ACKNOWLEDGEMENTS

This report was written by Alessandra Vanoli, Mike Drummond and Trevor Sheldon at the NHS Centre for Reviews and Dissemination (CRD) and the Centre for Health Economics (CHE), who are leading the development of the NHS Economic Evaluation Database project.

We express our gratitude to Susan Mottram, Julie Glanville and Bridget Carter of the Information Service for their participation in the development of the NHS Economic Evaluation Database system; and to Margaret Anderton, Donna Clayton and Paula Press for their administrative and secretarial assistance to the project.

We also thank the following health economists who contributed to the production of structured abstracts of economic evaluations:

Karen Bloor,
Mark Deverill,
Paul Dolan,
Teresa Feighan,
Sean Forrest,
Barbara Graham,
Alison Hadnett,
Louise Hallam,
Bruce Hollingsworth,
Sarah Howard,
Marilyn James,
Karl Kantor,
Tom Jefferson,
Emma Jeffreys,
Anna Jillings,
Ioana Littlewood,
Roshni Mangalore,
Douglas McCulloch,
David McDaid,
Miranda Mugford,
Jo Ann Mulligan,
Stephen Palmer,
Glenn Robert,
Di Sanderson,
Tony Scott,
Russel Slack,
Anne Spencer,
Andrew Street,
Rod Thomas,
David Torgerson,
JaneWolstenholme.

We are also grateful to the advisory group members who are assisting the progress of the project:

Professor Martin Buxton ,Health Economics Research Group, Brunel University.

Karl Claxton, Department of Economics and Related Studies, University of York.

Dr. Jonathan Cooke, Department of Pharmacy, University Hospital of South Manchester.

Dr. Bernard Crump, Department of Public Health Medicine, South Birmingham Health Authority.

Professor Cam Donaldson, Health Economics Research Unit, Aberdeen.

Professor David Eddy, Department of Health Policy and Management, Duke University, USA.

Professor Mathias Graf von der Schulenberg, Institut fur Versicherungsbetrieblehre, Hannover, Germany.

Dr. Simon Harding, Department of Health, London.

Professor Akinore Hisashige, Technology Assessment and Decision Science Unit, University of Tokushima, Japan.

Dr. Dee Kyle, Department of Public Health, Bradford Health Authority

Dr. Bryan Luce, Centres for Public Health Research and Evaluation, Arlington, U.S.A.

Dr. Miranda Mugford, National Perinatal Epidemiology Unit, Oxford.

Dr. Nick Phin, Department of Public Health Medicine, South Humberside.

Dr. John Posnett, York Health Economics Consortium, University of York.

Professor Joan Rovira, Centre d'Estudis en Economia de la Salut i de la Politica Social, Barcelona, Spain.

Professor Frans Rutten, Institute for Medical Technology Assessment, Erasmus University, The Netherlands.

Alan Shiell, Department of Public Health, University of Sydney, Australia.

Professor George Torrance, Centre for Health Economics and Policy Analysis, McMaster Health Sciences Centre, Canada.

TABLE OF CONTENTS

INTRODUCTION 1

1. METHODS TO DEVELOP THE DATABASE 3

2. RESULTS 9

3. ACCESSING AND SEARCHING THE DATABASE 14

4. MARKETING AND DISSEMINATION 16

5. EVALUATION OF THE NHS ECONOMIC EVALUATION DATABASE 18

6. PLANS FOR RESEARCH LINKED TO THE NHS ECONOMIC EVALUATION DATABASE PROJECT 20

REFERENCES 23

APPENDIX 1: SEARCH STRATEGIES 24

APPENDIX 2: CHE/CRD JOURNALS CURRENTLY HANDSEARCHED 26

APPENDIX 3: EXTENDING SEARCH STRATEGIES 28

APPENDIX 4: CRITERIA FOR INCLUSION/EXCLUSION OF STUDIES IN THE DATABASE 30

APPENDIX 5: GUIDANCE FOR WRITING CRITICAL ABSTRACTS FOR THE NHS ECONOMIC EVALUATION DATABASE 31

INTRODUCTION

Health technologies should only considered for use when their effectiveness and safety have been demonstrated. However, decision makers are becoming increasingly aware that, because of finite resources, the resource implications of health care interventions also need to be considered. If information on both costs and effectiveness are available, then resources should be allocated with a view to increasing (social) efficiency, taking into account policy on equity.

Economic evaluations are conducted to provide information about the 'parameters' (e.g. cost-effectiveness ratios, cost-utility ratios) which may help the development of more efficient health care programmes. However, reviews of studies have demonstrated that the quality of economic evaluations is highly variable and their reporting often inadequate.

Health care decision making should be informed by the most reliable studies. In order to make information more easily accessible about the cost-effectiveness of health technologies and to provide assessments of the quality of these studies, the NHS Centre for Reviews and Dissemination has been commissioned by the Department of Health to develop and maintain a database of critical abstracts of economic evaluations of health care.

The NHS Economic Evaluation Database contains structured abstracts of economic evaluations of health technologies, and covers studies in all languages published from 1994 onwards. Papers are abstracted if they are full economic evaluations of health care interventions or forms of organisation of health care relevant to the NHS. A detailed abstract structure has been developed, to help critically appraise each study and ensure that the information is of maximum use to the intended audience of health care professionals, managers, policy makers, and academics.

