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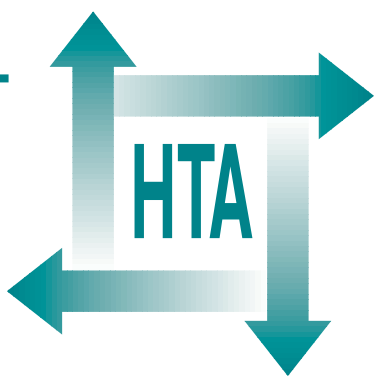
Health Technology Assessment
NHS R&D HTA Programme



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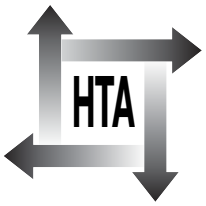

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‘Early warning systems’ for identifying new healthcare technologies

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NHS R&D HTA Programme

The overall aim of the NHS R&D Health Technology Assessment (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. Research is undertaken in those areas where the evidence will lead to the greatest benefits to patients, either through improved patient outcomes or the most efficient use of NHS resources.

The Standing Group on Health Technology advises on national priorities for health technology assessment. Six advisory panels assist the Standing Group in identifying and prioritising projects. These priorities are then considered by the HTA Commissioning Board supported by the National Coordinating Centre for HTA (NCCHTA).

This report is one of a series covering acute care, diagnostics and imaging, methodology, pharmaceuticals, population screening, and primary and community care. It was identified as a priority by the Methodology Panel and funded as project number 94/10/02.

The views expressed in this publication are those of the authors and not necessarily those of the Standing Group, the Commissioning Board, the Panel members or the Department of Health. The editors wish to emphasise that funding and publication of this research by the NHS should not be taken as implicit support for the recommendations for policy contained herein. In particular, policy options in the area of screening will be considered by the National Screening Committee. This Committee, chaired by the Chief Medical Officer, will take into account the views expressed here, further available evidence and other relevant considerations.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

The editors have tried to ensure the accuracy of this report but cannot accept responsibility for any errors or omissions. They would like to thank the referees for their constructive comments on the draft document.

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Contents

List of abbreviations

BPA	British Paediatric Association
BT	British Telecommunications
CCOHTA	Canadian Coordinating Office for Health Technology Assessment
CEPOD	Confidential Enquiry into Peri-Operative Deaths
CMP	Changing Medical Practice
CON	Certificate of Need
CT	computerised tomography
DHSS	Department of Health and Social Security
DIHTA	Danish Institute for Technology Assessment in Health Care*
DIPG	Drug Information Pharmacists Group
DIS	Drug Information Services
DRG	Diagnostic related group
DSI	Danish Institute for Health Services Research and Development
EWS	early warning system
FDA	Food and Drug Administration
FinOHTA	Finnish Office of Health Technology Assessment
FT	full time*
HTA	health technology assessment
HTAIS	Health Technology Assessment Information Service
IDE	investigational device exemption
IFN-β	interferon-β
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
LSI	large-scale integration*
LVAD	left ventricular assist device
MDA	Medical Devices Agency
MRC	Medical Research Council
NPC	National Prescribing Centre
NRR	National Research Register
OST	Office of Science and Technology (UK)
OTA	Office of Technology Assessment (USA)
PC	personal computer*
PCM	pulse code modulation*
PET	positron emission tomography
PICU	paediatric intensive care unit
PLA	product licensing application
PTCA	percutaneous transluminal coronary angiography
rhDNAase	recombinant human DNAase
SBU	Swedish Council on Health Technology Assessment
SDAT	senile dementia of the Alzheimer type
SERNIP	Safety and Efficacy Register of New Interventional Procedures
SGHT	Standing Group on Health Technology
SMAC	Standing Medical Advisory Committee
STG	Steering Committee on Future Health Scenarios
WTE	whole-time equivalent

* Used only in tables and figures

Executive summary

Background

The introduction of new healthcare 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 an 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 healthcare system (either through the adoption or non-adoption of the technology), and can also help to fulfil a number of other objectives.

This report determines which sources might be used to provide such intelligence and considers how an early warning system (EWS) might operate.

Aims

- To explore the most useful sources for identifying new healthcare technologies.
- To make recommendations to assist the establishment and operation of an EWS in the UK.

Methods

The methods comprised:

- a 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 about preferred sources for identifying new healthcare technologies
- retrospective case studies to learn how specific innovations could have been identified before their introduction to the NHS.

Results

Four separate methods were adopted as there is no definitive way of establishing the best information sources for identifying new healthcare technologies.

1. Literature review

The literature review identified five scientific attempts at identifying new healthcare technologies which used formal and empirical methods but which did not assess those methods. 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 healthcare technologies.

2. Telephone enquiries

The telephone enquiry of existing EWS also suggested that liaison with experts is indispensable. 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 and Efficacy Register of New Interventional Procedures (SERNIP), also have an important contribution to make.

3. Delphi study

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 and biotechnology companies, specialist medical journals (i.e. those containing early case reports, case series and uncontrolled studies), principal medical journals, medical engineering companies, private healthcare providers, newsletters and other bulletins from other national and regional health technology assessment agencies and sentinel groups of expert health professionals.

4. Case studies

The case studies suggest that particularly important documentary sources include key pharmaceutical journals, specialist medical journals and Food and Drug Administration (FDA) licensing applications in the USA. Conference reports can also be useful.

From the results of the four methods, a threefold classification for potential sources for identifying new healthcare technologies was devised: **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.

The literature review and telephone enquiry showed that the establishment of an EWS is a recent concept for most countries. An EWS has been in operation in The Netherlands since 1988, and five other national organisations are currently attempting to establish such systems (Canada, Denmark, France, Sweden and the UK). These are often principally aimed at establishing research priorities for health technology assessment but may also seek to inform professional groups and other interested parties of imminent technologies.

Discussion

Of the many information sources identified by the various methods, each has its own advantages and disadvantages. There were some discrepancies between the sources recommended by the four methods, but widespread consensus that key pharmaceutical and medical journals, specialist medical journals and liaison with experts are important components of an EWS. 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 (e.g. the Internet and patient special interest groups) are becoming more prominent; their value to an EWS will need to be monitored.

Predicting when a technology will become widely diffused often requires 'watchful waiting' with the aid of experts.

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 methods:

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

An EWS, established at a national level, could help to inform the preparation of guidelines for commissioners of health care (whether health authorities or general practitioner consortia) in advance of the introduction of new innovations, the estimation of future expenditure implications, and the establishment of national priorities for researching cost-effectiveness. Such an EWS should be evaluated. The value of an EWS for health technology assessment purposes should be judged by the extent to which it facilitates timely research-based evidence on new technologies.

Research recommendations

Information sources

- To design a system for prospectively recording the information sources used to identify new technologies in order that their accuracy can be assessed at a later date when the value of the output from the EWS is known.
- To undertake further and more detailed case studies of technologies (preferably prospectively) to help understand the diffusion processes of new healthcare technologies and to assess information sources for identifying them before their introduction into health services.
- To determine the best methods for accessing expert opinion and for selecting experts. This will involve a systematic review of the literature on expert selection, management and knowledge retrieval.

Establishment and operation of an EWS

- To estimate the likely 'payback' from providing early warning of a variety of new healthcare technologies i.e. estimating costs and valuing early warning.
- To systematically review and experiment with models (assessed at two to three year follow-up) to estimate the likely impact of new healthcare technologies, in terms of cost, effectiveness and number of people affected.
- To determine through surveys of policy makers and other methods how much early warning is required for (1) strategic policy decision making and (2) day-to-day operational management decisions, which 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.

Chapter 1

Aims

The overall aim of the project was to develop a robust method for identifying new healthcare technologies to help a national health technology assessment (HTA) programme set research priorities. The *a priori* hypothesis (based on the findings of the Scenario Commission on Future Health Scenarios [1] in The Netherlands) was that the best source of information on future healthcare 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.

The aims of the project were to:

- make recommendations on the most useful sources for identifying new healthcare technologies
- make recommendations on the establishment and operation of an early warning system (EWS) in the UK as part of a national HTA system.

Subsidiary objectives were to consider how such an EWS might be put to a wider use within the NHS and make recommendations for further research in this area.

Chapter 2

Background and rationale for the study

Brief descriptions of the key concepts that are central to this area of study and examined in this report (health futures, 'new' healthcare technology, early warning systems, innovation and diffusion) are provided in appendix 1.

The need for an early warning system

New healthcare 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.[2–11] In some cases concerns are focused on the social and ethical implications of a new technology. However, in a fixed-budget, publicly funded healthcare system such as the NHS the focus is more often on the costs of new technologies. The cost implications of a new technology can be high if it involves expensive capital equipment (e.g. a whole body scanner), requires substantial time of highly skilled persons to operate it (e.g. renal dialysis) or likely to be used frequently (e.g. certain diagnostic tests or drugs). Other sectors, such as electronics, aviation[12] and agriculture, have undertaken extensive studies of technological innovation and diffusion;[13] yet 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.

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 healthcare costs.[14–24] The economic impact may take a number of forms:

- 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. Alternatively, new technologies may substitute for existing technology but at higher cost
- 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 increased resource use
- there may be non-medical costs associated with receiving the medical 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.[25–28] The NHS has tended to introduce technologies haphazardly before their effectiveness and appropriateness have been proven.[29–33] Stocking[34] 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
- 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 organisational 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 existing alternatives and there are large geographical variations in use.[35] In early 1998 the UK Medical Devices Agency (MDA) issued a hazard warning about one of these products which may lead to up to 5000 patients who have undergone hip replacement surgery having to be recalled and possibly having repeat operations (at a cost of £5000 per operation). Such devices are not required to undergo long-term clinical trials before being introduced. 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 1800 patients.*

Such concerns about the introduction of new healthcare technologies has led, in line with developments such as the NHS Research and Development strategy[30] and evidence-based medicine,[38] to increasing interest in improved NHS evaluation and control of technology. New technologies must be shown, by rigorous evaluation, to be potentially either less expensive for the same (or greater) effect, or more effective for the same cost than the technologies they may replace.

The responsibility for making decisions about new technologies, and for handling these consequences, falls to commissioners of health care (whether health commissions or general practice consortia). The recent introduction of interferon-β (IFN-β) led to the observation that (emphasis added):[39] '[commissioners] will need **early information** 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.

Examples of healthcare 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, 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 5 years. Analysts have speculated that Pulmozyme could bring its manufacturers Genentech $100–500 million worldwide.[40] 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 multiple sclerosis, 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 £1–3 million in 1996.[41] 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 6). The introduction of other types of healthcare technologies which 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'[42]).

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. If they 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.[43] Economic evaluation should, therefore, be viewed as a continuous process over time, progressing from early 'indicative' studies to rigorous comparative analysis.[44] The belief is that an EWS, by providing such early information as part of a HTA system, can help to minimise unnecessary costs, health disbenefits and policy confusion within the NHS.[45,46] Notwithstanding the Buxton paradox[47] 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.[48–51]

Many of the technologies in regular use today would have been hard to predict 25 years ago,[52] 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,[53] including those in the health sector.[1,54] However, whatever the method adopted

* Source: '5,000 hip operations may have to be repeated', *The Independent* (19 February 1998). Such failures have led to calls for the establishment of a registry of hip implants.[36] Similar pleas have been made with regard to other healthcare technologies, such as neurological implants.[37]

there are uncertainties inherent in all applications of futures work and forms of forecasting.[56,57*]

It is not easy to assess the effectiveness and costs of a technology before its introduction and diffusion.[58,59] 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.[60] It can be particularly difficult to determine at an early stage which new technologies are likely to be important for a healthcare 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 synthesised, 1000 underwent animal testing, ten were selected for human testing, and ultimately only one would enter the healthcare market[61] (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.[62] For example, progress in five different biomedical research programmes (X rays, tomographic techniques, instrumentation, mathematics and computers) were required in order to develop computerised tomography (CT) head scanners and subsequently CT body scanners. 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 high percentage of new medical devices have emerged not out of biomedical research, but through transfer of technologies that were developed elsewhere (e.g. lasers, ultrasound, magnetic resonance spectroscopy and computers).

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 (e.g. intravascular three-dimensional imaging increasing the use of stents) so increasing the number of potential adopters, 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 healthcare technologies, as the technology may itself create new categories of patients by virtue of new indications. In addition, new healthcare 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 (e.g. 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'.[63] Often these uncertainties surrounding the innovation and diffusion of new healthcare technologies make it very difficult to select the technologies most likely to have a large impact on a healthcare system.[‡] Treasure[64] 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

[*] Spilker[53] 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.

[†] 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.

[‡] Rogers[13] 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 healthcare 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.[65]

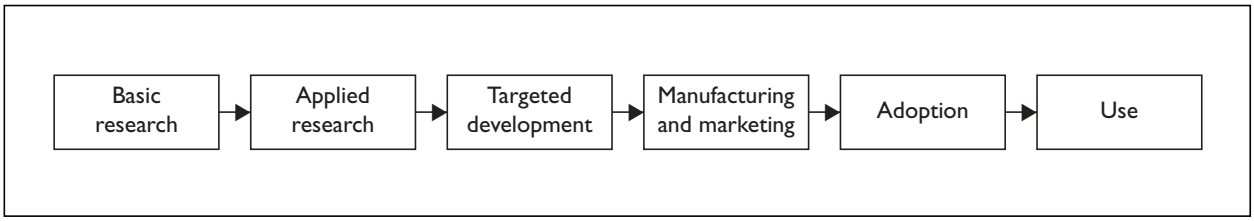

FIGURE 1 *A linear model of biomedical innovation*

as inoperable. Thoracolumbar sympathectomy illustrates what Treasure terms the 'research cul-de-sac'.

From the 1970s onwards, studies of biomedical innovation, and of the diffusion of medical technology, have become more frequent, and slowly a base of knowledge is emerging[66] but the basic mechanisms underlying medical research and development remain largely unknown.[67] The evolution of a new biomedical technology was initially thought of as a series of technical events which is usually described as linear-sequential[68,69] (known also as the 'science-push' model; *Figure 1*).

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.[70] In health, as in industry, innovation involves the interaction of the providers and users of research in a complex iterative process.[71–73] Bower[74] cites the major study by Sneader,[75] which 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 interrelations 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 research and development 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 misconceived 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.[76] So, as Lewit[77] suggests in the context of surgical procedures, 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. 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[53] suggests that most predictions of revolutionary change in medicine are 'pure hype' and that it is impossible to predict which ones will occur and when they will occur.

Diffusion research in the healthcare sector has focused on the role of opinion leaders and communication channels.[13] Stocking found that in 22 innovations which she studied there was one central person who had the idea, developed it, and was central in promoting it.[78] 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. 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,[79] whereas other valuable technologies have sometimes diffused only slowly, delaying either healthcare benefits or financial savings or both. Gelijns and Rosenberg[65] therefore suggest that the linear model captures 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.

Many high-cost, high-profile technologies have diffused rapidly, not always appropriately nor in a controlled way.[80] Their diffusion, evaluated or not, is disorganised and occurs at varying rates,* depending on the strength of various influences[81,82] (e.g. clinical enthusiasm for a new surgical technique[83]). Thus the development and uptake of an innovation is unpredictable and cannot be described in terms of standard processes.[84] This is not surprising given that the key features of the market for healthcare technology include a lack of information, and the separation of technology provision from its financial ramifications.[85]

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 which have potentially large implications for a health service. Appropriate research can then be commissioned to determine the desirability or otherwise of the technology. *Figure 2* illustrates this point and also illustrates the different time-frames that determine the purposes and methods of an EWS.[86]

	Technologies that are pushing towards the NHS – plausible futures	**Technologies we have to seek – preferable futures**
0–5 years (short term)	*Activity:* EWS *Purpose:* manage and control change	*Activity:* identify unfulfilled technologies/stem unnecessary ones *Purpose:* induce change
5 years +	*Activity:* basic science-orientated forecasting *Purpose:* long-term planning to anticipate likely	*Activity:* predicting desirable futures *Purpose:* design appropriate techniques

FIGURE 2 *Timescales and purposes of EWS*

An EWS intended to help set priorities for HTA research lies in the upper-left quadrant of *Figure 2*. It intends to help control and rationalise the adoption and diffusion of technologies that are being promoted by the healthcare industry and professional opinion leaders.[87] 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 professional 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 in *Figure 2*). For example, futurologists and researchers brought together by British Telecommunications (BT) 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.[88] Such initiatives may often be part of national attempts at technology forecasting. In the UK the Department of Health is establishing a group whose remit is to help develop new and emerging 'orphan' technologies. Adopting a longer-term approach and collaborating with the healthcare 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' either to help prevent the undesirable consequences of the irrational and haphazard introduction of new healthcare technologies or to promote the adoption of beneficial and cost-effective technologies.[89] Prediction strategies vary: some are quite broad and long-range, looking at futures in terms of societal, technical and demographic change[90] (bottom left quadrant of *Figure 2*), perhaps using scenario analysis,[91] and examples include industry (Shell[92]) and the Office of Science and Technology's Technology Foresight Programme.[93] More focused examples include

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

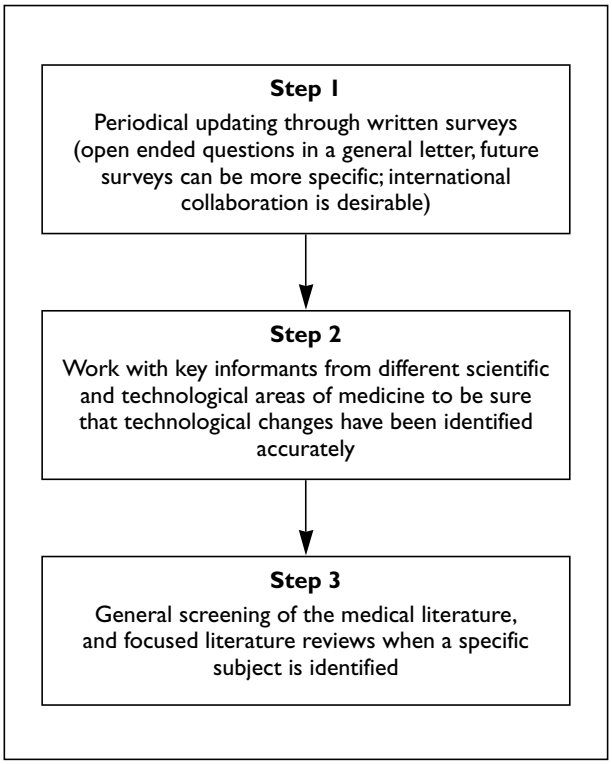

FIGURE 3 *STG process for identifying new healthcare technologies*

the Wellcome Trust's Unit for Policy Research in Science and Medicine (PRISM) report on cardiovascular research[94] and the UK's Standing Group on Health Technology's own forecasting exercise[95] and other local initiatives.[96] Some are technology, and/or speciality, 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 and Development Programme, whose report in 1995[97] is the first of a series of NHS appraisals of scientific growth areas which aim at a clearer view of the likely implications of major research discoveries for the NHS over a 10 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 healthcare 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 the Safety and Efficacy Register of New Interventional Procedures (SERNIP), began with the 'detection' of new techniques through the literature, communications, and conference reviews.[98*] 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 healthcare technologies are infrequent and, if done at all, are often undertaken 'in-house' and therefore rarely published.[99]

In the USA, 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 Food and Drug Administration (FDA).[100] 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 the FDA,[†] through its premarket approval process, gathers information on drugs and devices that are being developed, but no existing system adequately identifies developing technologies that will require evaluation.

