevertheless, participants generally felt that there is still scope for sharing methodological experience as well as results.

'Specialist' medical journals

According to the Delphi participants new 'diagnostic strategies', 'procedures' and 'other medical and assistive devices' were best identified from specialist medical journals. Participants recognised that it will prove difficult to select those technologies which will remain in the research domain and those which will take off rapidly. There is consequently a possibility of spending too much time on things that in the end are not too significant in health care. Participants were asked:

Please suggest journals which you have used previously, or are aware of, which would enable a directory of journals to be developed which would allow the early detection of most new technologies through case-study/case series reports.

Few specific suggestions were received from participants. There were a number of broader methodological comments such as: 'perhaps a well-designed MedLine search at six monthly intervals would be easier than journal scanning and the output could be used to provide selected topics to an expert panel', and that it is 'difficult for early warning agencies to scan the huge scientific literature in order to detect potentially interesting technology'.

Appraisal of technologies

Having identified new and emerging health care technologies, the next step of an EWS is to assess their likelihood of making a significant impact on the health care system. The appraisal and synthesis of information will clearly be key in identifying genuine emerging technologies. Those processes could influence the selection of the most useful information sources and (at least partly) determine their overall importance and the importance of their component characteristics (for example timeliness, sensitivity and specificity). Participants were prompted for their views with the following question:

Who do you believe is best placed to appraise and synthesise information on new health care technologies, and on what basis should you highlight important technologies? Details of how such information is appraised and synthesised in other early warning systems would be helpful. For example, a non-medically

qualified researcher simply cataloguing all technologies that are reported as being 'new' or recently introduced by scanning the key medical journals. An additional sift could then be carried out by a panel of experts. Alternatively, a more senior and medically-qualified person could carry out this task without recourse to an expert panel.

A three-stage process involving a number of participants seemed to be favoured (figure 8). Some respondents felt that the use of 'panel of experts' would be cumbersome and probably only suitable for select topics or topic areas.

Figure 8 *A potential process for synthesising and appraising information on new health care technologies as favoured by Delphi respondents*

1	***Scientific catalogue***: medical librarian and research assistant with clinical/health service experience or background, routinely scan chosen information sources and catalogue technologies of relevance
2	***Discussion/cross-check:*** with chosen experts using (a) Delphi study and then (b) focus group/meeting
3	***Dissemination*** of information on selected technologies

Participants' comments included:

> 'appraisal and synthesis best in-house by experienced HTA staff, with specialist support as needed ... highlighting needs to be done in the broad context of a health care system - implying a working knowledge of issues in science, medicine, health services research and politics'
>
> 'initial sift ... should go further than merely cataloguing new technologies - it could include appraising such information against a pro forma (for example, cost, size of health problem etc.) A panel of experts could then assess this.'
>
> 'May be some scope for specialist librarian/information officer(s) to do routine scanning. But also need more authoritative reviews by experts'
>
> 'The task is to bring together an understanding of the science with a knowledge of the biology of disease and/or the principles and mechanics of health organisation'.

7.5 CONCLUDING THOUGHTS – DELPHI STUDY

From the results, a wide range of sources would need to be used if an EWS wished to be comprehensive. Depending on the resources available for establishing an EWS there may, therefore, be a need to decide which particular types of technologies are most likely to require early warning. The size of impact that the types of technology are likely to have and the speed of their diffusion will determine this decision. Time and resources can then be concentrated on identifying these types of technology and the most appropriate form of evaluative research. The marginal utility of using each of the recommended sources that have not been used before in earlier attempts to establish an EWS must be examined.

It was surprising how low 'sentinel groups of experts' were rated in the Delphi survey for many of the specific types of technology. This may be because participants saw experts as a combination of all the other sources rolled into one, with the same information simply being accessed through a different medium (talking rather than reading) but without any existing filtering mechanisms. Alternatively, or perhaps additionally, experts may not have been identified with one type of technology and so, despite their overall value, were not ranked highly when participants were asked to focus their thoughts on specific types of technology. The value of experts was raised directly with the participants when the results were fedback to them (see above), and the responses were much more positive regarding their potential contribution than the responses to the earlier rounds of the study had been.

Finally, there is a need to remember that the most appropriate sources may vary depending on the health care system concerned and the 'HTA-linked' legislation that may be in operation.

8 CASE STUDIES

Chapter Summary

Overall, the case studies suggest that in addition to experts particularly important documentary sources include key pharmaceutical journals, specialist medical journals and FDA licensing applications in the US. Conference reports can also be useful. The length of the likely early warning prior to the introduction of some of the technologies would have been relatively short. However, the payback analyses reveal the potentially significant benefits that may be gained from the operation of an EWS as well as highlighting some of the barriers to realising these benefits.

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INTRODUCTION

These nine case studies (sections 8.1 to 8.9) aim to illustrate whether the information sources recommended by the literature review, telephone enquiry and Delphi study would have identified the selected health care technologies prior to their initial introduction and early diffusion into the NHS. Where appropriate the case studies also highlight some of the possible limitations to the operation of an EWS. They also outline the likely payback which may have been realised had an EWS been operating as part of a national HTA programme prior to each technology's introduction into the NHS. Lessons which may inform policy making and strategy from these case- studies are synthesised and discussed in detail in chapter 9.

Each case study follows the same structure:

- a brief description of the technology,
- the chronology of its development,
- the timing and extent of its adoption by the NHS,
- an analysis of whether the recommended information sources from the preceding chapters could have provided early identification,
- a retrospective analysis of likely payback from an EWS, and
- a discussion of the issues that each case study raises for the establishment and operation of an EWS in the UK.

8.1 COMPUTED TOMOGRAPHY SCANNERS (HEAD)

Description of technology

This diagnostic technique combines the use of a computer and X-rays to produce cross-sectional images of conditions such as cancer (for the staging of tumours), strokes and head injuries. CT scanners are more sensitive to variations in bone and tissue density then X-rays are, and they produce images with greater resolution and speed, thereby reducing the patients' exposure to radiation[149].

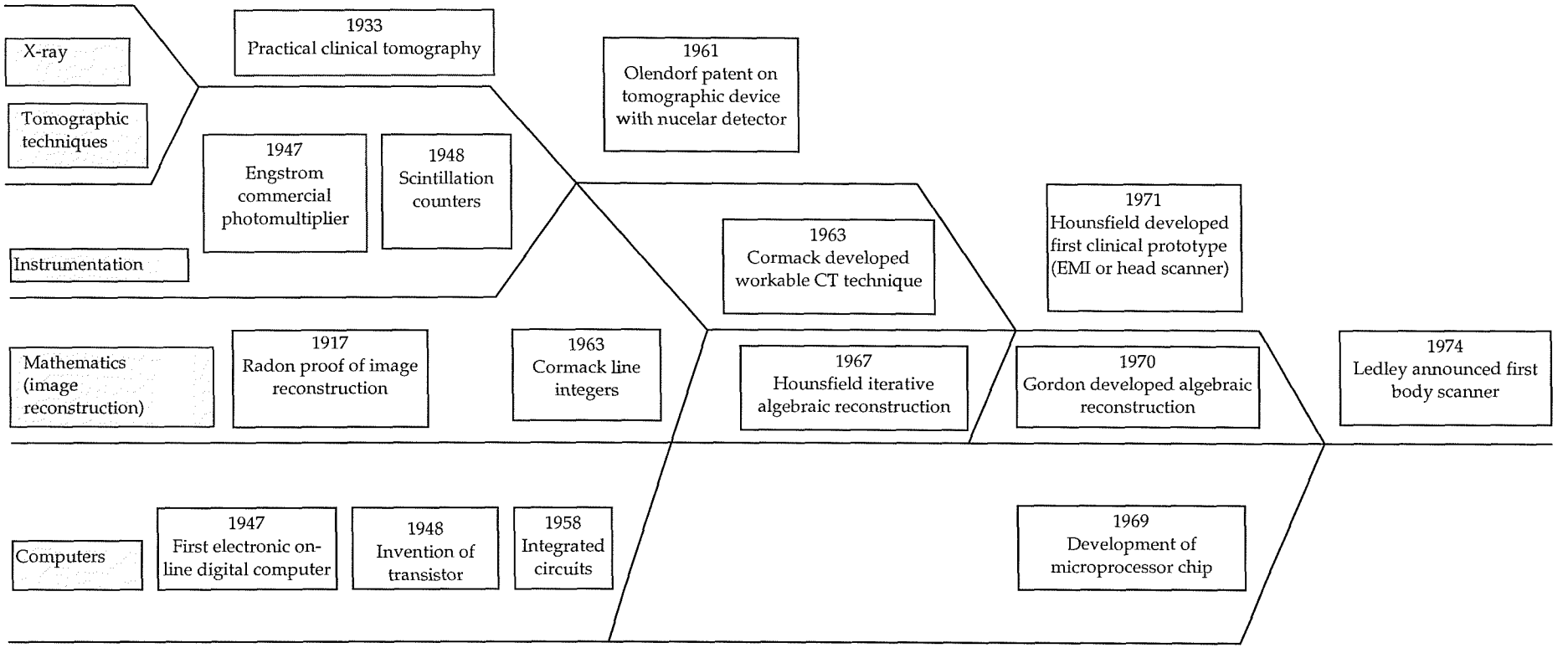
Early development

The early mathematical basis for the reconstruction of images from projections was established in 1917. However, the application of this knowledge was only able to take place with the development of the modern computer. During the 1950s the first workable CT instrument was constructed in the US and a patent was granted in 1961, with a paper published in the *Journal of Applied Physics* in 1963. However, this work received little or no attention from the medical community. In 1961 a second tomographic device was constructed in the US and received a patent in 1962. Again, and despite subsequent work, corporations and physicians showed no interest in commercial development[13].

The first commercial interest in CT occurred in Britain. EMI, a British electronics firm, developed a CT instrument in 1967[150] but no X-ray companies wanted to license CT technology. However, the British Department of Health and Social Security (DHSS) supported the construction of a prototype head scanner in the early 1970s. DHSS officials in the UK had visited EMI's laboratory in January 1969. The prototype instrument was installed in Atkinson Morley Hospital in London in September 1971. The ideas that had led to the notion of the scanner and the principles on which it worked were presented in a paper published in the *British Journal of Radiology* in 1973[151].

Figure 9 illustrates how progress in five different biomedical research programmes (in x-ray, tomographic techniques, instrumentation, mathematics and computers) was required in order to develop CT head scanners.

Figure 9 Development of the computed tomography (CT) scanner required progress in five different biomedical research programmes



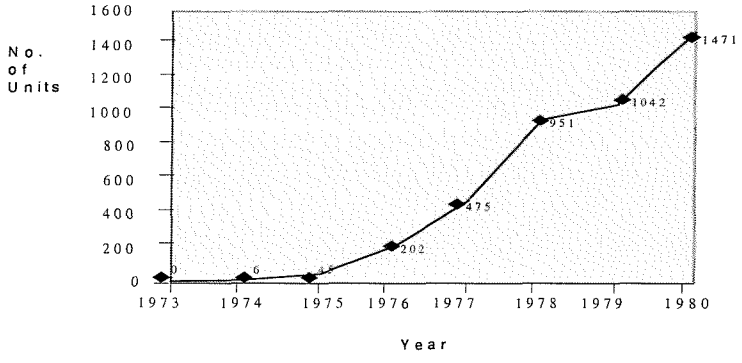
[Source: *Analysis of selected biomedical research programs. Vol 2.* Columbus Ohio: Battelle Columbus Laboratories, 1976]

Adoption

The first operational scanner unit was installed in London in 1971 and CT of the brain has been used in the UK since 1974. EMI installed almost all the scanners that became operational in this initial period of adoption. However, the extraordinary demand for, and the high profits associated with the manufacture of CT scanners led many companies to begin to develop them. By May 1978 thirteen companies had installed CT scanners in the US and EMIs share of that market had fallen to less than 50%[152]. The units moved through four generations of operating methods within four years.

The first clinical evaluation of a prototype brain scanner, funded by the DHSS, had begun at Atkinson Morley Hospital in 1971. In April 1972 the new instrument was announced at a UK press conference[153]. As it became obvious that CT brain scanning was a remarkable breakthrough the DHSS provided funds for five brain scanners and recommended that each region should purchase at least one brain scanner[13]. As early as 1974 the research team at Atkinson Morley Hospital was able to report on a clinical series of 650 patients[154]. By the spring of 1978 the UK had 52 scanners, or almost 1 per million population[13]; by 1985 there were 123 CT scanners in the UK and a further 26 on order. In 1990 there were 250 units or 4.3 per million population[155]. In the US the diffusion of CT scanners was extraordinarily rapid. Following the installation of the first scanner in 1973, six more scanners were installed that year and 39 more during 1974. During 1977, the rate of installation increased to about 40 per month[152]. Figure 10 shows the diffusion rates of CT in the US over the early years of its clinical availability:

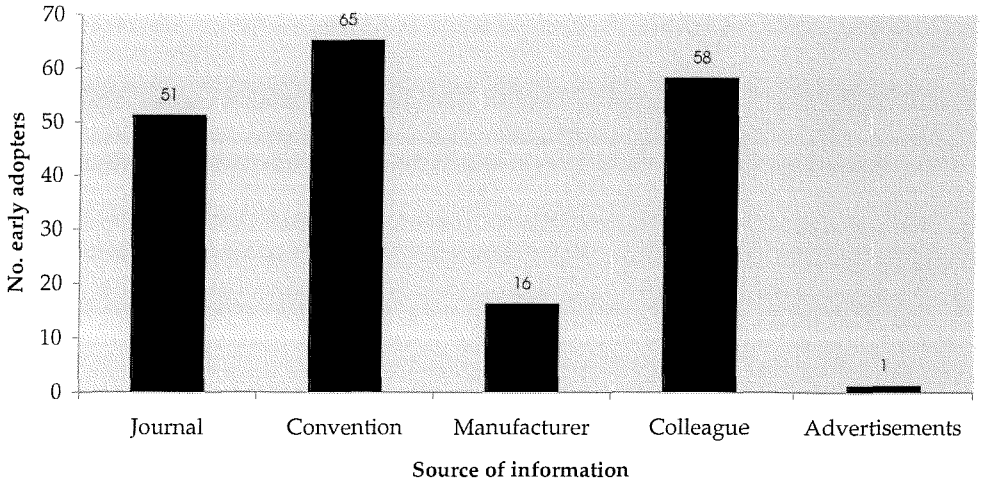
Figure 10 The rapid diffusion of CT in the US (1973-80)



[Sources: Banta HD. The diffusion of the computed tomography (CT) scanner in the US. *International Journal of Health Services*, 1980, **10**(2): 251-69 and OTA (as cited in Hillman BJ. Government health policy and the diffusion of new medical devices. *Health Services Research*, 1986, **21**: 681-711)]

Baker[156] reported on the relative importance of sources of information amongst early adopters in the US (figure 11). Early adopters acknowledged the almost equal value of medical conventions and the experience of colleagues.

Figure 11 *Conventions and colleagues were most important sources of information about scanners for early adopters (those ordering scanners 1973-75) as reported by Baker*



[Source: Baker SR. The diffusion of high technology medical innovation: the computed tomography scanner example. *Social Science & Medicine*, 1979, **13**: 155-62]

Creditor and Garrett related the early diffusion of CT scanners in the US to the appearance of literature on the subject of CT scanning by means of a 1973 to July 1976 MEDLINE search[38]. There were many journal papers on the use of CT scanners but almost all of them were uncontrolled case reports and very few examined effects on patient therapy or health outcomes[157]. Eighteen institutions were the sources of all the information published through 1975 and nine more contributed in the first seven months of 1976 (almost all were major university centres). Only thirteen clinical papers which provided data that allowed valid quantification of diagnostic accuracy had appeared in the English-language literature by June 1975. By this time 100 scanners had been ordered, suggesting that the rapid diffusion of CT scanning was not because the medical literature indicated its great usefulness. The single nationally funded multi-institutional study, performed from 1974 to 1977, was not reported until 1980[158]. Analyses such as these question the belief that decisions to invest in new health care technologies are based on scientific reports in the literature[38, 152, 156].

Potential information sources for early identification

There were a number of key points at which an EWS could have identified CT scanning as a major new health care technology prior to its introduction into the NHS during the period 1971-1974:

- US patents in 1961 and 1962 respectively;
- papers in 'specialist' medical journals in 1963 and 1973;
- information from EMI (manufacturers) from 1967 onwards;
- DHSS officials (government agency) visit to EMI's laboratories in 1969;
- press conference (media) in UK in 1972;
- US conference in 1972 (*International Conference on Particles and Radiation Therapy*, Los Alamos) and 1973 (*Radiological Society of North America Convention*, Chicago); and the
- report of the evaluation at Atkinson Morley Hospital, London in 1974 (or knowledge of the study whilst it was ongoing having begun in 1971).

Patents and papers in 'specialist' medical journals would have provided the earliest documentary evidence of the development of CT scanners (1961 and 1963 respectively). However, given the low specificity of these two sources, it is unlikely that they would have helped to alert policy-makers to the huge potential impact of CT scanners. In contrast, the 1969 visit to EMI's laboratory and subsequent DHSS involvement in the development and evaluation of this technology might have alerted an EWS via discussion with experts. A combination of the US conferences in the early 1970s and the *British Journal of Radiology* article in 1973 certainly should have provided early warning.

Payback from early warning

In contrast to the remaining eight case studies in this chapter the introduction of CT scanners into the UK was preceded by early warning and the close involvement of national policy-makers (although not as the result of the operation of a formal EWS). The discussion of the benefits of this early warning in the five categories of payback which follows below is based, therefore, on a comparison between the introduction of CT scanners into the UK and into the US where no such controlled introduction took place. Clearly there are significant differences between the health care systems, and the incentives and methods for introducing new technologies, in these two countries. These

differences, and the retrospective nature of the analysis, prevent definitive conclusions being drawn from such a comparison. However, the case study does allow some important issues to be raised. The remaining case-studies adopt a different approach by assessing the likely payback to the NHS had early warning been available in the UK.

There were ample opportunities to identify the likely introduction of the CT scanner in the US and to put in place evaluative research, as was the case in the UK. It is likely that although early warning may have been possible in the early 1960s (some ten years prior to the installation of the first scanner in London) it would not have been until the end of that decade that policy-makers and clinicians would have been alerted to the potential of CT scanning. Such timing would, and did, provide two years early warning and enabled the controlled introduction of CT scanning into the UK.

Knowledge

Early warning in the UK some two years prior to the installation of the first CT scanner enabled a clinical evaluation to be undertaken alongside the introduction of this technology. The knowledge gained from this evaluation allowed policy-makers to recommend the wider adoption of CT scanners beyond the initial study centre. However, little attempt was made in any of the early published papers (including the report of the evaluation undertaken at the Atkinson Morley Hospital) to assess the effect of improved diagnostic capability on the outcomes, or even treatment, for the various indications for which CT scanning was being proposed[38]. Key clinicians and policy makers may well have had an intuitive sense, or perhaps more empirical knowledge, regarding patient outcomes but this is difficult to assess retrospectively. A formal HTA focussing on patient outcomes could have been initiated much earlier had an EWS been operating at the time. Such information was not widely available until much later and certainly after the widespread adoption of CT scanners.

Benefits to future research and research use

CT scanners went through a number of phases of development and improvement in a relatively short space of time. Given these advances it would not have been possible for an early evaluation to prove to be the definitive study on CT scanning. However, an early evaluation would have provided valuable lessons and developed research expertise for subsequent studies, not only when attempting to take account of developments in CT head scanners but later when CT body scanners were introduced. In the longer term, experience of evaluating relatively expensive and innovative

diagnostic imaging machines would provide valuable grounding when evaluating technologies such as MRI[a] and PET.

Political and administrative decisions

In the US health planning agencies seem to have had very little effect and CT scanning was not fully evaluated before it spread into practice[152]. The lack of an EWS or a co-ordinated approach to HTA led to the widespread, and unplanned, diffusion of an expensive health care technology that had wide-ranging implications for the health care system. Although there were some efforts to control technology diffusion by the mid-1970s, most states in the US did not have viable regulations affecting hospital acquisition at this time. Certificate-of-need (CON) programs to review hospitals' capital expenditures were not established until 1974 and the earliest years of CT development therefore largely escaped effective CON regulation[152 b].

In contrast, in the UK the DHSS was involved at a very early stage and quite restrictive towards purchasers of the head scanner and set up an explicit evaluation plan intended to guide policy[13, 16]. The combination of early warning and a strong central policy-making body enabled a more rational introduction of this expensive technology than in the US, although a survey in the UK in 1987 found that there was considerable disparity in terms of the number of scanners between regions[159].

The experiences of the US and UK with CT scanners provide a comparative, albeit historical, illustration of how early involvement of national agencies may help to promote early evaluation and thereby improve the information base on which to take policy decisions.

Health sector benefits

In order to estimate the potential health sector benefits of early warning and evaluation of CT scanners in the US it is necessary to come to some judgement as to what would have been the 'right' level of diffusion of CT scanners in the US at any point after the initial adoption of the technology had begun. As a proxy, Lazaro's analysis of the number of CT scanners per million population in selected countries in 1990 presents a striking contrast between the US (26.8 per million) and countries where CT scanners

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[a] for example, one 1991 UK-based evaluation of the cost-effectiveness of MRI (Szczepura AK et al. Cost effectiveness of magnetic resonance imaging in the neurosciences. *BMJ*, 1991, **303**: 1435-9) was based on a controlled observational study design from a 1977 (US) study of CT head scanners (Fineberg HV et al. Computerized cranial tomography: effect of diagnostic and therapeutic plans. *JAMA*,1977, **238**:224-7)

[b] in the case of CT body scanners in the US, enthusiastic clinicians were able to purchase the scanners using charitable and philanthropic donations

were introduced in a controlled fashion, such as Sweden (10.5 per million) and the UK (4.3 per million)[155]. At a cost of approximately $500,000 for each installation at the time the estimated net expenditure for CT scanners in the US ranged from $180 million to $388 million in 1976[12]. In the early adoption stages capital investment costs were only partially offset by savings from reducing other diagnostic procedures. Whilst CT scanning is now generally acknowledged to be both cost-saving and beneficial to health this was not known at the time of its rapid and widespread introduction into the US[149]. Therefore, although in the long-term CT scanners have been proven to be cost-effective, their unwarranted and unplanned early diffusion lead to significant levels of unnecessary expenditure in the US. A sizeable reduction in the number of CT scanners introduced into the US in the early to mid-1970s would have represented significant cost savings.

Broader economic benefits

Early warning of emerging technologies may lead to wider economic benefits from commercial exploitation of innovations arising from R & D. In this respect the case of CT scanners provides an interesting example of the tensions that may arise between the need of the NHS for appropriate evaluation of a new health care technology and the interests of UK-based manufacturers. As described above CT scanners were developed in the UK by EMI who were responsible for all the initial installations. However, by 1978 twelve other companies had also installed scanners in the US. CT scanners are therefore often cited as an example of how NHS reluctance to adopt a new technology may lead to the UK losing a technology-production lead in potentially important areas of development. Whilst the scientific and manufacturing industry in the UK see this as a failure (in terms of the UK losing world market-leader status), the introduction and early diffusion of CT scanners in the UK may be seen as a relative success for policy-makers and the notion of early warning.

Lessons for an EWS

CT scanners provide an example of how complex the innovation and development of a health care technology can be[160]. Development paths such as those illustrated in figure 9 can make identification of a technology harder, as well as making prediction of the likely timing of its introduction less certain. Such complexity illustrates how difficult it is to accurately identify new health care technologies and their likely impact on a health service. Even so an EWS, via liaison with experts, would probably have detected CT scanners approximately five years before this technology exploded into use.

Documentary sources alone would not have been able to identify CT scanners as an important new health care technology prior to their widespread diffusion. This is because small-scale clinical reports did not begin to appear until 1975, and it is only in combination with other sources that the importance of the *British Journal of Radiology* paper in 1973 can be recognised. Use of conference and meeting abstracts, particularly in the US, may well have provided early warning of the likely rapid diffusion of CT scanning; Baker's analysis of where early adopters obtained information from suggests that conventions were the most common source. Newsletters and bulletins from other HTA agencies, would not appear, or would not have been expected, to provide any information on CT scanners prior to their diffusion into the NHS. The OTA did produce one of its first health reports on this subject in 1978[12]. A first draft of the OTA's evaluation was available and widely circulated in late 1976, but the diffusion of scanners during 1977 and 1978 was nevertheless very rapid. The basic conclusion of the report was that 'well-designed studies of efficacy of CT scanners were not conducted before widespread diffusion occurred'.

8.2 BIOSENSOR FOR HOME GLUCOSE MONITORING (MEDISENSE EXACTECH PEN)

Description of technology

Various definitions have been given to the term 'biosensor'. In general, they are classed as chemical sensing devices that operate within a biological environment. The majority of biosensors are microelectronic devices that use a biological molecule, usually a protein, as the sensing or signal transducing element. Clinicians have suggested that the patient populations who will benefit most from the introduction of biosensors are diabetics and the critically ill.

Hundreds of clinical biosensor designs have been reported but relatively few have emerged from the laboratory. Biosensor research and development is rapidly expanding at present. The MediSense ExacTech pen is one of several biosensors that are on the UK market for home glucose monitoring by diabetic patients and the glucose-testing market is currently growing at a rate of 15% per annum.

Early developments

The evolution of the first biosensor began in the mid-1950s, when an electrode designed to measure dissolved oxygen in the blood of patients undergoing surgery was invented

in the US[161]. By 1962 the 'oxygen electrode' had been extended to sense blood glucose levels[162]. This device never found its way into routine patient care. Nevertheless, it provided a conceptual base for subsequent work. The next major innovation came in 1969, when a system was built to measure urea in body fluids. Pickup reports that about twenty-five years ago, at the 50th Anniversary Insulin Symposium, implantable glucose sensors were beginning trials and devices to mimic normal glucose-insulin control system were thought to be feasible in the near future[163].

In the decades following the development of these electrochemical methods, roughly 100 different enzymes have been used in biosensors. Biosensors became commercially available in the mid-1970s with the launch of the Yellow Springs Instruments (YSI) glucose monitor[164] and Roche's lactate analyzer[165]. Further technological advances have led to the development of second-generation amperometric enzyme sensors.

MediSense opened in Abingdon in the UK in 1984 and, at that time, made use of research on biosensors previously carried out at Oxford University and the Cranfield Institute of Technology. The ExacTech pen took approximately five years to move from early commercial development to availability on the NHS and was the result of an intensive and expensive programme of research which began in the academic sector in the UK[166].

Adoption

The ExacTech pen received clearance for marketing by the FDA in December 1986 and the initial marketing of the product commenced in the US in 1987. The subsequent launch of the product in the UK was in the summer of 1988, and the ExacTech system became available on NHS prescription in August 1989.

In the same year the ExacTech pen was the subject of an independent evaluation commissioned by the Supplies Technology division of the NHS[167]. The study contained reports from five hospitals in the UK and compared the new device to several other instruments, such as the YSI glucose analyzer, in terms of precision and speed. The ExacTech pen generally compared well although errors were noted to occur if instructions were not adhered to and the meter was not started immediately[168].

Since the launch the ExacTech system has been improved several times to enable the availability of a more 'user friendly' device. At the initial marketing stage, the ExacTech pen was competing solely with colour changing enzyme strips which had a wide range of problems associated with them. The ExacTech system allowed new error checks to be

introduced to glucose monitoring and the timing function was entirely taken over by the device. The electronics were redesigned into popular credit-card and computer-mouse style formats. MediSense's sales showed exponential growth reaching $175 million by 1996[169]. Now, the improved ExacTech system competes with a variety of other home monitoring biosensors on the UK market; manufactured by Boehringer Mannheim, Bayer Diagnostics, LifeScan and Hypoguard.

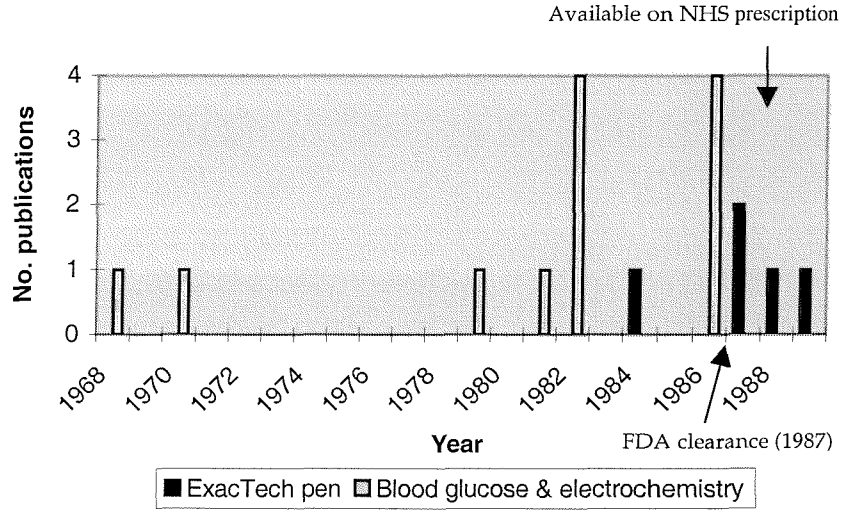
Potential information sources for early identification

Sources of information related specifically to the ExacTech pen prior to its UK launch in the summer of 1988 were:

- papers in scientific journals in 1984 (regarding a ferrocene-mediated enzyme electrode for amperometric determination of glucose by workers at Oxford and Cranfield[170]), 1987 and 1988[171] (from Cranfield regarding an amperometric enzyme electrode for glucose analysis);
- FDA clearance in December 1986; and
- a brief research report in a key medical journal (*The Lancet*) in 1987[172].

Less specifically, articles relating to the application of electrochemical instruments to analyse blood glucose date back to 1968 (see figure 12). Articles on 'biosensors' began to increase significantly in the late 1980s, with 42 papers indexed on MedLine with this term in 1988 and 72 in 1989.

Figure 12 *Increase in MedLine references to ExacTech pen and electrochemical instruments to measure blood glucose in the late 1980s*



Thus there were relatively few opportunities to identify the ExacTech pen from documentary sources prior to its launch in the UK, although there were at least three papers published within two years of it becoming available on prescription in the NHS[173,174,175]. However, *The Lancet* paper in 1987, together with notification of FDA clearance in the US in 1986, should have provided two years warning of the availability of the ExacTech pen on NHS prescription. In the late 1980's there were a large number of papers reporting generally on the development of biosensors for glucose analysis[176] as well as reports of animal studies of other specific biosensors that were in development.

The combination of an effective network of experts and regular liaison with biotechnology companies might reasonably have been expected to provide some early warning of this technology. Indeed some time after the introduction of the ExacTech pen, Cranfield Biotechnology Limited produced a report which predicted future application areas based upon two criteria: firstly, applications likely to emerge within a five-year timescale; and secondly, applications where 'substantial' product sales were expected[177].

Payback from early warning

It seems likely that an EWS using only documentary sources would have been able to provide approximately three years early warning of the introduction of the ExacTech pen. Close liaison with relevant experts may have lengthened this early warning by up to a further two years.

As with all of the remaining case-studies in this chapter an integral part of the analysis that follows addresses two questions. Firstly, what would have happened to the adoption and diffusion of the ExacTech pen from August 1989 (when it became available on the NHS) onwards if, following early warning, HTA research had begun in the mid-1980's? Secondly, what net benefits would such early warning and research have realised for the NHS?

Knowledge

As noted above the development of the ExacTech pen was an important step in the clinical application of biosensors, and emerged from a long period of academic and scientific research. However, recommendations for self-monitoring of blood glucose by diabetic patients need to be based on sound evidence and, following the adoption of the ExacTech pen and other similar devices, the effectiveness of home testing has been

questioned[178] and remains unproven[179]. It is in respect of the correct application of new scientific knowledge that an EWS may have enabled timely HTA research to take place.

Benefits to future research & research use

There was an absence of control groups in early studies and more recent work has suggested that regular self-monitoring of blood glucose may be inefficient[180]. The adoption of near patient testing has been an increasing trend in many clinical areas recently and an early evaluation of the ExacTech pen may have identified general issues that could apply equally to other technologies designed for this type of use. Subsequent studies could then have been more precisely defined and targeted in either method or scope. More generally an early evaluation could have increased the skills, knowledge and professional networks of researchers in this field as well as enhancing their ability to utilise later research.

Political and administrative benefits

An ongoing debate relates to which diabetic patients are more likely to benefit from self-monitoring of blood glucose. The monitoring of blood glucose control is a particularly important aspect of diabetes care since the achievement of good control in patients with insulin dependent diabetes mellitus (IDDM) reduces the risk of long-term diabetic complications[181]. It may be that only a relatively small proportion of the 10-15% of diabetics in Britain who have IDDM have the need to make frequent adjustments to their insulin dosage[180 a] and so would be most likely to benefit. An early evaluation could have provided decision-makers with an improved information base with which to justify recommending a policy of limiting the use of the ExacTech pen to IDDM patients.

Health sector benefits

Designing the most cost-effective packages of care for common conditions like diabetes mellitus is important because of the potential for health gain and the high costs of intervention. The MediSense pen starter kit costs less than £100 and there are approximately 1.4 million diabetics in the UK. Gallichan reports that in 1995 £42.6 million was spent on home monitoring of glucose in the UK[180] of which as much as approximately a third may have been for the ExacTech pen. Initially the purported benefits from self-monitoring of blood glucose concentrations included the provision of

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[a] in 1994 in Germany 305 million blood glucose strips were prescribed, costing approximately £169 million and almost half were prescribed to non-insulin dependent diabetes melllitus patients (source: Ernst C, Nowicki S. Self-monitoring of glucose by people with diabetes: patients with NIDDM should monitor urine rather than blood glucose. *BMJ*, 1997, **315**: 185)

more accurate information than from urine testing and that the information about everyday fluctuations may give encouragement to patients to become more active partners in their management[182].

However, it has been suggested more recently that 'the inappropriate use of self-monitoring of glucose is wasteful of NHS resources and can cause psychological harm'[180]. On the basis that hundreds of thousands of people undertake several tests per day and that every unnecessary blood test wastes 28 pence plus the costs of lancing devices, lancets and blood glucose meters, the potential waste of NHS resources is very high. However, at least one international organisation involved in diabetes research and care believes that 'home blood glucose monitoring is a cost effective, simple and relatively cheap tool for improving the quality of life and the prognosis of all people with insulin dependent diabetes and many with non-insulin dependent diabetes'[183].