Bibliographic details of costing studies, methodological papers and reviews of economic evaluations are also included in the Database, as well as selected records originally included in the DH Register of Cost-Effectiveness Studies (1994), and which have been mapped into the CRD abstract structure.

The NHS Economic Evaluation Database is a companion to the CRD Database of Abstracts of Reviews of Effectiveness, which is a collection of abstracts of good quality research reviews about the effectiveness of health care interventions and the organisation of health services. Both databases are accessible on-line free of charge.

The NHS Economic Evaluation Database, whilst potentially a useful resource, is only the start of a process of improving access to reports of economic evaluations and promoting the use of reliable results in health care decision making. CRD has identified key areas of the activities relevant for the effective implementation of the project. They can be classified in three broad categories: a) marketing and dissemination of the Database; b) assessing the use of the Database; c) research activity linked to the Database and to economic evaluations.

This report summarises the methods used for developing the Database, the progress made so far, the ways of accessing and searching the Database, and the plans for extending activities linked to the project.

Appendices include details of the search strategies of the relevant literature, criteria for inclusion/exclusion of studies, list of the journals handsearched, and the guidance developed by CRD for reporting critical summaries of economic evaluations.

1. METHODS TO DEVELOP THE DATABASE

Economic evaluations are currently located by searching Current Contents-Clinical Medicine, handsearching a range of journals and grey literature sources. For 1994-1995 Current Contents-Clinical Medicine was searched comprehensively. For 1993, only the journals kept by the NHS Centre for Reviews and Dissemination (CRD) and the Centre for Health Economics (CHE) at York were searched.

A weekly search of Current Contents-Clinical Medicine has been conducted since January 1995 using 'search strategy 1' (Appendix 1). Journals regularly received by CRD or CHE which are likely to have economic evaluations are handsearched (Appendix 2). Medline and the Cumulative Index of Nursing and Allied Health Literature (CINHAL) are updated monthly and a search is conducted using 'search strategy 2' and 'search strategy 3' (Appendix 1). Medline and CINHAL searches will be carried out retrospectively for 1995/1996 and this will continue on a monthly basis. Search strategies are being expanded (Appendix 3).

The records retrieved from these searches enter the process shown in Figure 1. The bibliographic details of the records are circulated to health economists in CRD and CHE. Using the exclusion/inclusion criteria (Appendix 4) we assess whether the paper should be rejected or whether to get the paper because:

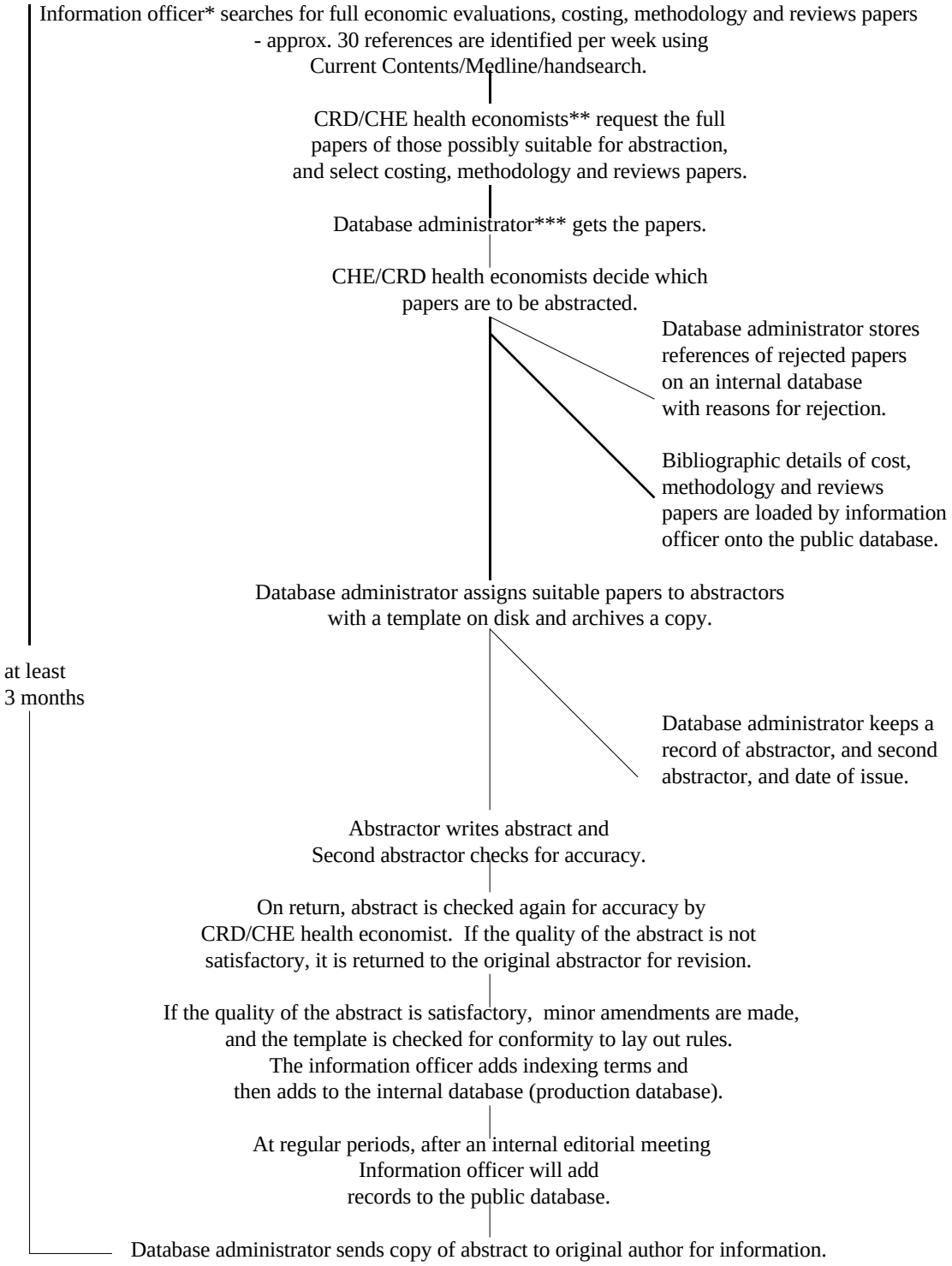
a) it appears to be a full economic evaluation that should be abstracted;
b) it appears to be a cost paper or a burden of illness study;
c) it appears to be a paper on the methods of economic evaluations;
d) it appears to be a paper reviewing economic evaluations.