The Netherlands was one of the first countries after the USA to identify the potential benefits of HTA.[101,102] 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 healthcare technologies, in collaboration with WHO Europe. The results of that project were first presented in Rotterdam in May, 1987. The report recommended the process

[*] A similar initiative has been launched in Australia: the Australian Safety and Efficacy Register of New Interventional Procedures (ASERNIP/s): http://www.racs.edu.au/open/asernip-s.htm.

[†] In 1981 the FDA prepared a list of emerging medical devices and drugs (see chapter 4 for further details).

shown in *Figure 3* for identifying new healthcare technologies.[1] The STG organised the first International Health Futures Network (IHFN) meeting in 1991 in response to a request from the EC 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 healthcare technologies. In 1993 Jorgenson attempted unsuccessfully to establish a European system for early identification of emerging healthcare technologies.* 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.† However, national HTA agencies have very limited resources which restricts their ability to perform continuous early identification of emerging healthcare technologies. Coordination, he argued, would bring together these limited efforts, and whilst comprehensive medical 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 EWSs for new technologies. In September 1997 the Danish Institute for Health Services Research and Development and the Swedish Council on Health Technology Assessment in Health Care (SBU), in collaboration with the European Commission DGV, held a 'European Workshop‡ on Scanning the Horizon for Emerging Health 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 early warning systems
- to discuss and assess the feasibility of a European network of EWSs.

Two of the authors of this report (GR, AS) attended the workshop, and the conclusions[103] and resulting collaboration has helped to inform our thinking and recommendations.

None of the small number of existing studies has been evaluated and, with the exception of the STG in The Netherlands,[1] no ongoing, iterative process has resulted. There is, therefore, no agreed or empirically proven method of identifying and predicting the likely future impact of new healthcare technologies.

Some problems in developing methods in EWSs

Mowatt and co-workers[104] suggest that all systems for detecting new technologies require value judgements 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 judgements would have to be made by experts who have vested interests and an 'insider' perspective, they question whether the systems as designed would be effective or dispassionate enough to justify the amount of resources they would consume: 'Would they detect all emerging healthcare technologies? Would they correctly assess their potential? Would voluntary systems work?' Some commentators support these suppositions, suggesting that

* T Jorgenson, personal communication, based on a submission to the EC, December 1993.

† 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 UK's National Standing Group on Health Technology (SGHT) and Sweden would soon be initiating continuous processes for early identification of new medical technologies.

‡ The Canadian Coordinating Office for HTA also participated.

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.[105] 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'.[106]

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. As a rule of thumb, an EWS intended to help HTA research prioritisation will require at least 3 years early warning, although this will depend on the technology and on the type of research (e.g. more for a randomised controlled trial than for a review or modelling exercise. 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 (e.g. laparoscopic cholecystectomy). An EWS operating in the health policy context may require much less warning, perhaps 6 months for commissioners of healthcare services. 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. They 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 prioritisation exercise technologies which turn out to have large implications for the health service.

Timeliness of this report

The rapid speed with which new healthcare 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 health technologies which might have a significant impact on the NHS in the near future.

At the national level the main purposes to which an EWS may be put are:[107]

- to develop and prioritise a HTA research programme
- to assist with issuing guidance to service commissioners/purchasers about the use of new technologies and advances
- 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 determined by the selection of the information sources used and by the methods used to evaluate the technologies. It will also depend on understanding the complex process of adoption and diffusion which underpins the development and use of new healthcare technologies in a healthcare system.

This report aims primarily to determine the method for operating an EWS in the context of the UK's HTA programme. It sets out to achieve this by identifying and assessing, through a variety of methods, potential information sources for identifying new healthcare technologies.

The project builds on the work that has already been carried out by the authors on behalf of the UK's National Standing Group on Health Technology (SGHT).[90]

Chapter 3
Methods

We adopted four methods in order to achieve the stated aims of the project:

(1) A systematic review of the literature on health futures and forecasting in the UK and from healthcare systems overseas to assess information sources which have previously been used to identify new healthcare 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 assess potential sources for identifying new healthcare technologies
(4) Retrospective case studies of exemplar technologies to identify (with hindsight) information sources for providing 'early warning'.

Table 1 summarises where in the report the results of the four methods that informed the two primary objectives appear.

The results from each of the four methods are drawn together in the synthesis chapter (see chapter 7), and conclusions and recommendations are made in the final chapter of the report.

TABLE 1 *Structure of report (page numbers)*

Method	Objective 1: most useful sources	Objective 2: Establishment and operation of an EWS
Literature review	15–23	–
Telephone enquiry	23–25	25–27
Delphi study	29–37	–
Case studies	41, 43, 45, 48, 49, 51, 52, 53–54, 55 (both objectives)	

Systematic review of the literature on health futures and forecasting exercises

The purpose of the systematic review was to assess information sources which have previously been used to identify new healthcare technologies. In order to analyse the accuracy of published initiatives we presented the results to experts in particular fields and asked them to give their retrospective opinions on a sample of the predictions that were made.

The search strategies and results are presented on page 15. The databases used are described in appendix 2. We scanned the title and abstracts (where available) of all the references and retrieved all those which related to methods adopted in health futures studies which focused on healthcare technologies, or forecasting methods (related to healthcare technologies) or strategies for identifying new healthcare technologies. We also retrieved those studies which related to the more general area of the application of futures methodology in health care.

As a supplement to the published literature we carried out an e-mail survey of members of the International Society of Technology Assessment in Health Care (ISTAHC). We contacted 92 members of the society whose e-mail addresses were published in the 1997 members directory, representing 24 countries* and a wide range of disciplines and organisations. We asked them for brief details of any EWS which had sought to identify new technologies either in one particular area, or across the wide spectrum, of health care. The responses were used to help identify interviewees for the telephone enquiry.

* The countries were USA, Argentina, Sweden, Japan, Australia, Canada, Israel, France, Germany, Brazil, UK, Denmark, The Netherlands, Greece, Spain, Portugal, Italy, Hong Kong, South Africa, Finland, Ireland, Mexico, New Zealand and Switzerland.

Telephone enquiry of coordinators of EWSs

In order to inform all aspects of the establishment and operation of an EWS we carried out a semi-structured, telephone enquiry of coordinators of existing EWSs in six countries (The Netherlands, Denmark, France, Canada, Sweden and the UK). Participants were identified either from the published literature, the responses to the e-mail survey or from the project team's own network of informal contacts. The questionnaire focused on the aims, methods and level of support of each of the EWSs. The pro forma for the questionnaire is at appendix 3. The participants are listed in the acknowledgements to this report.

A Delphi study to assess potential sources for identifying new healthcare technologies

We used a Delphi study to devise and develop a classification of healthcare technologies and a list of the potential sources for identifying each type. We used this method because of the lack of documented evidence[108] on the use of information sources in an EWS and because it allowed consensus development over a wide geographical area.[109] The Delphi study involved 37 participants whom we identified through our own informal networks and a cascade to other nominated individuals. It became clear during the early phase of the project 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 healthcare technologies. The individuals were selected because they could claim expertise either on:

- particular information sources for identifying new healthcare technologies (e.g. the pharmaceutical literature) or
- specific types of healthcare technologies (e.g. medical devices) or
- operating or planning EWSs in other countries.

We formulated an initial list of potential information sources and sent it to all Delphi participants, together with a set of criteria for assessing the ease with which the sources could be used for extracting and assessing information. We also proposed a basic classification of healthcare technologies (drugs, devices, procedures, settings, and information technology).

In round 1 we asked participants to:

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

We then summarised the responses and included them in round 2 of the survey, when we asked participants to use the criteria to assess information sources for each agreed type of technology. We asked them 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)
- 'how good?' (the effectiveness of the technology)

In round 3 we asked participants 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. We also asked specific questions that we felt had been raised by the earlier rounds and which we felt would benefit from further elaboration and discussion. We fed the final results of the Delphi study back to the participants. Again, the participants are listed in the acknowledgements to this report.

Retrospective case studies of exemplar technologies

Given the lack of empirical evidence with which to assess the results of the Delphi study we carried out nine retrospective case studies (*Table 2*) to assess the ability of potential sources to identify new and important healthcare technologies.

We chose these particular case studies in order to ensure examples of each of the broad types of healthcare technology (drugs, devices, settings and procedures). In addition, not all of the case studies are currently emerging examples; using old and contemporary examples provided an opportunity to reflect on the actual diffusion of some of the

TABLE 2 *Selection of case studies*

Technology	Type	Timing of introduction to NHS
IFN-β	Drug	Contemporary
Dornase alfa	Drug	Contemporary
Donepezil	Drug	Emerging
Medisense ExacTech® pen	Device	Emerging
Left ventricular assist devices	Device	Emerging
Telemedicine	Device	Emerging
CT scanners	Device	Old
Paediatric intensive care units	Setting	Contemporary
Laparoscopic cholecystectomy	Procedure	Old

technologies into the NHS and the benefits that might derive from the operation of an EWS.

Clearly 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 7.

The sources of data for the 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 which were used are shown in appendix 3. 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. In an exploratory study of this type, case studies are well suited for answering the questions of the how and why, for example **how** an EWS using the information sources recommended by the Delphi study might have identified certain healthcare technologies and **why** there might be differences between the different types of healthcare technology.

Chapter 4

Literature review and telephone enquiry

Results of literature review

The retrieval from the literature review is shown in *Table 3*.

In total, after extraction of duplicates, there were 4160 references. We were only specifically interested in references which described either:

- methods adopted in health futures studies which sought to identify new healthcare technologies or
- scientific attempts at identifying new healthcare technologies.

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 healthcare 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, that is, 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
- 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 study is concerned.

Although ideally it was the type I literature which we were seeking to inform this report, no such studies were identified by the literature search. However, *Box 1* gives the bibliographic details of the five studies[1,95,110–112] which adopted formal and empirical methods to identify future healthcare 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 pages 16–23, 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 EWSs in The Netherlands[1] and the UK[95]).

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 (e.g. in one speciality or concerning one particular

TABLE 3 *Results of literature review*

Database	Years	Search strategy	Retrieved
OVID MEDLINE	1966–9/1998[a]	[exp FORECASTING\] and [(TECHNOLOGY\ or technology.ti.ab.rw.sh) or (exp TECHNOLOGY\)]	1214
OVID Core Biomedical Collection	1993–7/1998[a]	[future.ti.ab.tx,ct] and [technology.ti.ab.tx.ct]	2186
HealthSTAR	1975–8/1998[b]	[forecasting (mh) or future (tw) or future (kw)] and [explode technology or technology (tw) or technology (kw)]	815
HTAIS (ECRI – US)	1990–1996[c]	'Methods for identifying new healthcare technologies'	31

[a] *Final electronic search was carried out on 1 September 1998*
[b] *Final electronic search was carried out on 1 September 1998, and results exclude MEDLINE references*
[c] *Search was carried out on 11 March 1996 by ECRI*

BOX 1 Scientific attempts at identifying new healthcare technologies: bibliographic details

Food and Drug Administration. Forecast of emerging technologies. US Department of Health and Human Services, June 1981

Banta HD, Gelijns AC (eds). Anticipating and assessing health care technology, vol I. General considerations and policy conclusions. Report of the Scenario Commission on Future Health Care Technology. Dordrecht: Martinus Nijhoff, 1987[a]

Spiby J. Advances in medical technology over the next 20 years. *Community Med* 1988;**10**(4):273–8

Technology Foresight Programme. Notes on the Delphi survey. Companion paper B to the health & life sciences panel report. Office of Science and Technology. London: HMSO, 1995

Stevens A, Robert G, Gabbay J. Identifying new healthcare technologies in the United Kingdom. *Int J Technol Assess Health Care* 1997;**13**(1):59–67

[a] *Summarised in Banta and co-workers.[114] All these citations relate to the same project undertaken in The Netherlands during the mid 1980s*

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 7.

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 but which were not focused on identifying new healthcare technologies and often took a longer-term perspective. There are numerous examples[113] 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. Exemplar papers which together provide an introduction to this area are referenced 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 healthcare technologies in a particular speciality or across health care as a whole, but only three initiatives[1,110,111] provide any critique of the various sources which might be adopted for the purposes of an EWS.

Scientific attempts at identifying new healthcare technologies

This section reviews the studies in *Box 1* (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 healthcare technologies
- 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 healthcare 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.[*] Three of the studies[1,110,111] 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[110] 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 (e.g. monitoring 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 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 healthcare technology, and to find experts who will respond to surveys with helpful information.[1]

[*] Professor D Banta and Dr J Spiby, personal communications, 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.

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
- a commitment to improving these methods.

Spiby[111] 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 panellists would interpret in the same way, providing useful feedback and the implementation of an arbitrary endpoint. In a related report, Spiby[99] very briefly reviewed other methods that could have been adopted to identify new healthcare technologies (e.g. trend extrapolation, econometric methods and scenarios). 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 used by three reviewers (GR, AS, JG) 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, that is, would all five substantial advisory panels to the UK's SGHT* have been informed by the findings?
- Did they take an international perspective or not?
- Did they focus on an appropriate (short to medium term) time-frame; ideally, technologies likely to be introduced within 5 years?
- Did they incorporate any 'checkback' methods?

Table 4 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.

The FDA[110] 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 we identified. This study used scientific experts inside and outside the FDA to identify emerging healthcare 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 organisations; and ten 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
(3) identify any major factors which might affect it when it would first arrive on the market or reach FDA (e.g. technical feasibility, health risk, cost or public acceptance).

TABLE 4 *Summary assessment of earlier studies*

Study	Empirical	Triangulation	Explicit sample	Generalisable	International	Time (years)	Check back
FDA	✔	✗	✔	✔	✗	1–10	✗
STG	✔	✔	?	✔	✔	4–15	✗
Spiby	✔	✗	✔	✔	✗	Up to 20	✗
Technology Foresight Programme	✔	✗	✔	✔	✗	20+	✗
Stevens and co-workers	✔	✔	✔	✔	✗	Up to 5	✗

* The five panels are: acute sector; primary and community care; diagnostics and imaging; population screening; and pharmaceutical.

In total 429 individual citations were condensed into 168 distinct technologies. These technologies were organised by the FDA's major programme areas: biologics, medical devices, radiological health, human drugs, animal drugs and feeds, foods and agency-wide technologies. As Spiby[99] 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. The time-frame adopted was somewhat longer than that anticipated for the purposes of HTA prioritisation (up to 15 years as opposed to less than 5 years). However, the eight most frequently mentioned new technologies were predicted to arrive within 5 years.

Banta and co-workers[114] is the first publication relating to a large-scale analysis of future healthcare technology, initiated by the government of The Netherlands, and carried out formally from 1985 to 1988. The study was formulated by the STG, which aimed to develop an EWS for healthcare technology and involved both the early identification of future developments in healthcare technology and prospective assessments of a number of high-priority technologies.* 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 healthcare technology assessment, as the Commission recognised that a system for identifying future healthcare technology would be of limited benefit on its own. Later volumes looked at specific future technologies.

The project identified the following problems when analysing future healthcare technologies as reported in volume I of their report:

- the lack of urgency of long-range issues has meant that the future has often received less attention than the 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
- 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 (e.g. drug registration). A variety of other sources were considered such as the published literature, news services, biomedical and bioengineering conference proceedings, and others (e.g. *Scrip*). For drugs and devices, additional sources were patent and licensing applications, investigational new drug (IND) and investigational device exemption (IDE) documents released by the FDA in the USA 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 research and development 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 healthcare technology in the USA. 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 healthcare 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: 4–6 years and 7–15 years. A total of 100 usable responses were received, and the resulting list was organised into 17 categories. A later paper[60] summarised the methods used in the STG study and made recommendations as to the establishment of an EWS for HTA purposes. 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

* Assessments were reported in the following areas: (1) developments in the regeneration, repair and reorganisation of nervous tissue; (2) healthcare applications of lasers; (3) developments in genetic screening; (4) the new biotechnology vaccines; (5) computer-assisted medical imaging; and (6) home care technology.

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

Spiby[111] reports on a study which comprised 210 people (derived from 66 people selected according to their professional post who were then asked to nominate a further five people each) being requested to identify what they saw as the three most significant changes likely to occur in medical technology which 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.[112] Foresight panels worked in 15 sectors, including one on health and life sciences.* 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 10–20 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 (out of 464 invited to participate; a response rate of 32%) was carried out between September and November 1994. Time periods for which predictions were made were 1995–1999, 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 healthcare communities.

Stevens and co-workers report on 1 year's work in the UK to identify new healthcare technologies likely to have an impact within the time period 1996–2001.[95] Three main strategies were used: (1) scanning of medical, pharmaceutical and scientific journals for an 18 month period beginning in 1994, and a 'watching brief' on pharmaceuticals going through clinical trials, (2) evidence from other initiatives in the UK (e.g. CMP) and Europe (e.g. Health Council of The Netherlands), and (3) a national postal survey of approximately 3500 individuals. From these sources 1099 new and emerging healthcare 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. Of these technologies, 66% 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 procedures (41.4 and 37.8%, respectively) were more commonly mentioned than devices 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.[99] 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 1960s.[99] Of 21 predictions forecast to occur within the 1970s to 1980s only two (a drug for dissolving gallstones 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.