A HTA systematic review 'Monitoring blood glucose control in diabetes mellitus: a systematic review based protocol' is currently ongoing in the UK and is scheduled to be completed by early-2001. The review is costing £52,333 and is considering self-monitoring and monitoring in health care settings for patients with diabetes. The combined cost of an EWS (£250,000 per annum based on the cost of the current EWS in the UK) and such a review theoretically offers substantial payback to the NHS when compared to the annual expenditure on home glucose-monitoring. Such research could assist in developing timely evidence-based protocols which could be used by those involved in the care of people with diabetes.

Broader economic benefits

Cranfield Biotechnology Centre, which is affiliated with Cranfield University, jointly invented and subsequently developed the ExacTech pen (the market leader device) which is marketed by MediSense. Several staff and students from Cranfield were employed by MediSense to establish the manufacturing company[a]. In May 1998 it was announced that MediSense would be creating 700 new jobs in the south-east of England at a new £30 million plant in addition to its existing facilities in the UK.

In addition, commentators at the time of the initial introduction of the ExacTech pen suggested that the device's success could 'catalyze interest in a wide range of convenient mediated meters with applications in medicine, the food industry, fermentation, environmental monitoring and military situations'[168].

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[a] personal communication, Prof APF Turner, Cranfield Biotechnology Centre, 1999

Lessons for an EWS

As noted above, biosensor research began in the 1950's and 1960's and the history of the development of such devices has been closely related to advances in biotechnology, materials science and electronics. Thus, the development and likely use of biosensors *per se* would have been relatively easy to predict as long ago as the 1960s. However, commercial secrecy and uncertainty would have meant that it would not have been straightforward to predict when, and precisely which, biosensors would begin to make a real impact on the NHS. In this regard, this case study illustrates how it can be difficult to identify specific products prior to their introduction to the NHS from a number under development and to select which will have the earliest and largest impact.

Scientific journals would have provided early warning of the ExacTech pen but more useful (as they are less labour intensive to search and are likely to have a higher specificity) were the article in *The Lancet* and notification of clearance from the FDA. In addition, biosensors were identified as an important emerging health care technology by the STG report (whose results were published in 1988) and by the Delphi survey undertaken by Spiby in the same year. Although both these reports were published after the launch of the ExacTech pen in the UK the work supporting them had been carried out prior to the launch.

8.3 LEFT VENTRICULAR ASSIST DEVICES (LVADs)

This case-study draws, in part, on a paper written by myself and others on the experiences of Papworth NHS Hospitals Trust with LVADs in the UK from the 1980's onwards[184].

Description of technology

LVADs are mechanical devices that aim to provide safe and effective long-term circulatory support. They are designed to address the needs of patients requiring either a bridge to heart transplantation, a bridge to recovery following heart transplantation or as a permanent solution for severe heart failure.

Evaluating LVADs, in common with other device-based health care technologies, is complicated by the fact that there are several different types manufactured by different companies: the HeartMate 1000 IP, HeartMate VE, Novacor, Jarvik 2000, and the AB-180. The two HeartMate devices and the Novacor device, which are specifically designed for long term mechanical circulatory support, have received safety approval within the UK

in the form of the CE mark. In addition, the Jarvik 2000 and the AB-180 devices are in the process of becoming CE marked, and are likely to start clinical trials in the near future[185].

Early developments

It was not until the 1960s that technology was sufficiently advanced for clinical implantation of mechanical assist devices to be undertaken[186]. In 1975 impetus was provided by the US government which created a programme for developing and clinically testing a LVAD. At that time clinical trials for a two-year implantable LVAD were expected to begin in an estimated three to five years. Targeted efforts beyond that included the development of a five-year implantable LVAD and electrically energized engines. Researchers saw the longer term implantable LVAD as a significant step, possibly a decade away[187].

With early LVADs, patients were tethered to bulky power systems, which meant they could never go home. During the ensuing decade, major technological barriers were overcome, and ventricular assistance was shown to be not only safe in humans, but also capable of supporting the heart until ventricular function was substantively restored. The events shown in table 24 occurred within a relatively brief time frame and established mechanical circulatory support as an effective therapeutic manoeuvre pending cardiac transplantation:

Table 24 Development of mechanical cardiac support 1975-85

Year	Development
1975	Authorization given to begin clinical trials of a LVAD to be used temporarily in patients unable to resume cardiac function at the completion of open-heart surgery
1978	First bridge to transplant with an electrically powered assist device and first successful cases of bridge to transplantation with mechanical device
1982	Implantation of Jarvik 7 total artificial heart as a permanent cardiac substitute
1984	First long term transplant survivor (supported for 9 days) with Novacor electrical implantable system
1984-85	Three further Jarvik 7 total artificial hearts implanted. But, despite encouraging experience, the overall costs, together with devastating neurological complications, terminated the programme
1985	Jarvik 7 used successfully as a bridge to transplant. Total of 163 Jarvik 7 were implanted clinically including forty consecutive patients by Cabrol in Paris (the largest series)

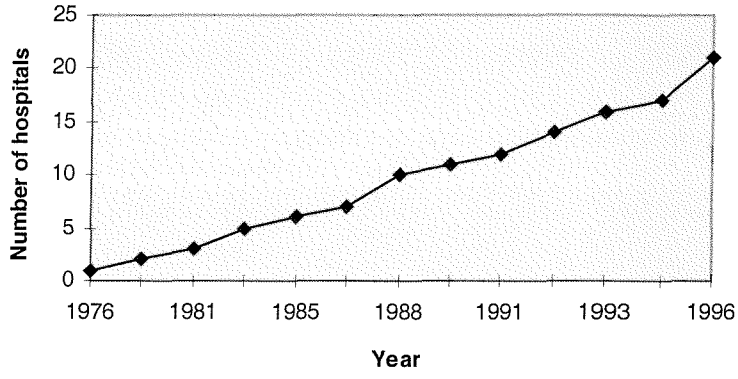
The development of LVADs has progressed over the last twenty years to a stage where the devices are smaller, quieter, more reliable and less likely to cause complications. Prolonged bridge to transplantation led to the concept of permanent mechanical support

for patients with chronic heart failure who are not transplant candidates or stand little chance of receiving a donor organ. The technology is continually developing with the goal of a completely internalised system and power supply.

Adoption

In a survey of University HealthSystem Consortium member hospitals in the US, respondents were asked when they began using LVADs[188a]. Figure 13 shows a steady increase in the adoption of LVAD technology in the US since 1976:

Figure 13 Steady increase in adoption of LVADs in the US during period 1976-96



[Source: UHC Clinical Practice Advancement Centre. *Technology Report: Ventricular Assist Devices.* Illinois: University HealthSystem Services Corporation, December 1997]

Two LVADs, the Thermo Cardio Systems 'Heartmate' devices[189, 190] (used in the UK at the John Radcliffe hospital in Oxford) and the Novacor system (used at Papworth hospital, Cambridge), have proven track records for prolonged bridge to transplantation[191]. There is now extensive clinical experience (so far limited to heart transplant candidates) with both the pneumatic and electric Heartmate systems. Clinical trials with the Heartmate electric device began at the Texas Heart Institute in 1991 and as of July 1995, 46 implants had occurred with 28 patients receiving a transplant. The average duration of support was 100 days with a range of 1 to 503 days. The use of similar devices as a bridge to recovery is at an earlier stage of clinical development and acceptance. Between 1986 and July 1995 the pneumatic device was implanted in 422 patients worldwide.

In the UK, investigators at Papworth hospital began to design a trial of the Novacor LVAD in 1992 and the protocol was finalised in 1994. A pilot study began in August

[a] unfortunately, no comparable UK data is collated centrally

1994 but problems with recruitment to the trial have delayed any further formal evaluation[a]. Patient availability and lack of suitable referrals has also been a problem in early US studies. However, after seven years of effort and preparation, a US RCT of LVADs as a 'destination therapy' began in 1998, using a protocol very similar to the one which was proposed for the UK trial in 1992. The US REMATCH trial will need the co-operation of 11 centres to recruit 140 patients over two years and results will be available in 2002[b]. Although the devices have been in use now for many years and are continually being developed, to date, very few patients have had LVADs implanted in the UK: funding (the devices currently cost in the region of £40-60,000 each), patient selection and remaining technological limitations are currently restricting availability.

In recent years, efforts have been made to evaluate the benefits of using an LVAD as permanent therapy (sometimes known as 'destination therapy') for those patients in heart failure who are unsuitable for heart transplantation. The effectiveness of these devices remains unknown as their evaluation has been hindered by issues arising from research funding systems (in the US as well as the UK) and attitudes to experimentation involving potentially life saving technologies, as well as methodological difficulties. Recent research has been directed toward developing a totally implantable, electronically activated system intended for long-term use. A new generation of LVADs use a small, external power supply worn on a belt or holster and patients are able to leave hospital and resume near-normal lives[192]. The Jarvik 2000 intra ventricular artificial heart is an innovative new approach in the development of a permanent fully implantable system. Preliminary work in Texas and Oxford suggests that the Jarvik 2000 can function free of thrombus for many years with insignificant heat generation and negligible haemolysis. If long term clinical trials are successful the Jarvik 2000 intra ventricular pump may prove preferable to transplantation both from the standpoint of durability and quality of life. A trial of the Jarvik 2000 device is planned for 1998/99 with 20 patients recruited over two years as a bridge to myocardial recovery in those who would otherwise have been considered for heart transplantation. The potential diffusion of, and access to, this technology, if proved safe and effective, may be great and would affect cardiological practice throughout the UK.

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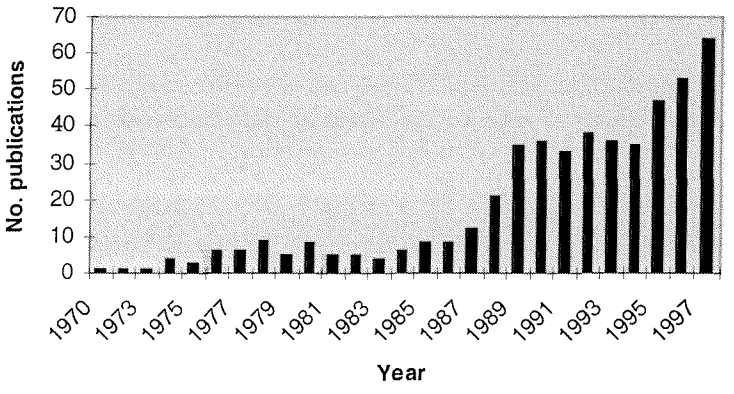
[a] ethically it was not considered possible to randomise to LVAD implantation or transplantation, so a very narrowly defined clinical group of elderly patients formed the study population. As a result of low referrals, only 18 patients were considered for inclusion over a period of 15 months; there was a high proportion of unsuitable patients (7/18) and of patients unwilling to take part (5/11). Developments elsewhere also led to the use of LVADs outside the trial and outside any context of a formal evaluation.

[b] personal communication, Rose E, Columbia-Presbytarian Medical Centre, New York, 1998

Potential information sources for early identification

LVADs have been the subject of published papers throughout the 1970s to 1990s (see figure 14), with a marked increase from the late 1980s onwards. Retrospective case series dating back to 1981 have reported on the various developmental stages of these devices[193]. Some small comparative trials of LVADs used as bridge to transplantation (for example, a paper in the *Annals of Thoracic Surgery* in 1994 reporting on clinical experience with the HeartMate LVAD[190]) have also been published. The evaluation judged by an independent review[185] to have the best methodological quality was a cohort study published in 1995[194]. Similarly, case studies on LVADs as a bridge to myocardial recovery date back to 1986[195].

Figure 14 Increase in MedLine references to LVADs from late 1980's onwards



As well as the growing number of papers in the peer-reviewed literature, there has been increasing interest in the devices from the popular media, but the distinction between an orthotopically sited total artificial heart and an implanted LVAD has not been made in the lay press[88 a].

Experience with LVADs in the UK has, until very recently, been limited to two centres: the John Radcliffe and Papworth hospitals. In 1985 a team of two surgeons and one technician from Papworth hospital underwent two weeks of training at the University of Utah in the use of the Jarvik series of total artificial hearts and VADs. Subsequently, the Papworth team provided technical assistance in the first Jarvik TAH implant in Paris in 1986 and later that year implanted their own first patient with a Jarvik TAH as an elective bridge to transplant. In 1989 one surgeon and one technician underwent

[a] for example, a *Sunday Times* article in 1995 stated that the implantation of a new artificial heart was a 'first' for Oxford, whereas a headline in the *Times* on 24 April 1997 ('Tiny pump gives diseased hearts a chance to recover') subtly changed the emphasis away from replacing a heart towards supporting patients while their heart recovers

training in the use of the Hemopump (a high-speed axial pump for LVAD applications), in Houston. Papworth subsequently became one of two investigational sites in the UK. Following implantation in five patients the device was withdrawn for modifications based on the clinical experience.

There may also have been potential for identifying LVADs via the involvement of the FDA in the US; Myers reports that clinical studies have been conducted under an investigational device exemption approved by the US FDA to evaluate the devices for safety and efficacy[196].

Payback from early warning

LVADs could have been identified from the literature as a potentially important new health care technology from the mid-1970s onwards, some 15 years prior to their initial introduction to the NHS. Closer involvement of UK clinicians and technicians in the development and use of these devices seems to have begun in the mid-1980s. Given the still relatively low numbers of patients implanted with these devices in the UK this would have provided sufficient early warning to enable a HTA programme to instigate research or propose interim monitoring measures, the results of which could have helped inform the rational introduction of this technology into the NHS.

As with the other case-studies in this chapter an integral part of the analysis presented here addresses the counterfactual, specifically: following early warning of the likely significance of LVADs what would have been the net cost and benefit accruing to the NHS of formal HTA research of these devices during the early 1990s?

Knowledge

Given the problems encountered world-wide in designing studies and recruiting sufficient patients to evaluative studies, the involvement of the two UK centres with expertise in LVAD use in a collaborative study would undoubtedly have been beneficial. At the very least a UK-based study, or even shared data collection and monitoring, would have had added value by allowing an assessment of the external validity of results of US-based studies to be made. Such analyses would have helped to inform decision-making regarding the use of LVADs in this country. In the absence of such research decisions regarding the use of LVADs have been made on an arbitrary basis (see below). Whilst informal networking between the UK centres and the US investigators has clearly taken place this has not proved sufficient to enable a definitive study to report (and 2002 is the earliest date by which one is expected to do so) despite

the technology undergoing a very long and relatively well-publicised development phase.

Benefits to future research and research use

By combining data from all the centres which have been using LVADs since the early 1990s, clinical experience could have been modelled (and perhaps included in an international collaboration) using, for example, Bayesian methodology to update estimates and beliefs as data accrue. Importantly, such models allow systematic use of sensitivity analyses to explore how changes in one or more variables alters the conclusions of the study, thereby identifying threshold values of variables, below or above which LVADs are likely to represent good value for money. Information on thresholds is also of value in planning future assessments of the technology by providing a focus for data collection and sample size collection. Co-ordinated data collection and data monitoring in the UK may therefore have allowed for better targeting of future research.

At the broader policy level, the NSCAG can only fund a small number of evaluations given the often high cost of specialist services. Beyond NSCAG there is currently no acceptable way in the UK of ensuring that low volume, high cost surgical interventions, such as LVADs, do not slip into general use unevaluated. The introduction and adoption of LVADs has offered an opportunity to provide an exemplar of how potentially life-saving surgical interventions should be introduced into the UK health system but, to date, this opportunity has not been taken. Whatever the study design, multicentre (maybe multinational) collaboration is needed as effective evaluations of such technologies require a concentration of research efforts in a small number of well placed centres with experience in treating appropriate patients. In the UK the co-ordination of such national evaluations may well be a role for the recently established NICE working with NSCAG.

Political and administrative benefits

Currently, in the absence of any formal evaluation, there are no contracting arrangements for LVADs in the UK. Rather agreement to provide treatment either as a bridge to transplant or as a more permanent therapy, have been made on a 'one-off' basis to individual health authorities who need to make arbitrary decisions about significant financial commitments at very short notice. Partly to replace such *ad hoc* commissioning, NSCAG are at present considering an application from a consortium of

UK cardiac centres to fund LVAD therapy, which would also include an associated evaluation. There is perhaps a lesson to be learned from the early experience with evaluation of heart transplantation in the UK. In parallel to the commissioning of the research, which unusually for the early 1980s included measures of cost as well as clinical effectiveness, the Supra-Regional Funding system (the precursor of NSCAG) ensured that only two UK centres were designated to provide the service, for the duration of the evaluation. This highly effective system for the planned introduction of new technology is now continued through the work of the NSCAG. Provision of LVAD therapy via NSCAG, through the designation of a limited number of centres in which expertise can be developed and in which data registries can be established, would be a preferred option to the current *ad hoc* activity, and could have been initiated several years ago.

Health sector benefits

It is difficult to assess quantitatively the likely payback from an earlier HTA of LVADs, given that to date we still have relatively little information on the effectiveness of these devices. Recent UK heart transplant figures may give an indication of the potential numbers of LVAD recipients when used as a bridge to transplant. For the period January 1998 to December 1998, 264 heart transplants were performed in the UK[a]. A large number of potential transplant candidates, estimated at between 20-40%, die whilst on the waiting list before a donor heart becomes available[197]. Mortality figures from myocarditis and cardiomyopathy may give some indication of the possible numbers that may benefit from LVADs as a bridge to recovery: in England & Wales in 1997 there were 57 deaths from myocarditis and 1,594 deaths from cardiomyopathy. The cost of the LVAD device is quoted as being approximately £52,875, with the implantation procedure costing on average £9,604. This compares to heart transplantation procedure costs of around £23,949 on average, with follow up costs quoted as £3,500 per annum. At a net cost of approximately £35,000 and with a (minimum) potential patient group of around 1,750, LVADs could theoretically cost the NHS in the region of £6 million per year.

However, the still low numbers of patients being implanted with these devices places the emphasis not on any potential cost savings that the NHS may have realised had evaluative research and controlled introduction been in place, but rather on the substantial patient benefits that may not have been realised. This is particularly

important given the high proportion of patients who die whilst on the waiting list for a donor heart.

It is admirable that a RCT (the US REMATCH trial) is being done at last but the results would have been more useful and timely if it had started six years ago, particularly as during this period there have been only minor refinements to the technology. In contrast, by 2002 there may well be highly significant changes to LVAD technology in that a fully implantable system may by then be available: dispensing with lines to an external power supply will have a crucial effect on infection morbidity. It is also highly possible that by 2002 the first clinical trials of other alternatives, including xenotransplantation, will be underway. In the interim a potentially beneficial, and high cost, technology may have been under utilised; early warning and mechanisms for encouraging collaborative evaluation may have helped to maximise the experience and knowledge generated by the use of LVADs in various centres, not just in the UK but world-wide. In doing so health policy-makers could have ensured a more equitable use of these devices than has been seen in the UK.

Broader economic benefits

There are no obvious broader economic benefits (either in terms of commercial exploitation or reduction in working days lost) that might have followed on from an earlier evaluation in the UK of already patented LVADs.

Lessons for an EWS

It would not have required a particularly sophisticated EWS to identify this technology; LVADs have been in development for some time and information regarding progress has been publicly and widely available. The experience of individual clinicians and technicians at the Papworth and John Radcliffe hospitals in the UK could have enabled LVADs to have been identified as an emerging technology as long ago as 1985.

In addition to further emphasising the role of experts, this case-study again highlights the potential role of specialist medical journals in providing early identification. However, this is a labour intensive source to search particularly as the development of LVADs has been taking place since the 1960s. This difficulty could be overcome: the high number of articles in specialist medical journals from the late 1980s onwards suggests that routine MEDLINE searches could signal when the number of papers is increasing (particularly those reporting case studies and case series) and prompt timely

[a] statistics prepared by the UK Transplant Support Service from the National Transplant Database, 1999

discussion with experts. With the exception of a 1980 paper in *JAMA*[198], there does not seem to have been a great number of papers in principal medical journals describing LVADs. It is difficult to assess retrospectively how useful liaison with medical engineering companies would have been. The postal survey undertaken by Stevens et al in 1995 (and published in 1997) identified LVADs as a new health care technology that would have important implications for the NHS within a five year time frame. However, LVADs were not one of the most commonly mentioned of the 1,100 technologies identified in the survey.

8.4 TELEMEDICINE

Description of technology

Telemedicine is defined as remote, telematic care using information and communication systems to give patients with their health care workers access to relevant information sources wherever they are located. The term therefore encompasses a wide range of telecommunications and information technologies and many clinical applications. For example, in describing a possible scenario for future management of stroke patients using telemedicine, a recent report highlights the important potential role of telemedicine in strengthening the interface between the primary, secondary and community sectors of care, and in possibly shifting the focus of care away from a centralised service to one which is patient centred[199].

Early developments

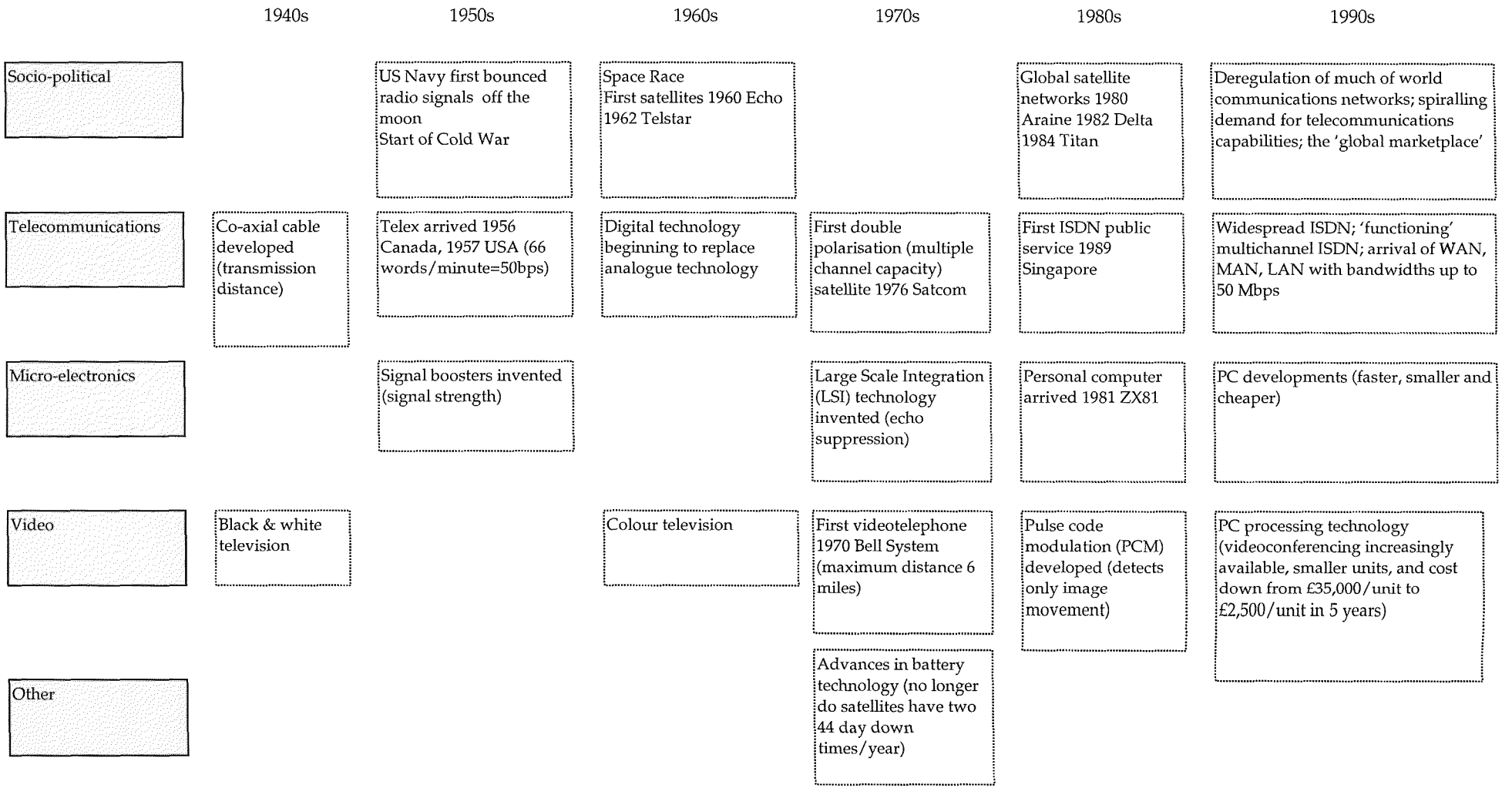
Early programmes of telemedicine in the 1950s[200] failed to achieve physician and patient acceptance[201]. These early attempts to establish telemedicine services failed principally because of the costs of technology, poor image quality, the structure of care services and staff training issues[202]. A cycle of technological development has led to renewed activity, followed by a waning of interest when expectations were not realised, continued approximately every decade[203].

In the US, NASA played an important part in the early development of telemedicine, providing much of the technology and funding for early demonstration projects[204]. From around 1978 to the mid-1980s there were few studies undertaken on telemedicine. With the exception of a twenty-year-old telemedicine programme in Newfoundland, none of the projects implemented before 1986 had survived beyond their original grant funding cycle. A resurgence of interest has occurred from around 1990 onwards. This has been

due to further technological advances (such as the deployment of high-speed, high-bandwidth telecommunications systems and the invention of devices capable of capturing and transmitting digital images[205]) combined with reduced costs, programmes of health care reform emphasising the need for improved efficiency, and a demand by rural patients and clinicians for equal access to high quality health care irrespective of location.

As with CT scanning, technological advances have been required in a number of fields over a lengthy period of time in order for telemedicine to begin to realise its potential:

Figure 15 Development of telemedicine required technological advances in a number of fields over a lengthy period of time



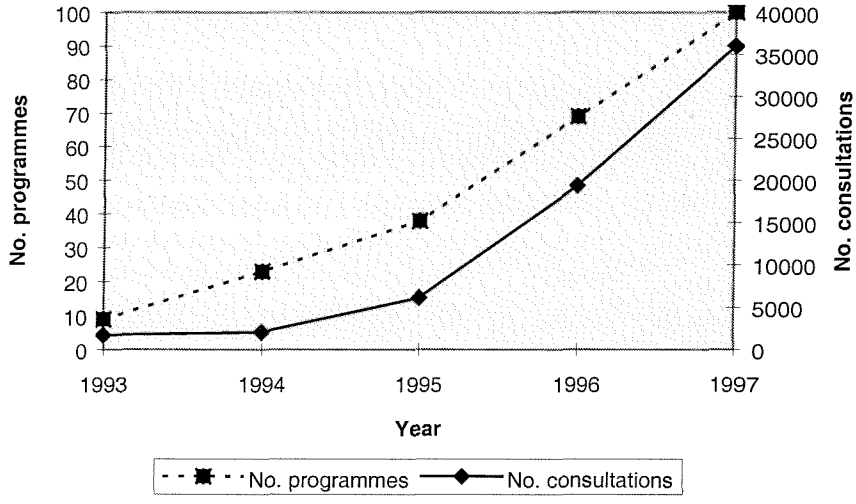
[Source: Mowatt G, Bower DJ, Brebner JA et al. When and how to assess fast-changing technologies: a comparative study of medical applications of four generic technologies. *Health Technology Assessment*, 1997, **1**(14)]

Adoption

The development of telemedicine has essentially been technology-driven. Technology providers have been keen to generate new markets for their products by funding telemedicine research and attempting to stimulate both medical and popular interest in such applications. As with all information technologies costs have fallen sharply over the last decade; interactive video equipment that cost more than $100,000 in 1992 can today be purchased for less than $20,000 and has more capabilities[205].

Telemedicine projects are being implemented in the US at an accelerating rate. In 1990, four telemedicine projects for patient consultations were active in North America. Since then the number of programmes has been doubling yearly (figure 16) and activity (number of consultations) trebled from 1995 to 1996[206]:

Figure 16 Telemedicine in the US: interactive video-mediated programs, 1993-97[a]



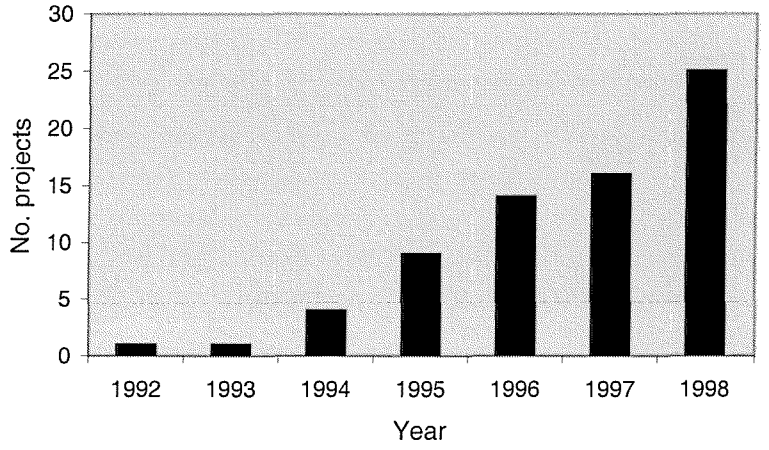
[Source: Grigsby B, Allen A. *4th Annual Program Review - A cooperative study by Telemedicine Today and the Association of Telemedicine Service Providers,* http://www.telemedtoday.com/articles/4annual.htm]

Research has progressed furthest in the image orientated subspecialties such as teleradiology and telepathology and there have been one or two studies concerned with teleconferencing. Teledermatology seems to be a much more recent application of telemedicine than teleradiology. The most common specialities, in terms of number of consultations in 1996 in the US, were: radiology (13,653), mental health (3,460), emergency/triage (2,574), cardiology (2,017), dermatology (1,807) and surgery (1,351)[206].

[a] 1997 figures are projected from data from first four months of that year

A 1995 *Lancet* editorial commented that the recent resurgence of interest had yet to have a major impact on mainstream medical services in the UK. The editorial made a number of predictions as to the likely impact of telemedicine on medical practice in the year 2000[207]. In order to take stock of the level and range of work in the UK, in 1996 the DHs R & D Directorate commissioned a survey of telemedical activity. The report provided details on 65 projects surveyed in the UK, of which 24 fall strictly into the category of telemedicine projects providing remote telematic health care services to patients[199]. The UK National Database of Telemedicine Projects contains a regularly updated list of telemedicine projects in the UK:

Figure 17 Increasing number of telemedicine projects starting each year in UK during period 1992-98



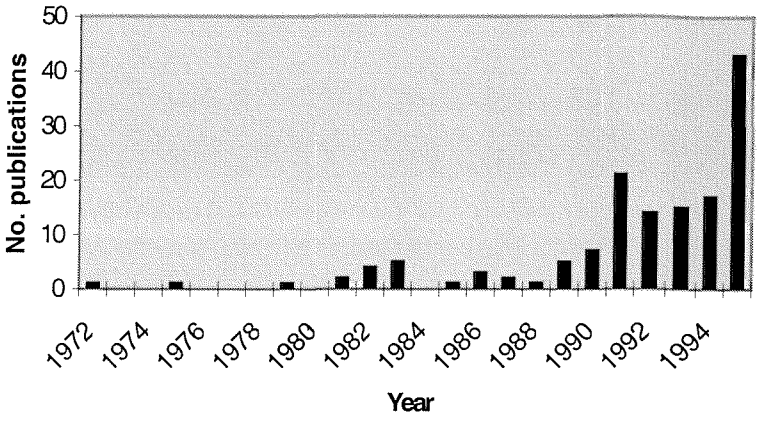
[Source: UK National Database of telemedicine, http://www.dis.port.ac.uk/ndtm/uktm.html]

Current services in the UK include some teleconferencing services such as mainland provision of trauma advice to oil rigs and remote fetal diagnosis on ultrasound images. Most UK activity to date has so far been locally driven pilot projects; larger scale activities are being planned and in a recent call for R & D proposals to the HTA programme in the UK 58 out of 349 (17%) were related to telemedicine[203].

Potential information sources for early identification

In 1995 it was reported that telemedicine had been the subject of over 100 articles listed on MedLine, and the theme of recent conferences in the US[207]. In the medical literature the first reports on teleradiology appeared as early as 1972 but numbers of references remained relatively low up until 1990, with a generally increasing trend from then onwards, culminating in a major increase during 1995[133]:

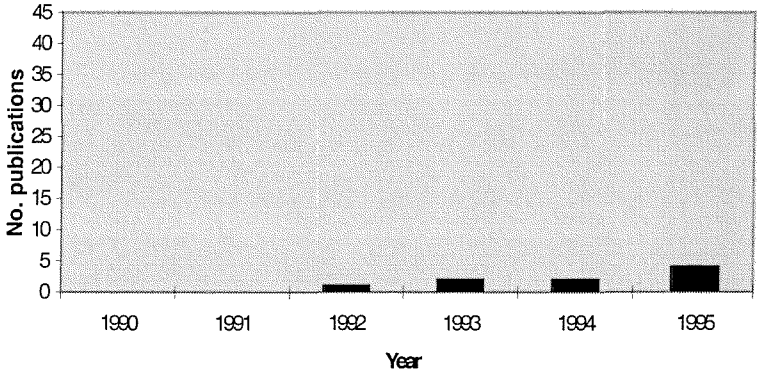
Figure 18 Increase in MedLine references to teleradiology in 1995



[Source: Mowatt G, Bower DJ, Brebner JA et al. When and how to assess fast-changing technologies: a comparative study of medical applications of four generic technologies. *Health Technology Assessment*, 1997, 1(14)]

Other applications of telemedicine in different specialties, such as dermatology, have seen fewer publications:

Figure 19 Fewer MedLine references to teledermatology, 1990-95



[Source: Mowatt G, Bower DJ, Brebner JA et al. When and how to assess fast-changing technologies: a comparative study of medical applications of four generic technologies. *Health Technology Assessment*, 1997, 1(14)]

In addition to the published literature telemedicine has long been the subject of conferences and symposia. Via a search of MedLine and the Index of Scientific & Technical Proceedings 57 conferences held during the period 1980-96 relating to telemedicine were identified[133]. The 1981 survey of expert opinion undertaken by the FDA reported four citations on 'information transmission and storage to improve health

care'[142]. The citations mentioned teleradiology in particular and predicted 1989-90 as the likely year when this technology would become an issue for that organisation.