The full reports of the studies which appear to be full economic evaluations, cost/burden of illness studies, reviews or methodological papers are obtained and then assessed by CRD/CHE health economists. Using the same criteria as above, we decide

Figure 1

ADMINISTRATION OF THE NHS ECONOMIC EVALUATION DATABASE

FLOW DIAGRAM



**Susan Mottram*
***Alessandra Vanoli, Trevor Sheldon, Mike Drummond*
****Margaret Anderton*

if the paper is to be selected for abstraction, or if it is a cost paper, a methodology paper or a reviews paper, or if it has to be rejected. The bibliographic details of the costing, methodology and reviews papers are included in the Database. The papers that are to be abstracted are passed to one of a number of health economists whom we commission to write abstracts, with a disk containing a template based on the abstract structure that we have developed.

The abstract of each study provides information on the following dimensions: economic study design, description of the assessment of effectiveness, estimation of benefits used in the economic analysis, costing methodology, methods for synthesis results, handling of uncertainty.

Studies are not selected for inclusion on the basis of their quality. The user of the Database is provided with information about the quality of the studies in the commentary field of each abstract. The quality of the studies has been appraised by the abstractors on the basis of various factors. So far, no overall quality scoring method has been used given that no valid, reliable and interpretable instrument has been developed.

The contents of the abstract structure as well as the most common elements influencing the quality of economic evaluations on which the abstractor based his/her assessment, are reported in the "Guidance for writing critical abstracts for the NHS Economic Evaluation Database", included in Appendix 5. The abstract structure used is summarised below (Fig. 2).

Contents of the abstract structure for the NHS Economic Evaluation Database

Accession number
Addition date
Edit date
CRD status
Record status
CRD reviewer
Author(s)
Title
Source information
Journal volume
Publisher
ISBN
Series information
Pages
Date of publication
Publication type
Language of publication
English summary available
Correspondence address
Health technology
Disease
Type of intervention
Hypothesis/study question
Economic study type
Study population
Setting
Dates to which data relate
Source of effectiveness data
Modelling
Link between effectiveness and cost data (for case A - single study - only)

(Case A: Single study)
Study sample
Study design
Analysis of effectiveness
Effectiveness results
Clinical conclusions

(Case B: Review/synthesis of studies)
Outcomes assessed in the review
Study designs and other criteria for inclusion in the review
Sources searched to identify primary studies
Criteria used to ensure the validity of primary studies
Methods used to judge relevance and validity, and for extracting data
Number of primary studies included
Method of combination of primary studies
Investigation of differences between primary studies
Results of the review

(Case C: Estimates of effectiveness based on opinion)
Methods used to derive estimates of effectiveness
Estimates of effectiveness and key assumptions

Measure of benefits used in the economic analysis
Direct costs
Indirect costs
Currency
Statistical analysis of costs
Sensitivity analysis
Estimated benefits used in the economic analysis
Cost results
Synthesis of costs and benefits
Author's conclusions
CRD commentary
Implications of the study
Other publications of related interest
Subject index terms
Country codes
Source of funding
Copyright comments

A strict process of quality control has been implemented to ensure that the structured

abstracts are accurate, comprehensive and understandable (Fig 3). When the abstract is completed, it is sent to a second abstractor for quality checking. This is then given a final quality check and edited by a CRD/CHE health economist. If the quality of the abstract is satisfactory, we pass the completed abstract to the information officer, who checks the format and then loads it onto the database. If the quality of the abstract is not satisfactory, we return the abstract to the original abstractor for revision.

Figure 3

SYSTEM OF QUALITY ASSURANCE FOR FINAL OUTPUT
FLOW DIAGRAM

When the abstracts are returned after being checked by second abstractors,
CRD/CHE health economist makes final check of the contents.

Database administrator incorporates on file
the final corrections, checks spelling,
checks fields names, formats for loading
and returns disk and hard copy to
CRD/CHE health economist.

CRD/CHE health economist checks that the corrections
have been correctly included and passes
the records to information officer.