* The other sectors were: agriculture, natural resources and environment; chemicals; communications; construction; defence and aerospace; energy; financial services; food and drink; information technology/electronics; leisure and learning; manufacturing, production and business processes; materials; retail and distribution; and transport.

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. We have assessed retrospectively all studies that (1) provide likely dates with their predictions (or some indication of time period) prior to 1998, and (2) make predictions across the broad spectrum of health care (as an EWS for HTA would be expected to do).

Of the technologies identified by the FDA survey 25% were related to the areas of genetic engineering or advances in CT. *Table 5* shows the eight most frequently mentioned new technologies in the complete survey.

TABLE 5 *Most frequently mentioned new technologies*

Technology	Time of predicted arrival
Hybridoma technology (e.g. monoclonal antibodies)	1983–1984
Magnetic resonance imaging	1983–1984
DNA-produced interferon/antigen	1983–1984
Risk assessment	1985–1986
Computerised instrumentation	1985–1986
CT	1985–1986
Immunoassays	1980–1982
Chromatography/mass spectrometry	1985–1986

Of the 168 distinct new technologies which were identified, 38 were related to the Human Drugs Program (approximately 25%). As three of the case studies in chapter 6 are pharmaceuticals, we have chosen to focus on this particular area of the FDA survey. The ten technologies in this programme which were the subject of three or more separate citations are shown in *Table 6*. Retrospective analysis by one practising clinician in this field 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 1980–1982 and 1983–1984, 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 with different focuses than that predicted in 1981 ('mind-altering drugs' and 'computerised drug analysis and testing').

In volume II of the STG report, 18 chapters examine technological capabilities in specific areas of health care. Rather than provide a superficial examination of each of these 18 areas, we assess the predictions made in just two: '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 6, were made during the period 1985–1987. The aim of these area-specific chapters was to anticipate future healthcare 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 7*).

Generally, these predictions are correct but the majority of them do not say anything about timing which limits 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 8*).

The predictions related to 'artificial and transplanted organs and tissues' seem to have been made with a longer time-frame in mind than 5 years and, again, the lack of suggested dates 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 healthcare 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
- information technology.

The study predicted the likely availability of the advances in *Table 9* within 10 years (i.e. 1997). Retrospective analysis of these predictions by

TABLE 6 *New technologies related to the US Human Drugs Program*

Number of citations	Technology	Time of predicted arrival	Retrospective analysis
9	Using DNA to produce insulin	1980–1982	Correct; date may have been a little early
6	Computerised drug analysis and testing	1983–1984	Correct; is available in clinical setting but of limited use
6	Using DNA to produce new pharmaceuticals	1983–1984	Correct
5	Computerised drug manufacturing and process control	1980–1982	Correct
5	Microencapsulation of drugs	1983–1984	Came later in 1990–1991
4	Mind-altering drugs, e.g. endorphin-releasing drugs	1987–1988	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	1980–1982	Has not happened yet and seems long way off still
3	Artificial blood	1983–1984	Still several years away from being a practical proposition
3	Identifying particulates and detecting trace chemical contaminants in drugs	1983–1984	Correct
3	New synthetic hormones from DNA technology	1980–1982	Correct; dates vary for different drugs

TABLE 7 *Technological developments in medical imaging and other diagnostic technologies: 1988 onwards*

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)	Although still considered primarily a research tool, this imaging technique is beginning to be used for routine clinical diagnosis in the USA and Japan, although the technology is still at an early stage of development. With development of cyclotrons, PET scanning may become more widely available
Digitalisation	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 levels, 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 5 years or so, but some experts are sceptical that it will ever become completely operational
Other diagnostic technologies	* Endoscopy using fibre optics * Flow cytometer (with monoclonal antibodies) * Two-dimensional gel electrophoresis (with monoclonal antibodies) * Automated genetic diagnosis

TABLE 8 *Artificial and transplanted organs and tissues: 1988 onwards*

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

TABLE 9 *Innovations predicted to occur during the period 1987–1997*

Innovations predicted to occur during the period 1987–1997 by the Spiby survey	Accuracy of prediction
Diagnostic innovations	
• Monocolonal 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
– magnetic resonance scanning	Correct
– nuclear medicine and positron detection	Still research based
Therapeutic interventions	
• Drug 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 centralisation	No
• Optical disk storage and communication will be used with X rays and other diagnostic images	Not yet

practising clinicians 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.

The survey also suggested several advances that would not be realised by 1997, all of which were correct:

- 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 ageing process
- the production of a safe cigarette.

In the Technology Foresight exercise undertaken by the UK Office of Science and Technology (OST), the four predictions in *Box 2* were made for the period 1995–1999 based on respondents who rated their expertise on each particular topic as 'familiar', 'knowledgeable' or 'expert'.

BOX 2 Predictions likely to occur between 1995 and 1999

- 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. ultramicroscopy)
- 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 non-peptide molecules which mimic the activity of peptides

In the postal survey undertaken by Stevens and co-workers, of the 48 most frequently mentioned new or emerging technologies that were identified as being likely to have an impact on the NHS within the next 5 years (*Table 10*), 23 were predicted to make their impact during 1995 and a further 13 were predicted to make their impact during the period 1996–1997.

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

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 EWSs 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 USA, 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 EWSs.

We were unable to include Norway and Finland 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 (e.g. 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 (The Netherlands and Sweden) but mostly through telephone contact (The 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 and 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 ten 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 and to comment on technologies identified by other sources (usually 3–5 experts are consulted per technology).

TABLE 10 *Technologies predicted to occur during the period 1995–1997*

1995	1996–1997
Magnetic resonance imaging	Implantable vascular stents
Minimally invasive surgery	Recombinant human DNAase (rhDNAase) 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 disease
Angioplasty	Alendronate for osteoporosis
Interferon for chronic granulocytic leukaemia and hepatitis C in haemophilia patients	Fludarabine for lymphoma and chronic leukaemia
Lasers for dermatology	Combined therapy for HIV/AIDS
Ultrasound	Intracytoplasmic sperm injection
Revision of joint replacements	CT advances
Helicobacter 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 levels	

TABLE 11 *Documentary sources used by existing EWSs*

Country	Medical journals	Scientific journals	Pharma-ceutical journals	Marketing journals	Internet	Conference abstracts	HTA reports	Other pharma-ceutical sources	News-papers
The Netherlands	✔	✔	✔			✔			
Sweden	✔					✔	✔		✔
UK	✔	✔						✔	
Denmark	✔	✔	✔		✔				
France	✔	✔		✔		✔			
Canada	✔	✔	✔		✔	✔			

Scanning documentary sources is also widely adopted by existing EWSs (*Table 11*). 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 and Canada). 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 the Canadian Coordinating Office for Health Technology Assessment (CCOHTA) already have access to through its library collection. Appendix 7 details the Internet sites which CCOHTA has identified.[115]

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.

A small feasibility study of information sources and potential informants was undertaken in

1997 by the Danish Institute for Health Services Research and Development (DSI). The informants were members of the DSI, scientific medical societies, drug and 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 makers in the health service) and clarify their specific need for information concerning emerging medical technologies. Eleven of 17 respondents, from a total sample of 46 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 (*Table 12*). 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:

Establishment and operation of an EWS

National HTA organisations have tried to establish an EWS (or at least to systematically identify new healthcare technologies at a given time), and *Table 13* summarises the aims and involvement of experts in the six organisations which are currently operating an EWS. In addition, to the six national initiatives described, and although the USA does not operate a national HTA system as such, there are, or have been, a number of projects undertaken in the USA which are similar in scope to an EWS (although not necessarily for the explicit purposes of HTA). Initiatives similar to the EWSs in Europe and Canada are undertaken at both the federal level and within the private sector in the USA by organisations with an interest in the evaluation of healthcare technologies.

Some earlier initiatives (e.g. in Norway and Finland) have not been continual but have looked at future technologies at one particular time. Norway initiated a study on future healthcare technology in early 1985, sponsored by the Council for Medical Research.[116] 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 Health Technology Assessment (FinOHTA) sent a questionnaire to all Finnish hospital districts, specialist associations and other parties.[*] The respondents were asked to identify different health technologies that needed assessment and place them in four categories. The results have not been formally published and are only available in Finnish, but a total of 1005 technologies were identified.

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.

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.[117] 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

TABLE 12 *Quality of information sources – Danish feasibility study*

Significance[a]	Hit rate[a]	Objectivity[a]
Principal medical journals	Scientific medical societies	National medical journals
Conferences and meetings	Expert and research networks	Principal medical journals
Scientific medical societies	National medical journals	Key scientific journals
Expert and research networks	Press releases from manufacturers	Other journals

[a] *Top four in descending order*

[*] K Lampe, Medical Office, IT and Communications, FinOHTA, August 1997, and H Sintonen, September 1997, personal communications.

TABLE 13 *Current national HTA programmes*

Country: organisation and 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 (ten members each) are part of the routine operation of the EWS	50–100 technologies are identified each year, 20 are considered in detail and ten have reports written or are prioritised for research and development. 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 eight 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. One or two 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
UK: University of Southampton (1995–1996); University of Birmingham (1997–)	National HTA prioritisation and health policy planning	< 5 years before adoption	Two or three experts used to check on each technology identified by other sources (by telephone)	The EWS directly informs the UK's SGHT, and thus the NHS research and development strategy, of important new healthcare 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 research and development 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 ten 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
Canada: CCOHTA, 1997	Ongoing 1 year pilot project for purpose of health policy planning (planning, budgeting and prioritising for provincial review)	1–2 years before adoption	Use postal surveys and 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. Three to five experts are used to advise on each specific technology	Identify over 1000 technologies each year, consider 6–12 in detail and write reports on 6–10. Results are published in the *Issues in Emerging Health Technologies* newsletter and on the Internet. Selective communications are also sent to provincial decision makers on 'hot' topics

policy relevance) by 16 staff members with specific tasks
- priority setting (can either disseminate warning or monitor for future possible action)
- dissemination (bulletins, advisory board)
- 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 which may qualify for application of specific legislation (e.g. the Hospital Provisions Act or the Population Screening Act) as well as listing 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 1 year pilot project was initiated in June 1997 with support from federal, provincial and territorial governments 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
- 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 and co-workers[118] indicate there are a number of organisations and initiatives that either explicitly or implicitly have a role in providing early warning of healthcare technologies in the UK. As well as the Forecasting Secretariat to the national SGHT, 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 which provide information on new drugs on a regional and national basis, via the DIS and National Prescribing Centre (NPC). Further details on these additional contemporary sources in the UK are given in appendix 5.

All of the EWSs are mainly concerned with relatively short time horizons, commonly less than 2 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 will be of great importance to have the information 0–2 years before introduction of the technology. Only five respondents find it of great importance to have the information as early as 5–10 years in advance.

Each of the EWSs 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 EWSs varies from 80 to 1000.

In terms of staffing an EWS for HTA, *Table 14* details the current staff employed on each of the six existing EWSs.

TABLE 14 *Permanent staff – EWSs*

Country	Staff
The Netherlands	Lecturer FT; research assistant (0.5 WTE); 2 library staff (0.25 WTE); secretary; 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); 10 members of scientific board (10 days per annum)
UK	Director (0.2 WTE); project manager FT; horizon analyst FT; health economist FT; information scientist FT
Canada	Information scientist (0.5 WTE); 2 medical/pharmaceutical researchers (part-time); health economist (part-time)
France	Researcher FT; librarian (part-time)
Denmark	Researcher (part-time); librarian (part-time); secretary (part-time)

FT, full-time; WTE, whole-time equivalent

Chapter 5

Delphi study: information sources for identifying new healthcare technologies

Potential information sources

Introduction

The relative usefulness of the many available sources of information about new healthcare 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.

This chapter reports which of the sources are 'best' at identifying new healthcare technologies and how feasible it is to use them in an EWS. '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.

Sources used by HTA agencies

The sources that other national HTA programmes have adopted are:

- the published literature (scientific, pharmaceutical and medical) using scanning and focused searching (The Netherlands, Canada, the UK, Sweden, Denmark, France)
- expert opinion by way of either (1) written surveys either focused (Norway) or general (the UK, Denmark, Canada, Finland) or (2) in-depth interviews (The Netherlands, Norway, Sweden, Finland, Canada, France)
- newsletters; links with other agencies; other EWSs (The Netherlands, Canada, the UK, Sweden)
- conferences (The Netherlands, the UK, Sweden, France, Canada)
- patents (The Netherlands – STG)
- licensing applications (The Netherlands – STG)
- news services; financial press (Sweden, The Netherlands – STG)
- IND/IDE documents (The Netherlands – STG)
- the Internet (Denmark, Canada)
- marketing journals (France).

Other potential sources

In addition the project team has identified further sources, some of which have been included as they have been used by other 'futures'-orientated healthcare exercises which have been reported in the literature:

- financial markets
- specialist registers (SERNIP, MDA, DIS and SMAC)
- research funding sources (NRR and MRC)
- regulatory organisations (EU regulations)
- pharmaceutical, biotechnology and medical engineering companies
- private healthcare providers
- patient special interest groups.

International Delphi study

The content of the three stages of the Delphi study are described in detail in chapter 3 and summarised in *Figure 4*.

Classification of healthcare technologies

Because each type of healthcare technology must be expected to draw on somewhat different information sources, we suggested an initial classification of healthcare technologies to the 37 participants in round 1 of the Delphi study. We received 31 responses (84%), 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).[119] Another suggestion focused on the need to

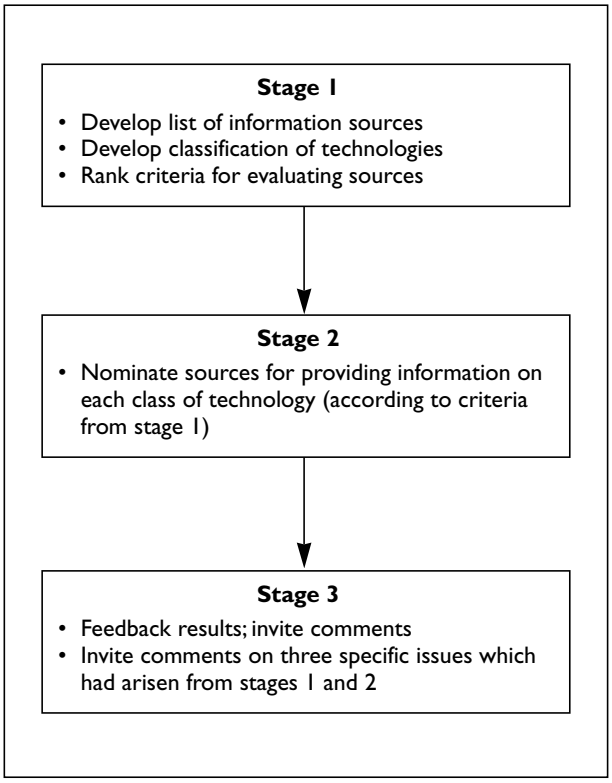

FIGURE 4 *Content of the three-stage Delphi study*

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 we decided to separate technologies by the sectors in which they are most likely to originate (e.g. pharmaceuticals from the pharmaceutical sector, other medical and assistive devices from medical engineering and procedures from clinical experience), as this would be most likely to highlight specific sources for identifying technologies at an early stage of their development. Our final classification of healthcare technologies is shown in *Box 3*.

Baseline list of sources

We compiled a list of potential information sources for identifying new healthcare technologies from existing or previous EWSs and other similar initiatives (*Box 4*).

Participants were invited to comment on this baseline list. Ten participants replied that no single source will identify most or all new healthcare technologies and that a composite approach was required rather than relying on just one of the information sources shown in *Box 4*. Three participants highlighted that few, or any, of the sources explicitly aimed to provide early warning of new healthcare 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 (e.g. 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

BOX 3 Classification of healthcare technologies by type

- Pharmaceuticals
- Diagnostic strategies
- Procedures
- Procedural devices
- Other medical and assistive devices
- Healthcare settings or treatment delivery systems
- Information technology
- New professions

BOX 4 Baseline list of information sources on new healthcare technologies

1 Key medical journals (e.g. *British Medical Journal, New England Journal of Medicine, The Lancet*)
2 Key pharmaceutical journals (i.e. *PharmaProjects, Scrip, InPharm*a)
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 healthcare 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)

BOX 5 Additional sources as suggested by Delphi participants

14 Internet (suggested by three respondents)

15 Funding proposals and trial registers in other countries (suggested by two respondents)[a]

16 Stock market analysts/venture capitalists (suggested by two respondents)

17 Newsletters and bulletins from other HTA organisations (suggested by two respondents)

18 Specialist industry sector journals (suggested by two 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, USA) which ranks (using criteria such as the number of people currently researching an 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; cofactors 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

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 healthcare 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 healthcare technologies. *Box 5* shows the additional suggestions from the 31 participants (84%) who replied.

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 15*).

There is some overlap between these categories (e.g. 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

TABLE 15 *Classification of information sources*

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 healthcare providers, drug information services
Tertiary	Drawing on other agencies' efforts to identify new healthcare technologies	Other EWSs or 'horizon'-scanning initiatives

users.[60] In round 1 of the Delphi study the project team suggested a list of criteria by which each of the potential information sources could be judged, and asked the participants to comment on it. In round 2 participants ranked the criteria in terms of their importance for assessing the potential information sources (from 1 (least important) to 5 (most important)). The scores which the 18 respondents (58% of the round 1 respondents) gave to each of the suggested criteria for assessing the value of the various possible information sources are presented in *Table 16*.

TABLE 16 *Criteria for assessing information sources*

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, and so '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 healthcare 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 healthcare 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.

Results

Table 17 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 and biotechnology companies were clearly seen as being the most effective sources 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.