Payback from early warning

Telemedicine would have been relatively easy to identify as a potentially important new health care technology at virtually any time over the past thirty years through the vast literature (and conference exposure) which has evolved around the subject. Early cost-effectiveness evaluations on prototypes that probably differed considerably from later models designed for serial production would not necessarily have been helpful. However, it is important to be able to have advance warning of when such technologies are sufficiently stable that a full evaluation is justified.

Knowledge

Telemedicine applications must be examined individually. However, there is a dearth of systematic empirical research regarding the true effects on telemedicine on costs, quality and accessibility of care[208]. The 1995 *Lancet* editorial commented that 'although much is claimed, the economic benefits of telemedicine have yet to be proved' and the Norwegian Centre for Health Technology Assessment suggested that this situation had not changed significantly by 1998[209]. Research is still needed on how such technology can be integrated into health care delivery systems in a way that improves the effectiveness and efficiency of those systems.

Benefits to future research and research use

Early identification may have enabled the development of a broad economic model to define costs and benefits more carefully which could then have been applied to a range of telemedical applications.

Political and administrative benefits

Introducing a telemedicine service is a complex intervention and one which it is difficult to assess. Telemedicine raises questions of transfer of resources from hospitals to primary care settings, accessibility and acceptability of services for patients, and major issues of education, substitution and re-skilling for health care staff[210]. However, there has been very little work on the impact of telemedicine on the structure and process of care.

The majority of the small R & D and EU-funded evaluations of telemedicine have covered a range of clinical areas[203]. They did demonstrate that individual patients could

be treated effectively, often in remote situations, when it might otherwise have been impossible. However, the evaluations have taken place in highly select and atypical situations, and did not necessarily seek to answer the question of whether telemedicine was cost-effective or provided direct practical benefit to the wider generality of healthcare provision. Without concerted research, the development of telemedicine will remain uncoordinated, with activity focused in specialist areas led by academic research and commercial organisations. Greater coordination between service providers could have been encouraged at an earlier stage in the application of telemedicine in the UK. Given some of the high profile IT disasters that have littered the NHS during the first half of the 1990s, such a proactive approach with the early involvement of policy-makers would have provided political and administrative benefits.

Health sector benefits

The potential benefits of the application of telemedicine include a reduction in follow-up appointments and in the number of medical interventions, tests and investigations that are required, increased patient satisfaction and improved patient health status. Telemedicine therefore holds out the prospect of a net reduction in the cost of delivering services, improvements in the quality of services (including increased patient satisfaction), improved efficiency and improved equity (by improving accessibility of services). As such a full evaluation of the likelihood of telemedicine projects being able to deliver such benefits is urgently required.

The HTA programme in the UK is funding two primary research projects. The first, 'Virtual Outreach: a randomised controlled trial and an economic appraisal', is costing £903,069 and is scheduled to be completed by early 2003. The second project, 'Randomised controlled trial of asynchronous and synchronous telemedicine in dermatology – RCT-ASTID', is costing £602,704 and is due for completion by mid-2003. These two projects are the most expensive studies funded to date by the HTA programme since its inception in 1993. Given the wide range of potential applications of telemedicine, the wide variation in the costs of different applications and the wide range of clinical areas in which it might be applied, it is not possible to quantitatively assess the likely payback to the NHS of individual assessments of telemedicine *per se*. Rather telemedicine should really be seen as a process which has system-wide implications rather than a discrete technology in itself. The need for HTA to take account of these issues is discussed further in section 9.3.

Broader economic benefits

Telemedicine offers the potential of a decreased burden on the national economy in terms of the amount of time patients require away from their work in order to attend a consultation.

There is also the potential to realise the commercial opportunity of the sale of telemedical services overseas. Over the last few years, there have been a number of commercial organisations with telemedicine products keen to enter the NHS market[203]. In Australia sales in the telemedicine industry represented approximately $24 million in 1997, mainly from the videoconferencing industry[211]. The market there is expected to grow considerably in 1998 and to $54 million by 1999.

Lessons for an EWS

It is difficult to retrospectively assess how two of the sources recommended in the three preceding chapters for identifying new information technologies (the Internet and other HTA agencies) might have added to the information that could be accessed through specialist medical journals.

The task for an EWS would be how to predict when telemedicine will finally begin to have an important impact on health care provision. Telemedicine should be driven by the health needs of patients and health professionals and not the possibilities of the technology[203]. The large capital outlay and organisational implications of this technology, manufacturers marketing and the fact that it has been around for a long time suggest that this technology required 'watchful waiting': that is liaising with experts to indicate when technological developments and an appropriate organisational environment would allow widespread diffusion of telemedicine to take place. Other instrument-based medical technologies may show a similar pattern of diffusion and would therefore require the same approach.

8.5 PAEDIATRIC INTENSIVE CARE UNITS (PICUs)

Description of technology

Intensive care is a low volume, high cost specialty which requires a highly trained, multidisciplinary team together with specialised tertiary expertise and diagnostic facilities.

The British Paediatric Association (BPA) report in 1987 describes PICUs as providing '..for the needs of critically ill children [aged 4 weeks to 16 years] requiring constant

individual nursing care and immediate availability of skilled medical help, with access to a full back-up of specialists skilled in the management of the critically ill child and specialised investigatory facilities. A PICU should be able to provide artificial ventilation, invasive cardiac monitoring, renal dialysis, intracranial pressure monitoring, complex intravenous nutrition and drug scheduling"[212].

Early developments

The first PICU was established for respiratory care (tracheotomy, muscle relaxant and mechanical ventilation) under the management of paediatric anaesthetists in the US in 1964. Then in the 1970s and early 1980s, an epidemic of Reye's disease demanded a multisystem approach to paediatric intensive care (PIC), introducing the use of intracranial pressure monitoring. Multidisciplinary PIC expanded the role from post-operative, pulmonary and cardiac units into general monitoring and stabilisation areas for a wide variety of childhood diseases.

In 1985 the BPA established a working party to 'investigate and report on the facilities, organisation and staffing (including training) for intensive care of infants outside the neonatal period and older children, and to make recommendations for the Association'. The Paediatric Intensive Care Society was established in the UK in 1987 and in 1989 the Confidential Enquiry into Perio-Operative Deaths concluded that the needs of children in single surgical specialities are not always fully met. There was a need for dedicated intensive care facilities for children and appropriate staffing in specialised units. In 1991 increasing public and professional concerns about the impact of NHS reforms on the provision of highly specialised services (including PICUs) and the lack of progress in implementing the 1987 BPA report, led to the establishment of a second BPA working party. This group carried out a national survey of PIC facilities, workload and working practices and, in December 1993, published 'The Care of Critically Ill Children"[213]. A Centre for Reviews & Dissemination (CRD) report concluded that '. . while the BPA report is a useful source of information and summarises the views of a range of professional groups, it does not constitute sufficient basis for determining national or local policy for the care of critically ill children in Britain"[220].

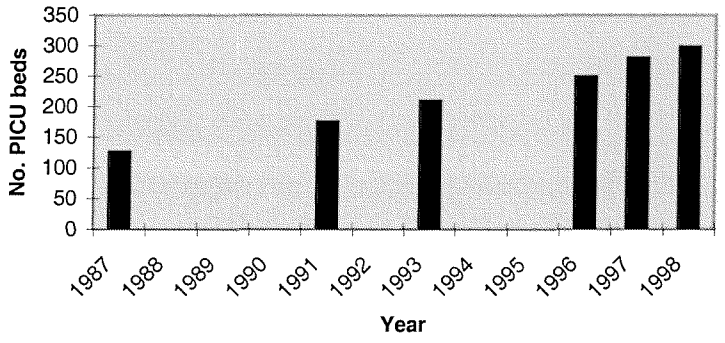
In January 1994 the NHS Executive medical director (in EL(94)10) asked purchasers to develop "..a strategic plan for the purchasing of paediatric intensive care, taking into account local needs and resources likely to be available within the overall context of children's services.' In 1996 a National Coordinating Group on PIC was established by the NHS Executive and regional co-ordinators for PIC were appointed in order to:

- coordinate the implementation of the planned additional intensive care beds
- ensure that the necessary medical and nursing training was available to meet needs, and
- to produce medium term plans to develop the provision of PIC.

Adoption

In the UK PIC has evolved incrementally as a distinct category of child health care but only in a fragmented fashion and a significant number of children are still managed outside a PICU[214]. Information about the provision and use of PICUs has not been collected routinely. Figure 20 shows the increase in the number of PICU beds in the UK from 1987 to 1998, based on estimates from a number of reports during that period:

Figure 20 Increase in PICU beds in the UK, 1987-98 (based on numerous sources)

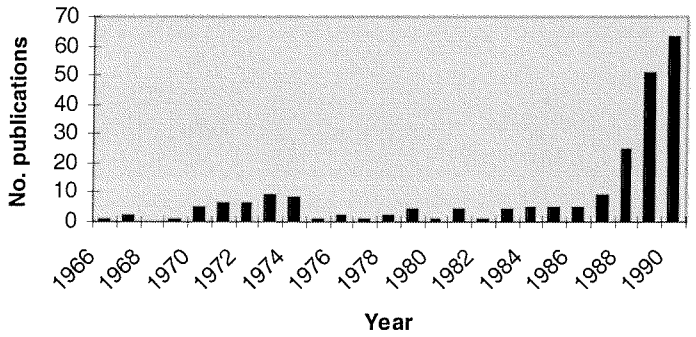


The 1987 working party reported that there were 22 PICUs in the UK which provided a total of 126 beds. In 1993, Shann suggested that there were too many small PICUs in Britain (twenty-two plus use of adult intensive care units) and it would be better if there were only 12-14 units[215]. The 1993 BPA report stated that whilst, in 1991 there had been 175 designated PICU beds (including general and sub-speciality beds), in 1993 there were 209. However, many PICUs reported that one or more of their beds were, in effect, permanently closed, because of lack of staff. Three regions had no identified PIC beds reflecting a wide regional variation. In addition, the figures include some units that are more correctly classified as high dependency units, small satellite units and single specialty units (for example, burns, cardiac and neurosurgery units). In April 1996 the NHS Executive in the UK established that there were a total of 249 intensive care, specialist intensive care and high dependency beds for critically ill children in England[216], and, in March 1997, updated this figure to 280 beds in 29 centres of differing sizes[217].

Potential information sources for early identification

Much of the published literature relating to PICUs is from the US and Australia[218]. Figure 21 shows the number of MedLine references over the period 1966 to 1990, with a particular increase in the late 1980s:

Figure 21 Increase in MedLine references to PICUs in the late 1980's



Whilst there is little information in the peer reviewed literature on PICUs in the UK, there have been a host of expert working groups and committees and, given the emotive nature of this technology, a high public profile which has been maintained by media attention.

Payback from early warning

The maximum length of early warning, based on the initial development of PIC in the US in the 1960s, would have been in the region of twenty years. However, it is likely it would not have been until the early 1980s and the formation of expert working groups, and the publication of their reports, that relatively late warning of the introduction of PICUs into the UK would have been available. The high public profile accorded to this issue throughout the mid- to late-1980s would have ensured that three years early warning would have been available prior to significant numbers of PIC beds becoming available in the UK.

Knowledge

There is relatively little evidence in the UK on the standards which provide the best outcomes for critically ill children. No such standards have as yet been laid down[219] and worldwide very few studies have addressed the need for PIC. The CRD review of the BPA's 1993 report on 'The Care of Critically Ill Children' found that[220]:

> "There is a significant diversity of professional opinion over detailed recommendations in this area . . . Of particular note, is the lack of British research in this area."

The review recommended that any future changes in the provision of services should be informed by better information based upon comprehensive and accurate data collection, and carried out in a controlled manner which can be evaluated and costed[220]. Ideally, a multicentred, case-mix adjusted trial comparing outcomes in well-resourced, local centres with those in regional paediatric ICUs is needed to provide the answer that clinicians and government agencies are still seeking[221].

Benefits to future research and research use

There remains an urgent need for developing severity of illness scoring system and for long-term outcome studies so that any future reorganisation of the PIC service is informed by research and audit[222]. A report from the MRC in 1996[223] emphasized the importance of a more integrated approach to research into intensive care, recommending:

- the development and validation of risk adjustment methods and their correlation with organizational factors
- the need for health technology assessment of specific interventions employed in PIC, and
- the development of accurate and objective outcome measures other than mortality.

One recent proposal is that a lead centre in each region should be responsible for data collection, audit and developing joint protocols with other hospitals in their region. An EWS could have enabled such initiatives to have begun much earlier and consequently may have resolved some of the continuing debates regarding PIC in the UK at a much earlier date.

Political and administrative benefits

PIC has developed in an *ad hoc*, unplanned way during the past twenty years[219] resulting in '. . extremely fragmented care for critically ill children in the UK'[224]. The currently available dedicated general PIC beds are spread across England in 29 centres of differing sizes. Reportedly, there are wide regional variations in the UK in terms of criteria for admission to or exclusion of a child from PIC.

The introduction of the internal market has further inhibited the rational development of high cost, low volume services such as PIC[214]. Additionally, as with many technologies, the process of disinvestment may be more difficult if research results are only available after diffusion, as resistance to giving up a service will be even greater than the pressure for it's creation[72]. However, this is the situation that the UK now faces with the need to find a 'drastic solution . . . for improving outcome'[225] by either closing or amalgamating small units[226]. The extent of this problem might have been diminished had appropriate research and monitoring of performance been initiated at an earlier date soon after the introduction of dedicated PIC facilities in the UK.

Health sector benefits

Between September 1996 and February 1997, over 460 children were refused admission to PICUs in the UK[214], and the '. . the lack of *any* coherent national policy on children's intensive care to date has allowed the development of a service with major deficits'[227].

A 1991 survey showed that 12,282 children receiving intensive care were looked after in 273 different PICUs, adult ICUs or children's wards with an average of only 47 admissions per unit per year. Such an analysis led commentators to suggest that '. . this is well below the minimum number of admissions needed for optimum care, and is the main reason that critically ill children in the UK are getting suboptimal care at inflated cost'[224]. The main benefit of timely research would therefore have been in improving the quality of services and improving the efficiency of health services, with a consequent increase in health gain.

Broader economic benefits

There are no obvious broader economic benefit that might have followed on from an early evaluation of PICUs in the UK.

Lessons for an EWS

PICUs are a good example of a technology where over reliance on peer-reviewed journal publications may not have been sufficient to identify a new and important health care technology. Early notification of the introduction of PICUs into the UK would have had to rely on monitoring of developments overseas (in this case in the US and Australia in the late 1970s and early 1980s). Media publicity and liaison with experts would have been more likely to alert policy- and decision-makers to the importance of planning the rational introduction of PICUs in the UK but at a later date.

There remains a need for prospective audit with the aim of establishing exactly where critically ill children are cared for and the outcome of that care. Early warning could have enabled monitoring and data collection systems to have been established much earlier and consequently resolved some of the questions that still remain regarding the cost-effectiveness and ideal configuration of PIC services in the UK.

8.6 BETA INTERFERON (IFN-β) FOR MULTIPLE SCLEROSIS

Description of technology

IFN-β is the first new product for multiple sclerosis (MS), a chronic incurable disease that is relatively common and has a variable course[228].

Early development

Interferons were first described in 1957 as proteins that are secreted by virus-infected cells and act to prevent other cells from becoming infected[229]. IFN-β was first cloned and expressed in bacteria in 1980 but was found unsuitable for clinical use in that form[230].

Genetic engineering enabled scientists to make synthetic IFN to replace the scarce, impure and prohibitively expensive natural human IFN, which resulted in a large supply of IFN at reasonable costs for clinical trials[231]. The potential usefulness of IFN as a treatment for MS was first considered in the late 1970s. Its discovery was not haphazard but the result of numerous human clinical trials with various IFNs conducted over a 13-year period[232]. It was finally marketed in the UK in December 1995.

Adoption

In spite of well organised information supplied by patient interest groups and high expectations of the use of IFN-β, currently only 1.5% of MS patients in the UK receive the drug at a cost of approximately £11 million per annum (less than the cost of a recently proposed HTA trial). This contrasts starkly with the higher levels of prescribing in most other European countries (6-23%) and the US (16%)[233].

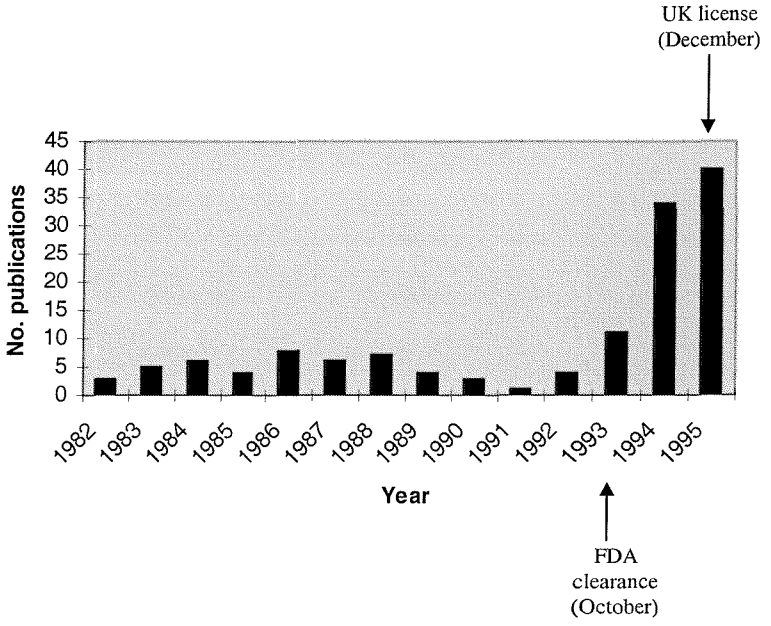
A wide spectrum of views amongst neurologists in the UK has been reported regarding the place of IFN-β in treating MS, and such differing opinions have been noted to occur within a single health authority[234]. A *Drugs & Therapeutics Bulletin* in February 1996 drew the conclusion that there was insufficient evidence to recommend the use of IFN-β[235] as did others[236,237]. However, a number of commentators have supported the use of IFN-β on the basis that it can reduce the number of relapses, regardless of its effect, or

otherwise, on long-term disability[238,239,240,241]. As a consequence, in the years after its licensing there were great disparities in prescribing of IFN-β across Britain, in spite of the attempt by the DH to ensure the orderly introduction of the drug. It has been suggested that a small number of enthusiastic neurologists and an 'active patient interest lobby' dictated policy at national level[242] but others have praised the role of patient interest groups (such as the Multiple Sclerosis Society) for making evidence available in 'a balanced and intelligible form'.

Potential information sources for early identification

Journal papers reporting open studies of IFN-β began to appear in the early 1980s. The number of papers stayed relatively stable each year comprising reports of continuing trials[243,244,245,246] and the occasional editorial[247]. Just before the launch of IFN-β in the UK in December 1995 there was a sharp increase in the number of papers published. Many of the papers published in 1994 and 1995 were editorials[248] or reviews (many in pharmaceutical journals) on the potential role of the drug following the publication of the phase III trial results in 1993[249]:

Figure 22 MedLine references to IFN-β in multiple sclerosis began to appear in early 1980's



As for regulatory procedures FDA approval of the drug came in October 1993 and the EC awarded marketing authorisation in 1995 subject to an annual review of the drug's safety, efficacy and pharmacokinectic data because of the paucity of such information available at that time. For most drugs an unfettered five-year approval would be

expected but for IFN-β particularly close review was introduced because 'comprehensive information on quality, safety and efficacy cannot be provided'. In Australia, the Pharmaceutical Benefits Scheme decided not to offer reimbursement for IFN-β, indicating that in its view the drug is not cost-effective.

Schering, the manufacturers of IFN-β, circulated information to health authorities and clinicians but McDonald issued a position statement in 1994 on behalf of the Association of British Neurologists giving the opinion that 'the widespread use of IFN-β can not yet be recommended'[250]. The DH issued an executive letter in 1995 providing guidance on the introduction of IFN-β. Purchasing authorities were asked "to initiate and continue prescribing of IFN-β through hospitals"[251]. This is the first time that the NHSE has issued such a directive.

Payback from early warning

This anaylsis draws on the discussion and conclusions of an *ex-ante* payback analysis carried out by myself and others on a proposed ten-year trial of IFN-β which was submitted to the UK HTA programme in 1998[252].

As with the other case-studies in this chapter an integral part of the analysis presented here addresses the counterfactual, specifically: what would have happened to the level of prescribing of IFN-β following it's licensing in the UK in 1995 if, following early warning of the likely importance of IFN-β, HTA research had taken place in the early to mid-1990's?

As discussed above, the length of early warning regarding IFN-β would have provided sufficient time to allow a HTA to be performed and for the results to potentially influence the adoption of the technology. An EWS could have been expected to have identified IFN-β as an emerging technology up to thirteen years prior to its introduction in the UK in December 1995[a]. A more reasonable assumption may be that HTA research could have begun after, or alongside, the phase II and phase III clinical trials in 1992-93 some two to three years prior to its introduction to the NHS. This is when the likely importance of IFN-β as a novel treatment for MS became apparent.

Knowledge

A trial begun in the early to mid-1990s would have been likely to provide important information prior to the launch of IFN-β in the UK on:

[a] the recent bid to the HTA programme entailed a ten to fifteen year trial

- the quality of life of MS patients,
- the long-term progression of disease,
- how early indications of MS might relate to longer-term disability, and
- better information on the full range of resources, including those outside the NHS, devoted to the support of MS patients.

To date, such long-term information has still not been generated elsewhere.

Benefits to future research and research use

Recent reports have indicated that it remains difficult to design trials to adequately assess the effectiveness of treatments for MS[253, 254]. The most important issue has been maintenance of blinding to treatment allocation. Patients may guess their treatment based on the presence of adverse events that are more common in the IFN-β treated group and this may affect outcome measurement.

Whilst it is unlikely that a trial designed at the beginning of the 1990s would have been able to overcome all such difficulties, the very fact that a trial had at least been initiated then may well have helped to progress thinking on trial design issues beyond the current state of knowledge. Importantly a trial may have provided assistance in determining appropriate outcome measures when evaluating treatments for MS which remains a point of some contention in this clinical area.

Political and administrative benefits

The uncertainty regarding IFN-β, in the absence of any authoritative national guidance, has inevitable led to variations from one part of the country to another when so many health authorities and their neurologists are taking such complex decisions[234].

A timely trial may have produced much needed cost-effectiveness information, as to date there has still been no economic evaluation run alongside a large randomised trial of IFN-β and the debate on cost-effectiveness has relied on modelling studies. For the trial to be of most use, it would have to improve the evidence-base for decision-makers; the key policy question concerns not simply whether there is a net advantage to the patients but the quality of life. The emphasis in the trial would have to have been on determining the length of the duration of benefits (and side-effects) that have been found by the short-term studies reported to date, i.e. what are the long-term effects of IFN-β on disease progression and disability in MS patients, and what implications do these effects have for the cost-effectiveness of the drug.

The answer to the question of what impact such a trial which began in the early 1990s would have had on the actual diffusion of IFN-β in the UK from 1995 onwards is partly dependent on the likely results of that hypothetical trial. The trial could have shown that IFN-β provides:

- No net overall clinical benefit and is not cost-effective,
- Net overall clinical benefit but is not cost-effective, or
- Net overall clinical benefit and is cost-effective.

The implications of the second of these, and this is the alternative which with hindsight (based on the results of subsequent clinical trials and modelling studies of cost-effectiveness) would have been the most likely, would have in turn been dependent on the response of policy makers to the trial results. There would have been two possible broad responses:

- that the DH and health care commissioners imposed stricter restraints on the prescribing of IFN-β: prescribing would therefore have been reduced in the light of cost-effectiveness information, or
- that the DH and health care commissioners imposed no or weak restrictions on the prescribing of IFN-β: IFN-β would have been prescribed to a higher proportion of those qualifying within the licence.

What is not clear is the extent to which, in reality, the relatively low levels of prescribing in the UK has been due to the policy directive from the NHS Executive[251]. The restrictive licence terms, uncertainty amongst some UK neurologists as to the benefits of treatment with IFN-β[a], and the fact that neurologists see a relatively low proportion of patients may all have been important contributory factors in restraining prescribing in the UK. It could also be argued that the dissemination of secondary reviews of the evidence of the likely effectiveness, and modelling studies of the cost-effectiveness, of IFN-β has been sufficient to obviate the need for a much more expensive and time-consuming RCT.

The fact that to date the results of timely HTA primary research may not have actually had a huge impact on the diffusion of this technology, is not to dismiss the political and administrative benefits of timely HTA primary research on IFN-β completely. In the

[a] whilst the clinical trials throughout the 1980's and early 1990's have each added to the evidence that there does appear to be a statistically significant difference between standard treatment and IFN-β in terms of delayed progression and lower relapse rates, the clinical importance of these differences is uncertain, as is the effect of the observed differences on the quality of life of a MS patient compared to

future, the evidence suggests that all of the pressures for prescribing IFN-β will be for an upward trend. The size of this increase may ultimately depend upon the continuing determination of central and local policy makers to constrain the availability of IFN-β, unless firm evidence of an acceptable cost-effectiveness ratio is found. Thus the likelihood that the legal, political and policy context will encourage continued restraints on the use of pharmaceutical products on the basis of their cost-effectiveness may become of paramount importance in trying to determine the usefulness of having conducted a timely trial. A trial would provide a firmer evidence base for a policy on future use; the results of a trial could help to support and justify such a policy to maintain prescribing at least at current levels.

Health sector benefits

Of the 80,000 MS patients in the UK, approximately 28,400 suffer from the relapsing-remitting form of the disease which was the initial broad indication for which IFN-β was licensed in the UK. At a cost of approximately £9,000 per patient per annum this represents a potential total cost to the NHS of £255 million; Walley and Barton suggest that if the drug were used strictly in accordance with the selection criteria in the reported phase III trials then the drug costs would be around £120 million[65]. If levels of prescribing were to reach those in the US and most European countries, expenditure on IFN-β would rise by £116 million in the UK. The current EWS in the UK costs approximately £250,000 per annum and the recently proposed HTA trial of IFN-β was costed at £20 million. Theoretically, therefore, early warning and timely HTA research, combined with a willingness of policy-makers to explicitly ration prescribing of IFN-β, could have had a potentially huge payback to the NHS. A further consideration is that if the trial had given a clear message that cost-effectiveness is a key consideration then it might have discouraged the pharmaceutical industry from putting investment into other products and indicators that they perceive as unlikely to look attractive in cost-effectiveness terms.

However, the likely size of the payback of timely HTA research may be significantly less than may appear at first sight as there are other factors, other than the potential application of evidence-based research to practice, which have limited the widespread diffusion of IFN-β. It is clear, from the relatively low proportion of MS patients in the UK who are currently receiving the drug, that some of the more dire predictions of the

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the effect of other, non-clinical interventions

expenditure implications of IFN-β for the NHS have not been realised[255]. This point is discussed further in section 9.3.

Broader economic benefits

There are no obvious broader economic benefits that might have followed on from an early evaluation of IFN-β in the UK.

Lessons for an EWS

As the development of IFN as a treatment for MS required at least fifteen controlled studies over a thirteen-year period, reports were being published in specialist medical journals during that time. Parallel to these reports were presentations at conferences, particularly in the US. In addition, as it became clear that IFN would be licensed in the US there were high profile reports in principal medical journals. Scientific journals also reported on the development of IFN-β. The initial advertising of the drug by the pharmaceutical company to doctors and commissioners of health care would also have provided early warning, as would FDA clearance in the US. In addition, there was a high profile role for patient interest groups in highlighting the importance and arrival of IFN-β, and they too, as can also be seen with dornase alfa for cystic fibrosis (CF) (section 8.7), can provide early warning. It is difficult to assess retrospectively how much, and when, information may have been available from pharmaceutical and biotechnology companies.

This case study illustrates how a new health care technology which is likely to have major policy implications could have been predicted significantly early by an EWS. In particular early warning could have helped to '. . persuade the manufacturer or the NHS R & D to look into further whether one can predict which patients are going to respond and which patients are not going to respond'[256].

8.7 DORNASE ALFA FOR CYSTIC FIBROSIS

Description of technology

Dornase alfa is a new treatment for CF which has been shown to improve lung function and reduce infective exacerbations in patients with CF.

Early development

The idea of using dornase alfa to treat the thick mucous secretions associated with CF was first conceived in 1988 by Genentech. The further rapid development of dornase alfa is shown in table 25:

Table 25 Rapid development of dornase alfa for cystic fibrosis, 1990-1994

Date	Progress
May 1990	IND submitted
Feb 1991	Phase I completed
Nov 1991	Phase II completed
Dec 1991	Phase III began. In less than a year, more than 900 patients with CF, from over 50 institutions, completed a 6 month phase III clinical trial satisfactory to the FDA; a landmark in clinical research on CF (Davis 1994)
Nov 1992	Phase III unblinded
January 1993	Phase III results reported at 36th Annual Conference on Chest Disease, Intermountain Thoracic Society and 1993 cystic fibrosis conference
March 1993	Product licence application (PLA) submitted (Wordell 1993)
August 1993	FDA Advisory Committee
January 1994	Licensed in the UK

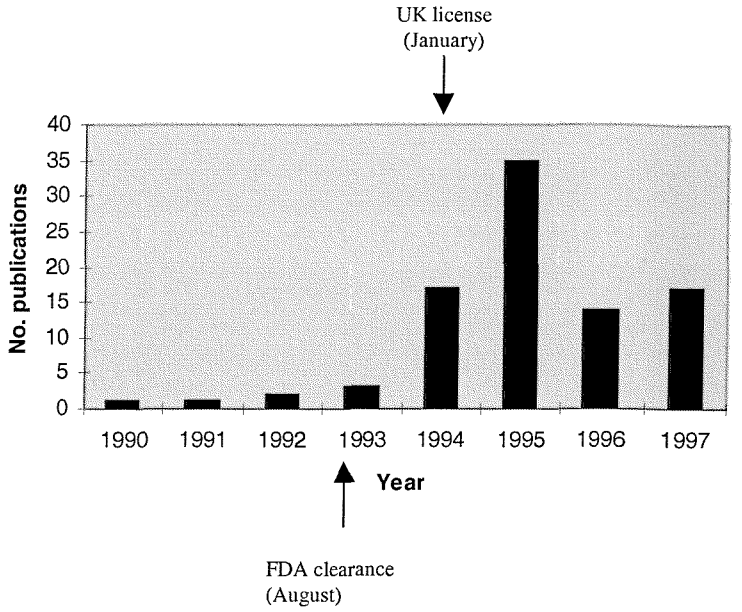
Adoption

There is considerable pressure to prescribe dornase alfa despite the demonstrably marginal benefits and its high cost. Other commentators have suggested that dornase alfa should not be added to the formulary as evidence supporting the use of the drug has not yet been published[257]. The Cystic Fibrosis Trust has been examining how best to establish guidelines for the use of dornase alfa. The manufacturers of dornase alfa, Genentech, estimated in 1996 that just under 20% of all CF patients in the UK, (1,200), were receiving the drug[258].

Potential information sources for early identification

As with IFN-β the number of papers on dornase alfa grew slowly and stayed relatively stable each year (reporting continuing trials[259,260,261,262]) until just before the launch of the drug in the UK in January 1994, when there was a sharp increase in the number of papers published. An editorial on the 'evolution of therapy for cystic fibrosis' which reviewed the implications of Fuch's study appeared in the same edition of the journal which carried the phase II trial. Again many of the papers published in 1994 were editorials or reviews (many in pharmaceutical journals) on the potential role of the drug following the publication of the phase III trial results in 1994:

Figure 23 Increase in MedLine references to dornase alfa just prior to launch in 1994



In addition to the peer-reviewed literature, before licensing in the UK in January 1994, dornase alfa was discussed at various conferences. The phase I study was presented at the American Thoracic Society's meeting, Anaheim, California, in May 1991 and phase III results were presented at the 36th Annual Conference on Chest Disease, Intermountain Thoracic Society, in January 1993 and at the 1993 Cystic Fibrosis Conference.

Pharmaceutical journals reported on the progress of dornase alfa through the regulatory system. In May 1993 'Bio/technology' reported that Genentech's new drug had moved from initial cloning to product licence application (PLA) filing in less than five years and in June 1993 'Drug Therapy' reported that Genentech Pharmaceuticals had filed a PLA for dornase alfa on March 30, 1993[263]. A PLA report was also made in December 1993 by 'Hospital Pharmacy'[264]. In November 1993 a consortium of four regional drug information centres produced a monograph on dornase alfa, a new drug in clinical development[265]. The monograph was intended as 'advance evaluated information for NHS managers and budget holders'. 'Scrip' reported that dornase alfa had been refused reimbursement in Australia. The FDA in the US, the Committee for Proprietary Medicinal Products in the European Union and the Medicines Control Agency in the UK all recommended the drug for licensing[266].

As with IFN-β there was an active patient interest group which publicly raised the issue of dornase alfa: the Parliamentary Health Committee was alerted to the impending problem of cost for dornase alfa by the CF Trust in September 1993 ('Dornase alfa - a

statement from the CF Trust'). Roche Products Ltd. circulated a standard letter alerting clinicians to the 'imminent introduction of a new treatment for cystic fibrosis which will have significant budgetary implications' in December 1993 (Tierney E. Letter. Roche Products Ltd., 14 December 1993). In February 1994 the Cystic Fibrosis Trust in the UK issued a statement on the use of dornase alfa. In June 1994 the Family and Adult Support Services of the CF Trust issued a further statement regarding the prescribing of Pulmozyme[a].

Payback from early warning

In the case of dornase alfa there probably would theoretically have been early warning (from conference reports) up to four years before licensing of the drug in the UK, which is considerably less than IFN-β. This is mainly due to the very rapid development of dornase alfa. However, as with IFN-β an economic evaluation would only realistically have begun after (or preferably alongside) the phase III trial which was reported in 1994. This means that there would have been less opportunity for the results to inform and influence the initial adoption of dornase alfa then for many of the other case-studies examined in this chapter. Modelling studies using the results of the phase II trial could have begun earlier than this.