Information officer adds the indexing terms and any cross references,
checks readability of the text
loads the records onto the production database,
checks that the records have been
loaded correctly and makes any necessary amendments.

CRD/CHE health economist checks
the records in the production database
and gives final approval for transfer to public database.

Once a month information officer transfers the records from the production database
to the public database and checks that this process took place correctly.

The records are then publicly accessible on the database.

It has been ascertained that, for an average of more than thirty references retrieved every week, the whole process of identification, filtering, abstracting, checking, editing, revising and loading onto the administrative and public databases takes at least three months.

The abstractors are supervised by Alessandra Vanoli, health economist at CRD/CHE who is co-ordinating the NHS Economic Evaluation Database project. All the 31 commissioned abstractors have attended training sessions held by CRD. Further meetings of support are held when required. An international advisory group is assisting in the development of this project.

2. RESULTS

Using the administration process described, 531, 1409, 1214 and 595 records were retrieved searching Current Contents for 1996 (until May), 1995, 1994 and 1993 respectively. The monthly results of the search for 1995 and 1996 are shown in detail in Table 1.

Table 1

1995 References **Current Contents was searched weekly until the end of December**	
Average number of references retrieved per month	117
Average number of references selected per month (initial decision)	66
Average number of studies considered suitable to receive structured abstracts per month (final selection)	33
Average number of methodological papers per month	1
Average number of costing papers per month	6
Average number of reviews papers per month	4
Average number of rejections (final selection)	14

1996 References **Current Contents was searched weekly until the end of May**	
Average number of references retrieved per month	113

On average, using the current search strategies, we expect to retrieve about 1500 references by year, of which 800 will be considered as relevant. Of these, about 400 will be abstracted as full economic evaluations, 150 will be costing studies, methodology papers, and reviews, and 250 will be rejected.

An example of a structured abstract included in the NHS Economic Evaluation Database is reported below.

Example of a structured abstract included in the NHS Economic Evaluation Database

BIBLIOGRAPHIC DETAILS

Author (s):
O'Brien B, Anderson D R, Goeree R

Title:
Cost-effectiveness of enoxaparin versus warfarin prophylaxis against deep-vein thrombosis after total hip replacement.

Source Information:
Canadian Medical Association Journal
1994, 150(7), pp. 1083-1090

Publication type:
Journal article

Correspondence address:
Dr Bernie O'Brien, Department of Clinical Epidemiology and Biostatistics, Rm 3H25, McMaster University Health Sciences Center, 1200 Main St. W, Hamilton Ontario, L8N 3Z5 Canada

Record status:
This record was compiled by CRD commissioned reviewers according to a set of guidelines developed in collaboration with a group of leading health economists.

DETAILS ABOUT CLINICAL EVIDENCE: REVIEW OF STUDIES

Study designs and other criteria for inclusion in the review:
Randomized controlled trials (RCTs) comparing enoxaparin or warfarin with any other prophylactic agents between Jan. 1982 - Dec. 1992. Primary studies were included if they met the following criteria: a) English language; b)RCTs comparing enoxaparin or warfarin with any other prophylaxis against DVT in patients undergoing elective total hip replacement; c) prophylaxis started no later than 24 hours after surgery and continued for at least 7 days; d) the warfarin dose was adjusted to maintain a prothrombin time of 14 to 16 seconds, a prothrombin time ratio of 1.2 to 1.5 or an international normalised ratio of 2 to 3; e) the enoxaparin dosage was 30 mg twice daily; f) DVT was confirmed by bilateral venography.

Sources searched to identify primary studies:
Not stated.

Criteria used to ensure the validity of primary studies:
Not stated.

Methods used to judge relevance, validity and for extracting data:
No judgement criteria were applied by the authors for assessing validity of primary studies.

Number of primary studies included:
Four RCTs of enoxaparin and six RCTs of warfarin, not compared directly one with the other, were included in the review.

Method of combination of primary studies:
Overall risk of DVT with each drug was separately estimated as the sum of events divided by the sum of patients at risk.

Investigation of differences between primary studies:
Homogeneity of rates between studies was tested by Chi-square analysis. Test results of heterogeneity for overall rates of DVT were significant (P<0.05) for the enoxaparin trials but not for the warfarin trials. The author explored the impact of this with sensitivity analysis

Results of the review:
Comparing the overall risk of DVT with RCTs of enoxaparin and the overall

SUBJECT OF STUDY

Health technology:
Prevention of deep vein thrombosis (DVT) after total hip replacement using low-molecular-weight heparin derivative or low dose warfarin.

Disease:
Cardiovascular diseases.

Type of intervention:
Primary prevention

Hypothesis/study question:
Is enoxaparin more cost-effective than low-dose warfarin in preventing DVT after total hip replacement? Low-dose warfarin has been chosen as a comparator since it is the most commonly used cheap anticoagulant.

KEY ELEMENTS OF STUDY

Economic study type:
Cost-effectiveness analysis.

Study population:
Patients undergoing total hip replacement.

risk of DVT with RCTs of low-dose warfarin therapy, the difference in pooled rates of DVT overall and of distal DVT was -7.1 (95% CI: -2.8 to -11.2) and 8.2 (95% CI: -11.9 to -4.5) respectively. For proximal DVT the difference in the pooled rates was not statistically significant at the 5% level.