Respondents were most prepared to suggest likely information sources for identifying

TABLE 17 *Results of the 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 and biotechnology companies	Pharmaceutical and biotechnology companies	Principal medical journals	Key pharmaceutical journals	Principal medical journals
Diagnostic strategies	Specialist medical journals	Principal medical journals	Newsletters and bulletins from other national/ regional HTA agencies	Specialist medical journals	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	Medical engineering companies	Medical engineering companies	Principal medical journals
Other medical and assistive devices	Specialist medical journals	Specialist medical journals Newsletters and bulletins from other national/ regional HTA agencies	Newsletters and bulletins from other national/ regional HTA agencies	Specialist medical journals	Newsletters and bulletins from other national/ regional HTA agencies
Healthcare settings/ treatment delivery systems	Private healthcare providers	Patient special interest groups	Private healthcare providers	Sentinel groups of expert health professionals	Principal medical journals
Information technology	Specialist medical journals	The Internet	Specialist medical journals	The Internet	(No suggestions)
New professions	Specialist medical journals	Specialist medical journals	Conferences Newsletters and bulletins from other national/ regional HTA agencies	Newsletters and bulletins from other national/regional HTA agencies Private healthcare providers Sentinel groups of expert health professionals	Sentinel groups of expert health professionals Newsletters and bulletins from other national/ regional HTA agencies

[a] *Where two or more sources are shown, they received the same number of recommendations*

'pharmaceuticals' and 'diagnostic strategies'; few were able to recommend particular sources for 'other medical and 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 healthcare technologies:

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

It is important to note that each of the sources can be accessed or searched in a number of ways, and each has its own disadvantages (*Table 18*).

We fed back the results of the study and asked participants for their views. 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 emphasise 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 or a new technology may appear in specialist journals of scientific journals (e.g. *New Scientist* or *Nature*) whilst speculative applications derived from the basic discoveries would probably appear in the more populist journals (e.g. *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 PET scanners in nuclear medicine, cardiology and oncology journals. When we fed back this comment in

TABLE 18 *Disadvantages of recommended sources*

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 and 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 make them a more important source of information than drug companies
Private healthcare providers	Only limited range of potential technologies will be of interest to private providers. May be difficult to access
Newsletters and bulletins from other national and 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

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.

Issues on which further comments and elucidation were sought

In round 3 of the study we asked participants to respond to prompts concerning issues which had arisen out of the earlier rounds and which we wished to explore further. Sixteen responses were received (89% of the round 2 respondents) 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.[60,95] 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 'healthcare settings and delivery systems' and 'new professions'. Further clarification was sought from participants with the following prompt:

> 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 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 healthcare 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 healthcare 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 (e.g. a 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 (e.g. the results of a Delphi study of peers) would add excitement to discussions
- the judgement 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
- the interaction and challenging of judgements 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 healthcare 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 speciality 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 (cardiorenal, oncology, etc.), another recommended co-nomination of members as had been used by the UK OST in their recent Technology Foresight exercise.[93] 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 healthcare 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 (e.g. pharmaceuticals) or sources (e.g. medical journals). We asked participants to:

> Please give your views on the scope for international collaboration with relation to early warning systems for new healthcare 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 EU (perhaps building on existing European programmes on research and development, such as EUR-ASSESS). The potential for involvement of other English language countries (the USA, Canada, Australia) was also highlighted. One respondent saw a potential role for the International Network of Agencies for Health Technology Assessment (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
- 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. We asked participants:

> 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.

We received few specific suggestions 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 healthcare technologies, the next step of an EWS is to assess 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. 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 (e.g. timeliness, sensitivity and specificity). We prompted participants for their views with the following:

> 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.

A three-stage process involving a number of participants seemed to be favoured (*Figure 5*). Some respondents felt that the use of 'panel of experts' would be cumbersome and probably only suitable for select topics or topic areas.

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 healthcare 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.) This could then be assessed by a panel of experts.

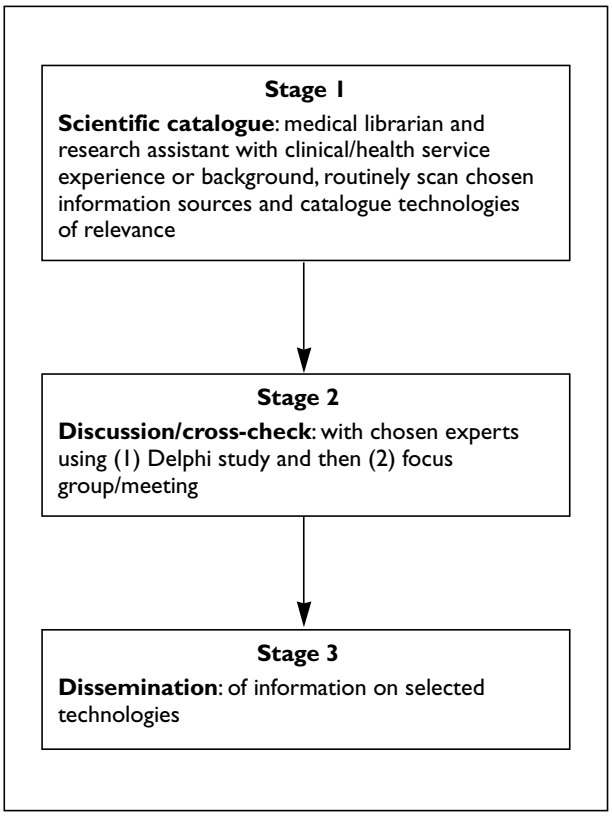

FIGURE 5 *Process for synthesising and appraising information on new healthcare technologies*

> 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.

Summary

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'. This decision will be determined by the size of impact that the types of technology are likely to have and the speed of their diffusion. 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 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 fed back 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 healthcare system concerned and the 'HTA-linked' legislation that may be in operation.

Chapter 6
Case studies

Introduction

These case studies aim to illustrate whether the information sources recommended by the literature review, telephone enquiry and Delphi study would have identified the selected healthcare technologies prior to their initial introduction and early diffusion into the UK's NHS.

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 information sources recommended in the Delphi survey could have provided early identification and, finally, a discussion of the issues that each case study raises for the establishment and operation of an EWS in the UK. Where appropriate the case studies also highlight the potential benefits of an EWS as well as some of the possible limitations to its operation.

CT scanners (head)

Description of the technology

This diagnostic technique combines the use of a computer and X rays to produce cross-sectional images of conditions such as cancer (staging of tumours), strokes and head injuries. CT scanners are more sensitive to variations in bone and tissue density than conventional X ray techniques, and they produce images with greater resolution and speed, thereby reducing the patients' exposure to radiation.[120]

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 USA, 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 USA and received a patent in 1962. Again, and despite subsequent work, corporations and physicians showed no interest in commercial development.[59,121]

The first commercial interest in CT occurred in Britain. EMI, a British electronics firm, developed a CT instrument in 1967[122] but no X ray companies wanted to license CT technology. However, the British Department of Health supported the construction of a prototype head scanner in the early 1970s. Department of Health and Social Security (DHSS) officials in the UK had visited EMI's laboratory in January 1969. The prototype instrument was installed in Atkinson Morley's 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.[123]

Figure 6 illustrates how progress in five different biomedical research programmes (in X rays, tomographic techniques, instrumentation, mathematics and computers) were required in order to develop CT head scanners. Such a development path can make identification of a technology harder, as well as making predictions of the likely timing of its introduction less certain.

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 of the scanners that became operational during 1973 and 1974. 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, 13 companies had installed CT scanners in the USA.[124] The units moved through four generations of operating methods within 4 years.

In 1971 the first clinical evaluation of a prototype brain scanner, funded by the DHSS, was performed at Atkinson Morley's Hospital in London. As early as 1974 the team at Atkinson Morley's Hospital was able to report on a clinical series of 650 patients.[125]

In April 1972 the new instrument was announced at a press conference.[126] The DHSS provided funds for five brain scanners and, as it became obvious that CT brain scanning was a remarkable breakthrough, the DHSS recommended that each region should purchase at least one brain scanner.[121]

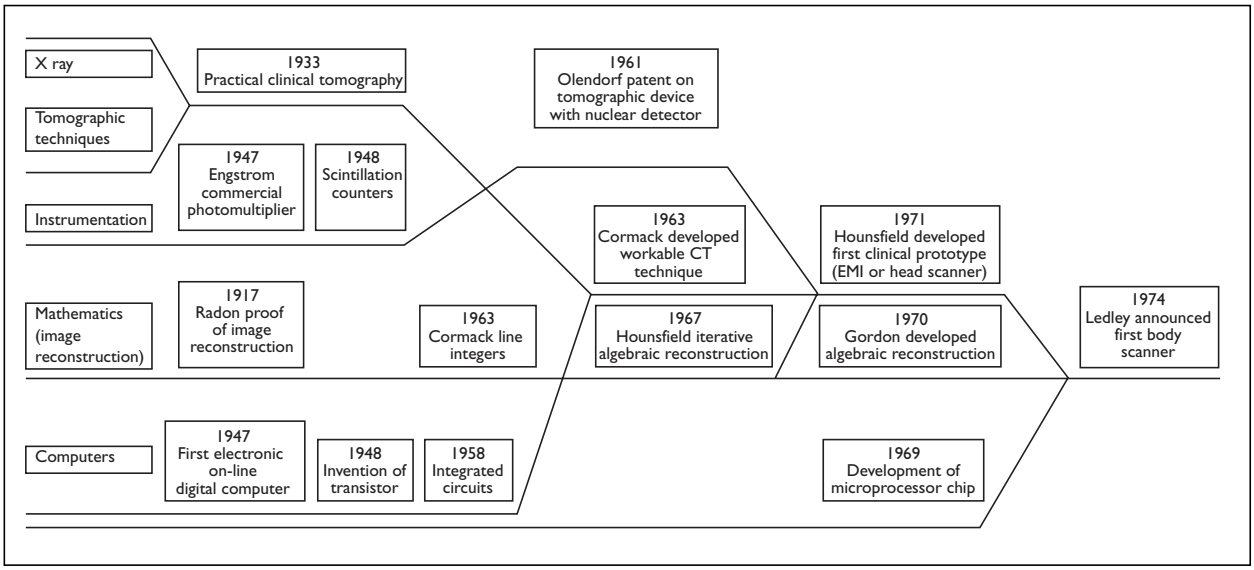

FIGURE 6 *Development of the CT scanner (Source: Analysis of selected biomedical research programs, vol 2. Columbus, Ohio: Battelle Columbus Laboratories, 1976)*

In the spring of 1978 the UK had 52 scanners, or almost one per million of the population.[121] 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 of the population.[127] This compares to 4.6 per million population in the USA as long ago as 1978.[121] In the USA 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.[124] *Figure 7* shows the diffusion rates of CT in the USA over the first 7 years of its clinical availability:

Baker[128] reported on the relative importance of sources of information amongst early adopters in the USA. Early adopters acknowledged the almost equal value of journal articles, medical conventions and the experience of colleagues (*Figure 8*).

Conventions and colleagues were the most common source of information for early adopters and although there were many articles on the use of CT scanners, almost all of them were uncontrolled case reports; very few examined effects on patient therapy or health outcomes.[129] This questions the belief that decisions to invest in new medical technology are based on scientific reports in the literature;[14,124,128] the single nationally funded multi-institutional study, performed from 1974 to 1977, was not reported until 1980.[130] Creditor and Garrett[14] related the early diffusion of CT scanners in the USA to the appearance of literature on the

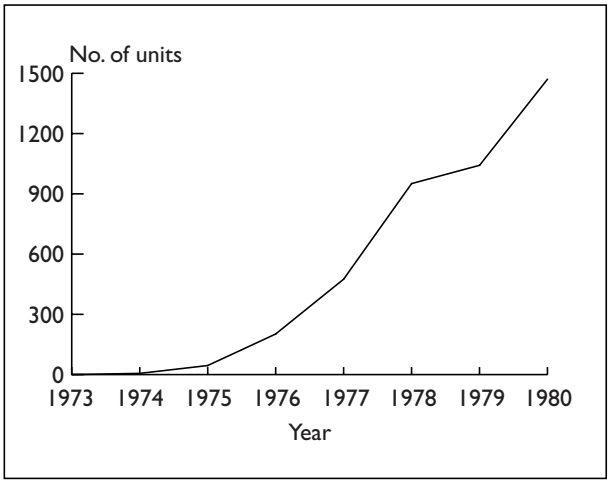

FIGURE 7 *The diffusion of CT scanners in the USA since the introduction of the first human imaging prototype (Sources: Banta[124] and OTA, as cited in Hillman[120])*

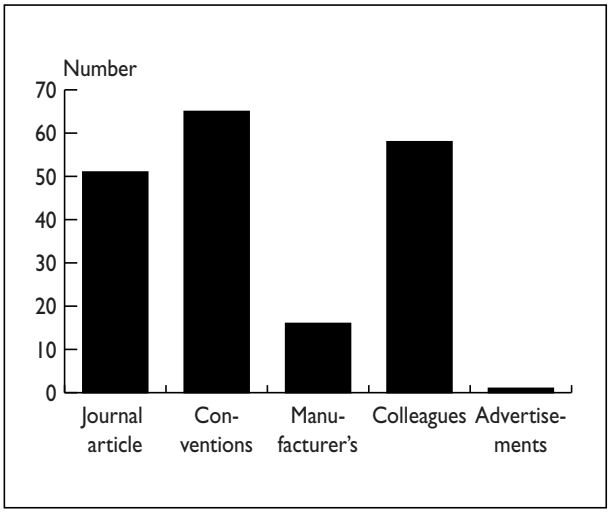

FIGURE 8 *Sources of information about CT scanners for early adopters (those ordering scanners 1973–1975)[128]*

subject of CT scanning by means of a 1973 to July 1976 MEDLINE search. They posed the question as to whether the 13 clinical papers which provided data that allowed valid quantification of diagnostic accuracy, and which had appeared in the English language literature by June 1975, justified the ordering of 100 units. They concluded that the rapid diffusion of CT scanners was not because the medical literature indicated its great usefulness. They noted that 18 institutions were the sources of all the information published through 1975 and that nine more contributed in the first 7 months of 1976 (almost all were major university centres).

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 healthcare technology prior to its introduction into the NHS in 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)
- report of the evaluation at Atkinson Morley's Hospital, London in 1974 (or report of the study whilst it was ongoing having begun in 1971).

Although the patents and papers in 'specialist' medical journals would have provided the earliest documentary evidence of the development of CT scanners (1961 and 1963, respectively) it is unlikely that these sources would have helped to alert policy makers to the huge potential impact of CT scanners given the high sensitivity and low specificity of such sources. In contrast, the 1969 visit to EMI's laboratory and subsequent DHSS involvement in the development and evaluation of the technology might have alerted an EWS via discussion with experts. Taken together, the US conferences in 1972 and 1973 and the *British Journal of Radiology* article certainly would have provided early warning.

Lessons for an EWS

CT scanners provide an example of how complex the innovation and development of a healthcare technology can be.[131] Such complexity illustrates how difficult it is to accurately identify new healthcare technologies and their likely impact on a health service. Even so, an EWS, via liaison with experts, would probably have detected CT scanners approximately 5 years before this technology exploded into use. However, documentary sources alone would not have been able to identify CT scanners as an important new healthcare technology prior to their widespread diffusion; small-scale clinical reports did not begin to appear until 1975, and it is only in combination with other sources that we can recognise the importance of the *British Journal of Radiology* paper in 1973. Newsletters and bulletins from other HTA agencies, would not appear, or would not have been expected, to have provided 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. 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'.

In the case of CT scanning, particularly in the USA, use of conference and meeting abstracts may well have provided early warning of the likely rapid diffusion of this technology; Baker's analysis of where early adopters obtained information from suggests that conventions were the most common source.

Biosensor for home glucose monitoring (Medisense ExacTech pen)

Description of the 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.

Biosensor research and development is rapidly expanding at present. Hundreds of clinical biosensor designs have been reported but relatively few have emerged from the laboratory. The Medisense ExacTech pen is one of several

biosensors that are on the UK market for home glucose monitoring.

Early developments

The evolution of the first biosensor began in the mid-1950s,[132] when an electrode designed to measure dissolved oxygen in the blood of patients undergoing surgery was invented in the USA. By 1962 the 'oxygen electrode'[133] had been extended to sense blood glucose levels. 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 levels in body fluids. Pickup[134] reports that about 25 years ago, at the 50th Anniversary Insulin Symposium, implantable glucose sensors were beginning trials, and devices to mimic the normal glucose–insulin control system were thought to be feasible in the near future.

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 glucose monitor[135] and Roche's lactate analyser.[136] Further technological advances have led to the development of second-generation amperometric enzyme sensors.

Adoption

Medisense opened in Abingdon in the UK in 1984 and, at that time, made use of research on biosensors previously done at Oxford University and the Cranfield Institute of Technology.

The ExacTech pen received clearance for marketing by the FDA in December 1986, and the initial marketing of the product commenced in November 1987 in the USA. The subsequent launch of the product in the UK was in the summer of 1988, and the ExacTech system was available on NHS prescription in August 1989. From early development to availability on the NHS the ExacTech pen took approximately 5 years.

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. The ExacTech system allowed new error checks to be introduced to glucose monitoring, and the timing function was entirely taken over by the device. 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 1988, were:

- papers in scientific journals in 1984 (regarding a ferrocene-mediated enzyme electrode for amperometric determination of glucose by workers at Oxford University and the Cranfield Institute of Technology[137]), 1987 and 1988[138] (from the Cranfield Institute of Technology regarding an amperometric enzyme electrode for glucose analysis)
- FDA clearance in December 1986
- a brief research report in a key medical journal in 1987.[139]

Less specifically, articles relating to the application of electrochemical instruments to analyse blood glucose date back to 1968 (*Figure 9*) and 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.