Knowledge

Existing evidence for the use of dornase alfa is primarily in the form of one large, good quality six-month RCT which examined its efficacy in CF patients. This RCT suggests that the use of dornase alfa reduces the risk of respiratory exacerbations, and improves lung function as measured by FEV_1 and FVC[262]. At present there is no evidence from any RCTs to indicate whether or not the improvement in lung function is sustained in the longer term, or whether the use of dornase alfa is associated with a reduction in mortality. The only long-term evidence that is presently available does suggest that dornase alfa treatment improves lung function, but this evidence is from two open extensions and not from RCTs.

Benefits to future research and research use

At the present time further research is still needed to[267,268]:

- identify which patients would benefit the most from this expensive treatment,

[a] 'The prescribing of Pulmozyme', Cystic Fibrosis Trust, June 1994

- look at the long-term cost effectiveness of dornase alfa (and see whether long-term benefits can be predicted from short-term results), and
- rule out the possibility of longer term adverse effects, an issue that is particularly important with a substance such as dornase alfa that has the potential to be used therapeutically on a life-long basis.

Political and administrative benefits

Since it was licensed in 1994, the use of dornase alfa has become a focus of attention in the management of CF due to controversy surrounding its effectiveness and economic issues[269]. There does appear to be some evidence that early reviews did affect the early prescribing of dornase alfa. A number of reviews have evaluated the use of dornase alfa for CF patients. These included a CCOHTA overview[270], a Northern and Yorkshire Regional Drug and Therapeutics Centre report[271], and a Trent Institute for Health Services Research guidance note for purchasers[272]. A recent Cochrane systematic review (published in October 1998) has also evaluated the use of dornase alfa[273]. Better, earlier, empirical research may have helped further and provided an improved information base which policy- and decision-makers could have taken into consideration when considering their responses to the introduction of this drug. .

In 1994 dornase alfa was considered by the South & West Development and Evaluation Committee (DEC) on the basis of a report written by myself[274], who returned a decision that the proposal was "not proven"[a]. This was one of the first attempts to calculate the cost-utility of this drug and the results were published as a letter to the *British Medical Journal* in September 1995[275]. Since the 1994 report was written the results of the main phase III (RCT) have been published in full[262], as have two longer term open label extensions to another RCT[276,277]. Although the published evidence appears to support the use of dornase alfa for all patients, expert opinion has suggested that limiting dornase alfa treatment to certain groups of patients, may be a more reasonable approach, given the high cost of the drug and the varied response to treatment. Such guidelines[278,271,272] are based on consensus rather than published evidence. Although there are slight variations in detail, all the guidelines published to date suggest that a trial of therapy and objective evidence of benefit is needed to justify continuing treatment with dornase alfa.

[a] the proposal in question was that CF patients within the Wessex region receive a daily dose of 2.5mg of Dornase alfa, and for those patients over 21 years of age, Dornase alfa should be available on a twice daily basis

Guidelines such as these are important because research has shown that there is a wide variability of responses to dornase alfa in individual patients, and that it is difficult to identify any predictors of individual responses[27]. In addition, there appears to be natural biological variability within CF patients in terms of their lung function test results, particularly over the short term. Expert opinion suggests that there are identifiable subgroups of patients showing improvement, little or no change, and deterioration after treatment with dornase alfa.

Health sector benefits

The 1995 UK mid-year CF population has been calculated as 6,657 but births outnumber deaths by 160 per year, which suggests a CF population of 7,750 by the year 2000, with all the increase being in the adult age range. At once daily dosage dornase alfa costs approximately £7,440 per patient per year. This represents a total potential cost of approximately £57.5 million. However, only approximately 20% of CF patients throughout the UK are receiving treatment with dornase alfa[279,280]. As with IFN-β therefore, it is clear from the relatively low proportion of CF patients in the UK who are currently receiving the drug, that some of the more dire predictions of the expenditure implications for the NHS have not been realised.

In comparison to the national average, data collected during 1995 from the South & West CF database indicated that only 12% of the 664 patients being cared for within the South & West region were identified as receiving dornase alfa. Whilst dornase alfa use within the former South & West region does not appear to have increased in recent years, in part as a consequence of the 1994 DEC decision[a], there are variations between different health authorities within the region. According to county of residence there were 24 patients receiving dornase alfa therapy in Avon, 13 in Cornwall, 8 in Dorset, 6 in Hampshire and only 3 in Gloucester. As with IFN-β it appears that rather than aiming to counter inflated predictions of the potential cost to the NHS of new technologies, the main benefit of early warning and timely research may often be to help with ensuring equity in terms of access to new treatments.

The NHS R&D HTA programme has commissioned a trial, entitled "A cross-over, comparative study of hypertonic saline, daily and alternate day dornase alfa in cystic fibrosis". This project began in September 1998, costs £126,458 and will last for 24

[a] personal communication with CF experts within the South & West region, 1998/99, as cited in Christopher F, Chase D, Milne R. *Dornase alfa for cystic fibrosis patients with mild to moderate lung disease.* Southampton: Wessex Institute for Health Research and Development; Development and Evaluation

months. The project objectives are to compare the efficacy and acceptability of daily and alternate day dornase alfa with hypertonic saline in 50 children aged 5-17 years with CF, with reference to lung function, subjective and objective clinical criteria and cost effectiveness. As with a number of the other case-studies in this chapter therefore the costs of operating an EWS and undertaking HTA research is minimal when compared to the potential cost and/or benefit implications of the technology under consideration.

Broader economic benefits

There are no obvious broader economic benefits that might have followed on from an early evaluation of dornase alfa in the UK.

Lessons for an EWS

Early warning provided by pharmaceutical and biotechnology companies was evident from the Roche letter that was widely distributed in December 1993. Principal medical journals would have been a key source and provided early warning; key articles were in the *New England Journal of Medicine* and the *Journal of the American Medical Association* in 1992, two years before the licensing of dornase alfa in the UK. In 1993 *The Lancet* also carried a paper describing dornase alfa, and key pharmaceutical journals reported on the rapid progress of dornase alfa trials and the process of the drug through the various licensing procedures in different countries.

This case study illustrates how an EWS can potentially identify rapidly developed and marketed drugs at an early stage (in this case, from a conference report four years before licensing). However, reliance on peer reviewed publication and FDA licensing would have resulted, at most, in only one years early warning for the NHS. The high priority accorded to the drug by patient interest groups and the close monitoring of its progress through pharmaceutical and principal medical journals should have indicated that dornase alfa was likely to have important implications for health services and patients. The postal survey undertaken by Stevens et al in 1995 (and published in 1997) identified dornase alfa as one of the most important new health care technologies that would have 'moderate' implications for the NHS during 1996-7.

8.8 DONEPEZIL FOR ALZHEIMER'S DISEASE

Description of technology

Donepezil (Aricept) is a new drug treatment for use in mild to moderate dementia due to Senile Dementia of the Alzheimer Type (SDAT), which was licensed in the UK in March 1997.

Early development

Animal studies with donepezil began in the early 1980s. In 1990 pre-clinical studies showed donepezil to have a high degree of selectivity for acetylcholinesterase in the central nervous system and to be lacking in peripheral activity. There have been three randomised controlled trials of donepezil, of which only one has been published in full US multicentred, randomised, double-blind placebo-controlled trial[281]. This was a 12 week study of 161 patients with mild to moderately severe Alzheimer's disease showed that 5mg donepezil daily improved cognitive function. However, the drug failed to influence day to day functioning, quality of life measures and rating scores of overall dementia. A European multicentre study has been completed but data are not yet available. One phase III trial has been published in abstract form.

Adoption

Until 1997 only one other drug was available for the treatment of dementia (Tacrine) whose licensing in the UK was delayed and is not being actively marketed. In October 1997 the *Drugs & Therapeutics Bulletin* failed to recommend the use of donepezil for the symptomatic treatment of mild to moderately severe Alzheimer's disease[282]. Marketing of donepezil is currently focused on specialist services, although it can be prescribed in primary care. Following on from tacrine and donepezil there are a large number of other drugs for Alzheimer's in development:

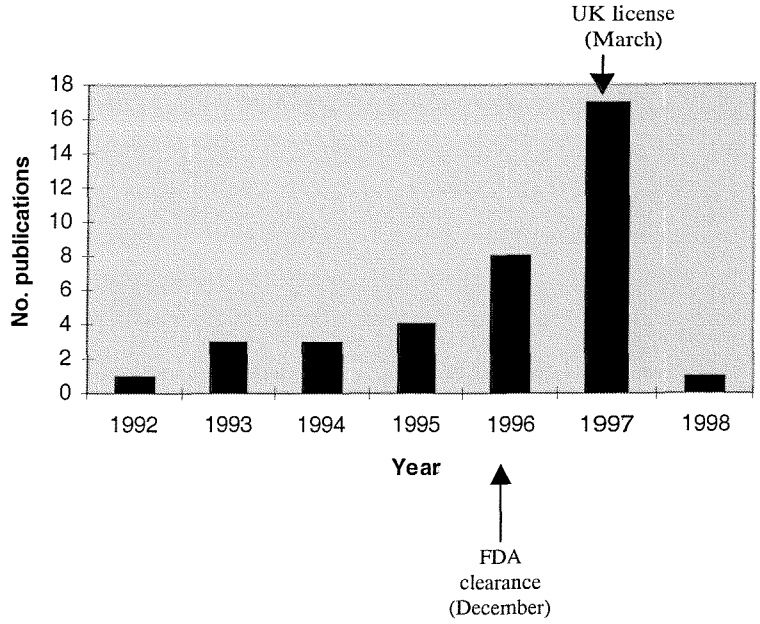
Table 26 *Large number of other acetylcholinesterase inhibitors for SDAT in development at time of donepezil's introduction*

Drug	Development status in 1997
Eptastigimine	Phase III
Galanthamine	Phase III in the UK; launched in Austria
Idebenone	Application for release filed in Germany
Metrifonate	Phase III
NXX 066 (Quilostigimine)	Possibly available 1999
Physostigimine	Phase III in the UK
SDZ-ENA-713 (Exelon)	Phase III
Zifrosilone	Possibly available 1999

Potential information sources for early identification

Prior to the licensing of donepezil in the UK in March 1997 there were 17 papers in pharmaceutical journals from 1990 onwards (and 12 in the year of approval) and six papers in specialist medical journals prior to 1997 (from 1980 onwards):

Figure 24 *Seventeen MedLine references to donepezil in pharmaceutical journals during period 1990-1997*



FDA clearance for donepezil was granted in December 1996. Melzer cites reports in the lay press that heralded the arrival of donepezil in the month before, and the month of, it's licensing in the UK[283]. In March 1996, also in the lay press, the Alzheimer's Disease Society was cited as 'introducing a note of caution' regarding donepezil.

Payback from early warning

There were numerous opportunities to identify donepezil in the early stages of its development suggesting that up to five years early warning might have been realised. However, it is likely that only one year's early warning would have been available following publication of the phase III trial results.

Knowledge

Much of the discussion relating to the introduction of donepezil has been around the real clinical significance of the statistically significant results reported in the trials, all of which have been funded by the manufacturer[284]. Trial evidence of the longer term effects of donepezil are not available and trials of longer duration, carried out on patients more representative of the general population of the elderly are required[285]. Outcomes used in studies to date have not included measures of dependency and effects on carers.

Benefits to future research and research use

One of the difficulties in establishing the effectiveness of donepezil in routine clinical practice has been the lack of valid measures of the quality of life of dementia patients. Early warning in the early-mid 1980s of the host of drugs in development for dementia could have provided the impetus for the development of such measures. This may have enabled a more rational introduction of these drugs into clinical practice in the mid-1990s, possibly as part of clinical trials incorporating the refined measure[286].

Political and administrative benefits

The debate about the cost-effective-effectiveness of donepezil continued after licensing[282]. Early warning in combination with HTA research could have enabled more timely preparation of prescribing guidelines. However, simply developing guidelines is insufficient. An independent review of guidelines available in the UK since the introduction of donepezil in 1997 found that none of 15 different sets of guidelines (developed nationally, regionally, locally and by independent groups) fulfilled criteria for high-quality evidence-based guidelines and substantial variability was evident in all areas of recommendation[287]. Such lack of consistency would inevitably lead to inequalities in the health care delivered in different geographical areas.

Such findings provide further evidence for the need for a national body to encourage true evidence-based guidelines not only on drug treatment but also on wider issues such as diagnosis, investigations and the best treatment setting for delivering drug and other

therapies[287]. This requirement is discussed further in chapter 9 in relation to the work of NICE in the UK.

Health sector benefits

At the higher dose preparation the cost per patient per year of donepezil is approximately £1,200 (1997 prices). As there are approximately 240,000 potential recipients living in the UK, this represents a potential cost to the NHS of £288 million per year.

In addition to some short-term observational studies which have included collecting medical cost data[288], economic evaluations using modelling approaches have been undertaken outside the UK and suggest that, in the long-term, the costs of donepezil may be offset by reductions in the cost of care due to enhancement in cognitive functioning and the delay to more costly disease stages and settings[289, 290]. However, such findings are largely dependent on assumptions regarding the long-term efficacy of the drug and longer-term empirical data is required to confirm these findings and those of other early evaluations[291292]. A recent Cochrane Systematic Review concluded that, whilst modest improvements in cognitive function were produced and clinicians rated global states more positively in donepezil-treated patients, there were no improvements on patient self-assessed quality of life[285]. The review states that data on many important outcomes are not available and that the practical importance of reported changes to patients and their carers remains unclear.

Broader economic benefits

There are no obvious broader economic benefits that might have followed on from an early evaluation of donepezil in the UK.

Lessons for an EWS

There were numerous opportunities to identify donepezil: animal studies can be traced back to 1980 and the early 1990s saw the publication of a number of studies in specialist medical journals. However, at the time of the drug's introduction there had been three RCTs, of which only one had been published in full. Most references in pharmaceutical journals only occurred after FDA approval in the US.

As with dornase alfa and IFN-β there were plenty of opportunities to track donepezil through clinical trials. However, given the wide range of related acetylcholinesterase inhibitors for SDAT it was probably not until the publication of the phase III trial results

in 1996 in a specialist medical journal, that the importance of donepezil could have been identified. The postal survey undertaken by Stevens et al in 1995 (and published in 1997) identified 'drugs for Alzheimer's' as one of the most important new health care technologies which would have 'major' implications for the NHS during 1996-7.

This case study highlights the difficulty of choosing which of a host of new drugs being developed at approximately the same time for the same indication is likely to be the most important. For example, it is possible that an EWS might be distracted by one of a new class of drugs falling by the wayside. However, it is important to know that a number of drug companies are interested in developing similar products and this enables the class of drugs to be spotted and trials methodology to be developed.

8.9 LAPAROSCOPIC CHOLECYSTECTOMY

Description of technology

Cholecystectomy is the most common treatment for gallstones. The laparoscope provides twenty times magnification and the dissection technique used in laparoscopic cholecystectomy is similar to that in open surgery except that it is carried out using long handled instruments and visualized on a television screen.

Early development

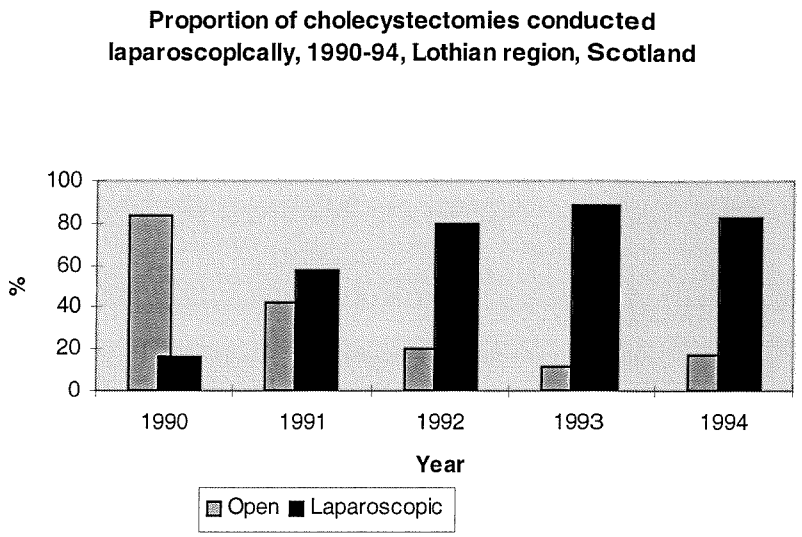
Laparoscopes were available in the 1960s but the imaging systems and instrumentation were not of a sufficient quality to allow for their use in therapeutic investigations[293]. Later refinement of high resolution video cameras and the development of appropriate instruments led to their adoption for medical applications. In Lyons, France, in March 1987, the first human laparoscopic cholecystectomy using a gynaecological instrument was performed[294]. Concurrently, three centres (in France and the US) began further development of the technique so that by 1988 it was already being performed in the US and other countries.

Adoption

Cuschieri and colleagues performed the first operation in the UK in 1989 in Dundee. The key feature of laparoscopic cholecystectomy was its rapid introduction and diffusion into the NHS: it became the standard treatment for symptomatic gall stones within seven years of the procedure first being performed[295]. Grundfest[296] suggests three reasons for the basis of the growth in laparoscopic procedures: the first and overwhelming reason is patient demand; second, the cost is low (at least for the patient);

and third, clinicians realise that less invasive surgery is good medicine. In Scotland the number of laparoscopic cholecystectomies performed in 1990 rose from 107 to 3,418 by 1995[a]. Data from the Lothian Surgical Audit illustrates the rapid introduction of laparoscopic cholecystectomy between 1990 and 1994[297]:

Figure 25 Rapid increase in proportion of cholecystectomies conducted laparoscopically, 1990-94, Lothian region, Scotland



[Source: Parliamentary Office of Science and Technology, 1995. Data supplied by Lothian Surgical Audit]

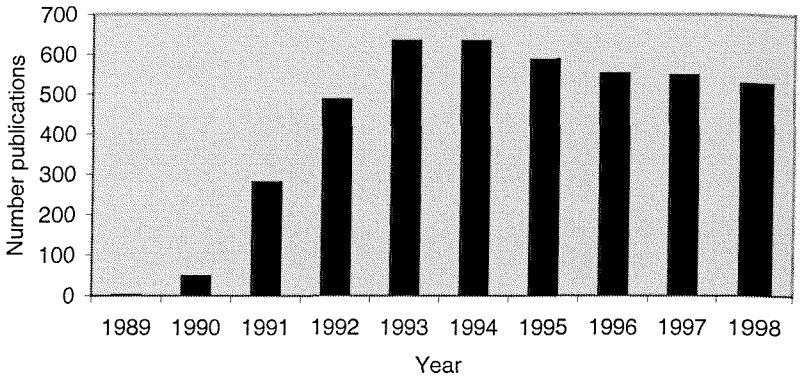
Less than three years after its introduction to the UK the majority of gall bladder operations was being undertaken using the laparoscopic procedure by surgeons who have had little or no experience in the technique[298].

Potential information sources for early identification

Mowatt[133] reports that a single reference on laparoscopic cholecystectomy appeared in 1989 after which annual numbers increased steadily, peaking at over 600 references over the period 1993/94 (figure 26). The beginning of a decline in publication numbers began in 1995. Thus over a relatively short period, a significant amount of publishing activity was generated (one paper in 1989, increasing to 47 papers in 1990). In addition, media reports of the apparent (short-term) benefits of laparoscopic cholecystectomy led to patients becoming aware of the procedure. This coverage in the popular media began around the same time as reports began to appear in the clinical literature.

[a] source: Information & Statistics Division, NHS in Scotland

Figure 26 MedLine references to laparoscopic cholecystectomy, 1989-98



However, the initial opportunities to identify laparoscopic cholecystectomy as an important development were when innovators presented videotapes of the first procedure at surgical society meetings in 1989 (not during scientific sessions, but in the technical exhibition hall). Afterward the procedure underwent rapid diffusion, particularly in the US. Mowatt et al cite seven conferences that took place in 1990[133].

The earliest trials began in 1990 and the largest study of laparoscopic cholecystectomy was a report of the experience of twenty surgical groups in the Southern US in 1991. The European experience from seven centres in France, Germany and the UK was also reported in 1991.

Payback from early warning

Unlike IFN-β and dornase alfa, laparoscopic cholecystectomy has diffused very widely and very quickly with the likelihood of much less, perhaps only one years, warning of its imminence. Such a short period of time would clearly have limited the extent of any payback from the operation of an EWS.

Knowledge

In 1989, before widespread diffusion, Cuschieri stated that prospective RCTs were needed to define indications for the laparoscopic approach and to confirm the benefits of this procedure against the standard cholecystectomy[299]. However, Russell[295] suggests that during the period 1987-1994 no more than ten trials comparing laparoscopic with conventional forms of cholecystectomy were published worldwide. Of three peer-reviewed RCTs comparing laparoscopic and minilaparotomy cholecystectomy published in Britain since 1992, only one randomised more than 100 patients, justified this with a calculation of sample size and analysed the results by intention to treat. Sculpher argued that one key characteristic of laparoscopic cholecystectomy was the

extent to which it had diffused widely as a result of perceived short-term benefits[354] with little consideration of long-term outcomes. A 1992 survey of surgeons and research ethics committees on the necessity and ethics of an RCT to compare laparoscopic with open cholecystectomy[300] showed wide support for a trial comparing the techniques. Respondents with more experience in laparoscopic cholecystectomy were less convinced of the need for a trial.

As Diehl indicates the rapid adoption of laparoscopic cholecystectomy in the US by surgeons in community practices was '. . . stimulated by demand from patients aware of the procedure's apparent virtues in comparison with conventional surgery, preceded any formal evaluation of its benefits and risks by academic centres'[301]. To date, there has been no large-scale RCT of laparoscopic versus open cholecystectomy, and few of the smaller RCTs included any economic analysis[133]. The short amount of early warning, the need for rapid generation of results to influence clinical practice before widespread diffusion occurred and for long-term follow-up, and the potential difficulties in recruiting patients, might mean that observational studies would have been needed to supplement RCTs[354].

Benefits to future research and research use

Laparoscopic cholecystectomy is one of a large number of applications of minimal access surgery. The biggest impact to date has been in gynaecology, urology and thoracic, orthopaedic and general surgery. However, minimal access surgery is finding wider application within areas such as paediatric, cardiovascular and neurosurgery. Generally the benefits and disbenefits of minimal access surgery are similar across all these specialties. Good quality evidence from well designed trials in one specialty would have assisted in the evaluation of the application of minimal access surgery in other specialties.

Political and administrative decisions

At the time of the introduction of laparoscopic cholecystectomy there was no consensus to withhold new techniques until they were properly evaluated. Nor was there any mechanism, such as SERNIP, for centralised monitoring to control the diffusion of unevaluated procedures[69, 133].

Guidelines on minimally invasive surgery were not issued by the Royal College of Surgeons until June 1994 (and even then were only advisory)[302]. In 1996 Downs et al published a systematic review of laparoscopic cholecystectomy from those trials with at

least 50 patients in each group[303]. The work was commissioned by the DH in the UK. The main findings prompted the conclusion that surgeons should not be encouraged to replace mini-cholecystectomy with laparoscopic cholecystectomy. As Hatlie indicates, in the US context, "... a rapid response to the market's demand for new treatment modalities that involve less pain or a shorter recovery period may be wholly appropriate. If the pace of implementation is also pushed by surgeon's interests in keeping or expanding their marketability, the revenue interests of surgical centres or anaesthesiologists, or manufacturers' desire for new equipment sales, more troubling issues arise"[304]. Similar concerns could equally be held to apply to the introduction of laparoscopic cholecystectomy in the UK.

Health sector benefits

The capital costs incurred in setting up a theatre for laparoscopic cholecystectomy (video equipment, basic instruments etc.) would be around £30,000 and the operation itself costs approximately £1500 to £2000 compared to over £2000 for an open cholecystectomy. A DH sponsored review published in 1994 concluded that laparoscopic cholecystectomy may be slightly less expensive than conventional surgery when instruments can be re-used, and similar in cost when disposables are used[298]. However, minimal access surgery could increase the demand for surgery, either by lowering the threshold for surgical intervention, or by allowing operations on patients whose conditions precluded conventional surgery.

This case study highlights a particular potential benefit of an EWS that applies to the introduction of all new health care technologies and as has been noted in the earlier PICU case-study: the difficulty of disinvesting from widely adopted technologies. In the context of surgical procedures, and as certainly applies to laparoscopic cholecystectomy, McGinn and Terzic allude to the "resistance of the already converted enthusiasts to any suggestions that the new procedure may not be as good as the experts suggest"[305]. A combination of early warning, timely HTA and mechanisms for ensuring that research findings have an impact on clinical practice can help to overcome this problem by preventing ineffective, or non cost-effective, technologies from ever being widely adopted.

Broader economic benefits

There are some potential broader economic benefits that might have followed on from an earlier evaluation of laparoscopic cholecystectomy. One of the main claims as to the

benefits of laparoscopic cholecystectomy was that accelerated recovery time should reduce demand for sickness and other social security payments, and increase the 'productivity' of patients who are able to return to work more quickly. The 1994 DH review concluded that while the impact of minimal access surgery on NHS costs was likely to be limited there were '. . . substantial gains for the Exchequer in reduced sickness and other benefits'[298]. An early evaluation could have confirmed whether these wider benefits would actually have been realised.

Lessons for an EWS

In the case of laparoscopic cholecystectomy at least, liaison with experts and monitoring of conferences would seem to have been the only sources of early warning.

In the case of laparoscopic cholecystectomy advance warning of this new procedure could only have been received one to two years prior to it being first performed in the UK and three-four years before it was in common usage. Because of this speed of diffusion there were very few opportunities to identify laparoscopic cholecystectomy sufficiently early. The rapid introduction of laparoscopic cholecystectomy occurred because of a few product champions who were sited in general hospitals, not only in teaching or academic centres. This is because most of the techniques did not require particularly expensive capital outlay, and in surgery, innovation occurs equally in non-teaching and teaching centres

9 SYNTHESIS OF RESULTS

Chapter Summary

A combination of sources will be required in order to ensure that all types of technologies and all important technologies are identified. Using more than one source will provide corroboration, increase the likely accuracy of any predictions and increase the amount of useful information regarding a new technology.

Existing EWS seek to identify all types of health care technologies likely to emerge within five years. They generally have a staff of no more than five WTE and use a variety of mechanisms for accessing expert opinion (although there is as yet no empirical evidence to suggest the 'best' way of doing so). On average, information on ten to twelve technologies is disseminated each year by existing EWS via a wide range of mechanisms and products. Close collaboration with HTA programmes, as well as with other national and international early warning initiatives, is recommended.

An EWS can potentially assist in the development of timely guidelines for health care professionals, enable early monitoring of new technologies through registers, enable 'watchful waiting' where appropriate, allow longer term effectiveness information on new technologies to be available sooner, lengthen methodological lead times, and help to ensure that research with realisable and worthwhile payback is commissioned. There are however a number of factors which may limit the success of an EWS. In particular, there is a need to design and implement new routes to incorporate the results of research in guidelines or policy mechanisms, and, by doing so, improve the relationship between knowledge, evidence and policy or decision-making.

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INTRODUCTION

This chapter draws together the results of the four methods as described in chapters 5-8 as they relate to the choice of information sources to be used by an EWS (section 9.1), the establishment and operation of an EWS (section 9.2), the likely value of an EWS to the NHS (section 9.3) and, finally, on ways in which the value of an EWS might be increased (section 9.4).

9.1 INFORMATION SOURCES

There were some discrepancies between the information sources which were recommended for identifying new health care technologies by previous initiatives (type II papers from the literature review), the telephone enquiry of existing national EWS, the Delphi study and the retrospective case studies (see table 27):

Table 27 Recommended information sources from each method: summary table

Source	Literature review	Telephone enquiry	Delphi study	Case studies
Primary				
Patents	x		x	
FDA licensing	✓		✓	✓✓
Pharmaceutical & Biotechnology companies	x		✓✓	✓
Medical engineering companies	x		✓✓	
Secondary				
Pharmaceutical journals	✓	✓	✓✓	✓✓
Medical journals	✓	✓✓	✓✓	✓✓
Scientific journals	✓	✓✓	x	
Specialist medical journals	✓		✓✓	✓
Conferences	✓	✓✓	✓	✓
Experts	✓✓	✓✓	✓✓	✓✓
Patient interest groups	x		x	✓
Private health care providers	x		✓✓	
Drug Information Services	x	✓	x	✓
Internet	x	✓	x	
Media	✓	✓	x	✓
Tertiary				
Other countries' EWS activities	✓	✓	✓✓	

Key:

Literature review
- ✓✓ = used by all previous studies
- ✓ = used by at least one previous study
- x = not used

Telephone enquiry
- ✓✓ = used by at least 4 of EWS
- ✓= used by some (1-3) of EWS

Delphi study
- ✓✓ = consensus that this source is a minimum requirement for an EWS
- ✓ = no consensus but from comments received may be useful
- x = not recommended

Case studies
- ✓✓ = in my opinion this was the best source for at least one of the case studies
- ✓ = in my opinion this source may have been helpful for at least one of the case studies

Blank cells indicate no evidence available as method was not used to assess specific source

The following reviews of the various potential information sources are presented in the order in which they appear in table 27.

Primary sources

Patents

Both the literature review and the Delphi study indicated that this source was not of particular use to an EWS. In the case of CT scanners, patents might have appeared to be a very important source but the very small proportion of products for which patents are issued that reach the health care market actually makes this source inefficient[81]; in the first month of 1987 alone the US patent office issued 6,418 patents, of which 423 were classified as medical patents[306]. As well as the inherent uncertainty and poor specificity of using this source to try and identify the small proportion of patented technologies that may eventually be important, Delphi respondents emphasised how patents would only provide part of a long term view and would be a very labour intensive source to search.

FDA licensing

Licensing applications and approvals in the US are significant because pharmaceutical companies often seek to introduce new products there first. In the mid 1980s, the STG highlighted the potential role for examining 'investigational new drug' and 'investigational device exemption' documents released by the FDA. The results of the Delphi study did not recommend FDA licensing as an information source for an EWS. Rather, respondents selected, with some reservations (see below), liaison with pharmaceutical & biotechnology companies as the best source for identifying new drugs. One Delphi participant commented that 'spotting when North American licensing applications' are submitted would generate a very high hit-rate but give limited early warning. In contrast, from the case studies (biosensors, LVADs, IFN-β, dornase alfa and donepezil) it was apparent that monitoring the regulatory control of drugs and devices in the US via the FDA would commonly provide one to two years early warning. However, not all drugs are necessarily licensed in the US before they are approved in the European Union (for example, Exelon for Alzheimer's disease), although the applications are often submitted earlier. The FDA web-site (http://www.fda.gov) provides an easy and cost-effective way to monitor licensing applications in the US. In 1996 the FDA approved more new products (51 molecular entities and 8 new biologic agents) than in any year of its history.

Pharmaceutical, biotechnology and medical engineering companies

Neither the results of the literature review nor the telephone enquiry mentioned these sources. Banta noted that, in general, manufacturers have not been co-operative in releasing information on CT scanners that they have sold[152]. Similarly, comments received in the Delphi study, whilst recognising the potential benefits of liaising with relevant companies, noted a number of potential barriers to the close involvement of private companies in an EWS, such as:

- potential problems with the extent of disclosure of information due to commercial sensitivity,
- that companies may release news only just before actual marketing, and that
- information from private companies can be unreliable.

Despite these reservations the Delphi respondents chose this source as one of the minimum requirements for a comprehensive EWS. Some respondents highlighted press releases on early trials, strategy seminars and annual reports as being helpful ways of accessing information from companies. It is difficult to assess the potential role of pharmaceutical & biotechnology companies and medical engineering companies through the case studies. However, the retrospective evidence suggests that there has often been a strong profit-orientated technology push from manufacturers, although there has also been a degree of receptiveness on the part of health care providers. For example, British Telecommunications in the UK has developed the CARE project, initiating a series of telemedicine trials designed to gain an insight into the potential impact of telehealth services. In the cases of IFN-β and dornase alfa, pharmaceutical companies were clearly involved in promoting their products directly to clinicians prior to licensing in the UK and having these clinicians among an expert panel would have provided a few months early warning. Prospectively liaising with such companies would provide earlier warning, presuming that they are willing to co-operate in this way. In the late 1960s, liaison regarding the development of CT scanner between EMI Ltd. and the relevant government department of the time provided sufficient early warning to allow the controlled introduction of this expensive technology into the UK. Such an approach may be given greater emphasis given that NICE sees early warning as providing a '. .chance to do some provisional selections, have provisional discussions with the industry about their new technologies and to identify what is likely to be coming'[28].

Secondary sources

Pharmaceutical journals

Banta specifically cites *'Scrip'* as a publication that enables drugs in development to be tracked through from initial development to marketing[81]. Three of the six national EWS's interviewed in the telephone enquiry reported that they used pharmaceutical journals as a source of information for identifying new and emerging drugs, and this source was also recommended by the Delphi study. As noted, drugs are the easiest type of health care technology to monitor due to the formal requirements of the licensing process and the publication, and presentations at conferences, of the results of phase I-III trials. Approximately 20% of all drugs in phase I trials, and 66% of drugs which undergo phase III trials, currently reach the market[307], making the systematic scanning of journals which report on such trials a relatively specific source. Respondents to the Delphi study generally felt that pharmaceutical journals would provide good, regular updates of progress but no great detail on particular technologies. The three drug case studies all revealed that pharmaceutical journals (for example, *Hospital Pharmacy, Biotechnology, Drug Therapy, American Pharmacy*) would have provided early warning and reasonable specificity. In all of the three case studies a large number of reports appeared at key stages of the licensing process, such as at the time of submission of an application to the FDA or announcement of FDA approval, but such events occur relatively late in a drugs development.