ECONOMIC ANALYSIS

Measure of benefits used in the economic analysis:
Life-years gained.

Direct costs:
Quantities and costs were analysed separately. Only health service costs were considered: prophylactic drugs, diagnostic tests and treatment (hospital stay and therapy). The estimation of the quantities (length of hospital stay, duration of proph

CONCLUSIONS AND CRITICAL COMMENT

Author's conclusions:
Enoxaparin is more effective than warfarin but will increase the cost per patient. On the basis of current Canadian guidelines, a cost of Can$29,120per life-year gained would give evidence for adoption. However, the author recognises that there are many threats to the validity of inference drawn from the meta-analysis. The author stresses the uncertainty around the estimates because of the limited data available.

CRD commentary:
Because there is no evidence of a systematic search of the literature for trials of effectiveness, it is not clear the extent to which all relevant studies were included. The analysis pooled the DVT rate in enoxaparin arms of trials and compared it with the pooled DVT rate of low dose warfarin. However, since these come from separate trials there is no evidence that the groups of patients were comparable. Therefore, it is not clear that the difference observed between the groups can be attributed solely to the treatments. This study is therefore hypothesis generating. More detail about the sensitivity analysis methods used would have been useful.

IMPLICATIONS OF THE STUDY

Implications of the study:
A well designed RCT directly comparing enoxaparin with low dose warfarin is needed.

Copyright: University of York, 1995

3. ACCESSING AND SEARCHING THE DATABASE

The NHS Economic Evaluation Database has been available on-line since October 1995. CRD does not charge for the use of the Database. It is possible to access the CRD host computer via one of the following routes:

- Wide Area Network Access (Internet, Janet, NHS-Wide Network);
- Non-Network Access (direct dial using a modem).

Over the Internet or Janet, the CRD host computer can be reached by making use of the Telnet network terminal program. Users should change the settings of their Telnet program to select DEC VT100 terminal emulation and if possible the CED Multinational Character set (8 bit) option should also be selected.
The Internet (and Janet) address to the CRD host computer is: **nhscrd.york.ac.uk**.
Users can also access the Database (using Telnet) from the CRD World Wide Web pages. The URL is: **http://www.york.ac.uk/inst/crd/info.htm**

If users have a modem and communications software on their PC or network, they can access the Database dialling the following telephone number: **01904 431732**
Users should check that their communications software options is set up as follows:

* ASCII asynchronous transmission
* DEC VT100 terminal emulation (optional)
* No Parity
* 8 Data Bits
* 1 Stop Bit

Once connected to NHSCRD, users will enter the username and password, which is <**crduser**> in both the cases.

The database can be searched in two ways: using the Menus and using the Command Line searching. The first method is the easiest, however the Command Line searching is faster and more direct.

The search through menus is guided by the instructions provided by the database software. Using the menus, a word can be searched in all fields or in a specific field, i.e. Author, Title, Date, Subject indexing and Journal title. The possibility of refining a search is also offered by a specific prompt, widening or narrowing the search previously conducted. For example, the user may be interested in cost-utility analyses carried out in the UK. A range of operators and wildcards for refining a search is also available for refining a search.

Command line searching facilitates a more direct and accurate searching. Moreover, Command line searching enables the user to combine searches together, with a saving of time. However, Command line searching is more complicated than searching using the Menus. A good knowledge of search operators and their order of precedence is in fact required to perform a command line searching in an appropriate way.

Once the search has been completed, several options are offered for displaying the results of a search. So, the user can see the full record; bibliographic details and results; brief bibliographic details; title only. Finally, the records retrieved can be saved to a file for printing out after users have left the Database. Alternatively, it is possible to print all - or just selected records - directly.

A Databases Introductory User Guide explaining the basic ways of searching is freely available at CRD. A more comprehensive and detailed CRD Manual, reporting practical examples of using operators and searching is being prepared and will be available shortly at a charge of £10.CRD is currently exploring ways of enhancing the access to and searchability of both its databases. In particular, we are looking at the options for offering the Centre's databases on the NHSnet which has growing importance in the networking of the NHS.

4. MARKETING AND DISSEMINATION

Several marketing activities have been implemented so far to publicise both the NHS Economic Evaluation Database and the Database of Abstracts of Reviews of Effectiveness (DARE), along with the Cochrane Library which contains interalia the Cochrane Database of Systematic Reviews.

Information about the Databases was mailed to medical and health libraries in the UK by CRD Information Service staff. Open days for medical/health libraries have been held and more are planned. As well as introducing participants to the work of CRD in general, the open days have emphasised the importance of the databases and the effort that goes in to ensuring that the information contained in them is of high quality.

In addition to the open days, the Information Service staff have been responding to requests from groups of health librarians to give talks and database demonstrations locally. So far, these have taken place in Reading, Hemel Hempstead, Birmingham, Liverpool, and further sessions are planned in Aberystwyth, South Wales, Kent and Scotland.

Moreover, further presentations describing the NHS Economic Evaluation Database have been given (European Union Concerted Action on the Harmonisation of the Methodology of Economic Evaluation of Health Technologies - HARMET - European Workshop, 17-18 June 1996, York; Faculty of Public Health Conference Medicine, Summer Conference, 4-5 July 1996, Cardiff).

An information sheet describing the features of the CRD databases has been prepared.