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 2 years of it becoming available on prescription in the NHS.[140–142] However, *The Lancet* paper

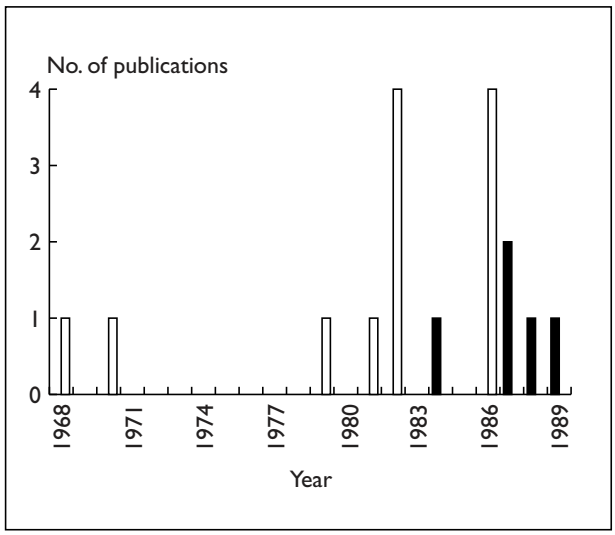

FIGURE 9 *MEDLINE references to the ExacTech pen and electrochemical instruments to measure blood glucose, 1968–1989 (■, ExacTech pen; □, blood glucose and electrochemistry)*

in 1987, together with notification of FDA clearance in the USA in 1986, should have provided 2 years warning of the likely introduction of the ExacTech pen.

The combination of an effective network of experts and regular liaison with biotechnology companies might reasonably have been expected to have provided some early warning of this technology. Indeed, some time after the introduction of the ExacTech pen, Cranfield Biotechnology Limited produced a report[143] which predicted future application areas based upon two criteria: (1) applications likely to emerge within a 5 year timescale; and (2) applications where 'substantial' product sales were expected.

In the late 1980s there were a large number of papers reporting generally on the development of biosensors for glucose analysis[144] as well as reports of animal studies of other specific biosensors which were in development.

Lessons for an EWS

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. It seems likely that an EWS using only documentary sources would have been able to provide approximately 3 years early warning of the introduction of the ExacTech pen. In addition, biosensors were identified as an important emerging healthcare technology by the STG report (whose results were published in 1988) and by the Delphi survey undertaken by Spiby in the same year.[111] 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.

This case study also illustrates how it can be difficult to identify specific products prior to their introduction to the NHS and, more importantly, how to identify which specific product from a large number under development will have the largest and most imminent impact. As noted above, biosensor research had been begun in the 1950s and 1960s, 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, but 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.

Left ventricular assist devices (LVADs)

Description of technology

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

Early developments

It was not until the 1960s that technology was sufficiently advanced for clinical implantation of mechanical assist devices to be undertaken.[145] Impetus for efforts was provided by the US government, which, in 1975, created a programme for developing and clinically testing an LVAD. At that time, clinical trials for a 2 year implantable LVAD were expected to begin in an estimated 3–5 years. Targeted efforts beyond that included the development of a 5 year implantable LVAD and electrically energised engines. Researchers saw the longer-term implantable LVAD as a significant step, possibly a decade away.[146] 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 19* occurred within a relatively brief time frame, and established mechanical circulatory support as an effective therapeutic manoeuvre pending cardiac transplantation.

The development of LVADs has progressed over the last 20–30 years to a stage where the devices are smaller, quieter, more reliable and less likely to cause complications. The technology is continually developing, with the goal of a completely internalised system and power supply.

Adoption

As part of a survey of LVAD use at University HealthSystem Consortium member hospitals in the USA, respondents were asked when they began using LVADs.[147] *Figure 10* shows that adoption of LVAD technology has been consistently increasing since 1976.

Two LVADs have previously been considered suitable for long-term cardiac support. Both the Thermo

TABLE 19 *Development of mechanical cardiac support*

Year	Development
1975	Authorisation given to begin clinical trials of an 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 First successful cases of bridge to transplantation with mechanical device
1982	Implantation of the Jarvik 7® total artificial heart as a permanent cardiac substitute
1984	First long-term transplant survivor (supported for 9 days) with the Novacor electrical implantable system Paracorporeal Pearce/Donachy LVAD
1984–1985	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 devices were implanted clinically, including 40 consecutive patients by Cabrol in Paris (the largest series)

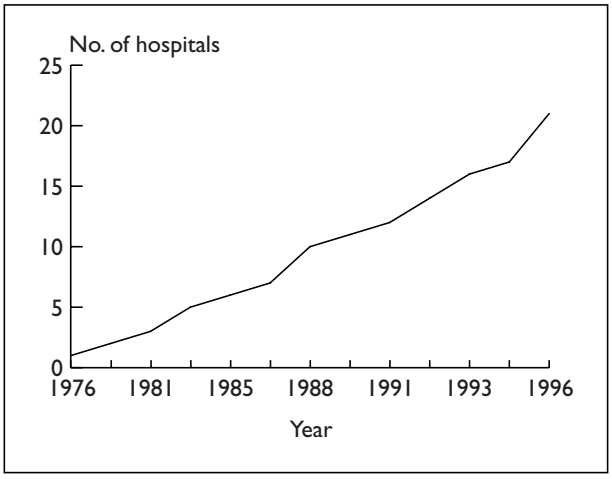

FIGURE 10 *Cumulative adoption of LVADs in the USA – University Health System Consortium members (US)*

Cardio Systems HeartMate® devices[148,149] used in the John Radcliffe Hospital, Oxford, and the Novacor system used in the Papworth Hospital have proven track records for prolonged use as a bridge to transplantation.[150] In the FDA-approved clinical trial of 116 patients versus 46 control patients with an endpoint of survival at 60 days after transplantation, 71% of the HeartMate patients survived to undergo transplantation versus 36% in the control group; after the transplant the group supported by the LVAD had a survival rate of 65% versus 30% for controls. Clinical trials with the 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 1–503 days. The use of similar devices as a bridge to recovery is at an earlier stage of clinical development and acceptance.

There is now extensive clinical experience (so far limited to heart transplant candidates) with both the pneumatic and electric HeartMate systems. Between 1986 and July 1995 the pneumatic device was implanted in 422 patients worldwide. Recent research has been directed towards developing a totally implantable, electronically activated system intended for long-term use, and 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.[151] Prolonged bridge to transplantation use 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 Jarvik 2000® intraventricular artificial heart (an axial flow pump) 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 proved successful the Jarvik 2000 intraventricular pump may have proved preferable to transplantation both from the standpoint of durability and quality of life. A trial of the Jarvik 2000 device is planned for 1998–1999, with 20 patients recruited over 2 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.

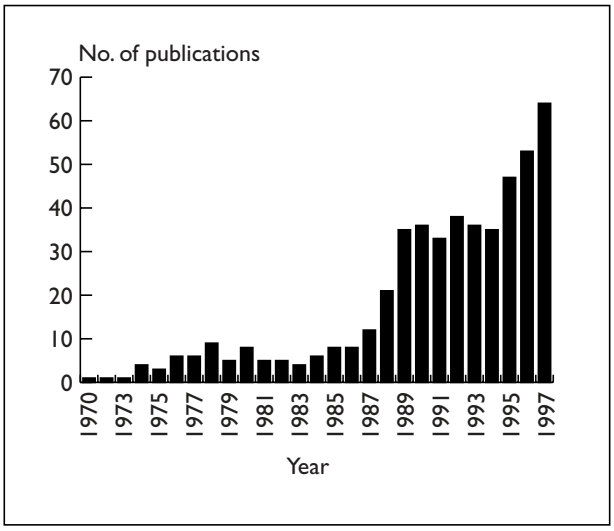

FIGURE 11 *MEDLINE references to LVADs, 1970–1997*

Potential information sources for early identification

LVADs have been the subject of published papers throughout the 1970s to 1990s (*Figure 11*), with a significant increase from the late 1980s onwards. Retrospective case series have reported on the various developmental stages of these devices as well as some small comparative trials of LVADs used as bridge to transplantation (e.g. paper in the *Annals of Thoracic Surgery* in 1994 reporting clinical experience with HeartMate LVAD[150]).

As well as the increasing 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.[64] 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.

Experience with LVADs in the UK has been limited to two centres. In 1985 a team of two surgeons and one technician from the Papworth Hospital underwent 2 weeks of intensive training at the University of Utah, Division of Artificial Organs, in the use of the Jarvik series of total artificial hearts and VADs. Subsequently, the Papworth team provided technical assistance in the first Jarvik total artificial heart implant in Paris in 1986 and later that year implanted their own first patient with a Jarvik artificial heart as an elective bridge to transplant.

In 1989 one surgeon and one technician underwent training in the use of the Hemopump® (a high-speed axial pump for LVAD applications), in Houston. The Papworth Hospital 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.

The 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 1994, but problems with recruitment to the trial (only three cases and three controls) has delayed any further formal evaluation.[152]

Lessons for an EWS

Certainly the case of LVADs 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 discussion with experts. With the exception of a 1980 paper in the *Journal of the American Medical Association*,[153] 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 and co-workers in 1995 (and published in 1997) identified LVADs as a new healthcare technology which would have important implications for the NHS within a 5 year time-frame, but LVADs were not one of the most commonly mentioned of the 1100 technologies identified in the survey. Perhaps most importantly, 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.

There may also have been potential for identifying LVADs via the involvement of the FDA in the USA; Myers[154] reports that clinical studies have been conducted under an investigational device exemption approved by the FDA to evaluate the devices for safety and efficacy.

Telemedicine

Description of the technology

Telemedicine is defined as 'remote, telematic care using information and communication systems to give patients with their healthcare workers access to relevant information sources wherever they are located'. 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.[155]

Early developments

Although telemedicine has been around since the 1950s,[156] the early programmes failed to achieve physician and patient acceptance.[157] 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.[158]

In the USA, NASA played an important part in the early development of telemedicine, providing much of the technology and funding for early demonstration projects.[159] From around 1978 to the mid-1980s there were few studies undertaken on telemedicine. With the exception of a 20 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, due to factors such as further technological advances combined with reduced costs, programmes of healthcare reform emphasising the need for improved efficiency, and a demand by rural patients and physicians for equal access to high-quality health care irrespective of location. Telemedicine projects are being implemented in the USA at an accelerating rate. In 1990, four telemedicine projects for patient consultations were active in North America. In 1993 there were ten, and by 1994, there were at least 50 programmes active or in various stages of planning and implementation.

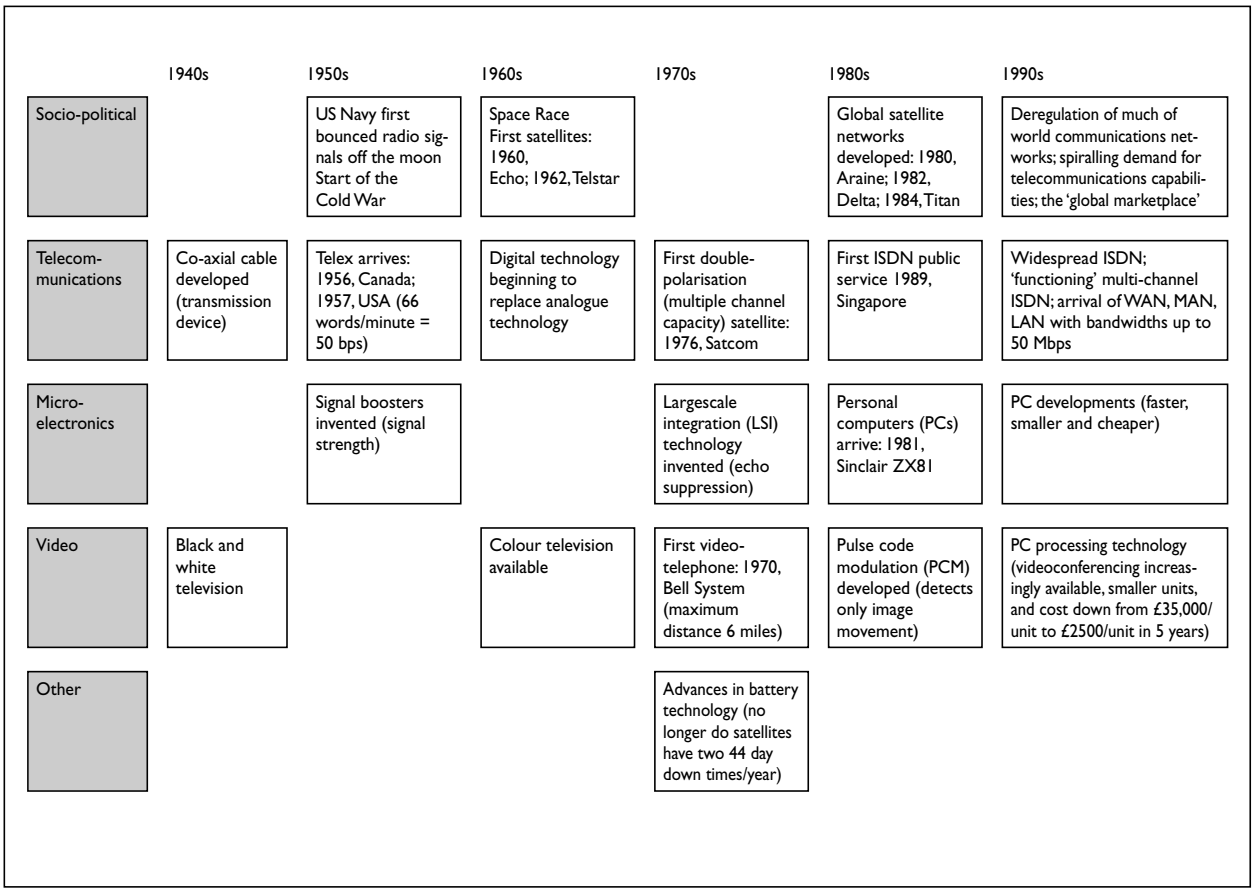

FIGURE 12 *Development of telemedicine*

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 12*).[104]

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. An editorial in *The Lancet* in 1995 commented that the recent resurgence of interest had yet to have a major impact on mainstream medical services, and made a number of predictions as to the impact that telemedicine will have on medical practice in the year 2000.[160] In order to take stock of the level and range of work in the UK, in 1996 the Department of Health's Research and Development Directorate commissioned a survey of telemedical activity. That study identified the status of activity in the UK in telemedicine. 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 healthcare services to patients.[155] Current services in the UK include some teleconferencing services, including mainland provision of trauma advice to oil rigs and remote fetal diagnosis on ultrasound images. In 1994 the Riverside Community Health Care Trust installed a link to enable nurse practitioners working in a walk-in minor treatment centre in London to access accident and emergency advice from consultants at the Royal Victoria Hospital in Belfast. Most UK activity to date has so far been locally driven pilot projects. Internationally, larger-scale activities are being planned.

Teledermatology seems to be a much more recent application of telemedicine than teleradiology. A number of studies related to telemedicine have been published or are underway. 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.

The trajectory of telemedicine will be restrained by the lag in setting standards for computer interaction, the need for open computer systems architecture, legislation and the regulation of medical practice, resistance by providers and reimbursement issues.

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 USA.[157] However, a recent paper by Bashshur[161] considers there to be a dearth of systematic empirical research regarding the true effects on telemedicine on costs, quality and accessibility of care.

In the medical literature the first reports on teleradiology appeared as early as 1972, but numbers of references remained relatively low up to about 1990, with a generally increasing trend from then onwards, culminating in a major increase for 1995* (*Figure 13*).[104]

Other applications of telemedicine in different specialities have seen fewer publications (*Figure 14*).

In addition to the published literature, telemedicine has long been the subject of conferences and symposia. Mowatt and co-workers identified 57 conferences which related to telemedicine during the period 1980–1996 (MEDLINE and Index of Scientific and Technical Proceedings).[104] The 1981 survey of expert opinion undertaken by the FDA reported four citations on 'information transmission and storage to improve health care'. The citations mentioned teleradiology in particular, and predicted 1989–1990 as the likely year when this technology would become an issue for that organisation.

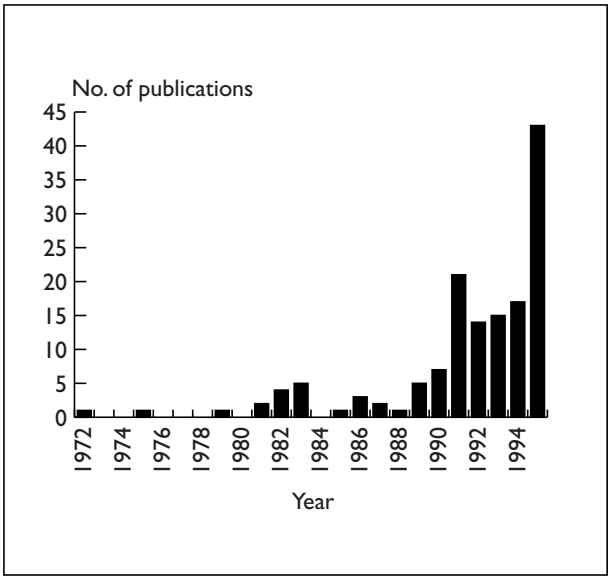

FIGURE 13 *MEDLINE references: teleradiology, 1972–1995*

* Search strategy: as cited in Mowatt and co-workers.[104]

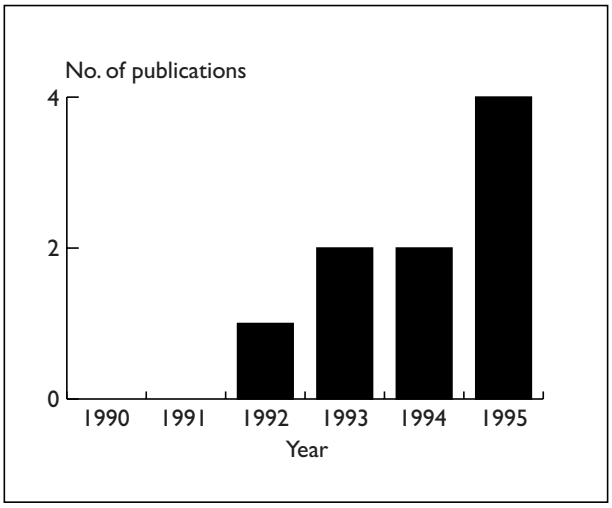

FIGURE 14 *MEDLINE references: teledermatology, 1990–1995*

Lessons for an EWS

Telemedicine would have been relatively easy to identify as a potentially important new healthcare technology at virtually any time over the past 30 years through the vast literature (and conference exposure) which has evolved around the subject. It is difficult to retrospectively assess how the Internet and other HTA agencies might have added to the information that could be accessed through such documentary sources.