Medical journals

Wilkie detailed the sources of information used by health reporters and medical journalists[308]. He cited several journals *(Nature, Science, New Scientist, The Lancet,* and the *British Medical Journal)* as being useful to scan and stated that other journals are also monitored (*Journal of the American Medical Association,* the *New England Journal of Medicine, Scientific American* and trade and technical magazines, such as *Nursing Times*). This source is used by all existing EWS and was recommended by the Delphi study, although a majority of participants commented that principal medical journals 'mainly evaluate already established technologies' and those near to 'imminent clinical use'. However, as evidenced by our case studies, journal articles in leading medical journals can provide early warning via:

- reports of primary research (for example, a report of a phase III clinical trial of dornase alfa); or

- discursive pieces on the future of a particular technology, such as those type III papers identified by our literature review (for example, *The Lancet* editorial on telemedicine, the *New England Journal of Medicine* editorial on dornase alfa, the *Journal of the American Medical Association* paper on LVADs or series such as the 'medical advances' papers in the *British Medical Journal*); or
- news sections which may alert the reader to developments in areas of highly prevalent or serious disease.

However, journals can be time-consuming to scan and the articles that appear in them are subject to editorial selection. The use of medical journals as a source of early warning might be expected to produce relatively few potential new technologies but detailed information on each. These limitations of journal articles mean that other supplementary sources of information need to be used.

Scientific journals

The majority of existing EWS scan scientific journals but respondents in the Delphi study did not select such journals as being of primary importance in identifying new health care technologies. The main drawback highlighted in the Delphi study was that such a source would not provide any evaluation of the likelihood of the successful development of a technology nor the timescale in which the technology might be introduced. As with patents, scientific journals would tend to give very early warning and would be labour intensive to search, as only a proportion of developments would be relevant to a health care system. '*Nature*' and '*Science*' were particular journals that were cited frequently by respondents, and by Wilkie (see above), as being of some potential use.

Specialist medical journals

Specialist medical journals were helpful in a number of the case studies (providing particularly early warning in the cases of LVADs, biosensors, IFN-β and donepezil) and recommended in the Delphi study. However, this specific type of journal was mentioned by neither the literature review nor the telephone enquiry. As with all journals, there are methodological difficulties in using this source, as publication bias and editorial filtering of submitted papers may result in a false impression of the likely speed and timing of diffusion of a new technology. In addition, earlier work in the field of cardiovascular and pulmonary medicine and surgery found that 41% of articles (appearing in all types of journals) reported work that, at the time it was done, had no

relation to the disease that it later helped to prevent, diagnose or alleviate[309]. Comments in the Delphi study suggested that it is in specialist medical journals that reports of initial case-series of the application of a new technology will appear. Rosen reports that her research has shown that case-series reports have a strong influence on clinicians at the earliest stages of diffusion[9]. However, even papers in specialist journals sometimes only appear following the adoption of a technology (for example, papers on excimer lasers appeared mostly well after the technology had diffused). As well as early case series reports, reviews of the state of knowledge about an emerging technology (for example, the 1985 editorial concerning IFN-β that appeared in the *Annals of Neurology*) can be helpful. As with many of the documentary sources, specialist medical journals will be labour intensive to search and an attempt to construct a sample of key journals via the Delphi survey elicited very few suggestions. These difficulties might be best overcome through iteration with experts in specific areas of health care.

Conferences

Four of the national initiatives (the Netherlands, Canada, France and Sweden) specified conferences as one of the sources which they were using to inform their respective EWS. Conferences are potentially very useful but a major problem identified by respondents to the Delphi survey was how to take account of the potentially high false-positive rate and analyse such a huge amount of information. Only a third of studies reported at conferences are eventually published, so the information presented may bear little relation to the potential of the technology[a]. Consequently, conference and meeting abstracts were not recommended as a source of information on new technologies by the Delphi study. This seemed due to concerns about low specificity and the large effort that would be required to scan such a source. However, many respondents to the Delphi study did recognise the potential value of a source that would often provide much earlier warning than that from other documentary sources, as well as providing a means of tapping into research networks in specialised fields. Conferences can be seen as a proxy indicator for the value of liaison with experts and a means of 'tapping' into the informal networks of opinion leaders (a key factor in determining the diffusion of technologies as evidenced by Stocking's analysis of 22 innovations[71]). A number of Delphi respondents commented on the importance of conferences in the development of networks and early dissemination of informal information on new technologies. In four of the case studies (CT scanning, telemedicine, dornase alfa and laparoscopic

[a] Source: personal communication, Andrew Booth, University of Sheffield (Delphi participant)

cholecystectomy) conferences would have been a useful source; 'conventions' were cited as the most important source of information about CT scanners for early adopters in the US[156].

Conferences are focused either on specific topics or disease areas or technological issues and thereby can enable a close watch to be maintained on specific areas of health care that may be particularly important to an EWS. Trends in citations at conferences may provide some indication of the rate of diffusion of a technology. The selection of particular conferences either on the basis of their international profile or specific subject area or if they are specifically focused on 'futures', can overcome many of the difficulties relating to the huge amount of information that would have to be assessed if all conferences were going to be monitored.

Experts

It is hardly surprising that experts seem such an important source but the pertinent question for an EWS is not whether to use experts but how to select and access them. The means of selection is particularly crucial but the best method for doing so is currently either assumed or arbitrary. All six of the national initiatives rated experts as an important source; they all use experts, with some having developed specific committee structures to inform their EWS, as well as using postal surveys to elicit information. All of the previously published papers in the type II literature had used experts in a systematic manner. The Delphi method has been commonly used for setting short-term research priorities[310,311,312,313]. The results of the Delphi study did not reflect a high rating for experts in identifying all types of new technology but open comments from respondents suggest that the use of experts was seen as a vital source for any EWS. The low ranking accorded to experts may have reflected the structure and design of my questionnaire. Whilst it is problematic to assess retrospectively the benefits of involving experts, six of the nine case studies (biosensors, LVAD technology, telemedicine, dornase alfa, donepezil and laparoscopic surgery) were predicted by previous studies which used experts as their main source of information. Another of the case studies (IFN-β) was briefly referred to in the STG report and used as an exemplar 'new' technology by Stevens et al in their postal survey. The final two case studies (CT scanning and PICUs) had begun to diffuse before any of the studies were carried out but 'colleagues' were cited as an important information source for early adopters of CT scanners in the US[156].

Clearly, the role of experts is a key to the operation of an EWS, although they should not be expected to exhaustively predict the future. As well as through meetings, postal surveys or telephone enquiries, expert opinion can also be accessed through reports that are produced for purposes other than an EWS (for example, reports such as those of the Genetics Advisory Group in the UK). Using experts in an open survey is likely to produce a long list of potential new technologies, often with little detail on each specific technology. However, compared to many of the alternative documentary sources experts are likely to be a less labour intensive source of information to use, ensuring a broad range of views which can be collated quickly and cheaply. As such, experts' views are recommended as a starting point for any EWS; they can then be filtered and updated by other sources, including more focused surveys in specific technological or specialty areas where necessary.

Patient special interest groups

Patient special interest groups, such as the Multiple Sclerosis Society, the Cystic Fibrosis Trust and the Alzheimer's Disease Society in the UK, have played important roles during the introduction of new technologies, for example in relation to drugs such as IFN-β, dornase alfa and donepezil respectively. However, comments in the Delphi study suggest that such groups may only be of limited use for identifying new health care technologies as they only have a narrow field of interest and are themselves reliant on other sources of information. Clearly, they are helpful in assessing the extent of public and media pressure that may develop for a particular technology but different patient groups will have more or less influence than others. Only in exceptional cases can patient special interest groups be considered as a primary source of information for early warning. The changing nature of consumer involvement in health care may mean that this source becomes more helpful in the future; this is exemplified by the integral role that such groups will be playing in the work of NICE.

Private health care providers

Delphi respondents did not recommend this source. They felt that, whilst it may be useful for identifying needs for new health care technologies, in terms of providing early warning, private health care providers may often follow rather than lead developments in the NHS. There was no reference to this source in the literature review or telephone enquiry, and the case studies did not reveal any opportunities at which private health care providers may have proved to be a helpful early warning source (although this is difficult to ascertain retrospectively).

Drug Information Services

In the UK a well established EWS for new drugs in development already exists in the form of the Drug Information Pharmacists Group (DIPG), which in collaboration with the NPC, has developed a structured approach to providing evaluated and rapid information on new drugs and medicines which is easily accessible through the internet[a]. One Delphi respondent commented that regional drug information services in the UK have 'built up impressive information sources for new drugs in development'. This includes continuous tracking of all new drugs likely to reach the UK market up to five years before marketing (see appendix 6 for full description). Modern day sources such as drug information services could not always be assessed by the retrospective case studies. They are likely to provide helpful corroboration, as indicated by the monograph on dornase alfa produced by the DIPG in November 1993. Direct monitoring of the FDA would still be required for decisions relating to devices.

Internet

The emergent EWSs in Canada and Denmark both specifically mentioned the Internet as a source of information. This serves to highlight the implications of developments in information technology for an EWS. The World Wide Web provides a very important means of accessing a huge amount of information relating to new health care technologies and their evaluation. The sites that have been particularly helpful are detailed in appendix 8. Many of the information sources that have been identified by the literature review, telephone enquiry, Delphi survey and case studies can be accessed directly via the Internet. For example, many journals are now available on the Internet in some form and conference reports on specific disease areas can be accessed through sites such as the 'Pharmaceutical Information Network'[b]). As the amount of information available on the Internet grows so the means of selecting which sites are the most important may become more difficult.

Media

Delphi respondents were divided as to whether media sources (such as newspaper cuttings and relevant television programmes) could provide helpful early warning. Whilst the media were sometimes seen as useful, disadvantages included exaggerated claims being made for new technologies and the potential for bias and manipulation.

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[a] http://www.ukdipg.org.uk/newprod.htm

[b] for example, recent meeting highlights relating to asthma can be accessed via: http://www.pharminfo.com/disease/immun/asthma/asthma_info.html#highlights

For instance a Daily Mail headline in June 1999 regarding etanercept (Enbrel), which is due to be launched in early 2000, read ' Does this new drug spell the end to the agony of arthritis?'[314]. Some respondents distinguished between the general news media and the financial press (see below).

Media sources were cited by the Swedish EWS as being a useful source, and marketing journals and literature are being used in France. Popular media coverage may have helped to highlight the likely importance of a number of the case studies, such as LVADs, PICUs and donepezil, but it seems that such coverage may only appear after the initial introduction of the technology. For the general news media and the financial press a lot of work would be required in order to ensure that these sources were systematic and comprehensive. One suggestion was to make use of Internet news services (such as Reuters).

Other sources - financial press & stock exchange monitoring

Senard points out that news from financial markets can provide early information on drugs, sometimes long before it reaches prescribers or the public from official or industry sources[315]. He cites the case of alpidem, an anxiolytic drug, which was launched by Synthelabo in France in October 1991. In June 1992 it was reported that the drug might be causing hepatic toxicity, and led to a pharmacovigilence study, which in turn led to the drug being withdrawn. The Synthelabo share price had risen progressively from 1990 but the setting up of the inquiry was followed by a 25% fall in share price. The withdrawal of alpidem was marked by a 12% fall in share price. However, for over a year while the enquiry was underway, the risks of alpidem remained confidential and sales of the drug actually increased. Richman argues that it is preferable to monitor company events rather than stock price movements and suggests specific computer-accessible sources that can be used for this purpose, such as the US Securities and Exchange Commission, the print news media and investments analysts' reports[316]. Additionally, companies traded on any of the US stock exchanges must file quarterly as well as annual reports[a].

Other sources - contemporary regulatory bodies

On 1 January 1995 a new set of European rules covering practically all non-pharmaceutical products became effective in the member states of the European Union for the marketing approval of implantable medical devices - namely CE markings,

[a] these are available via the world wide web at: http//www.sec.gov/edaux/searches.htm

which indicates that devices meet the essential requirements of the medical devices directives[317]. After 14 June 1998 all medical devices will have to bear the CE mark. Many of the member states of the EU currently have their own notified bodies dealing with the marketing approval of new medical devices. Notwithstanding new international requirements, *ad hoc* national initiatives to regulate the introduction of new, non-pharmaceutical, technologies have begun to be developed (for example, SERNIP in the UK).

Tertiary sources

Other countries' EWS activities

There seemed little role for newsletters from other HTA agencies although the existing initiative in Sweden specified such communications as a key source. These may have been overlooked in the case studies, not least because so few are as yet up and running properly, but, as a number of Delphi participants noted, they may be more useful for identifying current areas of technology assessment rather than 'ones to watch' for the future. There may, however, be potential for further developing international collaboration in this area as identified by the 1997 European workshop. The recent initiatives by HTA agencies in Canada ('Issues in Emerging Health Technologies') and Sweden (ALERT), which are placing a high emphasis on dissemination of their results, may prove valuable sources and so change the emphasis that should be placed on this source.

Concluding thoughts – information sources

In this thesis it has been assumed that different types of technologies will be identified through different, although not necessarily mutually exclusive, information sources. For instance, in the case of procedures that are not product-dependent (for example, arterial operations) the STG relied more heavily on expert opinion, informal documentation of scientific and technological developments, and professional meetings and publications, than on commercial product development databases. A combination of sources will be required in order to ensure that all types of technologies and all important technologies are identified. Using more than one source will provide corroboration, increase the likely accuracy of any predictions and increase the amount of useful information regarding a new technology. The classification of health care technologies that was developed as part of the Delphi study is only one way of classifying them; further sub-categorisation may highlight other sources for identifying new health care technologies.

9.2 ESTABLISHMENT AND OPERATION OF AN EWS

The principal methods for informing the following sections were the telephone enquiry and the literature review. Some of the issues were also highlighted by the case studies.

Scope

Time frame

In the context of a national HTA programme, it is not the aim of an EWS to provide exhaustive forecasts of the future. The length of early warning required is determined by the fact that appropriate research has to be prioritised, commissioned, and carried out and the findings have to be disseminated prior to the widespread diffusion of the technology into the health service. The telephone enquiry of coordinators of existing and planned EWS, revealed that current initiatives are concerned mainly with relatively short 'time-horizons'. Two of the respondents stated that they were interested in technologies which were likely to be adopted within one year, four respondents were interested in a time-frame of one to two years but only one respondent was interested in a time-frame of up to five years. It would be helpful to determine through surveys of policy-makers and other methods how much early warning is required for (a) strategic policy decision-making, and (b) for day-to-day operational management decisions. This will include determining what is the most appropriate balance between length of early warning and the level of certainty as to the likelihood of the importance of the new technology.

EWSs established for HTA purposes do not explicitly aim to identify 'desirable' long-term technologies but rather establish research priorities amongst those technologies that seem scientifically or clinically feasible in the relatively short-term. However, the results of the literature review indicated that an EWS can be used to try to influence the longer-term development of a health care system, the so-called 'preferable futures' approach.

Technologies

Much of the focus in the literature to date, and in discussions regarding the role of NICE[a], has been on ensuring the timely identification of new pharmaceuticals. However, EWSs should be concerned with identifying all types of health care technology. Not least this is because evidence for new pharmaceuticals is often better

[a] the list of technologies which NICE intends to evaluate immediately and in early-2000 includes 13 drugs, five devices, four procedures, one diagnostic technology and no health promotion interventions

than for other types of technology regardless of any early warning. Furthermore, as the case-study of laparoscopic cholecystectomy shows, there has until recently been no mechanism for the co-ordinated early identification of non-pharmaceutical advances even though their development may be rapid in comparison to new drugs[137].

Helzner suggests that the timely evaluation of devices (such as CT scanners, LVADs and biosensors) present a unique challenge[a]. In the telephone questionnaire the majority of the co-ordinators of existing EWS responded that either all types of technology were given equal attention or that drugs, devices and procedures & therapies were the main focus of their work. One of the EWS (France) does not focus on drugs at all but nominated devices, procedures & therapies and settings, as the types of technology which are concentrated upon.

Additionally, many significant health care technologies in the form of new services develop through the implementation of national policy initiatives. Examples include the development of Medical Assessment Units to relieve winter pressures on the NHS, NHS Direct to reduce waiting times and the increase in specialist nurses in areas such as Parkinson's disease and stroke as part of the initiative to reduce junior doctors' hours[b]. Such developments highlight 'policy' itself as an initiator of health care technologies, often in the form of complex services rather than single interventions.

Scale of operation

EWS can range from explicit international collaboration perhaps via national and regional organisations, to informal networking at the local district health authority or even clinical level. These different levels clearly have different scales of operation and orders of magnitude. Existing national initiatives commonly employ a core staff of no more than five WTE researchers, information service and administrative staff but have varying committee structures available to them and other means of accessing expert opinions.

In addition, the appropriate level of operation for an EWS may depend upon the specific type or types of technology which are the main focus of concern. The focus has been on a national EWS concerned with all types of health care technology, with the potential for

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[a] as they are generally characterized by: short development times, short life cycles, learning curve effects, provider experiences/expertise, complexity of procedures, small numbers of patients and technology explosion (Helzner E. *Industry and HTA*. Presentation at 15th Annual Meeting of the International Society of Technology Assessment in Health Care, Edinburgh, 1999)

[b] personal communication, Prof M Severs, University of Portsmouth, September 1999

greater international collaboration because of the likely economics of scale that could be realised from sharing methodologies and results (see below).

System

Methods for eliciting expert opinion

One of the key elements in an EWS, in addition to the monitoring of the chosen documentary sources, is a system for contacting and eliciting opinions from experts; this was another key lesson from the STG project. Experts can be used both to 'brainstorm' new developments and to filter information from other (documentary) sources. The lessons from the results of the literature review are that an EWS needs expertise and experience, and that Delphi studies are a useful method for achieving this. A fuller discussion of the advantages and disadvantages of this particular approach is given in appendix 1. The Delphi study described in this thesis highlighted the potential role of focus groups and e-mail discussion groups as well as Delphi surveys. Focus groups were felt to be a very labour intensive method to adopt although it was suggested that the cataloguing of information from documentary sources and/or a Delphi survey might precede them.

There was some uncertainty as to the best methods for accessing expert opinion and for selecting experts to contribute to an EWS. Resolving these issues may require a systematic review of the literature (including the sociological and social administrative literature) on expert selection, management and knowledge retrieval, possibly supplemented by triangulating to other sources such as 'experts' on expertise.

Prioritising technologies

The telephone enquiry of coordinators of existing and planned EWS also indicated that there is a need, having identified new technologies, to develop criteria for selecting those technologies which are in most urgent need of evaluation. There is an extensive literature regarding setting priorities for HTA which has not been summarised here[318,319,320]. The views of the co-ordinators of the six national EWS suggested slightly different criteria with which to select which emerging technologies should be highlighted. However, the following were commonly mentioned[127] and are similar to those summarised elsewhere[321]:

- expected health impact (burden of disease)
- efficacy or predicted efficacy of the technology

- type of development (innovativeness, innovation phase, speed of diffusion)
- economic consequences (investment cost, total economic impact), and
- policy relevance (regulatory decision, research agenda, controversial, ethical concerns).

Interface with HTA programme

The value of an EWS to a HTA programme will be determined to a very large extent by the responsiveness of the programme to the outputs of the EWS. One method of ensuring that the maximum benefit of an EWS is realised is through the 'fast-tracking' of particularly important technologies (or those that are likely to diffuse very rapidly) from their initial identification to appropriate evaluative research being commissioned. In this context an EWS should not aim to provide an exhaustive list of all potential new health care technologies with only limited planning of future research needs and research design but rather select the most important technologies and concentrate research planning on these.

Thus, in the context of the work of a national agency for HTA, simply identifying new health care technologies via an EWS is not enough; the next step is to perform early assessments[322,323].

Updating

Central to the operation of an EWS is, as the STG recommended in 1988, the need for consistent methods of updating information; the system that has been subsequently maintained by the Health Council has identified monitoring as its most important function. The rationale for this approach is that, as the case studies clearly show (with the exception perhaps of laparoscopic cholecystectomy), technologies do not suddenly appear with little prior warning but have been in development for a long time before they begin to diffuse. For example, the bases for the development of telemedicine and LVADs were first conceived in the 1950s and 1960s respectively. Often parallel developments in a number of other technological areas are required prior to the full potential of the innovations being able to be realised (for example, CT scanners, telemedicine, biosensors). As Buxton and Scheider suggest, Comroe and Dripps classic study[309] 'emphasizes the complexity of the science base for many current advances, the diversity of component elements on which they drew, and the long time lags between some scientific advances and their useful application'[324]. This pattern of technological

development highlights the need for a 'watchful waiting' approach by an EWS (see section 9.3 below).

Respondents to the Delphi study highlighted how different documentary sources might be used to monitor technologies at different stages in their innovation, development and adoption. They suggested a progression from reports of discoveries in scientific journals to reports of progress in developing the technologies in specialist journals and then onto key medical journals as the technology is adopted.

Dissemination

The EUR-ASSESS Subgroup on Dissemination and Impact has made recommendations for informing policy makers and communities of technology assessments[325], and many of these will be relevant to disseminating the results of an EWS.

Each of the six national initiatives reported that they are currently disseminating, or are planning to disseminate, detailed information on only a small number of technologies each year, usually ten to twelve. This dissemination is carried out via a wide range of mechanisms and products. This includes providing formal advice to government (the Netherlands) as well as more informal dissemination to politicians (Sweden, France, the Netherlands) and national and provincial health policy makers (Canada, Sweden, United Kingdom). Two of the initiatives (Canada, Sweden) have Internet sites that provide updated information on the technologies that they have identified and prioritised as being important. Newsletters are used by three of the initiatives (Canada, Sweden, and the Netherlands).

Collaboration

From the results of the literature review and the telephone enquiry it is apparent that the notion of early warning has only recently emerged from reflections on the nature and utility of health technology assessments. These have emphasized the importance of identifying a new technology as early as possible so that an appropriate evaluation can be initiated at a very early stage[a]. Of the existing national initiatives the Health Council of the Netherlands, which built on the work of the STG in the mid-1980s, has had the most experience of an EWS. Often it may be possible to make use of existing schemes or initiatives (such as, in the UK, the CMP group of the SMAC) and there is little point in

[a] Blume S. *Early warning in the light of theories of technological change*. European Workshop: Scanning the horizon for emerging health technologies, Copenhagen, 1997

reinventing the wheel. However, where such opportunities do not exist specific initiatives are required; even when they do exist, they may require supplementing.

The case studies illustrate the benefit of international collaboration. At the international level it would be beneficial to collaborate on definitions, co-ordination, standardisation and communication. In the longer term there may be a role for a more formal mode of collaboration, perhaps based within the EC or through INAHTA.

9.3 LIKELY VALUE OF AN EWS TO THE NHS

As Buxton and Hanney suggest, just as it is wrong to presume the value of a technology that is yet to be evaluated by research, so it is wrong to presume the value of research *per se*[326]. This applies equally to mechanisms intended to promote and assist research-based policy or decision making, such as an EWS.

This section establishes the criteria and outcomes by which the success, or otherwise, of an EWS should be judged and then reviews the available empirical evidence on the value of an EWS. The section then goes on to discuss some of the methodological difficulties of assessing the payback of an EWS, highlights six potential benefits based on the case-studies in chapter 8, and then discusses possible different levels of payback which may result from early warning of different types of technology. Finally, the section suggests some problems which may limit the value of an EWS and concludes by proposing some solutions.

Aims of an EWS

When assessing the value of the NHS R & D programme, of which the HTA programme is an integral part, the focus has been on the immediate benefits to the NHS[326]. Such an evaluative approach sees the incorporation of research findings into the production of relevant secondary outputs (such as national guidelines or local policies) as key indicators of future health service impact. Such outputs and their effects on health care services are appropriate outcomes by which an EWS should be measured. The introduction of new technologies entails an important additional criterion: these outputs must be realised in a sufficiently timely manner to be able to influence the adoption and diffusion of the technology in question. The direct benefits to the NHS of timely research theoretically include reducing the cost of delivering existing services, improving the quality of the process of care delivery, increasing the effectiveness of

services (leading to increased health) as well as potential equity gains[327]. Central to this thesis has been the recognition of the importance of linking the operation of an EWS and the provision of improved information by means of undertaking timely HTA research for the purposes of policy-making.

However, outputs from HTA research in the UK have often simply generated knowledge and not been formally linked to policy-making[a]. This makes it hard to value the contribution of an EWS to evidence-based decision making. The role of explicitly applying such knowledge to decision-making at a national level is one which NICE has been charged with fulfilling for 30-50 technologies each year. In the assessment presented here the generation of timely knowledge is used as a proxy for information which can and will inform decision-making. The caveats around some of the assumptions are discussed further below.

Existing evidence

Although work on identifying health care technologies as part of the HTA programme began in 1996, a formal EWS was only established in the UK in 1998. Consequently, there is little NHS-based evidence regarding the payback from such a system and existing empirical evidence for the value of an EWS is only informal and intuitive at best. Recently, however, the work of the EWS in the UK has been formally integrated into mainstream policy-making. The list of topics which NICE will appraise has been published[b] and the press release stated that 'the proposals for new interventions . . . are derived from a careful scrutiny of innovations likely to have a significant impact on the NHS, carried out on the Department's behalf by the National Horizon Scanning Centre at the University of Birmingham'. It has been suggested that the early identification of zanamivir (Relenza) and R064-0796 for the prevention and treatment of influenza through the operation of the Horizon Scanning Centre has facilitated the development of a proposal for a systematic review as well as allowed early consideration of the potential impact of these advances on the current immunisation programme in the UK[137].

The longest existing EWS anywhere is in the Netherlands where, since 1979, it has been possible to prohibit, or attach conditions to, the performance of certain new procedures

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[a] with the possible exception to date of the interface between the HTA programme and the National Screening Committee on matters relating to population screening issues

[b] NICE will begin to consider the following technologies in autumn 1999: hip prostheses, advances in hearing aids, routine extraction of wisdom teeth, liquid based cytology for cervical screening, coronary artery stent developments, taxenes for ovarian and breast cancer, inhaler systems for childhood asthma, proton pump inhibitors for the treatment of dyspepsia, interferon beta for MS and zanamivir & oseltamivir for influenza (NICE press release 6th August 1999).

in a hospital[328]. In this way the government is able to concentrate the performance of a given procedure in certain centres. As a result the licensed centres are able to build up and maintain appropriate levels of expertise, seeking thereby to guarantee quality. The system also ensures that no more centres than necessary invest in the infrastructure required for the procedure. Currently more than ten services are licensed in this way[a] [329,330]. During the past 15 years the Dutch government have made important policy decisions on the basis of Health Council reports addressing new and emerging technologies, including:

- the introduction of a national breast cancer screening programme on the basis of the Council's 1987 report, and
- a 1986 report on Artificial Reproduction which led to the controlled introduction of in-vitro fertilization and inclusion of this technology in the Hospital Provisions Act.

Such extensive experience with an EWS in the Netherlands there has been reported as being 'quite positive'[b] without any formal evaluation having been undertaken.

In summary, there is a lack of available empirical evidence on the value of an EWS to a health care system anywhere. By means of applying an existing model of estimating the payback from research, the case studies in chapter 8 have been used to illustrate both the potential and likely benefits that may result from early warning using the information sources recommended in chapter 7.

Assessing likely payback

The payback analyses of the case-studies presented in chapter 8 have sought, as far as possible, to estimate firstly, the 'theoretical potential payback' of EWS-instigated research, and secondly, (recognising that other factors may be important influences on the policy and decision-making process) the 'likely realisable payback'. These analyses have required some knowledge of each of the technologies, an assessment of the capabilities of the proposed research to deliver primary outputs, an understanding of the way the interfaces with policy can be expected and made to work, and a judgement of the likelihood of changing professional behaviour.

As far as the quantitative analysis of health sector benefits is concerned, the potential cost implications to the NHS of each of the technologies in the case studies far outweigh

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[a] various transplantations, neurosurgery, heart surgery, renal replacement therapy, radiation therapy, intensive care for neonates, in-vitro fertilization and clinical genetics

[b] ten Velden G. *Identification of new health care technologies by the Health Council of the Netherlands.* European

the likely costs of appropriate HTA research and the operation of an EWS. However, the likely value of any early warning will depend upon three factors:

- whether the potential cost implications of the technologies would actually be incurred by the NHS in the absence of an EWS and HTA research,
- whether sufficient and accurate early warning is likely to be given by an EWS and, if so,
- whether timely HTA research can change behaviour, and thereby achieve the expected potential benefits.

Consequently, the payback model has necessarily involved assumptions about the changes to policy and/or practice that might have been expected from timely research evidence. However, as outlined above, benefits from research have traditionally been thought of in terms of knowledge generation rather than evidence-based decision making. A typical analysis, though not from the UK, showed very favourable incremental cost per life-year gained ratios from seven RCTs but implicitly presumed that behaviour would automatically accord with new knowledge and made no attempt to assess how far practice could, in reality, change[331]. In fact, when the HTA research takes the form of clinical trials it can be argued that few individual trials are likely to have a major impact.

The originators of the payback model used in this thesis have noted that '...specific ways must be found of valuing research the objective of which is to produce knowledge which is spread and implemented as widely as possible'[326]. For this reason any similar attempt to assess the value of an EWS must '...give considerable attention to analysing how health services research has an impact because unless there is an understanding of how impact occurs it will be very difficult to know what it is we are trying to capture when assessing payback'. One of the retrospective case-studies in this thesis (CT scanners) appears to provide a comparative example between the UK and the US of the beneficial influence and very practical effect that the early involvement of decision-makers and evaluative research can have on the introduction of an expensive new technology. However, there are any number of other factors which may explain why the diffusion of CT scanners was markedly quicker in the US than in the UK. The relative influence of these factors is difficult to disentangle using hindsight.

Workshop: Scanning the horizon for emerging health technologies, Copenhagen, 1997

There is a clearly a need to undertake further and more detailed case studies of technologies (similar to those undertaken in this thesis but through prospective monitoring) to help understand the diffusion processes of new health care technologies and to assess how the results of timely HTA influences the adoption of a new technology.

Potential benefits of an EWS

The suggested uses to which information generated by an EWS may be applied have been outlined in chapter 2. All of the existing EWS which were included in the telephone survey aim to inform health policy planning, although two (Canada and Sweden) did not report having any direct input into national HTA research prioritisation. In the assessment presented here the primary outcomes used to assess the value of an EWS are the production of secondary outputs such as national guidelines or local policies, and their effect on health care services. In this context, the analysis of the likely payback from the case-studies highlighted six particular potential benefits of early warning which are particularly relevant.

Production and dissemination of timely guidelines

One of the main functions of NICE will be to produce and issue high quality, evidence-based guidelines on the appropriate use of particular interventions. NICE intends to provide information about how practice can be changed and will also develop implementation methodologies to help local clinicians.

The potential value and practical limitations of guidelines have been well-documented[332]. Guidelines may be particularly helpful for technology's which are intended for a patient group in which it is likely that the costs and benefits will vary over different sub-groups of patients (for example, the MediSense ExacTech pen, IFN-β or dornase alfa). Particularly if the cost of the technology is high these different sub-groups will have to be identified[72] in order to establish the socially optimal level of provision. By alerting, through early warning, manufacturers and NICE to the need for further sub-group analyses, those patients for whom the technology is most likely to be cost-effective can be identified; policy-makers can then determine whether to issue guidance which specifically targets the needs of these sub-groups. Guidelines similar to those developed for IFN-β can be developed, agreed with relevant parties (such as patient interest groups as was the case with dornase alfa and the Cystic Fibrosis Trust), and disseminated.

Guidelines will of necessity contain some value judgements themselves. They should not, therefore, seek to explicitly exclude specific categories of patients as there are a vast number of clinical situations, as in the case of donepezil, in which evidence is lacking[333]. As Eddy suggests 'interpretations [of guidelines] are almost never clear cut, and every new problem is likely to have some special feature that cannot be anticipated or captured in a terse set of instructions . . . developing guidelines for these problems will require judgement, interpolation and negotiation'[334]. Therefore, a combination of guidelines that are intended as educational tools (rather than as 'restrictive protocols'[332]) and a recognition that the most appropriate level for decision-making will differ for certain technologies may offer the best way forward. Such an approach explicitly recognises the inherent uncertainty in clinical practice and the inevitable existence of local variations in health care need and provision.

In a number of the other case studies there has been a clear need for nationally agreed guidelines to begin to reduce inequalities in access to certain health care technologies (for example, donepezil). This problem is not limited to drugs as there are, for example, wide regional variations in the provision and criteria for admission to a PICU. However, as the donepezil case-study reveals, the existence of numerous different sets of guidelines can itself lead to inequalities. If guidelines are not evidence-based, as would appear to have been the case with donepezil, this serves as a justification in itself for the establishment of NICE. NICE will, in turn, need early warning of new and emerging technologies in order to produce and disseminate guidelines in a timely manner. This will help to reduce policy confusion and overcome the difficulties associated with restricting the use of a new technology once it has already begun to diffuse. In the case of CT scanners, for example, early identification of an important new technology led to nationally promulgated advice, which drew on a timely evaluation, and recommended the adoption of the technology in the UK.

Establishing registers of new technologies

Undertaking evaluative research through an RCT can be problematic for technologies introduced simultaneously in more than one centre. In such cases the major benefit of early warning may be to lead innovators and researchers to collaborate and implement a register (as could usefully have been the case with LVADs and laparoscopic cholecystectomy). Early warning could facilitate such collaboration by identifying important new developments and then encouraging centres, either through the HTA

programme or NICE, to share data and their experiences. Such an approach has been suggested in the UK recently in the context of the introduction of a number of devices [61].

Registers aim to co-ordinate data collection on the early use of a new technology, in order to help monitor effectiveness and safety, and to share learning experiences between different centres. Such additional mechanisms are often required as routine data collection systems in the NHS are not framed in a way which allows monitoring of specific technologies to take place. One form of monitoring which has recently been proposed, particularly for fast-changing technologies, is the possibility of 'tracker trials'[335]. These aim to ensure that high quality research evidence is not postponed until the stability of a technology is reached and aim to avoid resistance to RCTs on the basis of a supposed lack of equipoise becoming entrenched.