Finally, several articles describing the potential usefulness of the NHS Economic Evaluation Database and DARE, and their interrelations have been published recently.[1-3] A summary description advertising the methods used to develop the NHS Economic

Evaluation Database, its contents and accessibility has been E-mailed in the UK and United States using health economist mail-lists.

Dissemination activities should be aimed at supporting people in the use of the database. Dissemination has two aspects: how to use the database and how to use the information included in the database.

A few strategies have been identified to achieve these aims:

(i) CRD could train people to search the database and to use the information contained in the database through worked examples (users could be asked on line if they want training, and a pilot test could be performed);

(ii) training could be included as part of courses already carried out by other centres (e.g. King's Fund College courses for managers);

(iii) CRD could target other institutions which carry out marketing activities to disseminate locally;

iv) local workshop for NHS staff could be organised;

v) a book of case studies illustrating the use of economic evaluations to inform decision making could be produced.

The dissemination of the database is linked to the evaluation process described in the following section about assessing the usefulness of the database and of the information/messages included.

5. EVALUATION OF THE NHS ECONOMIC EVALUATION DATABASE

The abstracts included in the NHS Economic Evaluation Database summarise and critically appraise economic evaluations in a rigorous and systematic way. Since the abstracts contain a description of the key features of the study only, users who wish to act on the basis of the study results are advised to refer to the original paper.

The records included in the database, can be useful in different ways, such as:

- to provide direct access to a comprehensive collection of international studies suitable to the NHS context;
- to identify gaps in research;
- to locate studies for conducting reviews of the literature;
- to facilitate the understanding of economic evaluations for non-experts (e.g. clinician or junior researcher);
- to facilitate the critical appraisal of the studies, which are of variable quality;
- to carry out research into characteristics and trends in economic evaluations.

Given the investment of scarce resources in the Database, it is important to assess how it has been used and what, if any, benefits have resulted. These are likely to be related to any improvement in NHS decision making that results from the access to better information on cost-effectiveness. However, these ultimate benefits will be difficult to measure. Therefore, a two-stage evaluation is proposed: a ‘process’ evaluation of the Database and an ‘impact’ evaluation of the overall project.

Process evaluation is aimed mainly at collecting information about the ways in which the Database is currently used and at understanding how it could be made more useful. This evaluation will be implemented putting on-line a survey form to be filled in by the users.

Impact evaluation is aimed mainly to better understand how economic evaluations can be used. This process may include two phases:

(I) to analyse if the information (or a core of information) provided by the database is of potential use for decision making. This could be done, for example, by considering a set of purchasing problems, and to investigate if the database contains relevant and useful results, or by taking a set of abstracts, and to investigate if they have results which contain useful messages for NHS decision makers.

(ii) to investigate whether, in practice, this information is useful in decision making and what are the problems in promoting its use. This might be in the form of a series of case studies. For this phase we will need to go out and explore these issues face to face with regular and potential users.

We will be assessing in what ways the Database information can help inform decision making, what specific types of decision the Database may be useful for, and ways in which the information can be made more relevant and usable. Ultimately, we want to record the ways in which decisions might have been affected by use of the database and whether activity or policy changed as a result.

6. PLANS FOR RESEARCH LINKED TO THE NHS ECONOMIC EVALUATION DATABASE PROJECT

A few research areas linked to the NHS Economic Evaluation Database project and to the evaluation process previously described, have been identified and are outlined below.

• Making studies relevant. It is not always obvious how to generalise and apply the results of economic evaluations. Not only are these studies of variable quality, but they might not be generalisable to local settings and to different countries. For example, a simple currency conversion - using any conversion factor one wishes - does not solve the issue of comparability of studies carried out in different countries. CRD, in collaboration with CHE, will conduct research to address these issues.

More specifically, we will investigate:

(a) who produces economic evaluations (industries, government, etc.), how they are currently used (guidelines, as means of control, etc.), and for what purpose (setting priorities, etc.);

(b) the ways by which to integrate economic evaluation findings into decision making and to increase up-take.

This research will be an extension of the database evaluation previously described.

• Assessing and grading the quality of studies. Studies are not excluded from the database on the basis of quality. The abstract included in the database contains a detailed assessment of the study, appraised on the basis of various factors which are of key importance in the conduct and reporting of economic evaluations. However, it would be useful to give a summary quality grading or profile so that users could rapidly identify the more reliable research results. However, no accepted standard for evaluating and summarising the quality of the studies is available.

We shall explore the development of methods of grading the quality of economic studies. Existing scoring systems will be evaluated and the question of weighting

factors aimed to judge the relative value of different dimensions examined with a view to producing a more detailed and useful grading system than is presently available.

- Systematic overviews of economic evaluations. The methods for conducting systematic overviews and syntheses of economic evaluations are not as advanced as those used for clinical evaluations and others areas such as educational research. The methods currently used for reviewing economic evaluations will be investigated and assessed. We will develop criteria for judging the quality of reviews of economic evaluations and contribute to the methods of economic reviews, such as developing methodologies to compare and summarise findings. Greater weight might be given to those good studies that are, in general, less subject to bias and misinterpretation. Particular attention might also be paid to studies in which the issue of generalisability of the results to other settings and patient/client groups was addressed. The analogy of meta-analysis, i.e. the statistical methods used to synthesise and combining results of effectiveness studies, will be taken into careful consideration.