The task for an EWS would be how to predict when telemedicine will finally begin to have a really important impact on healthcare provision. 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.

Paediatric intensive care units (PICUs)

Description of the technology

The British Paediatric Association (BPA) report[162] 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.

Early developments

The first PICU was for respiratory care (tracheotomy, muscle relaxant and mechanical ventilation) under the management of paediatric anaesthetists in the USA in 1964. Then in the 1970s and early 1980s, an epidemic of Reye's disease demanded a multisystem approach to paediatric intensive care, introducing the use of intracranial pressure monitoring. Multidisciplinary paediatric intensive care expanded the role from postoperative, 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 1987, and in 1989 the Confidential Enquiry into Perio-Operative Deaths (CEPOD) 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 1990–1991, 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, in 1991, to the establishment of a second BPA working group which carried out a national survey of paediatric intensive care facilities, workload and working practices. In December 1993 *The Care of Critically Ill Children* report was published.[163]

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'.

Adoption

Paediatric intensive care has evolved incrementally as a distinct category of child health care. Information about the provision and use of PICUs has not been collected routinely. *Figure 15* shows the increase in the number of PICU beds in the UK from 1987 to 1997, based on estimates from a number of reports during that period.

The 1987 working party reported that there were 22 PICUs in the UK which provided a total of 126 beds although a survey in 1986 suggested there were 17 PICUs in the UK. In 1993 Shann[165] suggested that there were too many small PICUs in Britain (22 plus use of adult intensive care units) and it would be better if there were only 12–14 units.

The 1993 BPA report stated that whilst in 1991 there had been 175 designated PICU beds (including general and subspeciality 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, and that three regions had no identified paediatric intensive care beds, reflecting a wide regional variation. In addition, the figures include some units which are more correctly classified as high-dependency units, small satellite units and single-speciality units (e.g. 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,[166] and, in March 1997, updated this figure to 280 beds in 29 centres of differing sizes.[167]

Potential information sources for early identification

Much of the published literature relating to PICUs is from the USA and Australia,[168] and *Figure 16* shows the number of MEDLINE references over the period 1966 to 1990, with a particular increase in the late 1980s.

The existence of expert working groups, and the publication of their reports, and a high public profile throughout the mid- to late 1980s, would have provided relatively late warning of the introduction of PICUs into the UK.

Lessons for an EWS

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. PICUs are therefore 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 healthcare technology. Even so, the early introduction of PICUs into the UK would have had to rely on monitoring of developments overseas (in this case in the USA and Australia), as such sources may have given earlier warning of the developments in PICUs in the late 1970s and early 1980s.

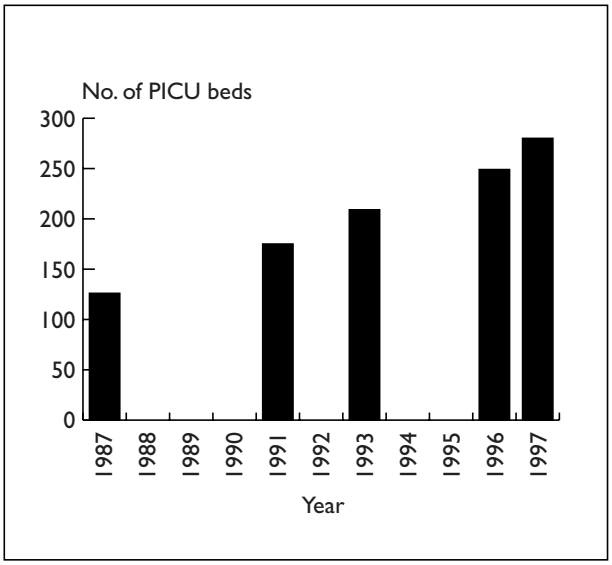

FIGURE 15 *PICU beds in the UK, 1987–1997*

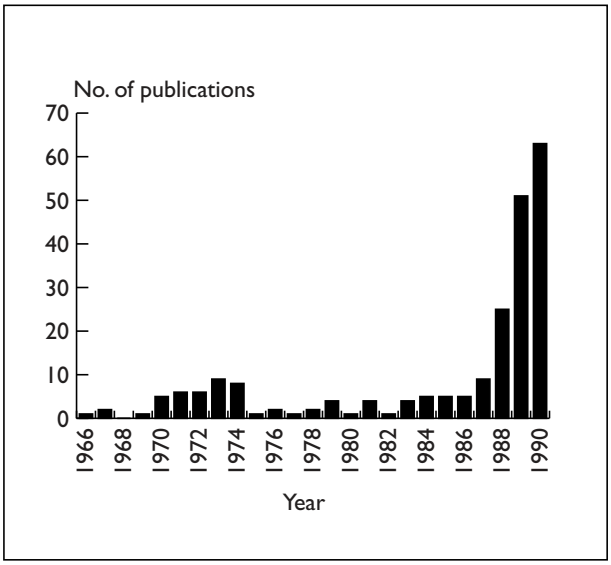

FIGURE 16 *MEDLINE references to PICUs, 1966–1990*

IFN-β for multiple sclerosis

Description of the technology

IFN-β is the first new product for multiple sclerosis, a chronic incurable disease that is relatively common and has a variable course.[169]

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.[170] IFN-β was first cloned and expressed in bacteria in 1980, but was found unsuitable for clinical use in that form.[171]

Genetic engineering enabled scientists to make synthetic IFN-β to replace the scarce, impure and prohibitively expensive natural human IFN-β, which resulted in a large supply of IFN-β at reasonable costs for clinical trials.[172] The potential usefulness of IFN-β as a treatment for multiple sclerosis was first considered in the late 1970s. Its discovery was not haphazard but the result of numerous human clinical trials with various interferons conducted over a 13 year period.[173] It was finally marketed in the UK in December 1995.

Adoption

A *Drugs and Therapeutics Bulletin* article in February 1996 drew the conclusion that there was insufficient evidence to recommend the use of IFN-β,[174] as did others.[175,176] 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.[177–180] As a consequence of this policy confusion, and in spite of the attempt by the Department of Health in Britain to ensure the orderly introduction of IFN-β, a year after its licensing there were great disparities in purchasing across Britain. It has been suggested that a small number of enthusiastic neurologists and an 'active patient interest lobby' dictated policy at national level,[181] 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, and the number of papers stayed relatively stable each year (reports of continuing trials[182–185] and the occasional editorial[186]) until just before the launch of IFN-β in the UK in December 1995, when there was a sharp increase in the number of papers published. Many of the papers published in 1994 and 1995 were editorials[187] or reviews (many in pharmaceutical journals) on the potential role of the drug following the publication of the Phase III trial results in 1993 (*Figure 17*).[188]

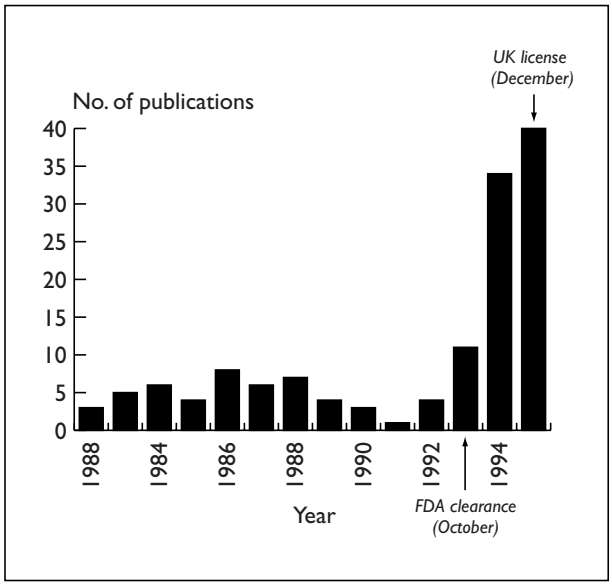

FIGURE 17 *MEDLINE references to IFN-β in multiple sclerosis, 1982–1995*

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 data. For most drugs an unfettered 5 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.

The manufacturers of IFN-β, Schering, circulated information to health authorities and clinicians, but McDonald issued a position statement in 1994 on behalf of the Association of British Neurologists,[189] giving the opinion that 'the widespread use of IFN-β can not yet be recommended.' The Department of Health issued an executive letter[190] in 1995 providing 'guidance' on the introduction of IFN-β. Purchasing authorities were asked 'to initiate and continue prescribing of beta interferon through hospitals'. This is the first time that the NHS Executive has issued such a directive.

Lessons for an EWS

As the development of IFN-β as a treatment for multiple sclerosis required at least 15 controlled studies over a 13 year period, reports were being published in specialist medical journals during that time. Parallel to these reports were presentations at conferences, particularly in the USA. In addition, as it became clear that IFN-β would be licensed in the USA 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 USA.

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, 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 major policy implications following the introduction of a new healthcare technology could have been predicted significantly early by an EWS.

Dornase alfa for cystic fibrosis

Description of the technology

rhDNAase is a new treatment for cystic fibrosis which has been shown to improve lung function and reduce infective exacerbations in patients with cystic fibrosis.

Early development

The idea of using rhDNAase to treat the thick mucous secretions associated with cystic fibrosis was first conceived in 1988 by Genentech. The further rapid development of dornase alfa is shown in *Table 20*.

Adoption

There is considerable pressure to prescribe rhDNAase despite the demonstrably marginal benefits and its high cost. Other commentators have suggested that rhDNAase should not be added to the formulary as evidence supporting the use of the drug has not yet been published.[192] The Cystic Fibrosis Trust has been examining how best to establish guidelines for the use of rhDNAase. The manufacturers of rhDNAase, Genentech, estimate that just under 20% of all cystic fibrosis patients in the UK (1200) are currently receiving the drug.[193]

TABLE 20 *Development of dornase alfa for cystic fibrosis*

Date	Progress
May 1990	IND submitted
February 1991	Phase I completed
November 1991	Phase II completed
December 1991	Phase III began. In less than a year, more than 900 patients with cystic fibrosis, from over 50 institutions, completed a 6 month Phase III clinical trial satisfactory to the FDA; a landmark in clinical research on cystic fibrosis
November 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[191]
August 1993	FDA Advisory Committee
January 1994	Licensed in the UK

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[193–197]) 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[197] appeared in the same edition of the journal which carried the Phase II trial, but 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 18*).

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,

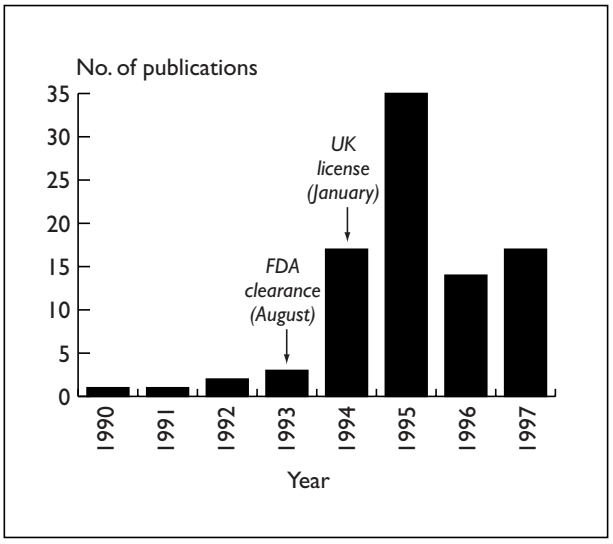

FIGURE 18 *MEDLINE references to dornase alfa, 1990–1997*

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 PLA filing in less than 5 years, and in June 1993 *Drug Therapy* reported that Genentech Pharmaceuticals had filed a PLA for dornase alfa on 30 March 1993.[198] A PLA report was also made in December 1993 by *Hospital Pharmacy*.[191] In November 1993 a consortium of four regional drug information centres produced a monograph on dornase alfa, a new drug in clinical development.[199] The monograph was intended as 'advance evaluated information for NHS managers and budget holders'. *Scrip* reported that rhDNAase had been refused reimbursement in Australia.

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 rhDNAase by the Cystic Fibrosis Trust in September 1993 ('DNase – a statement from the Cystic Fibrosis Trust'). In February 1994 the Cystic Fibrosis Trust in the UK issued a statement on the use of rhDNAase. In June 1994 the Family and Adult Support Services of the Cystic Fibrosis Trust issued a further statement regarding the prescribing of Pulmozyme®.*

Roche Products 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.†

The FDA in the USA, the Committee for Proprietary Medicinal Products in the EU and the Medicines Control Agency in the UK all recommended the drug for licensing.[200]

Lessons for an EWS

Early warning provided by pharmaceutical and biotechnology companies was evident from the Roche Products letter which 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, 2 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 identify drugs very early (in this case, from a conference report four years before licensing). This is particularly important in the case of dornase alfa, given the rapid pace at which it was developed and marketed. 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 and co-workers in 1995 (and published in 1997) identified rhDNAase as one of the most important new healthcare technologies which would have 'moderate' implications for the NHS during 1996–1997.

Donepezil

Description of the 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.

* 'The prescribing of Pulmozyme', Cystic Fibrosis Trust, June 1994.

† E Tierney, letter, Roche Products, 14 December 1993.

Early development

Animal studies with donepezil began in the early 1980s, and in 1990 preclinical 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, a US multicentred, randomised, double-blind placebo-controlled trial.[202] This was a 12 week study of 161 patients with mild to moderately severe Alzheimer's disease that showed that 5 mg of 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 (hydergine). In October 1997 the *Drugs and Therapeutics Bulletin* failed to recommend the use of donepezil for the symptomatic treatment of mild to moderately severe Alzheimer's disease.[202] 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 21*).

The debate about the cost-effectiveness of donepezil continued after licensing.

TABLE 21 *Other acetylcholinesterase inhibitors for SDAT*

Drug	Development status
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 1998
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 19*).

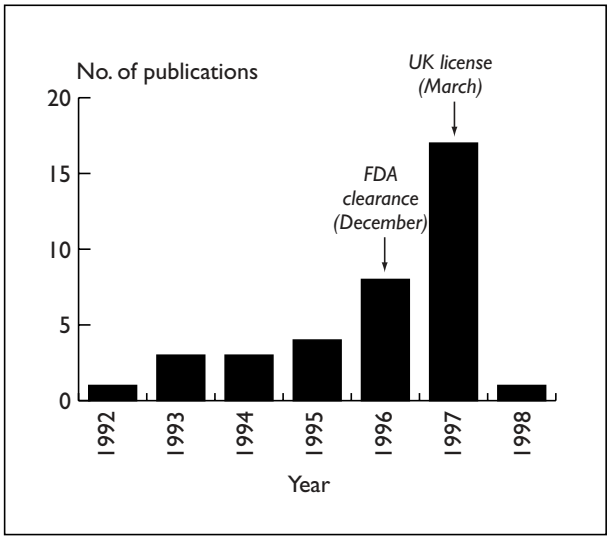

FIGURE 19 *MEDLINE references, donepezil, 1992–1998*

FDA clearance for donepezil was granted in December 1996. Melzer[203] cites reports in the lay press that heralded the arrival of donepezil in the month before, and the month of, its licensing in the UK. Also in the lay press in March 1996 the Alzheimer's Disease Society was cited as 'introducing a note of caution' regarding donepezil.

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 randomised controlled trials, of which only one had been published in full. Most references in pharmaceutical journals only occurred after FDA approval in the USA.

As with dornase alfa and IFN-β there were plenty of opportunities to track donepezil through clinical trials, but 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

and co-workers in 1995 (and published in 1997) identified 'drugs for Alzheimer's' as one of the most important new healthcare technologies which would have 'major' implications for the NHS during 1996–1997.[95]

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.

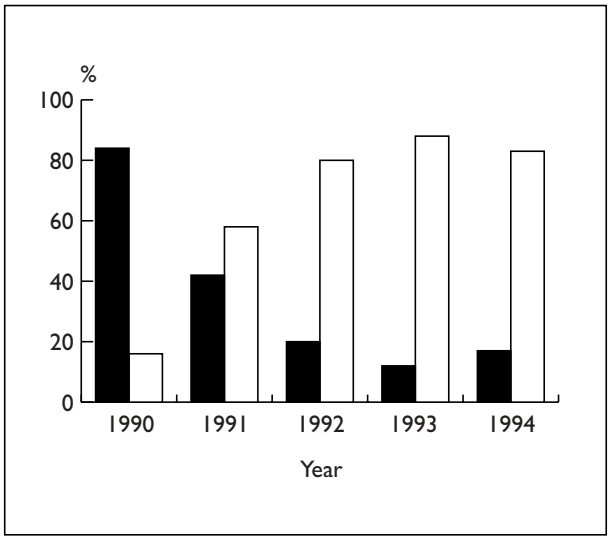

FIGURE 20 *Proportion of cholecystectomies conducted laparoscopically, 1990–1994, Lothian region, Scotland. (Source: Parliamentary Office of Science and Technology, 1995. Data supplied by Lothian Surgical Audit) (■, open; □, laparoscopic)*

Laparoscopic cholecystectomy

Description of the technology

Cholecystectomy is the most common treatment for gallstones. The laparoscope provides 20 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 visualised on a television screen.

Early development

In Lyons, France, in March 1987, the first human laparoscopic cholecystectomy using a gynaecological instrument was performed.[204] Concurrently, three centres (in France and the USA) began further development of the technique, so that by 1988 it was already being done in the USA and other countries. However, as Szczepura and co-workers[101] point out, 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; later refinement of high-resolution video cameras and the development of appropriate instruments led to their adoption for medical applications.

Adoption

The key feature of laparoscopic cholecystectomy was its rapid introduction and diffusion into the NHS. Grundfest[205] 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); third, physicians realise that less invasive surgery is in fact good medicine. The first operation in the UK was performed in 1989 in Dundee by Cuschieri and colleagues. Data from the Lothian Surgical Audit reveals the rapid introduction of laparoscopic cholecystectomy between 1990 and 1992 (*Figure 20*).[206]

Potential information sources for early identification

Mowatt[104] reports that a single reference on laparoscopic cholecystectomy appeared in 1989, after which annual numbers increased steadily, peaking over the period 1993–1994 at over 600 references per year; the beginning of a decline in publication numbers appeared to be indicated 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 literature began around the same time as reports began to appear in the clinical literature.