In the context of specialised services NSCAG encourages a similar approach by including a contract requirement that all services introduce an agreed form of inter-unit or international audit. Such a requirement recognises that in small and specialised services, measuring performance and auditing outcome is difficult, and hence in some cases only international comparisons are possible. There has been, and remains, a similar need for the co-ordinated provision and audit of performance of PICUs and LVADs. An example of how national collaboration can be beneficial is the experience amongst neonatologists in relation to extra-corporeal membrane oxygenation (ECMO). Clinicians agreed that all neonates who needed ECMO would be treated as part of a randomised trial, and this approach has been advocated by others[295]. Given the difficulties encountered in undertaking a RCT of LVADs in the UK (as described in the case study) a register-based approach would be a preferred option to the current *ad hoc* activity.

In the UK six implant registries currently exist: the UK National Pacemaker Database, the Heart Valve Registry, the National Breast Implant Registry, the UK CSF Shunt Registry, the Implantable Infusion Pumps Registry and the Arthroplasty Registry[336] [a]. Such an approach is not necessarily limited to devices and procedures and can be applied equally to drugs. This may have been the intention of the NHS Executive when it gave guidance on the prescribing of IFN-β, suggesting that 'decisions [about treatment in individual cases] should be made only by specialist neurologists (that is not by GPs)

[a] the UK HTA programme is currently funding two projects which are assessing the potential use of routine data for evaluating health technologies. One of these is compiling an up-to-date inventory of relevant routine data sources

to help ensure appropriate targeting of treatment ***and to ease monitoring and evaluation of its effectiveness***'.[337]

Enabling a 'watchful waiting' approach

Early warning can facilitate 'watchful waiting' of a technology's development in order to (a) allow others to carry out evaluations, or (b) maximise long-term benefits by delaying diffusion initially in order to take advantage of 'second generation' technology[72].

Under a 'watchful waiting' approach one possible aim is to allow policy-makers to slow down the process of the adoption of the technology while awaiting results and/or guidance from evaluations being undertaken elsewhere in the world. In this context the aim of an EWS is not primarily to inform a UK-based HTA. The theoretical benefits of applying such a policy have been illustrated in a number of the case-studies. International collaboration may enable the NHS to adopt a formal 'wait and see' policy towards the adoption of a technology which is being introduced, diffused and evaluated much more quickly in other countries. This is a potentially common scenario given that the UK represents only 4% of the world health care market and that trends in medical innovation and adoption generally tend to occur in the same fashion worldwide[338]. In the case of laparoscopic cholecystectomy the diffusion of the technique in Europe occurred at only half of the rate in the US. This was, in part, because the manufacturers were initially focussing on the US market and so were unable to meet European demands[97]. Given a limited amount of funding available for research and development, such an approach may help to ensure that the overall payback from HTA research is maximised.

The value of the second possible aim of a 'watchful waiting' strategy will depend upon the degree of obsolescence thought likely to apply to the technology or the amount of development or improvement likely to take place. For example, CT scanners went through four generations of operating methods within four years (mainly directed at the US market), the ExacTech pen was modified to make it more user-friendly, and LVADs have progressed from hospital-based power systems to much smaller and quieter devices which allow patients to leave hospital. Such an approach may also help to overcome the danger of evaluations being carried out too early, and their results then being forgotten or invalidated. For example, when changes in stenting and excimer laser technology took place whilst trials were in progress, doubts were subsequently raised about the external validity of the results by the time that they were published[62].

There can be additional economic benefits from waiting for further technological developments, as illustrated by the introduction of extracorporeal shockwave lithotripsy (ESWL) machines in France[339]. At first a German manufacturer of ESWL machines, Dornier, enjoyed a monopoly position in France. The first Dornier ESWL machine was installed in France in 1984 following years of development and a patent award in 1973. However, after 1985 this situation changed as, with the development of French machines, the purchase of foreign-made equipment was deferred in favour of French equipment that was under development. By 1988 28 ESWL machines had been installed in France: three of these were German and 25 French. The development of ESWL is a good example of the role that 'watchful waiting' and centralised planning of hospital equipment can play in the diffusion of a new health care technology.

Those technologies that require large-scale capital investment are particularly suited to a 'watchful waiting' approach. Technologies such as CT scanners and telemedicine have diffused relatively slowly in the UK compared to other countries. Stocking suggests that this is related to the way the fixed budgetary system operates in the UK engendering a sense of competing needs at local levels within local budgets and the difficulties in acquiring large capital sums for equipment purchase[55]. In addition, in a number of the case studies the development phases for the technologies were very long which would facilitate a 'watchful waiting' approach (for example, patents for CT scanners were first granted in 1961 and 1962, biosensors research dates back to the 1950s and the concept of telemedicine first arose in the 1950s).

Providing earlier information on longer term effectiveness

As has been illustrated by the case-studies, it is often particularly difficult to make policy decisions about a new technology's likely long-term effectiveness and cost-effectiveness on the basis of the results of short-term research studies. Indeed, once short-term efficacy has been reported, monitoring of longer-term effectiveness often becomes relatively neglected (for example, laparoscopic cholecystectomy).

In terms of the three drug case-studies presented in chapter 8, not only was information on longer-term cost-effectiveness lacking at the time of their introduction to the NHS but the practical importance of reported changes to patients and their carers was unclear. Earlier evaluations can clearly help but a change is also required in the way in which industry and the NHS interact. The chairman of NICE believes that:

> "..many of these things can be resolved if the economic aspects are included in the clinical trials starting way back . . . as NICE becomes more mature and as the industry becomes more accepting of the need for this sort of additional data-gathering . . . then this issue will be relatively resolvable"[340].

Whilst this may be true there is still some way to go before such an open and collaborative approach to evaluation between manufacturers and the NHS is likely to be achieved. In particular, manufacturers of health care technology will need to recognise that not all new technology's will necessarily be sufficiently cost-effective to the NHS to justify their introduction. In this regard the recent furore over NICEs recommendation to the Secretary of State that the new anti-flu drug zanamivir (Relenza) should not be available on the NHS does not augur well. The decision brought predictions from the chairman of GlaxoWellcome, the manufacturers of the drug, that 'if the government continues to make the environment antagonistic to the [pharmaceutical] industry then obviously it will start to move elsewhere [out of Britain]'[341].

In the absence of such a partnership, the existing situation is one in which RCTs of dornase alfa have been of insufficient duration to indicate whether lung function is sustained in the longer term, or whether the use of dornase alfa is associated with a reduction in mortality. Similarly, information on the long-term progression of MS and how early indications of the disease might relate to longer-term disability are still needed to inform policy-decisions regarding the prescribing of IFN-β. As a final example, longer trials of donepezil involving patients more representative of the general population of the elderly are required. Modelling studies will have some role to play but NICE will need to work closely with manufacturers in order to ensure that the requisite data begins to be collated at an earlier stage and is made available to decision-makers (either directly or indirectly through NICE-validated guidelines). Earlier warning to the NHS of impending technologies will assist in ensuring that appropriate collaboration with manufacturers can be initiated early in a technology's development .

Lengthening of methodological lead time

Earlier identification might enable the methodological lead-time for framing appropriate research questions or refining aspects of trial designs to be lengthened.

As table 28 shows it is likely that substantial early warning would have been provided for CT scanners, LVADs, telemedicine, PICUs and IFN-β. In contrast, the length of

early warning for the remaining four technologies (the MediSense ExacTech pen, dornase alfa, donepezil and laparoscopic cholecystectomy) would have been inadequate to enable sufficient HTA research to have been designed and initiated prior to these technologies being introduced into the NHS. This is not to say that early warning of a year or less is not useful, simply that the full potential benefits of early warning would have been limited by the nature of some of the technologies' development and relatively rapid introduction into the NHS.

Table 28 Likely length of early warning from case-studies

Case study	Date of introduction to UK	Maximum theoretical length of early warning (years)	Likely length of early warning (years)
CT scanners	1971	10	4
Biosensors	1988	4	2
LVADs	Early 1990s	15	5
Telemedicine	Early 1990s	40	10
PICU	Early 1980s	20	3
Beta interferon	1995	13	3
dornase alfa	1994	4	1
Donepezil	1997	5	1
Laparoscopic cholecystectomy	1990	3	1

Despite the relatively short length of early warning for donepezil, early (if non-specific) warning of the host of drug manufacturers developing drugs treatments for alzheimer's disease during the 1980's could still have been realised. This might have provided more time in which to develop and agree quality of life outcome measures which could then have been used later in a comprehensive RCT of donepezil. Similarly, difficulties remain with designing trials and developing outcome measures to adequately assess the effectiveness of therapies for MS. The recent proposal to the UK HTA programme intended using a primary outcome measure which was unlikely to be well known amongst health care commissioners[a]. Furthermore, it was not clear whether potential levels of change on the proposed measure would be likely to have a significant impact on quality adjusted life year (QALY) calculations. As the payback analysis of early warning of IFN-β makes clear, the ongoing policy debate with regard to IFN-β is not

[a] a UK HTA funded project, commissioned in 1995, entitled 'Improving the evaluation of therapeutic interventions in MS: development of a patient-based measure of outcome' is currently underway and

about such 'clinically meaningful outcomes' but rather the magnitude and length of any benefits to patients. early warning may have enabled more relevant outcome measures to have been considered and allowed for a longer and more informed debate regarding the type of information required by decision-makers. Early warning might also allow greater consideration of the practical implications of the proposed research (for example, the organisational issues relating to any assessment of telemedicine).

Commissioning research with realisable payback

The approach adopted here to measure payback implies a further, final benefit of an EWS. Naturally, if payback is a key concern then inevitably there should be a preference for carrying out research in areas where desired change can reasonably be expected. Consequently, research should be discouraged in those areas where there is an expectation, firstly, that results are not likely to influence practice and, secondly, where the likely speed of diffusion of the technology will not necessitate an early policy response (either to promote the adoption of a cost-effective technology or control the diffusion on an unproven technology).

In most cases, factors other than evidence-based research will often either serve to control the adoption of a technology or have a great influence on a technology's diffusion. For example, genuine clinical uncertainty regarding effectiveness, the acknowledged possibility of future technological developments or on-going evaluations in other countries may all serve to slow the diffusion of a new technology. Consequently, many of the large number of new technologies which are introduced into the UK each year can be left to diffuse naturally as led by the medical profession (although it may still be important to highlight some of these technologies so that registers, monitoring, and/or guidelines can be introduced at an early stage in the technology's diffusion if such policy responses become appropriate). Rather, the priority should be to carry out UK-based HTA research on those technologies which are likely to have important implications for the NHS as a whole and whose adoption is being 'pushed' prior to a full evaluation of their costs and effectiveness. Factors which may 'push' the adoption of a technology might include clinical enthusiasm, media campaigns, public opinion or inducements from manufacturers. By identifying such technologies early warning can enable a more rational approach to determining HTA research priorities.

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expected to be completed in early-2000

Although it was not directly the result of the operation of an EWS, I and others undertook a study of the 'payback' from a proposed UK HTA-trial of IFN-β, costing £10 million over a ten-year duration, which illustrates this potential benefit[252]. It was clear that the trial would generate knowledge benefits of wider relevance[a]. However, most of this knowledge could have been obtained in other ways. In a quantitative analysis of the benefits of the trial, three main scenarios were examined, reflecting different trial outcomes and the consequent levels of prescribing over a twenty year period (10 year trial and 10 years post-trial). Under only one of these could the proposed trial have been justified on cost-effectiveness grounds. This assumes the unlikely outcome that the trial shows IFN-ß to have no net benefit to patients. In contrast, the most likely outcome is that the trial would confirm some net overall clinical benefit at a considerable net cost. Following such a trial outcome it would be politically very difficult to maintain restraint on prescribing, which would have to be explicitly based on cost-effectiveness criteria, given the independent and strengthened evidence of some benefit to patients from the trial. There seemed to be no plausible way in which the trial and its resulting impact on therapy could have achieved a conventional threshold level of cost per QALY. The study concluded that the benefits of the proposed trial were highly dependent upon the policy adopted both during and after the trial, and the extent to which there is willingness to restrain prescribing of IFN-ß based directly on information of the high cost-effectiveness ratio of IFN-ß. Thus the policy-making environment was a vital factor in determining that the potential policy value of undertaking a 10-year HTA of IFN-β was relatively low.

The IFN-ß case-study in chapter 8 shows that even with an EWS it is likely that such a HTA trial could only have begun some two to three years prior to the licensing of the drug in the UK. The likely payback from early warning in this case was therefore minimised by the short period of early warning and the existence of factors which have been seen, in retrospect, to have limited the diffusion of this technology in the absence of any definitive HTA research. The challenge for EWS in the future will be to identify those important technologies for which early warning and timely research will be likely to make a significant contribution to ensuring their rational introduction, taking into account a host of other potential factors which may be expected to either promote or restrain the adoption of the technology. Prospective payback analyses can help to

[a] For example, knowledge on the understanding of MS particularly on disability and quality of life, of the non-healthcare costs associated with MS, and information to assist the interpretation of the long-term implications of short-term indicators of disease progression

provide a framework to consider these factors but, in the longer term, such a challenge can only be met through a greater understanding of the myriad influences on health care professionals behaviour and decisions relating to the introduction of new technologies.

Payback from early warning on different types of technologies

The case studies reveal significant differences in the factors that may impede the likely payback from early warning of various types of technologies.

There is an important contrast between early warning of drugs and other types of technology. At the point when a major new drug is licensed it has almost certainly already been used, via phase II and III trials, to treat significant numbers of patients worldwide. In contrast at the point when devices (for example, the MediSense ExacTech pen or LVADs) receive a CE mark or FDA approval, or perhaps a number of years after their approval, they will not have been used as widely. If similar lengths of early warning are to be applied to all types of technologies then the natural corollary is that we should be attempting to identify new drugs prior to pharmaceutical companies enlisting NHS patients into phase III trials. This contrast is due to the very different licensing procedures for the different types of technologies. Whilst it is compulsory to evaluate drugs before their widespread use is permitted, other health care technologies are not necessarily subject to the same constraints. There is some limited provision in the UK for regulating the introduction of new service developments. One of the objectives of NSCAG is to regulate the entry of appropriate specialised service developments into the NHS internal market[342]. NSCAG funds the service costs of new developments in those services for which it is likely to become the purchaser[a] to enable a full evaluation to take place. However, it can only fund a small number of evaluations.

Gelijns noted that the institutional structure within which development decision-making took place differed to some extent in the case of devices, drugs and surgical procedures[343]. The development of drugs and devices was largely sponsored by the pharmaceutical, biotechnology, and medical device industries, took place both in these industries and in academic and governmental clinical research settings, where investigators evaluated the likelihood of benefits and risks in patients. Procedures on the other hand were both technically developed and clinically evaluated by physicians in clinical practice. This does not mean, however, that evaluation of devices is without difficulties as the LVAD case-study illustrates. As described in the case-study, in 1992 a

[a] £70 million in 1996-97 of which 75% was for UK heart and lung transplant services

team at Papworth hospital designed a RCT to evaluate LVADs as a permanent therapy for patients unsuitable for heart transplantation. The first problem encountered was the cost of the technology. In negotiations with the DH and the company producing the device, there were problems in agreeing how to cover the capital cost of the technology during the clinical trial. In a drug trial, the company would be expected to supply the 'new technology' free for the period of the trial, but this is not typically the case with 'device technology' trials.

In summary, the ability of policy-makers in the UK to intervene and influence the adoption and diffusion of different types of technologies at different stages of their development and adoption will inevitably vary. As a consequence, the likely payback from early warning may be strongly influenced by the differences in the development and marketing of the various types of health care technology, as well as the existing 'licensing' mechanisms for each type where they exist.

Factors which may limit the value of an EWS

HTA results are only one of a number of factors that will influence a technology's adoption and diffusion[326], as health care issues are complex, multi-dimensional and grounded in individual experience[344]. These other factors could theoretically act as limitations on realising some or all of the potential benefits of an EWS. Firstly, the complex development paths of some technologies (for example, CT scanners and telemedicine) may limit the ability of policy-makers and researchers to know when is the 'right' time to perform an evaluation. Secondly, the speed of the introduction of some technologies can be so rapid (laparoscopic cholecystectomy) that there is little opportunity to perform any form of evaluation before it is in widespread use. Thirdly, the beliefs of health care professionals may hinder the rational use of new technologies and run counter to the prevailing evidence-base. Fourthly, changing political and professional environments within which research may take place are important. The research may produce very little payback if a political imperative overrides waiting for the research results, a fact clearly recognised by NICE which 'ultimately has to temper its advice in relationship to the people's elected representatives in parliament and in Government'[345]. Finally, and most importantly in the context of this thesis and as discussed below, adoption decisions concerning new technologies are frequently unrelated to the availability of good evidence regarding patient outcomes or cost-effectiveness.

Despite growing activity in economic evaluation and the encouragement being given to decision-makers to take note of the results, very little is known about the impact of economic evaluation on health care decision-making in the UK, particularly following the introduction of the internal market[346]. Whilst the importance of cost-effectiveness considerations are widely acknowledged there is very little evidence that such a criterion is applied to new health care technologies at a local decision-making level.

The rapid adoption of CT scanners in the US and Creditor & Garret's analysis of the lack of effectiveness evidence, as well as the conclusions of the OTA report in 1978, bear witness to the apparently small influence of evaluations on adoption decisions. Similarly, the analyses of published articles on telemedicine revealed a lack of empirical studies, and of cost-effectiveness information, in particular. However, it is reasonable to assume that the likelihood of potential benefits being realised would be accentuated by 'right' timing: preferably early rather than late, as information that arrives too late to serve its primary purpose will be of limited value. Such an assumption must take account of the need for continuing evaluation as the technology evolves, experience grows and the consequent influence of learning curve effects. There are examples which reflect to a limited extent that evaluations of new technologies which produce results that are positive and conclusive are more likely to have an impact on the provision of health care than results which are negative or equivocal[2].

There is still relatively little known about the specific influence of research on diffusion[a] [62,347,348] and the research base for bringing about individual and organisational change is incomplete[349b]. The indications are that commissioners of health care services have found it difficult to apply economic evaluations of individual technologies[350]. Coyle suggests that decision makers need to be closely involved in order to be influenced by the findings of research[351] and others have emphasised that ownership of the HTA process by managers is crucial to its success[352,353]. At the very least results of studies need to be generalisable to the UK; this lack of external validity has been an issue in the case of PICUs in the UK. Clearly, as Davies et al state[2]:

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[a] Rosen suggest three priority areas for research: (1) social influences which shape the use and interpretation of research could be further explored (2) characteristics of hospitals and other provider organisations, which determine how decisions are made and the extent to which promoting clinical effectiveness is considered important; and (3) explore how new commissioning organisations try to influence the use of new technologies and factors which determine their success [source: Rosen R. *Exploring the influence of research on the adoption and diffusion of new medical technologies. A study of technology adoption in the UK National Health Service.* Bristol; University of Bristol MD thesis, 1998]

[b] a Cochrane Collaborative group on effective professional practice has been established to collate evidence based reviews on interventions to change the behaviour of health care professionals [web address: http://www.abdn.ac.uk/public_health/hsru/epoc/]

> "..one prerequisite for HTA results to be translated into action to improve efficiency, is that the results are disseminated and recognised as relevant and usable by health care policy makers and health care professionals".

This point is exemplified by the lack of a trial of IFN-β at it's time of licensing which had focused on quality of life and cost-effectiveness rather than just short term clinical benefits.

In addition, the existing 'gold standard' amongst evaluation techniques, the RCT, may impose restrictions on the external validity of any findings. For example, the limitations of RCTs as trial protocols might impose atypical patterns of care on unrepresentative samples of patients which would make the observed resource use in the trial difficult to generalise into routine clinical practice[354]. In addition, long-term resource use would not be available if a trial is stopped once the clinical uncertainty has been resolved. Thus,

> "Any programme of management for technology as a whole must assume a pragmatic approach, avoiding the influence of those purists and academics who are unwilling to take action until all the data they want are available[355]."

Some proposed solutions

There is a need to design and implement new routes to incorporate the results of research in guidelines or policy mechanisms, and, by doing so, improve the relationship between knowledge, evidence and policy or decision-making.

Some commentators have called for the DH to clarify the status of guidance from NICE so that commissioners can measure their formal power to restrict the use of treatments by Trusts or individual practitioners[356]. It has been suggested that a 'Technology Gateway' will be introduced into health care, which will serve to screen entry into the health care system of new forms of practice and provide an exit mechanism for those that have been superseded or found to be unnecessary or ineffective[91]. In essence, 'the technology gateway will be the means by which the relationship between R & D, policy formulation and health care will be formalised[91]'. In a similar way the need for a regulatory framework to ensure commissioners and providers support research-linked technology adoption has been proposed[357]. NICE could be seen as entailing a move away from an 'old' model which focused on providing information regarding new

technologies and incentives to local decision-makers to a 'new' model which involves a formal mechanism for a centralised decision or recommendation[a].

Under the interim guidance issued by NICE recommendations could indicate that commissioners should only purchase specified technologies in the context of formal trials. Commissioners may be expected to fund evaluation research during the early use of selected new technologies and providers may be obliged to provide minimum data sets, to monitor outcomes and to participate in research on selected technologies. One alternative solution to the issue of funding of device trials in particular (as arose in the LVADs case-study) might be that industry is required to provide the technology for the duration of the clinical trial which must be performed before the technology can be marketed in the NHS. Another solution may be that the capital costs of technology are made an explicit component of the treatment or excess treatment costs of the research, which fall on NHS providers, and are funded from the R & D levy. Whichever solution is adopted, a gap in the research continuum would be bridged between the current single requirement for assessment of device safety, in the UK regulated by the MDA, and the requirement of the NHS for good evidence of relative clinical and cost effectiveness. In the context of procedures, although an EWS may not have provided sufficient early warning to initially proscribe the rapid adoption of laparoscopic cholecystectomy, it may have led to a policy of constraint to be implemented possibly with the involvement of SERNIP.

To some extent the precursor of the 'Technology Gateway' has been established through the advice in various NHS Executive Health executive letters (ELs), but it is unclear how widely these policy recommendations have been implemented[62]. Clearly there is a high level of expectation that this will be the role of NICE as the Chairman would '..envisage NICE as being a development of the R & D initiative in having determined the best practice and then disseminating them out to health professionals generally'[358]. The question is whether it will do it better than seems to have been done in the past? A solution will need to be found if the government's recent declaration on this issue is to be enacted:

> "the various industries which produce drugs and devices...will need to enhance their capacity to produce evidence of clinical and cost-effectiveness"[64].

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[a] Buxton M. *How will NICE impact on the use of new and existing technologies in the NHS?* Presentation at 'Priority setting in the NHS' conference, September 1999, London

When such evidence has not become available at the point that a product comes to market, NICE envisages recommending that in the first instance, the NHS channels the use of the new technology through well controlled research studies[359]. In order to overcome some of the obstacles which have prevented decision-makers from acting on the basis of research evidence in the past, these studies will increasingly need to take account of the organizational or 'system-wide' impact of new technologies (as any evaluation of telemedicine will have to do) and allow for the fact that this will often be shaped by local circumstances and therefore hard to generalize[a].

However, if effective and flexible evaluative approaches are not in place firstly to initiate timely evaluative research, or at least monitor the relative performance of the new technology, and secondly, to link the results with clinical decisions at the individual patient level, then little can be done to influence, let alone control, a technology's adoption and diffusion. Partly as a response to such concerns Sculpher has proposed an iterative, four-stage process of economic evaluation of a new technology[75b]. The first two stages (the 'early developmental' and 'maturing innovation' stages) are of particular interest in the context of an EWS. The first stage aims to establish the 'cost-effectiveness gap' offered by the existing technology and the scope for the new to be more cost-effective. It is undertaken when new developments are first being considered, or once there is the first evidence from small, uncontrolled case series amongst innovators (which may be identified through monitoring of specialist medical journals or conference reports). The second stage typically builds on small RCTs, using decision-analytical techniques to model available clinical data, and small-scale collection of resource use data alongside clinical trials. The combination of an EWS and an iterative approach to the economic evaluation of a new technology can:

- prioritise research in a particular area;
- help to make a decision as to whether further R & D spending on the technology is justified;
- test the implications for the planned product of different possible results from future trials (via modelling of the potential cost-effectiveness of the author technology);
- indicate whether it is likely that a proposed technology might be cost-effective;

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[a] source: Rosen R, Gabbay J. *Linking health technology assessment to practice. Progress has been made but fundamental problems still limit impact.* Work in progress, October 1999.

[b] As summarised by Buxton M, 'Economic evaluation early in the life cycle of a medical technology', European Workshop: Scanning the horizon for emerging health technologies, Copenhagen, 1997

- and aid the design of definitive studies, clarifying the key parameters, critical thresholds, and necessary differences for the new technology to be cost-effective.

The proponents of early appraisals of health care technologies in the UK (through the DEC approach) claim that 'none of the 100 reports produced so far has been significantly contradicted by later evidence[360]. Preliminary economic evaluation and modelling can, therefore, provide sufficient information to inform not just trial design and urgency but also policy and should be considered part of the research response.

Whatever mechanisms are developed in the UK it will be impossible to control all decisions concerning the adoption of new health care technologies, especially in a health care system that allows a great deal of freedom to health care providers such as the NHS. Factors outside the HTA process must inevitably set priorities for HTA-research and affect the adoption of HTA results. However, it is clear that a multi-faceted approach, with proactive research management, is going to be increasingly necessary in conducting health technology assessments[a].

Concluding thoughts – likely value of an EWS

The findings of commissioned HTA research that ultimately results from the establishment of an EWS, as well as the more general highlighting of new technologies likely to be the most significant, should provide valuable and timely assistance to decision-makers in the NHS. However, it is clear that if there are not mechanisms to use the results[346] then it does not matter what types of economic evaluations are undertaken, or when. In the UK, NICE has been the policy-makers' response to integrating an EWS, the commissioning of HTA research, the dissemination of research findings and the practical implementation of research recommendations.

In summary, the payback analyses of the case-studies in chapter 8 suggest that the operation of an EWS in the UK has the potential to:

- assist in the development of timely guidelines for health care professionals (particularly for sub-groups of target populations) which can result in more equitable access to new technologies across larger geographical areas (for example, IFN-β, dornase alfa, LVADs),
- assist early monitoring of new technologies through registries (for example, LVADs, PICUs, laparoscopic cholecystectomy) in recognised centres,

[a] source: Stevens A, Milne R, Lilford R et al. *Keeping pace with new technologies: systems are needed to identify and evaluate them.* Work in progress, October 1999

- enable 'watchful waiting' where appropriate (for example, CT scanners, biosensors, telemedicine, LVADs)
- allow longer term effectiveness information on new technologies to be available sooner (for example, IFN-β, domase alfa, donepezil),
- lengthen methodological lead time to, for example, assist in the development of appropriate outcome measures (for example, IFN-β, donepezil), and
- help to ensure that research with realisable and worthwhile payback is commissioned (for example, IFN-β).

10 CONCLUSIONS

10.1 TIMELINESS OF THIS THESIS

The paucity of empirical evidence means that one must be cautious in deciding which are the most useful sources of information for identifying new health care technologies and the best methods for operating an EWS. However, NICE intends that 'guidance should be available to the NHS as soon as possible after the launch or general dissemination of the technology'[a] and EWS are being established simultaneously in a number of countries (often by HTA agencies). Intuitively they would seem to offer obvious benefits. Therefore even early, tentative conclusions based on a thorough review of current knowledge will be valuable.

10.2 METHODS ADOPTED

My conclusions and recommendations are based on the results of four separate methods that approached the two study questions from different perspectives; each of these provided somewhat different findings, which emphasises the importance of a multifaceted approach. Such an approach was adopted as there is no single best method, and each has disadvantages. The literature review revealed very few relevant studies; the EWS coordinators who participated in the telephone enquiry are developing their systems by trial and error; the opinions of the participants in the Delphi study are necessarily subjective and open to bias; and the case studies can only be regarded as exemplars and inevitably raise questions of the representativeness of the technologies which were chosen[140]. However, the overall analysis of the results from the four methods (a form of triangulation) provides a more robust review of the important issues relating to EWS for identifying new health care technologies than any single method alone.

10.3 INFORMATION SOURCES

The choice of information sources that feed into an EWS will be influenced by the choice between:

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[a] Source: *Appraisal of health technologies* (appendix G), NICE Board Meeting, 21 July 1999 (http://www.nice.org.uk/updates/2107/app_g.htn)

a) earlier warning of a potential technology with little certainty of its likely impact in terms of its precise application and timing of introduction (examples include patents, conference abstracts and, perhaps, pharmaceutical & biotechnology companies), and

b) very clear and precise information of a specific technology but relatively late warning, i.e. shortly before introduction of the new health care technology. (Examples include key medical journals, newsletters & bulletins from other HTA agencies and FDA licensing).

The following two information sources were suggested from all four of the methods: key pharmaceutical journals and experts. In addition, 'specialist' medical journals, key medical journals, FDA licensing applications, conferences and liaison with pharmaceutical and biotechnology companies were highlighted, with reservations, as being potentially useful, additional information sources.

Therefore, for the purposes of identifying new health care technologies the following approach is recommended, using wherever possible resources which are available on the Internet:

- scanning of 'specialist' medical journals, key medical journals, FDA licensing applications, key pharmaceutical journals and conference abstracts, and liaison with pharmaceutical & biotechnology companies, to produce a database of potential technologies, and
- regular meetings and/or surveys of sentinel groups of expert health professionals in order to review and comment on the technologies identified by the other information sources.

It should be noted that some of the potential sources are changing (for example, HTA agencies and patient special interest groups) and may become capable of playing an increasing role and should be kept under review. Existing and future EWS should instigate systems for prospectively recording the information sources that they use to identify new technologies in order that their accuracy can be assessed at a later date when the value of the output is known.

10.4 OPERATING AN EWS

EWS's for identifying health care technologies should not be concerned with making exhaustive, long-term forecasts but with highlighting new and emerging high-impact technologies that are likely to materialize.

Experience of prioritising, commissioning and disseminating HTA research in the UK suggests that wherever possible the required length of early warning of a new technology is at least three years. The exact form and operation of the EWS (and the sensitivity and specificity, level of detail and timeliness which will be required from the chosen information sources) will ultimately depend upon the health care system of which it is a part and the purposes to which the EWS are to be applied. Important aspects of the operation of an EWS are:

- continuity, so that the important monitoring function of an EWS can be performed on those technologies which have a long development phase;
- that only a relatively small core staffing is required as long as there is access to experts either through formal committee structures or regular surveys and/or focus meetings;
- the need for collaboration with existing national and international programmes (for example, in the UK collaboration with regional DIS, SERNIP, SMAC-CMP, NSCAG and NICE) with the aim of ensuring adequate coverage of all types of technologies and providing sufficient early warning; and
- that the EWS should be part of a national programme to allow HTA research to be commissioned or run in parallel alongside early clinical trials.

10.5 VALUE OF AN EWS

The rationale for HTA in the UK, whatever the research technique adopted, is to maximise benefits to patients and to minimise costs to the NHS by determining which new technologies are clinically and cost-effective. Implicit in these objectives is the need for HTAs to be performed at the appropriate time in the technology's life-cycle. Early warning can provide an important lead in identifying new technologies for nationally controlled introduction[62]. In some, although not all, cases earlier identification of technologies could ensure that initial cost-effectiveness research took place prior to marketing and introduction into the NHS.

The main context of this thesis has been to examine the operation and likely value of an EWS for HTA purposes. However, the case-studies and synthesis chapter have shown that there are many other uses to which an EWS can be applied other than helping set priorities for HTA research. The most significant benefit of an EWS may be to help to establish what type of research or policy response at a national level is required, if any, for a limited number of important technologies. Thereafter, a combination of local circumstances and local interests may be left to determine the extent of commissioner and provider involvement in the introduction of new technologies.

10.6 FINAL THOUGHTS

Timely research-based evidence is the only rational way to establish the appropriateness of uptake of any health care technology. In order to facilitate such research, this thesis provides recommendations on information sources for identifying new health care technologies and on ways of operating an EWS. As only a few technologies will be subject to national evaluation and guidelines through NICE, it will be important to select those technologies from whose controlled introduction the NHS is most likely to benefit.

Further work is required to determine the best methods for accessing expert opinion and for selecting experts to contribute to an EWS. It will also be important to establish the ideal length of early warning for different potential audiences of an EWS, such as national policy-makers, clinicians and managers. Finally, the thesis indicates the likely value of an EWS and has suggested ways of increasing that value in the context of recent policy developments in the UK. The next step is to prospectively examine how the outputs and information from an EWS might best be used to inform and influence health care professionals behaviour, a task which is central to the establishment of NICE in the UK.

APPENDIX 1

KEY CONCEPTS

This appendix describes in more detail the following key concepts which are central to the subject of this thesis and which were briefly defined in chapter 3:

- technology, health care technology, and new health care technologies;
- futures and futurology (including an introduction to delphi studies, technology forecasting and bibliographic details of examples of health futures studies and texts);
- innovation and diffusion; and
- early warning systems.