Patrick and Erickson[4] have identified two ways in which a 'meta-analysis' of the findings of economic evaluations can be undertaken. The first refers to the case in which the analyst is interested to know whether a standardised measure of synthesis (e.g. cost-utility ratios) used to evaluate an intervention for a specific health condition, differs across studies. The idea is to test the results of different cost-utility ratios against the hypothesis of no difference between these ratios. However, as Patrick and Erickson pointed out, the application of the principles of meta-analysis requires comparability of the studies in terms of the methods used to assess the efficacy of the intervention (e.g. classification systems and preference weights). We think that the homogeneity of the methods used to carry out the cost analysis is also desirable. Moreover, the performance of quantitative synthesis generally requires information about the sampling distribution of the data, including the cost-effectiveness ratios, and the results of statistical tests, which is often lacking in economic evaluations.

The second type of 'meta-analysis' identified by Patrick and Erickson consists of ranking the cost-utility ratio for different interventions. But, once again, the lack of

comparability of the studies in terms of the methods used can be biasing and can lead to problems of interpretation of the results.

• Identifying the need for new economic evaluations. The database is a useful resource for identifying important health technologies which are in need of more economic evaluation. In the UK this will be of use to the NHS R&D programme and in particular the Health Technology Assessment Programme.

It should be recognised that new economic evaluations could be necessary not only to fill-in some gaps of the research (e.g. assessing new health technologies), or to improve the methodological analysis, but also to duplicate a good analysis, in order to verify the findings of evaluation performed on the same topics. Udvarhelyi et al.[5] found a lack of overlaps in topics for the sample of studies they investigated. They reported that this lack of overlap could reflect a lack of 'healthy competition among researchers.

• Identifying methodological issues in economic evaluations of health care. Researchers can also use the database as a data source or spring board for undertaking methodological research. For example the structured abstracts included in the Database can be used to compare principles and practice of conducting economic evaluations, and to monitor trends in evaluative practice over time. We are planning to explore ways of linking the database with the CRD Database of Abstracts of Reviews of Effectiveness, and to assess how well economic evaluations reflect the full clinical evidence on a given health technology.

This research will be aimed at improving the quality and usefulness of economic evaluations.

REFERENCES

1. Sheldon, T.A. (1996). Fast track to reliable research intelligence. *Health Director*, p. 7.
2. Sheldon, T.A. (1996). Where's the evidence, then? *IHSM Network (Institute of Health Services Management*), **3**(6), p. 6.
3. Sheldon T.A., Vanoli A. (1996). Providing research intelligence to the NHS: The role of the NHS Centre for Reviews and Dissemination. In Towse A. (ed.), *Putting the U.K Approach to the Conduct of Economic Evaluations of Pharmaceuticals into an International Context: An Examination of the Relative Effectiveness of the Australian, Canadian and U.K Approaches to the Use of Information from Economic Evaluations of Medicines*. Office of Health Economics, London. (Forthcoming).
4. Patrick, D.L. and Erickson, P. (1993). *Health status and health policy: allocating resources to health care.* Oxford University Press, New York.
5. Udvarhelyi, I.S., Colditz, G.A., Rai, A., Epstein, A.M. (1992). Cost-effectiveness and cost-benefit analyses in the medical literature: Are the methods being used correctly? *Annals of Internal Medicine*, **116**(3), 234-244.

APPENDIX 1 SEARCH STRATEGIES

Search strategy 1
Current Contents, Clinical Medicine (weekly search)

1. (economic$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ab,ti,kw,kp.
2. (expenditure$ not energy).ab,ti,kw,kp.
3. (value adj1 money).ab,ti,kw,kp.
4. budget$.ab,ti,kw,kp.
5. or/1-4
6. editorial.pt.
7. letter.pt.
8. note.pt.
9. table of contents.pt.
10. or/6-9
11. 5 not 10

Search strategy 2
Medline (monthly search)

1. economics.sh.
2. exp "costs and cost analysis"/
3. economic value of life.sh.
4. exp "economics, dental"/
5. exp "economics, hospital"/
6. exp "economics, medical"/
7. exp "economics, nursing"/
8. economics, pharmaceutical.sh.
9. exp "fees and charges"/
10. exp "budgets"/
11. (cost or costs or costed or costly or costing).ab,ti,kw,kp.
12. (economic$ or pharmacoeconomic$ or price$ or pricing).ab,ti,kw,kp.
13. or/1-12
14. letter.pt.
15. editorial.pt.
16. historical article.pt.
17. 14 or 15 or 16

18. 13 not 17
19. “animal” /
20. “human” /
21. 19 not (19 and 20)
22. 18 not 21*

Search strategy 3
Cumulative Index of Nursing and Allied Health Literature (CINAHL) - (monthly search)

1. economics.sh.
2. exp “costs and cost analysis” /
3. economic aspects of illness.sh.
4. economics, pharmaceutical.sh.
5. economic value of life.sh.
6. economics, dental.sh.
7. exp “fees and charges” /
8. budgets.sh.
9. (cost or costs or costed or costly or costing).ab,ti,kw,kp.
10. (economic$ or pharmacoeconomic$ or price$ or pricing).ab,ti,kw,kp.
11. or / 1-10
12. editorial.pt.
13. letter.pt.
14. news.pt.
15. or / 12-14
16. 11 not 15*

* **NB.** The complete strategy includes sets to ensure that the search omits references already retrieved in Current Contents or by hand searching locally held journals.