The opportunities to identify laparoscopic cholecystectomy 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); and afterwards the procedure underwent rapid diffusion, particularly in the USA. Mowatt cites seven conferences which took place in 1990.

In 1989, before widespread diffusion, Cuschieri stated that prospective randomised controlled trials were needed to define indications for the laparo-

scopic approach and to confirm the benefits of this procedure against the standard cholecystectomy.[207] The earliest trials began in 1990. The largest study of laparoscopic cholecystectomy was a report of the experience of 20 surgical groups in the Southern USA in 1991. The European experience from seven centres in France, Germany and the UK was reported in 1991. Guidelines on minimally invasive surgery were not issued by the Royal College of Surgeons until June 1994 (and even then were only advisory).[208]

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.

Stocking[34] suggests that the early 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.

Thus, in the case of laparoscopic cholecystectomy advance warning of this new procedure could only have been received 2 years prior to it being first performed in the UK and 3–4 years before it was in common usage. Because of this speed of diffusion there were very few opportunities to identify laparoscopic cholecystectomy sufficiently early.

Chapter 7

Synthesis of results

This chapter draws together the findings of the literature review, telephone enquiry, Delphi study and case studies into two areas of discussion:

- information sources
- the establishment and operation of an EWS.

Information sources

There were some discrepancies between the information sources which were recommended for identifying new healthcare technologies by previous initiatives (type II papers from the literature review), the telephone enquiry of existing national EWSs, the Delphi study and the retrospective case studies (see *Table 22*).

The following sections are presented in the order in which the information sources appear in *Table 22*.

Primary sources

Patents

Both the literature review and the Delphi study indicated that this source was not of particular

TABLE 22 *Recommended information sources from each method*

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

Key

Literature review:
✓✓= used by all previous studies
✓= used by at least one previous study
✗ = 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
✗ = not recommended

Case studies:
✓✓= in the opinion of the case study reviewer (GR) this was the best source for at least one of the case studies
✓= in the opinion of the case study reviewer (GR) 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

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 healthcare market actually makes this source inefficient;[64] in the first month of 1987 alone, the US patent office issued 6418 patents, of which 423 were classified as medical patents. 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 USA 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 and 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 USA via the FDA would commonly provide 1–2 years early warning. However, not all drugs are necessarily licensed in the USA before they are approved in the EU (e.g. 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 USA. In 1996 the FDA approved more new products (51 molecular entities and eight new biological 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[124] noted that, in general, manufacturers have not been cooperative in releasing information on CT scanners that they have sold. 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
- companies may release news only just before actual marketing
- information from private companies can be unreliable.

Despite these reservations this source was chosen by the Delphi respondents 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 and 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 healthcare providers. For example, BT 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 cooperate 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.

Secondary sources

Pharmaceutical journals

Banta specifically cites *Scrip* as a publication which enables drugs in development to be tracked through from initial development to marketing.[60] Three of the six national EWSs 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 healthcare 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,[209] 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 (e.g. *Hospital Pharmacy, Bio/technology, Drug Therapy* and *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[211] detailed the sources of information used by health reporters and medical journalists. 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, New England Journal of Medicine, Scientific American* and trade and technical magazines, such as *Nursing Times*). This source is used by all existing EWSs 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 (e.g. a report of a Phase III clinical trial of dornase alfa)
- discursive pieces on the future of a particular technology, such as those type III papers identified by our literature review (e.g. *The Lancet* editorial on telemedicine, the *New England Journal of Medicine* editorial on rhDNAase, 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

Scientific journals are being scanned by the majority of existing EWSs but respondents in the Delphi study did not select such journals as being of primary importance in identifying new healthcare 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 healthcare system. *Nature* and *Science* were particular journals which were cited frequently by respondents, and by Wilkie (see above), as being of some potential use.

Specialist medical journals

Although 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, this specific type of journal was not mentioned either in the papers assessed by 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.[211] Although comments in the Delphi study suggested that it was in specialist medical journals that reports of initial case series of the application of a new technology will appear, even papers in specialist journals sometimes only appear following the adoption of a technology (e.g. 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 (e.g. the 1985 editorial concerning IFN-β which 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 EWSs. 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.[212] 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[78]); 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 cholecystectomy) conferences would have been a useful source. 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 EWSs, 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.[213–216] The results of our own 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 our 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 and co-workers 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.

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 which are produced for purposes other than an EWS (e.g. 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, but compared to many of the alternative documentary sources experts is 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 speciality 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 healthcare 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 which 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.

Private healthcare providers

Delphi respondents did not recommend this source. They felt that, whilst it may be useful for identifying needs for new healthcare technologies, in terms of providing early warning, private healthcare 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 healthcare 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.* One Delphi respondent commented that regional DIS 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 5 years before marketing (see appendix 5 for a full description). Modern-day sources such as DIS, which 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 healthcare technologies and their evaluation. The sites which the authors of this report have found particularly helpful are detailed in appendix 7. Many of the information sources which have been identified by the literature review, telephone enquiry, Delphi survey and case studies can be accessed directly via the Internet (e.g. 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†). 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. 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

* http://www.ukdipg.org.uk/newprod.htm.

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

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 and stock exchange monitoring

Senard[217] 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. 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[218] 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. Additionally, companies traded on any of the US stock exchanges must file quarterly as well as annual reports.*

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 EU for the marketing approval of implantable medical devices – namely CE markings, which indicates that devices meet the essential requirements of the medical devices directives.[219] Since 14 June 1998 all medical devices have had 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 (e.g. 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.

Multiplicity of sources

One of the key assumptions in our approach has been to assume 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 (e.g. 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 healthcare technologies that we developed as part of the Delphi study is only one way of classifying them; further subcategorisation may highlight other sources for identifying new healthcare technologies.

Establishment and operation of an EWS

The principal methods for informing the following sections were the telephone enquiry

* These are available via web at http://www.sec.gov/edaux/searches.htm.

and the literature review; some of the issues were also highlighted by the case studies.

Value and purpose of an EWS

It is important to recognise that whatever systems are developed it will be impossible to control all decisions concerning the adoption of new healthcare technologies, especially in a healthcare system that allows a great deal of freedom to healthcare providers. However, the findings of the commissioned HTA research which ultimately results from the establishment of an EWS, as well as the more general highlighting of new technologies that are likely to be the most significant, should provide valuable and timely assistance to decision makers in the NHS.

Research-based evidence is the only way to establish the appropriateness of uptake of any technology. Earlier identification of technologies could ensure that initial cost-effectiveness research took place prior to marketing and introduction into the NHS. An iterative, four-stage process of economic evaluation of a new technology has been proposed by Sculpher and co-workers.[44,220] 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, and 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 randomised controlled trials, 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 research and development 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 candidate technology)
- indicate whether it is likely that a proposed technology might be cost-effective
- aid the design of definitive studies, clarifying what are the key parameters, critical thresholds, and necessary differences for the new technology to be cost-effective.

All the existing EWSs which were included in our telephone survey aim to inform health policy planning, but two (Canada and Sweden) did not report having any direct input into national HTA research prioritisation. In the context of a national HTA research programme, 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. Earlier identification enables the methodological lead time to be lengthened to allow for the framing of the most appropriate research question (e.g. developing or agreeing quality of life outcome measures to be used in a comprehensive randomised controlled trial) and consideration of the practical implications of the proposed research.

The evidence for the value of an EWS is only informal and intuitive at best. In The Netherlands, extensive experience with an EWS has been 'quite positive'.[117] Important policy decisions have been made during the last 15 years by the Dutch government on the basis of Health Council reports addressing new and emerging technologies. Examples include:

- the introduction of a national breast cancer screening programme on the basis of the Council's 1987 report
- a 1986 report on artificial reproduction led to the controlled introduction of *in vitro* fertilisation and inclusion of this technology in the Hospital Provisions Act.

Furthermore, the experiences of the USA and UK with CT scanners provide an example of how early involvement of national agencies can promote early evaluation and the rational diffusion of a new technology. There were ample opportunities to identify the likely introduction of the CT scanner in the USA and to put in place evaluative research, but the lack of an EWS or a coordinated approach to HTA led to the widespread, and unplanned, diffusion of an expensive healthcare technology which had wide-ranging implications for the healthcare system. Health planning agencies seem to have had very little effect in the USA. CT scanning was not evaluated before it spread into practice.[124] Although there were some efforts to control technology diffusion by the mid-1970s, most states in the USA did not have viable regulations affecting hospital

acquisition at this time. In the USA, certificate-of-need (CON) programmes to review hospitals' capital expenditures were established in 1974. Thus, the earliest years of CT development largely escaped effective CON regulation.[124] 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.[121] The combination of early warning and a strong central policy-making body enabled a more rational introduction of this expensive technology than in the USA.

Our case studies can also be used to illustrate the potential benefits that may result from early warning. For example, 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 to 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. Early warning could also have enabled more timely preparation of prescribing guidelines.

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 telephone enquiry of coordinators of existing and planned EWSs 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 1 year, four respondents were interested in a time-frame of 1–2 years but only one respondent was interested in a time-frame of up to 5 years. 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 healthcare system, the so-called 'preferable futures' approach, or can be concerned only with prediction or 'plausible futures'.

Technologies

Although much of the focus in the literature to date has been on ensuring the timely identification of new pharmaceuticals, EWSs are not concerned with identifying only one type of healthcare technology. In the telephone questionnaire the majority of the coordinators of existing EWSs responded that either all types of technology were given equal attention or that drugs, devices and procedures and therapies were the main focus of their work. One of the EWSs (France) does not focus on drugs at all, and nominated devices, procedures and therapies and settings as the types of technology which are concentrated upon.

Scale of operation

EWSs 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. Our focus has been on a national EWS concerned with all types of healthcare technology, but with the potential for greater international collaboration because of the likely economies 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 can be useful method for achieving this. Our own Delphi study 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 they might be preceded by the cataloguing of information from documentary sources and/or a Delphi survey.

Prioritising technologies

The telephone enquiry of coordinators of existing and planned EWSs 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 we have not attempted to summarise here.[221–224] The views of the co-ordinators of the six national EWSs suggested slightly different criteria with which to select which emerging technologies should be highlighted. However, the following were commonly mentioned, and are similar to those summarised elsewhere:[103,225]

- 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).

Interfacing with HTA programmes

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 healthcare 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 healthcare technologies via an EWS is not enough; the next step is to perform early assessments.[226,227]

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 (e.g. CT scanners, telemedicine, biosensors). This pattern of technological development highlights the need for a 'watchful waiting' approach by an EWS; 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, suggesting 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,[228] 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 10–12. 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, the UK). Two of the initiatives (Canada, Sweden) have Internet sites which provide updated information on the technologies which they have identified and prioritised as being important. Newsletters are used by three of the initiatives (Canada, Sweden, 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 emphasised the importance of identifying a new technology as early as possible so that an appropriate evaluation can be initiated at a very early stage.[79] 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 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, coordination, standardisation and communication. In the longer term there may be a role for a more formal mode of collaboration, perhaps based within the EU or through INAHTA.

Chapter 8

Conclusions and research recommendations

Timeliness of this report

The paucity of empirical evidence means that one must be cautious in deciding which are the most useful sources of information for identifying new healthcare technologies and the best methods for operating an EWS. However, EWSs are being established simultaneously in a number of countries (often by HTA agencies) and intuitively they would seem to offer obvious benefits. Therefore even our early, tentative conclusions based on a thorough review of current knowledge will we hope be valuable.

Our methods

Our conclusions and recommendations are based on the results of four separate methods which approached the two study questions from different perspectives; each of these provided somewhat different findings, which emphasises the importance of a multifaceted approach. We adopted this approach 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 are historical exemplars only. 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 EWSs for identifying new healthcare technologies than any single method alone.

Information sources

The choice of information sources which feed into an EWS will be influenced by the choice between

(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 and 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 healthcare technology) to the health system (examples include key medical journals, newsletters and bulletins from other HTA agencies and FDA licensing).

The following three information sources were suggested from all four of our methods: key pharmaceutical journals, key medical journals, and experts (although the last could be demanding of resources). In addition, 'specialist' 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 healthcare technologies we recommend the following approach 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 and biotechnology companies, to produce a database of potential technologies
- 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 (e.g. HTA agencies and patient special interest groups), and may become capable of playing an increasing role and should be kept under review.

Operating an EWS

EWSs for identifying healthcare technologies should not be concerned with making exhaustive, long-term forecasts but with highlighting new and emerging high-impact technologies that are likely to materialise. 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 3 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 healthcare system of which it is a part and the purposes to which the EWSs 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 national and international programmes that already exist (e.g. in the UK collaboration with regional DIS, SERNIP, SMAC CMP group) with the aim of ensuring adequate coverage of all types of technologies and providing sufficient early warning
- 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.

Research recommendations

Given the lack of empirical evidence on the practical value of an EWS it is important that any new initiative be evaluated and monitored. Our findings would support the commissioning of the following research.

Information sources

- To design into the establishment of an EWS a system for **prospectively** recording the information sources used to identify new technologies in order that their accuracy can be assessed at a later date when the value of the output from the EWS is known.
- To undertake further and more detailed case studies of technologies (similar to those undertaken here but preferably prospectively) to document help understand the diffusion processes of new healthcare technologies and to assess information sources for identifying them prior to their introduction into health services.
- To determine the best methods for accessing expert opinion and for selecting experts to contribute to an EWS. This will involve 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, paradoxically, experts on expertise.

Establishment and operation of an EWS

- To estimate the likely 'payback' from providing early warning of a variety of new healthcare technologies, that is, estimating costs and valuing early warning.
- To systematically review and experiment with models which can be assessed at two to 3 year follow-up for estimating the likely impact of new healthcare technologies, in terms of cost, effectiveness and number of people affected.
- To determine through surveys of policy makers and other methods how much early warning is required for (a) strategic policy decision making (e.g. HTA research prioritisation), and (b) day-to-day operational management decisions, which 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.

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Appendix 1

Key concepts

This appendix provides further introductions to the key concepts on which this report is based:

- futures and futurology (including an introduction to technology forecasting and bibliographic details of examples of health futures studies and texts)
- technology, healthcare technology, and new healthcare technologies
- early warning systems
- innovation and diffusion.

Futures studies and futurology

'Futures' is an extremely wide field, and futures studies fulfil many, and quite different, purposes.[229,230] Bezold[231] 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)
- 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.[229] Work on plausible futures identifies and forecasts the potential trajectories in key aspects of health care (e.g. healthcare 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.[232] Generally, the accuracy of forecasts, or of scenarios,[91,233] is secondary to whether the work either aids in wiser decision making or results in actions which create the futures we prefer.

Figure 21 sets the scope of this report in the context of the discipline of futurology. We are concerned with new healthcare technologies (sector) in the short term (time-frame) and making plausible predictions (outcome) as to which are likely to be important and introduced into the NHS.

Garrett[54] 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 organisations.

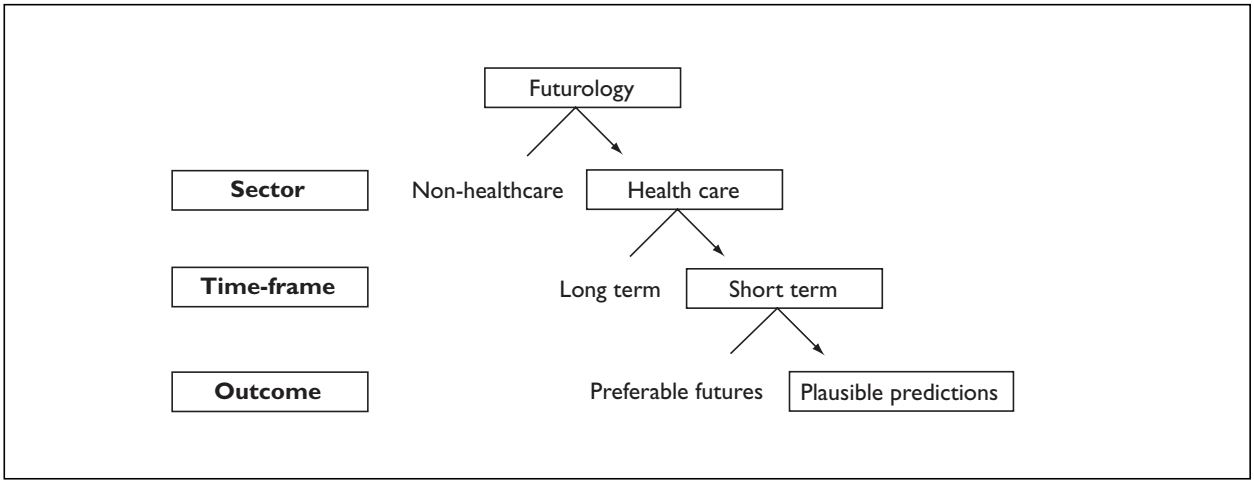

FIGURE 21 *Focus of this report within the context of 'futures' research*

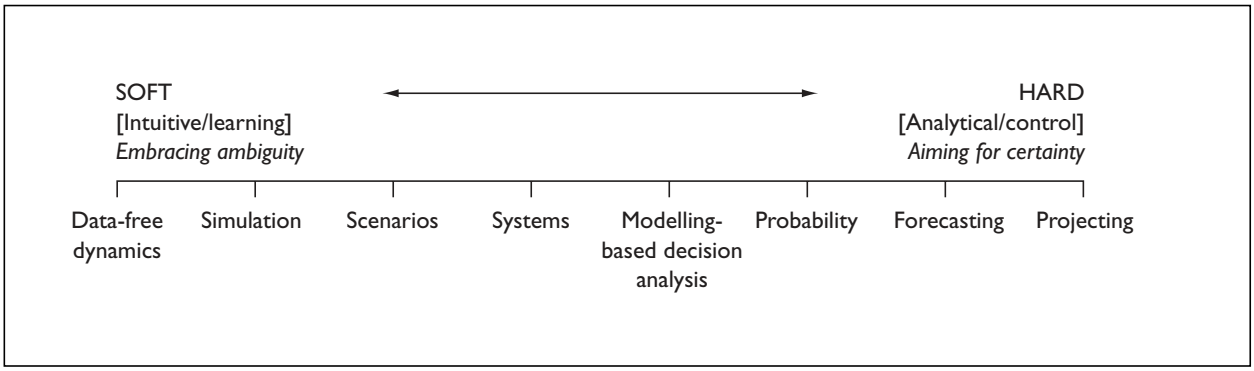

FIGURE 22 *A spectrum of futures methodologies. (Adapted from: Nicholson D, Hadridge P, Royston G. Some practical hints for newcomers to health futures.* Futures *1995;* ***27****(9/10):1059–65)*

Thus, the basic methods employed in futures studies range from analysing and soliciting opinion, to projecting and optimising, as illustrated in *Figure 22*.