Technology, health care technology and new health care technologies

Technology, health care technology

Technology has been defined as the 'systematic application of scientific or other organized knowledge to practical tasks'[361] or as 'human knowledge applied in production'[86]. A health care technology can be described in terms of its (1) physical nature and (2) purpose or application:

Table 29 *Descriptions of health care technologies can be by their physical nature or according to their purpose*

Physical nature	Purpose or application
Drugs	Prevention
Devices	Screening
Medical and surgical procedures	Diagnosis
Support systems	Treatment
Organisational and administrative systems	Rehabilitation

For the purposes of this thesis health care technologies have been described and classified in terms of their physical nature, as such a categorisation equates more closely to a technology's origin, development and adoption. In the 1970s, the US Office of Technology Assessment (OTA) defined 'medical technology' as 'drugs, devices, and medical and surgical procedures used in medical care and the organisational and supportive systems within which such care is provided'[362]. Another early broad definition of medical technology was 'the equipment, devices, drugs and procedures employed in the care of patients . . . including capital and human investment'[363]. Similarly, Stocking defines 'health care technology' as 'the drugs, equipment and procedures, used singly or in combination, and the health care support systems in which they operate'[55]. However, as Comroe and Dripps[309] pointed out most technologies are complex: that is they bring together

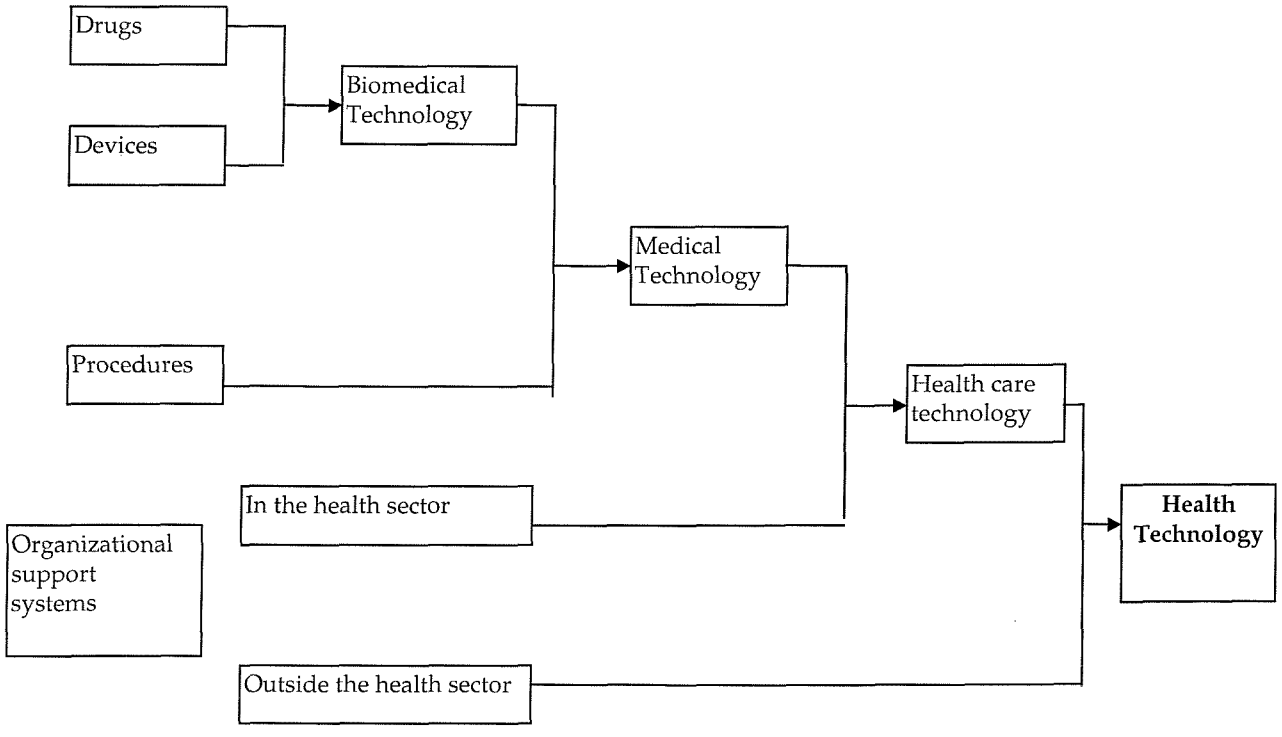
elements of 'hardware' (instruments, drugs) with a 'software' component (clinical knowledge and expertise gained through general training plus training specific to the application[25]).

The terms 'biomedical', 'medical', 'health care' and 'health technology' are all used in the literature, sometimes interchangeably and without definition. Within the context of the UK's NHS R & D programme 'health technology' covers pervasive, lower cost technologies as well as high-profile technologies. The reasons for adopting this broad definition are that[1]:

- different forms of technology are to a certain extent interchangeable over time;
- machines are so strongly intertwined with other aspects of health care (e.g. manpower, buildings and organisational systems) that the evaluation of machines alone would be of little interest; and
- using a broad definition emphasises the importance of not only evaluating machines, but that it is also important to evaluate what physicians and other health care providers do.

Liaropoulos[364] has provided a useful schematic representation of the different definitions of these terms (see figure 27). In this thesis the focus is on 'health care technology' (defined by Liaropoulos as representing drugs, devices, procedures and organizational support systems in the health care system) and that is the term used throughout:

Figure 27 Alternative definitions of technology in health by Liaropoulos



[Source: Liaropoulous L. Do we need 'care' in technology assessment in health care? *Int J Technol Assess Health Care*, 1997, 13(1): 125-127]

New health care technologies

Banta and Luce[57] suggested that the life cycle of a technology consist of five stages:

- future (not yet developed);
- emerging (prior to adoption);
- new (in the phase of adoption);
- accepted (in general use);
- and obsolete (should be taken out of use).

Similarly, Szczepura[365] defined 'new' technologies as those that had recently been introduced. The UK's existing EWS uses the following threefold classification:

Figure 28 Classification of 'new' technologies used by existing EWS in the UK

Emerging or new	Prior to launch or marketing, or within 6 months of launch or marketing, or localised to a few centres
Old	More than 6 months post launch
Old with new indication	More than 6 months post launch, but a new indication for use

The DH, in a document outlining the proposed SERNIP of the Medical Royal Colleges, defined a new interventional procedure as an 'invasive procedure which a clinician has read about, or has heard about, or has piloted (following Local Ethics Research Committee approval), but for which either the safety or the efficacy of the intervention has not been established. It does not include minor modifications of existing procedures where the safety and efficacy are not in question'. Rosen suggests that 'new' technologies can be distinguished from 'established' technologies by the following features[7]:

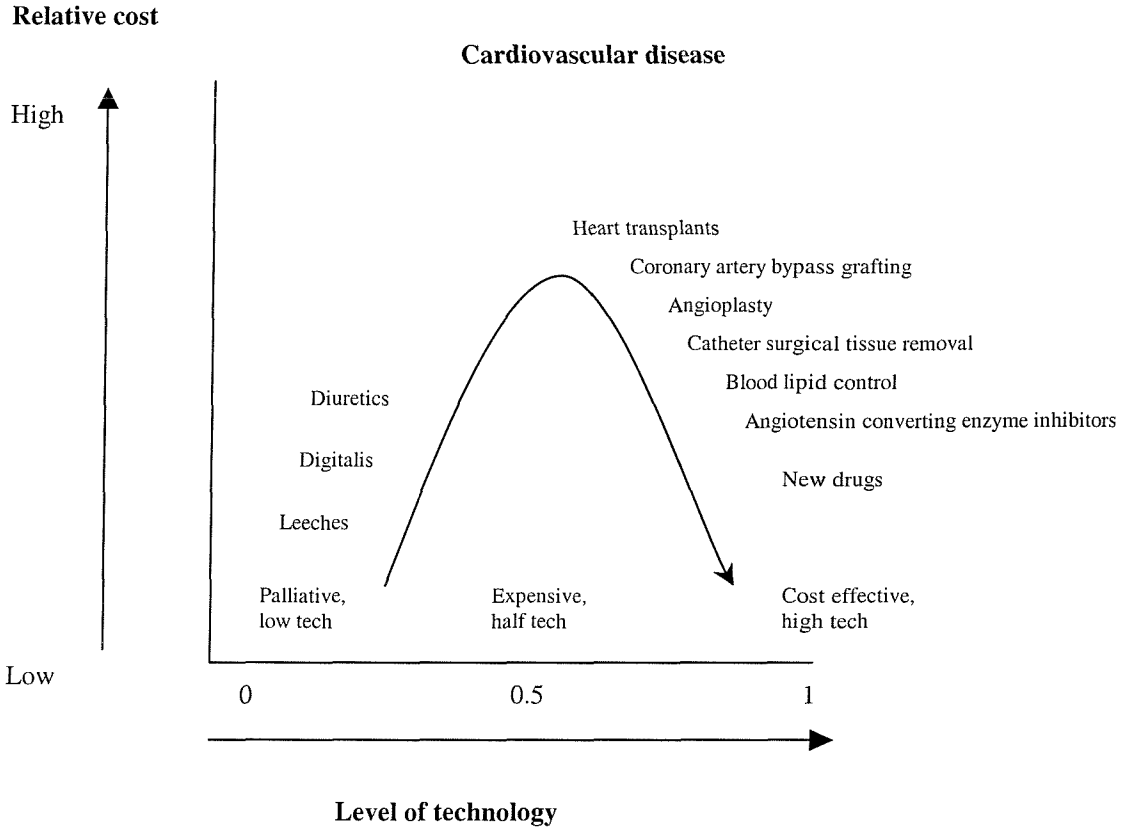
- equipment and techniques which have been available for clinical use for only a short time (although there is no clear time cut-off) and which are associated with a high degree of uncertainty about effectiveness (e.g. PET scanning)
- technologies which are still evolving when they are introduced into clinical practice, so that users will be both developing their skills, and modifying their applications (e.g. key hole surgery)
- finally, and most importantly, a strong body of evaluative research is unlikely to be available for decision makers.

However, there are difficulties in trying to establish clear criteria with which to define technologies at differing stages of their development. For devices, therapies and organisation changes it is difficult to determine whether technologies are new or emerging if they are marketed

before identification or are adopted but remaining localised to a few centres. For example, how many centres must adopt a technology and how diffuse must its adoption be before a new technology is not 'new' any more? Similarly, how do you classify a technology that is established in one area, seems effective but is not used elsewhere? In summary, there is no definitive, or quantitative, definition on a 'new' technology, but there is a general consensus that new health care technologies will have only recently been introduced to the NHS and not yet fully evaluated in terms of their effectiveness

Finally, figure 29 illustrates, using the example of cardiovascular disease, the range of technologies that are under consideration in this thesis and how different levels of new technologies might impact on the costs and cost-effectiveness of health care services[366]:

Figure 29 Different levels of technology used to treat cardiovascular disease



[Source: Pinto FJ. New paradigms for health care. In: *The economics of health care: challenges for the nineties.* London: Medeq, 1990: 17]

Futures and futurology

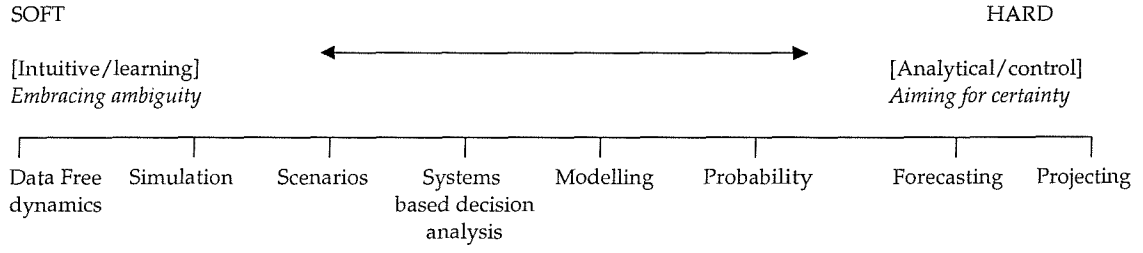
Futures studies

Garrett[130] classifies futures studies according to whether they are:

- quantitative, objective studies done by professionals, based on computer models and expert opinion, focused on economics, technology, and environment at the global or national level; or
- qualitative, normative studies done by 'lay' groups with a facilitator, using visioning workshops and citizen participation, focused on personal and social change in communities and organizations.

Thus, the basic methods employed in futures studies range from analyzing and soliciting opinion, to projecting and optimizing as illustrated below:

Figure 30 A spectrum of futures methodologies



[Source: Nicholson D, Hadridge P, Royston G. Some practical hints for newcomers to health futures. *Futures*, 1995, 27 (9/10):] 1059-65

Bezold[21] suggests that health futures will continue to focus on trends and forecasting the development of such areas as treatment breakthroughs, information and expert systems, mapping the human genome and its consequences, nanotechnology, privacy, ethics and health care expenditures and priorities, but the field is still immature. However, it will grow in importance as health care spending remains at 6-18% of the GNPs of developed countries.

Futurology

In the 1990s the World Futures Studies Federation and the World Future Society have hosted regular conferences on futures-related topics and serve as networks for futurists all over the world. *'Futures', 'Futures Research Quarterly', 'Futuribles', 'Technological Forecasting and Social Change'*, and other professional journals provide a forum in which ideas can be presented and criticised[21]. A European Symposium on Health Futures, organised by the Kings Fund, took place in London in November 1997. It aimed to provide an opportunity to "discuss, debate and learn about a range of 'Futures' techniques used to promote decision-making that is creative, flexible, values based and focused on the many factors and trends driving change in health systems in the

21st century". The Symposium was more concerned with futures methodologies at the 'softer' end of the spectrum, such as scenario analysis and simulation, rather than the more analytical approaches required by a HTA programme.

There are a number of useful world wide web sites which provide an introduction to ongoing futures research and commonly employed futures techniques:

- OECD International Futures Programme (http://www.oecd.org/sge/au)
- World Future Society (http://www.tmn.com/wfs)
- Institute for Alternative Futures (http://www.altfutures.com)
- World Future Studies Federation (http://www.fbs.qut.edu.au/wfsf/)
- Resources for futures research (http://www.well.com/user/leeshupp/future.html)
- Futures techniques (http://ag.arizona/edu/futures/fut/semtech)
- Foresight research centre (http://www.dur.ac.uk/foresight)

Delphi studies

Delphi studies involving experts have been adopted by previous initiatives and can realise savings in time and expense, recording opinions in a structured, systematic and quantitative fashion. In addition, one of their most important attributes is that the surveys are completed privately by individuals and so the opinions that are recorded are not biased towards those of the most vocal or influential experts. However, there are a number of methodological problems with this approach[367], many of which were identified by the respondents to the Delphi study in chapter 7 and have also been highlighted by the Office of Science and Technology's Technology Foresight programme[144] (which adopted the technique). Problems include:

- the way in which topics are often presented as terse statements; in areas where there are many divergent and complex trends the interpretation of results can become difficult,
- the selection of experts and the relative weighting of experts' opinions (as responses do not always indicate the knowledge or assumptions on which the opinion is based),
- the complexities of questionnaire design; and
- that there is no guarantee that the achieved consensus is the 'correct' answer.

Other approaches to utilizing expert opinions have also been suggested but these have also recognised the potential for experts to make incorrect forecasts. Treasure points out that even the best informed commentator in 1948 might have predicted that mitral stenosis would fade out and thoracolumbar sympathectomy for hypertension would become widespread[88]. As Spilker suggests, albeit with a longer term perspective, most of the guesses and predictions of future

revolutionary changes in medicine currently discussed in both professional and lay literature will turn out to be wrong[102].

Technology Forecasting

One form of futures study which often adopts similar methods as might an EWS for HTA purposes, albeit with a longer timescale in mind, is 'technology forecasting', sometimes known as 'foresight analysis'. This area is a subsystem of technology assessment and futures research; it is an attempt to consider possible future relations between science and technology and the needs of society and industry. Poole-Wilson highlights that the results of these studies are merely the consensual expression of expert opinions on the direction of the future[368]. These studies are often undertaken at a national level and involve the systematic investigation into the future development and application of technologies. Studies have a time horizon of 5-10 years or longer and are limited in the scope of the object of the study. This forecasting emerged in the 1960s in the US and in Japan. The Delphi technique has been used by Japan's National Institute of Science and Technology Policy which explores, every 5 years, the direction of technological growth in the long term (up to 30 years)), and has also been adopted by Germany and the Netherlands. Technology foresight exercises have also been conducted in France and Australia and by the European Commission. The US relies on review committees. The Health & Life Sciences panel in the UK OST Foresight exercise recommended greater effort and investment in:

Table 30 Key recommendations of Health & Life Sciences panel in the UK: areas requiring greater effort and investment

Area	Comments
Infrastructure for exploitation & development	Economic success in the expanding life sciences sector needs close links between industry, health services, & a strong research base in the life sciences & clinical medicine
'Integrative biology'	Research programmes which integrate molecular biology and genetics with cell and tissue biology, and whole organism studies
Neuroscience & the cognitive sciences	Research into progressive degenerative disease and non-specific age-related decline
Aging	Basic research into aging and disabling degenerative disease, coupled with technologies for sustaining reasonable quality of life for the elderly infirm
Genetics in risk evaluation & management	Understanding how genetic information can be applied to preventing and treating common multi-factorial disease
Drug creation & delivery	Building the molecular, chemical, and biological expertise that will support new classes of therapeutic agents
Advanced recombinant technology	Research into key metabolic pathways, metabolic engineering, and applications in the biological manufacture of industrial products
Diagnostic applications of molecular biology	Applying research into disease at the genetic, molecular and cellular levels to develop new generations of diagnostics
'Immune manipulation'	Research into the control of the immune system, & applications in specific interventions in inflammatory & immune disease, vaccines, transplants & other areas
Medical information technology	Innovative ways of using information and communication systems to inform and support clinical decisions, and medical practice in general

The following references provide a general introduction to futures methods and studies, and include examples of futures studies which have used Delphi methods or scenario analysis to inform discussion regarding the long-term development of health care and health care.

Table 31 Examples of futures studies and introductory texts to the discipline

First Author	Title	Source
Amara R	Futuring in health care	Health Care Strategic Management, 1985, 3: 26-29
Bezold C	Health care: Thinking ahead	World Health Forum, 1994, 15(2): 189-192
Bezold C	Scenarios for 21st-century health care in the US of America: perspectives on time and change	World Health Statistics Quarterly, 1994, 47(3-4): 126-139
Bezold C	The future of health futures	Futures, 1995, **27** (9/10): 921-5
Corlin RF	The future of medicine. A scenario analysis	JAMA, 1987, 258: 80-85
Driver JF	Forecasting without historical data: Bayesian probability models utilizing expert opinions	Journal of Medical System
Fenton TR	Assessment of artificial neural networks in health futures research	World Health Statistics Quarterly, 1994, 47(3-4): 177-184
Friesdorf W	Events which will influence intensive care units in the future. A Delphi study.	Technology & Health Care, 1997, 5(4): 319-30
Garrett	A way through the maze. What futurists do and how they do it.	Futures, 1993, 254-74
Garrett MJ	An introduction to national futures studies for policymakers in the health sector.	World Health Statistics Quarterly, 1994, 47(3-4): 101-17
Genugten ML	Scenario development and costing in health care: methodological accomplishments and practical guidelines	Utrecht; International Books, 1996
Leufkens H	Scenario analysis of the future of medicines	BMJ, 1994, 29: 309: 1137-40
Levine A	A model for health projections using knowledgeable informants	World Health Statistics Quarterly, 1984, 37: 306-17
Linstone HA	The Linstone lectures on technology forecasting and assessment 1. technology-forecasting 2. robotics 3. technology assessment, risk analysis and the multiple perspectives concept	Journal of Scientific & Industrial Research, 1987, 46: 1-19
Ono R	Assessing the validity of the Delphi technique	Futures, 1994,26(3): 289-304
Pollock AM	The future of health care in the United Kingdom	BMJ, 1993, 306: 1703-4
Preble JF	Future forecasting with LEAP	Long Range Planning, 1982, 15: 64-69
Ronning PL	Anticipating the future using life-cycle analysis	Hospital Technology Series, 1996, 15: 6-9
Sapirie S	What does 'health futures' mean to WHO and the world?	World Health Statistics Quarterly, 1994, 47(3-4): 98-100
Smith R	The future of health care systems	BMJ, 1997, 314:1495-6
Starkweather DB	Delphi forecasting of health care organisation	Inquiry, 1975, 12: 37-46
Wissema	Trends in technological forecasting	R & D Management, 1982, 12: 27-36
Zentner RD	Scenarios, past, present and future	Long Range Planning, 1982, 15: 12-20
Zimmerman S	Forecasting and its importance to health managers in the ever-changing health care industry	Hospital Cost Management & Accounting, 1996, 7: 1-8
Wyke A	21st-century miracle medicine. RoboSurgery, wonder cures, and the quest for immortality	New York; Plenum, 1997

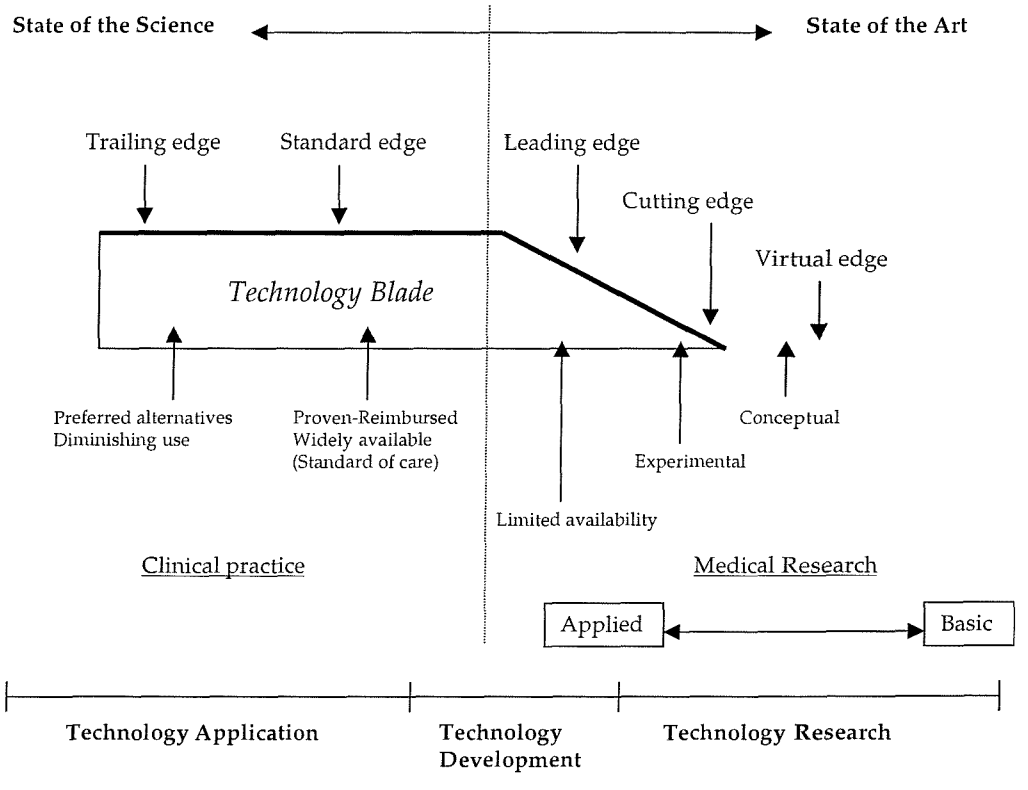
Innovation and diffusion

'Innovation' and 'diffusion' are key concepts in any attempt to establish early warning or 'horizon scanning' activities. Prior to determining the best sources for identifying new health care technologies it is necessary to have an understanding of the development and introduction of technologies into the NHS. Such an understanding enables the context for the identification and monitoring of new health care technologies to be established. There is a vast literature on the innovation and diffusion of technology, and so only the underlying themes are briefly referred to here.

Innovation

A useful distinction within the concept of innovation is between 'local' and 'global' innovation[369]. Global innovation being the first occurrence in an economy (or health care system) of a particular event, say the launching of a new product, whilst local innovation would be the first occurrence of an event in the unit of observation (a health authority or hospital). For the purposes of establishing an EWS in the UK the main focus of this thesis is on the broader definition of global innovation. Figure 31 illustrates the interface between innovation and diffusion:

Figure 31 The technology spectrum: the five stages of technology positioning

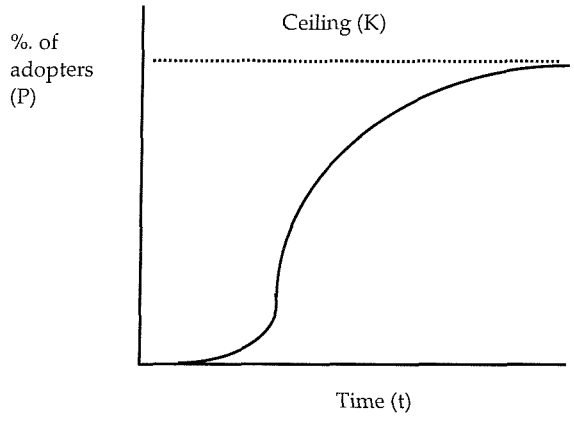


Source: Mikhail O, Swint JM, Brinker MR et al. Technology evolution. The technology spectrum and its application to orthopaedic technologies. *Int J Technol Assess health Care*, 1999, **15**(1): 254-263

Diffusion

Diffusion theory attempts to deal both with the factors that influence the demand for innovations or new technologies and the elements of the supply of such technologies that might influence their rate and pattern of spread. Rosenberg suggests that the diffusion of new technologies is an essentially economic phenomenon, the timing of which can be largely explained by expected profits and that supply side issues could be used to explain two characteristics of the diffusion process: its apparent overall slowness on the one hand and the wide variations in the rates of acceptance of different inventions, on the other[370]. Most discussions of diffusion share the conclusion that it is a process best represented by an S-shaped curve[25,27,371]:

Figure 32 The conventional diffusion of innovation curve: the S-shaped curve



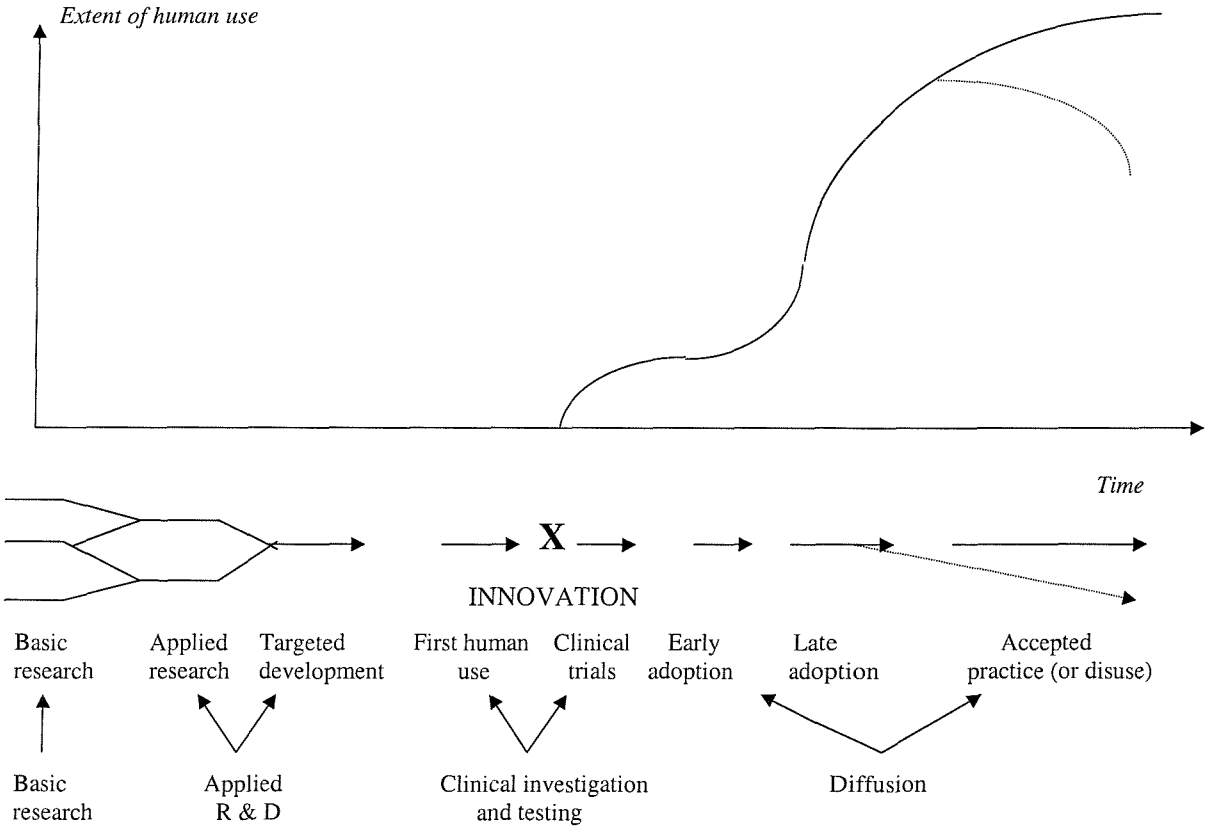
[Source: Warner KE. The need for some innovative concepts of innovation: an examination of research on the diffusion of innovations. *Policy Sciences*, 1974, 5: 433-51 1975]

As figure 32 shows, in S-shaped diffusion the spread of adoption is gradual at first but it picks up speed as positive experience diminishes both uncertainty about the value of the innovation and ignorance about how to use it efficiently. This slow phase has also been interpreted as reflecting problems of communication of information as well as caution on the part of users[1]. Eventually the trajectory of adoption begins to level off, as fewer and fewer individuals remain who have not yet adopted the innovation. It is important to note that the actual adoption of a technology by users constitutes only the beginning of an often prolonged process of diffusion in which important redesigning takes place, exploiting the feedback of new information generated by those users. Consequently, as forecasts about the number and characteristics of potential adopters are, implicitly, forecasts about the development of technology as well as about prices and incomes, they are notoriously unreliable. As Kaluzny noted, 'There is a need for caution in making generalisations about the health system based on innovation studies in other areas'[371]. However, Russell[372] suggests that the logistic function (or S-shaped curve) describes the diffusion of hospital innovations as well as it does the diffusion of innovations in other industries. Although there are

some case studies of technologies that show the S-shaped diffusion pattern quite well, the actual processes at work are more complex.

However, it is important to note that the diffusion of an innovation is only one stage in the process of technological change that covers the wide range of interacting events by which a technology evolves over time[27]. Figure 33 shows how the diffusion of a medical technology relates to the various stages of it's development and adoption, as well as the timing of the various stages of research. Clearly, an innovations may go through a series of false starts before it reaches a definable and, in many cases, marketable product. Once the innovation is in prototype form it has to be adopted by some of the key people in the relevant professional groups.

Figure 33 Stages in the development and diffusion of medical technologies



[Source: Office of Technology Assessment. *Development of Medical Technology: Opportunities for Assessment.* Washington, DC; Government Printing Office, 1976]

Greer[100] introduces the differentiation between 'formed' (complete) and 'dynamic' (still developing) technologies. She suggests that if medical technologies were retained in research laboratories until fully developed or 'formed' the assumptions of classical diffusion theory might be met. However, for technologies which develop as they diffuse, in a dynamic manner, a different pattern occurred. Here, dynamic medical technologies arrive in local medical communities through individual innovators, are promoted by idea champions and, as the

characteristics of the technologies and their results become observable, are then assessed by local opinion leaders.

These models and analytical approaches only provide the underlying skeleton of diffusion theory and there is much more to understand about how technologies actually diffuse, particularly in the case of health care technologies where the innovation may require the commitment of a number of people from different professional backgrounds and where adopters are part of large complex systems and organisations.

Early warning systems

There are four main stages to any HTA system: identification, testing, synthesis and dissemination[325]. The first of these stages, 'identification', comprises three tasks: firstly, monitoring new and emerging (as well as established) technologies; secondly, selecting from the identified technologies those in need of study, and finally deciding or prioritising which technologies to actually study. It is the first of these stages, the monitoring of new and emerging health care technologies, with which EWS are most often concerned. EWS can also help to select and prioritise those technologies in need of study.

The European Workshop in Copenhagen[127] defined an EWS as a mechanism for identifying emerging medical technologies (drugs, devices and procedures) of importance to a health service, and for disseminating this information with or without assessment of the technology's potential effects and consequences. Such mechanisms allow communication between on the one hand scientists and technological experts, and on the other policy makers and planners, usually in an open communication, and it can encourage public participation in monitoring important technological changes in the health services.

APPENDIX 2

DATABASES

The following electronic databases were searched as part of the systematic review to identify all articles, books and 'grey' literature related to health futures and forecasting (the search strategies and number of references retrieved are detailed in chapter 6):

MedLine: the National Library of Medicine's bibliographic database covers the international literature on biomedicine, including the allied health fields and the biological and physical sciences, the humanities, and information science as they relate to medicine and health care. Information is indexed from approximately 3700 journals world-wide. The searches used cover the period 1966 to the present.

HealthSTAR: HealthSTAR contains citations to the published literature on health services, technology, administration and research. It is focused on both the clinical and non-clinical aspects of health care delivery. The database contains citations and abstracts when available to journal articles, monographs, technical reports, meeting abstracts and papers, book chapters, government documents and newspaper articles from 1975 to the present.

ECRI's Health Technology Assessment Information Service (HTAIS) database: bibliographic information and abstracts on drug therapies, devices and procedures from research undertaken by ECRI, government agencies, academic centres, manufacturers, health care providers and many other world-wide sources. This is the first database of its kind and encompasses both peer-reviewed and 'grey' literature.

APPENDIX 3

DELPHI STUDY QUESTIONNAIRES

Stage 1

Stage 2

Stage 3

Sheet 1

Possible primary information sources for identifying new and emerging health care technologies:

As a baseline, the following give an indication of the types of sources which may be considered.

Please nominate any others or add comments/elucidate on those listed.

Comments might include whether you have had personal experience of using the source before in trying to identify new healthcare technologies and whether you feel is is a 'good' source (for all types of healthcare technology or for a specific type of technology), and any advantages/disadvantages of using the source. These comments do not need to be very detailed but sufficient to enable us to gain some understanding of the extent to which each of the sources has been used in the past and what you feel about their value in identifying new healthcare technologies.

Sources	Comments
The principal medical journals (i.e. British Medical Journal, New England Journal of Medicine, The Lancet, Journal of the American Medical Association)	
Key pharmaceutical journals (i.e. PharmaProjects, Scrip, InPharma)	
Key scientific journals (i.e. New Scientist, Nature)	
The financial press and press cuttings generally	
Patent literature	
Pharmaceutical companies	
Private healthcare providers (e.g. BUPA)	
Biotechnology companies	

Sheet 1

Medical engineering companies	
Sentinel groups of expert health professionals (e.g. postal survey of 'experts' in specific fields)	
Patient special interest groups	
Conference/meeting abstracts	
The results of other countries' horizon scanning exercises (e.g. the Netherlands)	

New suggestions:

Sources	Comments

Sheet 2

Assessment criteria for evaluating possible information sources:

The following represent a baseline set of criteria for evaluating potential information sources for identifying new healthcare technologies to be developed.

Please nominate any others (on the next page) and grade all the criteria (5 = essential; 0 = useless) which should be used when evaluating potential information sources. Any comments which you would like to make can be added in the 'comments' column

We have tried to provide brief explanations for each of the criteria that we have thought of to date.