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)
- Foresight research centre (http://www.dur.ac.uk/foresight).

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'. 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. These 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 USA 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 USA relies on review committees. In the UK, the Health & Life Sciences panel in the OST Technology Foresight exercise recommended greater effort and investment in certain areas (*Table 23*).

Bezold[229] 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 healthcare expenditures and priorities, but the field is still immature. However, it will grow in importance as healthcare spending remains at 6–18% of the gross national products of developed countries.

The references in *Table 24* provide a general introduction to futures methods and studies and examples of futures studies which have used Delphi methods or scenario analysis to inform discussion regarding the long-term development of health care.

Technology

Technology has been defined as the 'systematic application of scientific or other organized knowledge to practical tasks'[234] or as 'knowledge applied to a purpose'.[13]

Healthcare technology

In the 1970s, the US OTA defined 'medical technology' as 'drugs, devices, and medical

TABLE 23 *Key recommendations of the Health & Life Sciences panel*

Area	Comments
Infrastructure for exploitation and development	Economic success in the expanding life sciences sector needs close links between industry, health services, and a strong research base in the life sciences and clinical medicine
'Integrative biology'	Research programmes which integrate molecular biology and genetics with cell and tissue biology, and whole-organism studies
Neuroscience and the cognitive sciences	Research into progressive degenerative disease and non-specific age-related decline
Ageing	Basic research into ageing and disabling degenerative disease, coupled with technologies for sustaining reasonable quality of life for the elderly infirm
Genetics in risk evaluation and management	Research into the application of genetic information to the prevention and treatment of common multifactorial disease
Drug creation and 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, and applications in specific interventions in inflammatory and immune disease, vaccines, transplants and other areas
Medical information technology	Innovative ways of using information and communication systems to inform and support clinical decisions, and medical practice in general

and surgical procedures used in medical care and the organisational and supportive systems within which such care is provided'.[235] 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'.[236] Alternatively, Stocking defines 'healthcare technology' as 'the drugs, equipment and procedures, used singly or in combination, and the healthcare support systems in which operate'.[34] Liaropoulos[237] has provided a schematic representation of the different definitions of biomedical, medical, health care and health technology (*Figure 23*).

Within the context of the UK's NHS Research and Development 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
- using a broad definition emphasises the importance of not only evaluating machines, but that it is also important to evaluate what physicians and other healthcare providers do.

A broad definition of 'healthcare technology' has been used throughout this report: healthcare 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 healthcare professionals, and the use of equipment, pharmaceutical and healthcare procedures generally'.

'New' healthcare technologies

Banta and Luce[31] suggested that the life cycle of a technology consists 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).

Szczepura[238] defined new technologies as those which had recently been introduced. The UK's existing EWS uses a three-fold classification (*Box 6*).

TABLE 24 *Examples of futures studies and introductory texts to the discipline*

First author	Title	Source
Amara R	Futuring in health care	*Health Care Strategic Manag* 1985;**3**:26–9
Bezold C	Health care: thinking ahead	*World Health Forum* 1994;**15**(2):189–92
Bezold C	Scenarios for 21st-century health care in the United States of America: perspectives on time and change	*World Health Stat Q* 1994;**47**(3–4):126–39
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**:80–5
Driver JF	Forecasting without historical data: Bayesian probability models utilizing expert opinions	*J Med Sys* 1995;**19**(4):359–74.
Fenton TR	Assessment of artificial neural networks in health futures research	*World Health Stat Q* 1994;**47**(3–4):177–84
Friesdorf W	Events which will influence intensive care units in the future. A Delphi study	*Technol Health Care* 1997;**5**(4):319–30
Garrett MJ	A way through the maze. What futurists do and how they do it	*Futures* 1993;**25**:254–74
Garrett MJ	An introduction to national futures studies for policymakers in the health sector	*World Health Stat Q* 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 Stat Q* 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	*J Sci Industr Res* 1987;**46**:1–19
Nicholson D	Some practical hints for newcomers to health futures	*Futures* 1995;**27**(9/10):1059–65
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**:64–9
Ronning PL	Anticipating the future using life-cycle analysis	*Hospital Technol Ser* 1996;**15**:6–9
Sapirie S	What does 'health futures' mean to WHO and the world?	*World Health Stat Q* 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 Manage* 1982;**12**:27–36
Wyke A	21st-century miracle medicine. RoboSurgery, wonder cures, and the quest for immortality	New York: Plenum Press, 1997
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 Manage Account* 1996;**7**:1–8

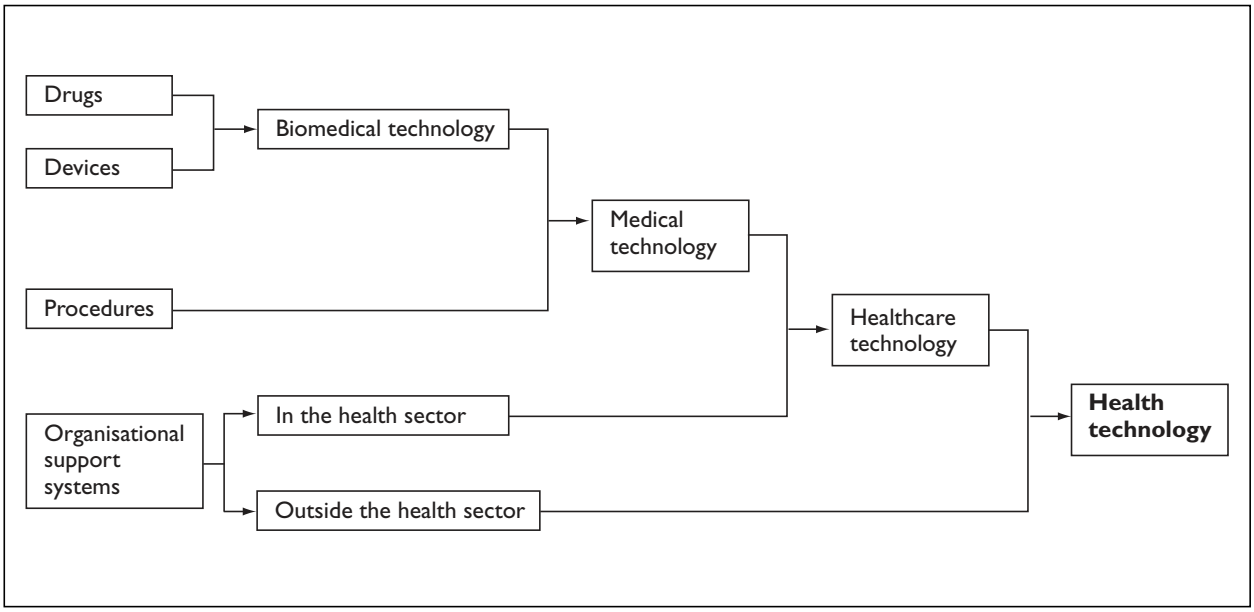

FIGURE 23 *Alternative definitions of technology in health*[238]

BOX 6 UK classification of 'new' technologies

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 Department of Health,* in a document outlining a proposed Safety and Efficacy Register of New Interventional Procedures (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'.

'New' technologies can be distinguished from 'established' technologies by the following features:

- 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. positron emission 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. keyhole surgery)
- finally, and most importantly, a strong body of evaluative research is unlikely to be available for decision makers.

However, for devices, therapies and organisation changes it is difficult to determine whether technologies are new or emerging if they are marketed before identification or put in place but remain localised to a few centres (i.e. how many and how diffuse before the new technology is not emerging any more and how do you classify a technology that is established in one area, seems effective but is not used elsewhere?).

In this report, 'new' healthcare technologies are those which have been relatively unevaluated and that are only just about to be introduced, or have only recently been introduced, to clinical practice.[43] Thus they comprise those technologies 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.[239] They may also be technologies localised to only a few centres, and for the purposes of this report may also be new applications of existing technologies.

* As cited by Mowatt and co-workers.[104]

Early warning systems

There are four main stages to any HTA system: identification, testing, synthesis and dissemination.[223] 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 healthcare technologies, with which EWSs are most often concerned. EWSs can also help to select and prioritise those technologies in need of study.

The European Workshop in Copenhagen[103] 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.

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 healthcare sector is to identify potential healthcare 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 EWSs and seek to provide a list of potential new healthcare technologies are, for example, scanning particular key medical journals or liaising with pharmaceutical companies.

Innovation and diffusion

'Innovation' and 'diffusion' are key concepts in any attempt to establish 'horizon scanning' activities. There is a vast literature on the innovation and diffusion of technology. The underlying themes are briefly referred to here as prior to determining the best sources for identifying new healthcare 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 healthcare technologies to be established.

An **innovation** is an idea, practice or object that is perceived as new by an individual or other unit of adoption.[13] Technological innovation in medicine covers the wide range of events that includes the discovery or invention, development and dissemination of a new healthcare technology.[240] A useful distinction within the concept of innovation is between 'local' and 'global' innovation;[241] global innovation being the first occurrence in an economy (or healthcare 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 our study is on the broad definition of global innovation.

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' (healthcare system).[13] The study of diffusion is concerned with three phenomena:[242]

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

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. Diffusion of an innovation is only one stage in the process of technological change which covers the wide range of interacting events by which a technology evolves over time.[13]

Most discussions of diffusion share the conclusion that it is a process best represented by an S-shaped curve (*Figure 24*).[13,58,61,66,239,243] As the figure 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

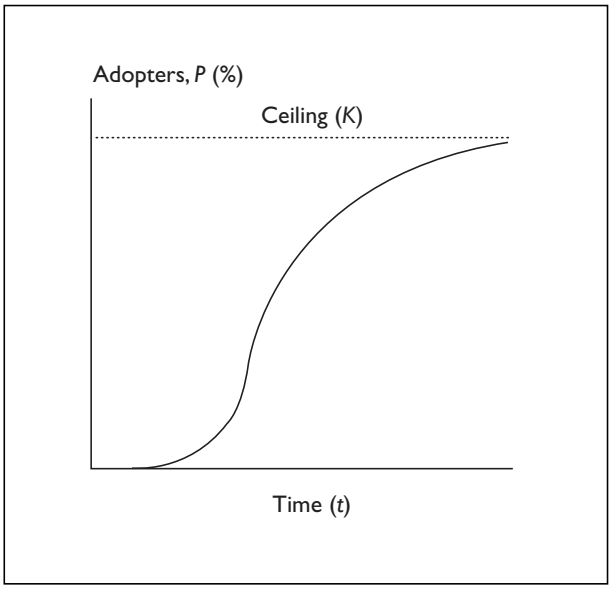

FIGURE 24 *The conventional diffusion of innovation curve (Source: Warner[242])*

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[240] noted, 'There is a need for caution in making generalisations about the health system based on innovation studies in other areas'. However, Russell[244] 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 which show the S-shaped diffusion pattern quite well, the actual processes at work are more complex.

Greer[76] 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.

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 4).

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 worldwide. 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

The HTAIS database provides bibliographic information and abstracts on drug therapies, devices and procedures from research undertaken by ECRI, government agencies, academic centres, manufacturers, healthcare 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

Search strategies: case studies

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)

IFN-β

(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 4

Questionnaire to coordinators of existing or planned HTA EWSs

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 category 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 source 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 and therapies
(d) Settings
(e) Information technology
(f) All the above 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 method if required)
(a) Postal survey
(b) Telephone
(c) Face-to-face/one-to-one 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 you 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 research and development

2.11 What do you do with the results?
Do you categorise the technologies you identify
(tick more than 1 category if required)
(a) by type (e.g. drugs/devices)?
(b) by size of likely impact on
– health?
– cost?
– planning?
(c) by time horizon?
(d) by 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 category if required)
(a) research and development programme?
(b) the health service?
(c) other (e.g. industry)?

2.14 *(If the EWS is used for HTA prioritisation purposes)*
After identification of a technology how long does it take to (give a minimum and maximum time if appropriate) to
– prioritise research?
– commission research?
– disseminate research findings once research is completed?

2.15 *(If the EWS is used for informing health policy)*
What does the 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 5

Contemporary sources for early warning in the UK

Forecasting Secretariat to the SGHT

In May 1995 the Department of Health established a Forecasting Secretariat to the UK's SGHT 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 CMP group of the SMAC.

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.[95] The survey requested information from participants on new and emerging technologies and treatments that are likely to affect the NHS in the next 5 years. Overall, approximately 3500 people were invited to participate in the survey. In total, 1100 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
- a named expert on the technology.

Appendix 6 is a compilation of the 48 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 5 years, and sometimes beyond.

Safety and Efficacy Register on New Interventional Procedures

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 .[246 *]

SERNIP registers new procedures and coordinates 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 specialities to include otorhinolaryngology and ophthalmology.

[*] Source: information sheet from Academy of Medical Royal Colleges, June 1996.

To April 1997 a total of 43 procedures had been considered. Twelve were considered safe and effective, 20 were of unproven safety and efficacy, ten were still under investigation and one (intraoperative autotransfusion (Haemocell 350®) IBS) has been proscribed by the committee.*

SMAC CMP group

The criteria for items to be included in SMAC advice to the Department of Health on 'changing medical practice' are listed in *Box 7*.

UK Drug Information Services

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.[247 †]

The UK DIS, coordinated through the network of regional DIS, have 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 25*).

The outputs are cascaded down to local DIS and hence to commissioners of health care and clinicians.

The UK's DIPG and the NPC in Liverpool announced in April 1997 that they were to collaborate in a venture to provide advance information on significant new drugs in development.‡ The initiative will build upon the UK DIS scheme entitled 'New drugs in clinical development' (see stage 3, *Table 25*). Collaboration between the 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.

BOX 7 SMAC CMP categories

(1) Categories of change will include:
  (a) incidence, mortality, regional variations and distribution of disease
  (b) developments in treatment and 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 and 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 health gain 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 speciality initiating a change should be indicated (e.g. for general practitioners)

(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 Hospital and Community Health Services spending over the next 4 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 £1 spent)
  – impact on other government spending
  – impact on economy

* SERNIP newsletter, May 1997.

† That is, general enquiry answering; evaluated information on new drugs; formulary support; current awareness bulletins; training in drug information; coordination of DIS.

‡ 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, or from the Internet at http://www.ukdipg.org.uk/newprod.htm.

TABLE 25 *Drug Information Services*

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 premarketing
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 premarketing; also uses drug companies as sources 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

Appendix 6

New healthcare technologies in the UK

TABLE 26 *New healthcare technologies in the UK, as identified in October 1995*[95]

Topic	Time	Size	Evaluated?
Magnetic resonance imaging	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	1996–1997	Moderate	Partially
Peripheral blood stem cells	Now	Major	Quite well
Picture archiving and 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	1998–2000	Moderate	Partially
Telemedicine	1998–2000	Moderate	Partially
rhDNAase for cystic fibrosis	1996–1997	Moderate	Quite well
Interventional radiology	Now	Major	Quite well
Angioplasty	Now	Major	Partially
Interferon for chronic granulocytic leukaemia 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	1996–1997	Moderate	Not well
Revision of joint replacements	Now	Major	Quite well
Genetic screening	1998–2000	Major	Partially
Helicobactor pylori eradication	Now	Moderate	Quite well
PET scanning	1998–2000	Moderate	Quite well
Phacoemulsification	Now	Moderate	Fully
Cochlear implants	Now	Moderate	Fully
Paclitaxels for ovarian and breast cancer	1996–1997	Moderate	Quite well
Nitric oxide for neonates	1996–1997	Some	Partially
Bone densitometry screening	Now	Major	Quite well
Anticoagulants for atrial fibrillation	Now	Moderate	Quite well
New anaesthetic vapours	1996–1997	Moderate	Quite well
Drugs for Alzheimer's disease	1996–1997	Major	Partially
Magnetic resonance angiography	1998–2000	Major	Partially
Digital radiography	1998–2000	Major	Quite well
Alendronate for osteoporosis	1996–1997	Major	Partially
Continuous positive airways pressure	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 and chronic leukaemias	1996–1997	Moderate	Quite well
Combined therapy for HIV/AIDS	1996–1997	Moderate	Partially
Epilepsy surgery	Now	Some	Quite well
Lipid-lowering drugs for raised cholesterol levels	Now	Major	Fully
Transfemoral endovascular (bifurcated) graft	1998–2000	Major	Partially
Intracytoplasmic sperm injection	1996–1997	Some	Partially
CT scan advances	1996–1997	Moderate	Partially
Voice-activated dictation technology	1996–1997	Moderate	Partially
Intra-arterial metallic stents	Now	Moderate	Quite well

Appendix 7

Catalogue of World Wide Web sites with information on new healthcare technologies*

Reuters Medical News/Reuters Health Information Services (http://www.reutershealth.com/frame_about.html). Highly recommended. Extremely easy to scan, useful categories, that is, 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 healthcare 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://www.nlm.nih.gov/databases/alerts/clinical_alerts.html). Clinical alerts are provided to expedite the release of findings from the National Institutes of Health-funded clinical trials where such release could significantly affect morbidity and mortality.

UK DIPG (http://www.ukdipg.org.uk/newprod.htm). See appendix 5 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 4 weeks). Stories are sourced wherever possible.

European Agency for the Evaluation of Medicinal Products (http://www2.eudra.org). The Agency aims to provide the EU member states and institutions with the best possible scientific advice on questions concerning quality, safety and efficacy of medicinal products for human and veterinary use. It coordinates single evaluations via a centralised or decentralised marketing authorisation system.

* With thanks to CCOHTA and Web Watch in the *Health Service Journal* for providing information on some of the Internet sites listed here. Many of the sites have links to other useful information sources on the Internet.

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This report was identified as a priority by the Methodology Panel.

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