Criteria	Grade	Comments
Coverage (i.e. sensitivity). Will the source identify all of the most important new technologies?		
'Hit rate' (i.e. specificity) Will the source identify a large number of false-positive technologies (i.e. incorrectly predicting a large impact)		
Objectiveness. Is the source objective in its assessment of what are likely to be important new healthcare technologies?		
Time efficiency; (i.e. how regularly do sources have to be accessed?) Would searching/monitoring these sources be heavily labour intensive?		
Correlation with other sources (i.e. robustness) Would it be possible to check the accuracy of this source against other sources?		
Elucidation of likely 'knock-on' effects. Does the source consider the implications of the introduction of new technology? (Helpful for considering likely impact of new technology)		
'Depth' of source (i.e. level of detail). Does the source provide a sufficient level of detail on the technology for it to be precisely identified and for its likely impact to be predicted?		
Explicitness of limitations. Does the source acknowledge the limitations of its 'early warning' capability?		

Sheet 2

Timeliness. Any of the sources, in order to be useful, will need to provide sufficient 'warning' (not necessarily early but appropriate), of new technologies, to enable evaluations to be carried out before their widespread diffusion		

Other criteria:

Criteria	Grade/comments

Sheet 3

Typology of technologies

There is a need for a typology of technologies for which one is 'horizon scanning' as different types of technologies will, presumably, require different primary information sources. For the purposes of this study we propose using the following typology of healthcare technologies:

- drugs
- diagnostic devices
- procedures/procedural devices
- health care settings
- information technology

Please comment/add further types to this list.

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Next step

The next communication will comprise a questionnaire by which each of the sources identified (sheet 1) will be ranked according to the criteria identified (sheet 2) for each of the types (currently five) of healthcare technology.

However, your collective answers may well alter how we are currently thinking about the sources, the criteria and the typologies. So please let us know your views!

This pro forma has been designed to answer: which primary sources are best able to give us relevant and timely information on eight particular types of healthcare technology? Please insert the most appropriate number(s) from sheet 1 into each box on this sheet which you feel reasonably happy to answer. Think of a lead time of 5 years before the initial adoption of the new/emerging health care technologies into a health service.

	Information required (nominate which source(s) is/are the best for each piece of information required for each type of technology)				
Type of technology	Indication of time to technology being used by health services ('when?')	Clarity about likely patient group to benefit from technology ('for whom?')	Information on unit costs of technology ('how much?')	Indication of probability of effectiveness of technology ('how good?')	Level of information re. potential displacement effects of adopting technology ('in place of what?')
A. Drugs/medicines					
B. Diagnostic strategies (including diagnostic devices, & population screening)					
C. Procedures (e.g. angioplasty)					
D. Procedural devices (e.g. coronary stents)					
E. Other medical & assistive devices (e.g. rehabilitation aids)					
F. Healthcare settings/treatment delivery systems (e.g. hospital at home)					
G. Information Technology (e.g. telemedicine)					
H. New professions (e.g. neonatal nurse practitioners)					

For some of the information required it may be that more than one source is useful or it may be that none will; in these cases please indicate all the sources which you think will be helpful or alternatively write 'none' in the appropriate box. If your personal experience of horizon scanning/health technology assessment is limited to specific types of technology then please only complete the rows relevant to those types of technology and put a line through the rest. If you would like to make any additonal comments/explanatory notes, then please do so on reverse of this pro forma.

Results

Analysis of stages 1 and 2 responses

You were most prepared to suggest likely primary information sources for identifying 'pharmaceuticals' and 'diagnostic strategies'; few of you were able to recommend particular sources for 'other medical & assistive devices' and 'new professions'.

The primary information sources which you rated as being the most useful in providing the five pieces of information ('when', 'for whom', 'how much', 'how good', 'in place of what') which are required in order to predict the timing of, and size of, the impact for each type of healthcare technology were as follow:

- *Drugs:* pharmaceutical & biotechnology companies; key pharmaceutical journals; principal medical journals
- *Diagnostic strategies:* specialist medical journals; FDA licensing applications in the USA; principal medical journals; pharmaceutical & biotechnology companies; newsletters & bulletins from other national & regional HTA agencies
- *Procedures:* specialist medical journals; principal medical journals
- *Procedural devices:* medical engineering companies; specialist medical journals; principal medical journals; conference and meeting abstracts
- *Other medical & assistive devices:* specialist medical journals; newsletters and bulletins from other national and regional HTA agencies
- *Healthcare settings/treatment delivery systems:* sentinel groups of expert health professionals; patient special interest groups; private healthcare providers; conference and meeting abstracts; principal medical journals
- *Information technology:* the Internet; newsletters and bulletins from other national & regional HTA agencies; private healthcare providers; specialist medical journals
- *New professions:* conference and meeting abstracts; private healthcare providers; sentinel groups of expert health professionals

Your responses (including the open comments received from some of the you to date) suggested eight what we shall term 'first order' information sources which would have to form the basis of any comprehensive early warning system for identifying new healthcare technologies: key pharmaceutical journals, pharmaceutical & biotechnology companies, 'specialist' medical journals, principal medical journals, medical engineering companies, private healthcare providers, newsletters & bulletins from other national & regional HTA agencies, and sentinel groups of expert health professionals.

Figure 1 illustrates which of these three sources were most commonly selected by you across the five pieces of information for each type of healthcare technology[1].

Please would you comment on these results. On reflection, do they seem correct?

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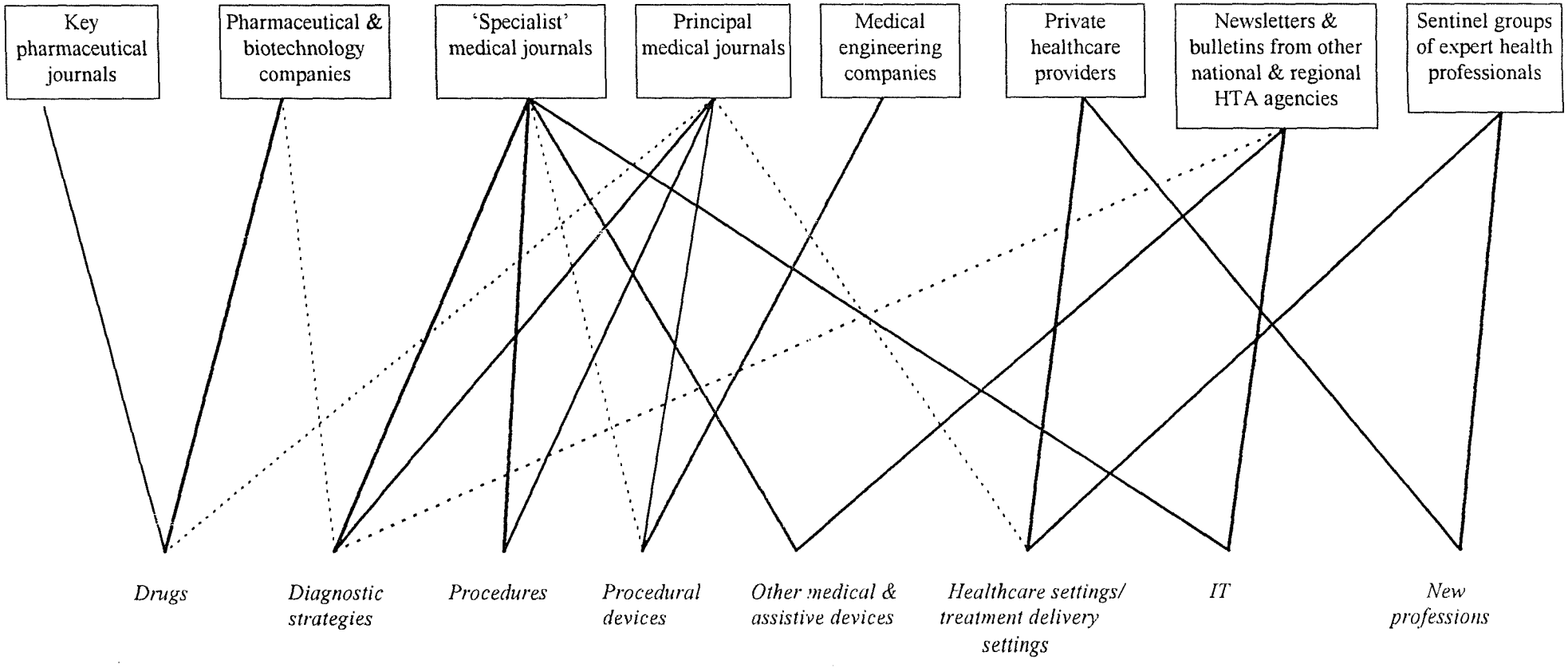
[1] with the exception of 'procedures', 'other medical & assistive devices', 'IT' and 'new professions' where only two sources were commonly mentioned. In the case of 'diagnostic strategies' 'pharmaceutical & biotechnology companies' and 'newsletters & bulletins from other national & regional HTA agencies' are both cited as tertiary sources as they scored an equal number of votes

Figure 1 **Primary, secondary and tertiary information sources for identifying new healthcare technologies (by type of healthcare technology)**



Commentary

Specific comments on stage 2 results

The following are particular issues on which we would like to invite your comments. These are the key issues which have resulted from the survey to date and we are taking this opportunity to share them with all of you as a prompt to aid further clarification and synthesis of views.

1. Use of sentinel groups of expert health professionals

In previously reported early warning systems and other health futures studies sentinel groups of expert health professionals have commonly been used as the main source of information. It is clear from open comments that we have received to date from some of you that this source would have to be, in your view, a key aspect of any early warning system. However, in the stage 2 responses the source was only commonly mentioned in relation to identifying new 'healthcare settings and delivery systems' and 'new professions'.

We would welcome your views as to the value of using such groups. What form should such groups take - focus groups, postal surveys, Delphi studies? On what basis should members of such groups be selected? What incentives should/can be used to ensure that invited experts participate in such exercises? Should expert groups be used as an initial source of information on new healthcare technologies or as a filter for information obtained from other sources or both?

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2. 'Specialist' medical journals

'Specialist' medical journals were recommended by you for identifying new 'diagnostic strategies', 'procedures' and 'other medical and assistive devices'. 'Specialist' medical journals refers to those journals which look at science application in medicine and contain the early case series, case reports and uncontrolled studies which strongly influence early adopters but are too small to make it into the 'big' journals. It is recognised that it will prove difficult to select those technologies which will remain in the research domain and those which will diffuse rapidly and, consequently, there is a possibility of spending too much time on things that in the end are not too significant in health care.

Please suggest journals which you have used previously, or are aware of, which would enable a directory of journals to be developed which would allow the early detection of most new technologies through case-study/case series reports:

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3. Other countries' horizon scanning exercises - scope for collaboration

So far you have not identified the use of the results of other countries' horizon scanning exercises as a particularly useful source of information although some of you had commented that this might be a useful starting point or cross-check. There does seem to be some scope for collaboration as most new healthcare technologies are international in their likely impact and this suggests the possibility of sharing specific tasks between agencies within a group of countries with each specialising in particular areas (e.g. pharmaceuticals) or sources (e.g. medical journals).

Please give your views on the scope for international collaboration with relation to early warning systems for new healthcare technologies.

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4. Processes for extracting, appraising and synthesising information

Having identified new and emerging healthcare technologies, the next step of an early warning system is to assess them in terms of their likelihood of making a significant impact on the healthcare system. The appraisal and synthesis of information will clearly be key in identifying genuine emerging technologies. The processes to be used to extract, appraise and synthesise the information from these sources could influence the selection of the most useful primary information sources and (at least partly) determine their overall importance and the importance of their component characteristics (e.g. sensitivity and specificity).

Who do you believe is best placed to appraise and synthesise information on new healthcare technologies, and on what basis should you highlight important technologies. Details of how such information is appraised and synthesised in other early warning systems would be helpful.

For example, scanning the key medical journals could be carried out by a non-medically qualified researcher simply cataloguing all technologies that are reported as being 'new' or recently introduced. An additional sift could then be carried out by a panel of experts. Alternatively, a more senior and medically-qualified person could carry out this task without recourse to an expert panel.

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5. Source specific comments:

The following are summaries of your comments on the 'first order' primary information sources for identifying new healthcare technologies. The summaries are presented in order to share all of the your views amongst the group. Any comments you would like to make are welcomed.

Principal medical journals

- useful to identify technologies now emerging but less so for identifying potential technologies to emerge within 5 years from now.
- good sources, broad coverage, will not cover all 'new' technology, but often give clues to imminent clinical use.
- should have 'pulled' it before it is in mainstream journals.
- important as an indicator of what is already happening; not very useful as a warning of what is over the horizon
- news sections (e.g. in BMJ, Lancet) may alert us to some developments in areas of highly prevalent or very serious disease but the early studies which strongly influence the use of new technologies by mavericks will be too small and poorly designed to merit publication in these ivy-league journals.
- tendency to consolidate rather than lead except for major megatrials.
- very labour intensive to hand scan but can be useful. Mostly for information on new uses of technologies which are already on the market.
- mainly look backwards and 'evaluate' already established technology
- reasonably good source but often too far removed from identifying practical emerging technologies and when they do, the woods are often obscured by the trees
- need to look at case reports etc. rather than completed studies. For example, in drugs we need phase II studies not phase III which would be too late
- individual journals a bit 'hit or miss' - need to scan several systematically
- these are valuable, especially medical progress in New England Journal of Medicine
- leaders can facilitate rapid review. Specialist journals can give earlier warning
- a secondary source yielding data in a very unsystematic way
- good but tend to give late warning of important technologies
- good in identifying areas; less good for technological detail

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Pharmaceutical & biotechnology companies

- barely release news before actual marketing which might be too late for health planning.
- problems with extent of disclosure but probably useful.
- press releases of early trials are a valuable source especially when they describe North American licensing applications
- probably useful, difficult to select best info'
- quite good if you can access some of their strategy seminars
- these (biotechnology companies) tend to hype their projects and so have not found them reliable
- hold good data but will wish to manage its use
- (biotechnology companies) earlier lead as many bio-tech innovations are sold onto pharmaceutical companies for development
- problem of confidentiality/secrecy
- good source but industrial secrecy prior to patent limits openess
- (biotechnology companies) potentially good source but low strike rate
- annual reports can be useful and reliable
- highly unreliable; influenced by need to maintain stockmarket value
- officially not forthcoming with commercially sensitive information
- unhelpful. Companies unwilling to declare their hands at an early stage of development

- in their field biotechnology companies are more forthcoming about future plans than 'conventional' pharmaceutical companies. Potentially useful

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Medical engineering companies

- barely release news before actual marketing which might be too late for health planning
- these tend to be highly focused and are able to give information - useful - on a limited area

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Key scientific journals

- covers things at research stage, remote from clinical use.
- often difficult to get a sense of timescale and imminence.
- long lead time before applications

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Sentinel groups of expert health professionals (e.g. postal survey of 'experts' in specific fields)

- a potential source, absolutely. My experience is, however, that it is hard to find incentives to make them participate.
- this has promise, was proposed in Australia but never got funded. Would need to be more interactive than just a postal survey
- would need to be more interactive than just a postal survey.
- good source for early notice; less good for views on usefulness.
- utility will depend on quality of question preparation, 'live interaction groups' are most productive; postal survey not the best method.
- some version of expert group consultation is most likely to access the new. Brief two round Delphi's might be a suitable mechanism.
- could filter data from a range of sources
- very important. They will pick up info from conferences where most early work on new technologies is disseminated
- excellent source
- gives a distribution rather than a focus
- could work but not postal survey
- potentially very powerful (though not necessarily via postal survey). Role in filtering/synthesising info.
- useful in theory but the best ones (experts) likely not to have time to respond

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Conference and meeting abstracts

- earlier than journals but how to select?
- quite an important source for first publication of drug information.
- major sifting problem
- difficult to assess systematically.
- only 33% get published; may bear little relation to potential of product
- very important. Volume of papers presented, as well as content
- can be very useful
- sometimes helpful, depends on conf. Discussion at conferences often more productive
- good source, if you can weed the good stuff out from the dross
- important; more so than journals for early notice
- often several months/years ahead of mainstream medical journals

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Specialist medical journals

- give earlier warning than principal medical journals. e.g. could spot the rapid increase in number of papers on excimer laser in ophthalmology journals or on PET scanners in nuclear medicine/cardiology/cancer journals

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Newsletters and bulletins from other national and regional HTA agencies

- high hit rate, short horizon

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Thank you very much for all your assistance. We shall forward a draft of the final report to you in September.

APPENDIX 4

SEARCH STRATEGIES: CASE STUDIES

All searches were carried out on MedLine 1966-98 unless stated. The profile of publications relating to telemedicine were based on the report by Mowatt et al[133].

CT scanners

1 computed tomography in ti.ab.sh (1963-75)

2 TOMOGRAPHY, X-RAY COMPUTED/ (1963-75)

Biosensors

1 BIOSENSORS/ (1963-89)

2 BLOOD GLUCOSE/an & ELECTROCHEMISTRY/is (1963-89)

3 ExacTech in ti.ab.sh (1963-89)

Left ventricular assist devices

1 left ventricular assist devices in ti.ab.sh

Paediatric intensive care units

1 paediatric intensive care units in ti.ab.sh (1989-98)

2 INTENSIVE CARE UNITS/ & PEDIATRICS/ (1963-98)

Beta Interferon

1 INTERFERON-BETA/ & MULTIPLE SCLEROSIS (1992-98)

2 INTERFERON TYPE 1/ & MULTIPLE SCLEROSIS (1983-91)

Dornase alfa

1 CYSTIC FIBROSIS/ & (dornase alfa in ti.ab.sh OR DEOXYRIBONUCLEASE 1/)

Donepezil

1 Donepezil IN ti.ab.sh OR E2020 in ti.ab.sh

Laparoscopic cholecystectomy

1 CHOLECYSTECTOMY, LAPAROSCOPIC/ (1963-90)

2 laparoscopic cholecystectomy in ti.ab.sh (1963-90)

APPENDIX 5

QUESTIONNAIRE TO CO-ORDINATORS OF EXISTING OR PLANNED HEALTH TECHNOLOGY ASSESSMENT EWS

Country/region:

Contact (name and telephone number):

1. ESTABLISHMENT OF THE EWS

1.1 Who initiated the establishment of the EWS?

(a) national government
(b) regional government
(c) local initiative
(d) other (specify)

1.2 In what year did/will the EWS become operational?

1.3 Is the EWS for:

(a) national HTA prioritisation
(b) health policy planning
(c) both
(d) other (specify)

1.4 What resources have been (will be) used to establish the EWS?

- in financial terms
- in terms of personnel time (level of staff and commitment, e.g. two part-time researchers; one full-time lecturer etc.)

1.5 What resources does (or do you envisage) the EWS consuming annually?

- in financial terms
- in terms of personnel time (level of staff and commitment, e.g. two part-time researchers; one full-time lecturer etc.)

2. OPERATION OF THE EWS

2.1 Which of the following categories of technologies do you aim to identify through the operation of the EWS (tick more than 1 box if required):

(a) emerging technologies(prior to adoption)
(b) new technologies (in the phase of adoption)
(c) new applications of existing technologies
(d) accepted (in general use)

2.2 If (a) above what 'horizon' are you most interested in?

(a) <1 year before adoption

(b) 1-2 years before adoption

(c) <5 years before adoption

(d) 5-10 years before adoption

(e) >10 years before adoption

2.3 Which written/publicly available information sources do you scan/monitor? (tick more than 1 box if required)

(a) medical journals

(b) scientific journals

(c) pharmaceutical journals/ bulletins

(d) conference/meeting abstracts

(e) others (specify)

2.4 Who does this scanning (level and number/wte of staff)?

2.5 Do you concentrate on any one of the following types of technology in particular?

(a) drugs

(b) devices

(c) procedures & therapies

(d) settings

(e) information technology or

(f) all given equal attention

2.6 Do you currently (or are you planning to) use experts/expert groups?

(a) to identify technologies initially

(b) to check/comment on technologies identified by other sources

(c) both (a) and (b) above

(d) other (specify)

2.7 How do you identify experts?

2.8 What methods do you use to gain views of experts? (tick more than 1 box if required)

(a) postal survey

(b) telephone

(c) face-to-face/1:1 meetings

(d) face-to-face/group meetings

2.9 How many experts do you use/contact?

- as part of the routine operation of the EWS (e.g. how many members of committees specifically established to advise EWS are there?)
- to advise on each specific technology (if do not use formal committee structures)

2.10 How many technologies do you/will you identify each year

(a) in total .....

(b) consider in detail .....

(c) write reports on or prioritise for R & D .....

2.11 What do you do with the results?

- do you categorise the technologies you identify by (tick more than 1 box if required)

(a) type(e.g. drugs/devices)

(b) size of likely impact on

- health

- cost

- planning

(c) time horizon

(d) other form of categorisation

(please specify)

2.12 How do you select technologies for prioritisation/further work?

- who selects?

- what criteria (e.g. size of impact technologies predicted to have)

2.13 Are the results fed in/disseminated to (tick more than 1 box if required)

(a) Research & Development programme

(b) The health service

(c) Other (e.g. industry)

2.14 (if EWS used for HTA prioritisation purposes)

After identification of a technology how long does it take to (give a minimum and maximum time if appropriate):

- prioritise research

- commission research

- disseminate research findings once research is completed

2.15 (if EWS used for informing health policy what does government/health service do with findings)

3. *LESSONS LEARNT*

3.1 What have been the biggest difficulties/barriers to the establishment and operation of an EWS?

3.2 What has worked well and why?

APPENDIX 6

CONTEMPORARY SOURCES FOR EARLY WARNING IN THE UNITED KINGDOM

Forecasting Secretariat to the Standing Group on Health Technology

In May 1995 the Department of Health established a Forecasting Secretariat to the UK's National Standing Group on Health Technology and its panels. The terms of reference for this Forecasting Secretariat were:

a) to develop and operate an agreed mechanism for identifying new and emerging health technologies, as well as existing health technologies which are expanding in their use

b) to develop and operate an approach to single out those health technologies which might have a significant impact on the NHS in the near future

c) to prepare briefings to the SGHT and its panels on those health technologies expected to have a significant impact on the NHS

d) to explore with relevant parts of the Department the value of possible approaches to disseminating information on new, emerging and expanding health technologies to decision-makers in the NHS

In 1995 the Forecasting Secretariat drew up a 'long list' of new and emerging technologies from the following sources:

- journals (scientific, medical and pharmaceutical)
- evidence and analysis from other similar exercises abroad
- conferences
- the work of the 'Changing Medical Practice' group of the Standing Medical Advisory Committee.

In addition, a national survey of all clinical directors, regional and district directors of public health and selected individuals in specialised medical fields in England, Northern Ireland, Scotland, and Wales was conducted[5]. The survey requested information from participants on new and emerging technologies and treatments that are likely to affect the NHS in the next five years. Overall, approximately 3,500 people were invited to participate in the survey. In total 1,100 new or emerging technologies were identified. Information was collated on each of these technologies relating to the:

- timing of their impact;
- size of their impact;

- reason for their impact (benefit, total cost, organisational, rapid diffusion, other);
- how well they have been evaluated to date; and
- a named expert on the technology.

Appendix 7 is a compilation of the forty-eight most frequently mentioned new or emerging technologies that were identified from the above sources as being likely to have an impact on the NHS within the next five years, and sometimes beyond.

Safety & Efficacy Register on New Interventional Procedures (SERNIP)

In 1996 the Department of Health gave its support to a new initiative being led by the Academy of Medical Royal Colleges to establish an 'intelligence centre' for new interventional procedures[a 373].

The Safety and Efficacy Register of New Interventional Procedures (SERNIP) registers new procedures and co-ordinates the experiences of clinicians developing new techniques in order to allow data to be rapidly accessed by other clinicians. This is a voluntary system, designed to support innovation and good professional practice in groups undertaking novel procedures. Information is invited from innovators of new procedures, those considering embarking on techniques learned from other doctors (often abroad) and from manufacturers of new devices. SERNIP was initially open to surgical, gynaecological, radiological and cardiological procedures but it is intended to widen the scope of specialties to include otorhinolaryngology and ophthalmology.

To April 1997 a total of 43 procedures had been considered. Twelve were considered safe and effective, 20 were of unproven safety and efficacy, 10 were still under investigation and 1 (intraoperative autotransfusion (Haemocell 350) IBS) has been proscribed by the committee[b].

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[a] Source: information sheet from Academy of Medical Royal Colleges, June 1996
[b] SERNIP newsletter May 1997

Standing Medical Advisory Committee (SMAC) - Changing Medical Practice (CMP) group

The criteria for technologies to be included in SMAC advice to the Department of Health on 'changing medical practice' are:

Figure 34 Criteria for technologies to be included in SMAC advice to the DH on changing medical practice

1.Categories of change will include:

a. incidence, mortality, regional variations & distribution of disease

b. developments in treatment & symptom control

c. investigative and diagnostic methods

d. methods of service delivery

e. patient expectations and quality of care

2. A change in a technique should normally be included only if in SMAC's view it:

a. is safe and effective

b. has completed research & development and achieved some modest (say 5%) diffusion into the NHS within the last 2-3 years, but not yet been fully diffused (say 75%)

c. will have a substantial incremental effect on the NHS in the next 2-3 years in terms of healthgain or costs or both

d. OR it would reduce clinical activity

3.*Where possible evidence for the effectiveness of, and costs of, the change should be presented or referenced. Implications outside the specialty initiating a change should be indicated (e.g. for GPs)*

4.*Three of the categories of changes listed under paragraph 1 (items b,c and d) may be grouped together under the narrower heading of medical advance. There are potentially hundreds of these each year. The criteria for deciding which ones to review in detail should include:*

- total potential health gain
- net (plus or minus) impact on total HCHS spending over the next four years
- impact on other NHS spending
- the number of people likely to benefit and their prognosis without treatment
- likely speed/ease of diffusion
- medical productivity (i.e. health gain per £ spent)
- impact on other government spending
- impact on economy

Drug Information Services (DIS)

The DIS in the NHS exist to promote the safe, effective and economic use of medicine by providing up-to-date, accurate and evaluated information and advice on drugs and drug therapy. Specialist drug information centres were established in 1969 at the London hospital and Leeds General infirmary. By 1992 there were 20 regional centres providing a range of services[a] [374].

The UK DIS, co-ordinated through the network of regional DIS, has developed a structured approach to providing evaluated and rapid information on new drugs and medicines. The work for this scheme is shared between DIS throughout the UK:

Table 32 Structured approach of the UK Drug Information Services to providing evaluated and rapid infomation on new drugs and medicines

Title	Content	Timing
Stage 1: new drugs in research (list 1)	Early intelligence on all new drugs likely to reach the UK market. Information content is brief as many products may never reach the market and early clinical information is scant. Contains prediction of possible broad cost implications. Approximately 300 drugs are continuously tracked	Continuous tracking up to 5 years before marketing
Stage 2: new drugs in research (list 2)	As stage 1 but restricted to selected drugs (up to 50) which are considered to have greater or closer market potential	Probably 6 months to 3 years pre-marketing
Stage 3: new drugs in clinical development	Comprehensive early intelligence evaluations of all new drugs, formulations and indications which are likely to have a significant impact on either prescribing practice or prescribing costs. Information provides estimates of potential costs, uptake, and place in therapeutics, both in primary and secondary care	Continuous tracking from about 2 years pre-marketing; also uses drug companies as a source of intelligence
Stage 4: new medicines on the market	Comprehensive, in-depth evaluations of most new drugs which are marketed. Currently excludes drugs in highly specialised clinical areas	Drugs identified through stages 1-3 and through product licence notifications

The outputs are cascaded down to local DIS and hence to commissioners of health care and clinicians.

The UK's Drug Information Pharmacists Group (DIPG) and the National Prescribing Centre (NPC) in Liverpool announced in April 1997 that they were to collaborate in a venture to provide

[a] i.e. general enquiry answering; evaluated information on new drugs; formulary support; current awareness bulletins; training in drug information; coordination of DIS

advance information on significant new drugs in development[a]. The initiative will build upon the UK DIS scheme entitled 'New drugs in clinical development' (see table 18 - stage 3). Collaboration between DIPG and the NPC is intended to produce a package of information comprising enhanced content and presentation of the current DIPG monograph. It is intended to identify at the earliest opportunity (up to 18 months before launch) those drugs that could develop into important new medicines for the NHS.

[a] further information on the collaborative venture can be obtained from Mrs Katrina Simister, NPC-DIPG New Product Co-ordinator, DIC, 70 Pembroke Place, Liverpool, L69 3GF, tel: 0151 7948112

APPENDIX 7

NEW HEALTH CARE TECHNOLOGIES IN THE UK

Table 33 New health care technologies in the UK, October 1995 as reported by Stevens et al

Topic	Time	Size	Evaluated?
Magnetic Resonance Imaging (MRI)	Now	Major	Quite well
Minimally invasive surgery (including laparoscopic surgery)	Now	Major	Partially
Drugs for treatment refractory schizophrenia	Now	Moderate	Quite well
Implantable vascular stents	1996-7	Moderate	Partially
Peripheral blood stem cells	Now	Major	Quite well
Picture archiving & communication system	1998-2000	Major	Quite well
Doppler measurement studies	Now	Moderate	Partially
Laser treatment of benign prostatic hyperplasia	Now	Moderate	Partially
Gene therapy advances	1998-2000	Major	Not well
Polymerase Chain Reaction (PCR)	1998-2000	Moderate	Partially
Telemedicine	1998-2000	Moderate	Partially
dornase alfa for cystic fibrosis	1996-7	Moderate	Quite well
Interventional radiology	Now	Major	Quite well
Angioplasty	Now	Major	Partially
Interferon for chronic granulocytic leukemia and hepatitis C infection in haemophilia patients	Now	Moderate	Quite well
Lasers for dermatology	Now	Moderate	Fully
Adjuvant chemotherapy in lung cancer	1998-2000	Major	Partially
Ultrasound	Now	Moderate	Partially
Near patient testing	1996-7	Moderate	Not well
Revision of joint replacements	Now	Major	Quite well
Genetic screening	1998-2000	Major	Partially
Helicobactor pylori eradication	Now	Moderate	Quite well
Positron Emission Tomography (PET) scanning	1998-2000	Moderate	Quite well
Phacoemulsification	Now	Moderate	Fully
Cochlear implants	Now	Moderate	Fully
Paclitaxels for ovarian & breast cancer	1996-7	Moderate	Quite well
Nitric oxide for neonates	1996-7	Some	Partially
Bone densitometry screening	Now	Major	Quite well
Anticoagulants for atrial fibrillation	Now	Moderate	Quite well
New anaesthetic vapours	1996-7	Moderate	Quite well
Drugs for Alzheimer's	1996-7	Major	Partially
Magnetic resonance angiography (MRA)	1998-2000	Major	Partially
Digital radiography	1998-2000	Major	Quite well
Alendronate for osteoporosis	1996-7	Major	Partially
Continuous positive airways pressure (CPAP)	Now	Moderate	Quite well
Expanding metal stents for oesophageal cancer	Now	Moderate	Quite well
Community placements for severe mental illness	Now	Major	Not well
Fludarabine in lymphomas & chronic leukemia's	1996-7	Moderate	Quite well
Combined therapy for HIV/AIDS	1996-7	Moderate	Partially
Epilepsy surgery	Now	Some	Quite well
Lipid lowering drugs for raised cholesterol	Now	Major	Fully
Transfemoral endovascular (bifurcated) graft	1998-2000	Major	Partially
Intracytoplasmic sperm injection (ICSI)	1996-7	Some	Partially
Computed Tomography (CT) scan advances	1996-7	Moderate	Partially
Voice activated dictation technology	1996-7	Moderate	Partially
Intra arterial metallic stents	Now	Moderate	Quite well

APPENDIX 8

CATALOGUE OF WORLD WIDE WEB SITES WITH INFORMATION ON NEW HEALTH CARE TECHNOLOGIES

With thanks to CCOHTA and Web Watch in the *Health Service Journal* for providing information on some of the Internet sites listed below. Many of the sites have links to other useful information sources on the Internet.

Reuters Medical News/Reuters Health Information Services (http://www.reutershealth.com/frame_about.html)

Highly recommended. Extremely easy to scan, useful categories, i.e. industry and regulatory. News archive to search news items for the past 1-2 years. Mainly US, with some Canadian and European coverage

PRNewswire/HealthBiotech (http://www.prnewswire.com/index.shtml)

Free of charge. Useful links to health care associations. Contact information for each news story is included.

Doctors Guide: Medical Conferences and Meetings (http://www.pslgroup.com/MEDCONF.HTM)

Good news service. Particularly good for news of upcoming conferences and also has conference highlights section from major medical conferences

CenterWatch Clinical Trials Listing Service (http://www.centerwatch.com)

Free of charge. Search by disease category or for new drug approvals

US Food and Drug Administration (http://www.fda.gov)

Information on new drug and device approvals

Pharmaceutical Research and Manufacturers of America (PhRMA) (http://www.phrma.org/)

Free of charge. Useful tables of drugs in development and the level of clinical trial they have reached. Charts organised by major disease types showing new drugs undergoing trials in the New Medicines in Development section

NIH Clinical Alerts (http://wwwindex.nlm.nih.gov/databases/alerts/clinical_alerts.html)

Clinical alerts are provided to expedite the release of findings from the NIH-funded clinical trials where such release could significantly affect morbidity and mortality.

UK Drug Information Pharmacists Group (http://www.ukdipg.org.uk/newprod.htm)

See appendix 6 for details

Pharmaceutical information network (http://www.pharminfo.com)

Assessments of therapeutics and advances in new drug development

EurekAlert (http://eurekalert.org)

Latest research advances in science, medicine, health and technology. Average of 20 news releases each day

Englemed (http://englemed.demon.co.uk)

Latest reports about health and medicine (within previous four weeks). Stories are sourced wherever possible

Doctors guide to the Internet - Medical News and Alerts
(http://pslgroup.com/DOCGUIDE.HTM)

Designed to help doctors harness the resources on the Internet. Has medical news and alerts, new drugs and conference information.

European Agency for the Evaluation of Medicinal Products (http://www2.eudra.org)

The Agency aims to provide the EU Member States and the Community institutions with the best possible scientific advice on questions concerning quality, safety and efficacy of medicinal products for human and veterinary use. It co-ordinates single evaluations via a centralised or decentralised marketing authorisation system.

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