APPENDIX 2 JOURNALS KEPT AT CHE/CRD CURRENTLY HANDSEARCHED

Aberdeen University, Health Economics Research Unit Discussion Papers
Aberdeen University, Health Economics Research Unit Option Appraisal Papers
Aberystwyth University, Department of Economics Research Papers
ACP Journal Club
Addiction
American Journal of Public Health
Annals of Internal Medicine
Archive of Internal Medicine
BMA Economic Research Unit Quarterly Bulletin
Bristol University, School for Advanced Urban Studies, Studies in Decentralisation and quasi markets papers
Bristol University, School for Advanced Urban Studies, Working Papers
British Journal of General Practice
British Medical Journal
Brunel University, Health Economics Research Group Research Reports
Brunel University, Health Economics Research Group Discussion Papers
Canadian Medical Association Journal
Centre for Health Economics Research and Evaluation (Australia) Discussion Papers
Clinical Therapeutics
Controlled Clinical Trials
Drug and Alcohol Review
Evidence - Based Medicine
Health Affairs
Health Care Financing Review
Health Direct
Health Economics
Health Economics Consortium Monitor
Health Policy
Health Policy and Planning
Health Service Journal
Health Technology Assessment Reports
Health Trends
Healthcare Management
International Journal for Quality in Health Care
International Journal of Epidemiology
International Journal of Health Planning and Management
Journal of Advanced Nursing
Journal of Epidemiology and Community Health
Journal of Health Economics
Journal of Health Politics, Policy and law
Journal of Medical Ethics
Journal of Studies on Alcohol

Journal of Public Health Medicine
Journal of the American Medical Association
Journal of the Royal College of General Practitioners
Journal of the Royal Society of Medicine
Lancet
London School of Economics, STICERD, Welfare State Programme. Research Notes
Medeconomics
Medical Care
Medical Decision Making
Milbank Quarterly
National Institute of Economic and Social Research Discussion Papers
New England Journal of Medicine
Nursing Standard
Nursing Times
Pharmacoeconomics
Preventive Medicine
Professional Nurse
Quality Improvement in Mental Health
Quality of Life Research
Social Science and Medicine
Statistical methods in Medical Research
World Health Forum
Social Policy and Administration
Statistics in Medicine

APPENDIX 3 EXTENDING SEARCH STRATEGIES

A number of Dialog on-line databases will be explored and searched, to expand the scope of current searching. A range of databases has been selected to cover specific subject areas. They include:

- Embase (formerly Excerpta Medica);
- Economics Literature Index;
- Dissertation Abstracts Online;
- Health Planning and Administration;
- PsycINFO.

A test search of the following On-line databases will be conducted to retrieve economic evaluations in journals not taken by CRD/CHE or not included on databases routinely searched. The results will be assessed to see how many articles are being selected before a regular search is conducted. An assessment of the output of searching will be compared to the effort involved in obtaining the result, before a decision is made. The financial implications will also be taken into account.

Embase

This contains biomedical literature and contains abstracts and citations from over 3,500 biomedical and pharmacological journals published throughout the world, and incorporates a large amount of European literature. A search strategy to retrieve economic evaluations, not in the journals taken in the Centre, or included on Medline or Current Contents, has been established on Embase, and a weekly print out of the results will be sent to the NHS CRD Information Service.

Economic Literature Index

This is an index of journal articles and book reviews from 260 economic journals and 200 monographs per year, and covers from 1969 to the present day. The database corresponds to the annual Index of Economic Articles and the index section of the quarterly Journal of Economic Literature.

Dissertation Abstracts Online

This covers more than 1.2 million doctoral dissertations and masters theses from American accredited institutions since 1861. It also includes thousands of Canadian dissertations, and a number of papers accepted abroad. All subject areas are covered. British and European dissertations are included in the database from 1988.

Health Planning and Administration

This contains references to nonclinical literature on all aspects of health care planning and administration, health insurance, financial management, personnel administration and manpower planning. It covers 1975 to present day. The references are drawn from Medline, the American Hospital Association's Hospital Literature Index, and National Health Planning Information Center (NHPIC).

PsycINFO

This contains international literature on psychology and related behaviour and social sciences, including psychiatry, sociology, anthropology, education, linguistics and pharmacology, from 1967 to present day.

BIDS

This provides access to the Social Science Citation Index, containing details of articles drawn from thousands of Journals world-wide. The data is supplied and owned by the Institute for Scientific Information Inc, USA.

APPENDIX 4 CRITERIA FOR INCLUSION/EXCLUSION OF STUDIES IN THE DATABASE

1 Papers to be Abstracted: Inclusion Criteria

Papers in any language are selected to receive a completed abstracts if they are full economic evaluations. These are studies in which a comparison of two or more alternatives is undertaken and both their costs and outcomes are examined. They are cost-benefit analysis, cost-utility analysis, and cost-effectiveness analysis (including cost-minimisation analysis and cost-consequence analysis).

2 Exclusion Criteria from Full Abstracts in Database

2.1 Studies which are not full economic evaluations. For example may include:

methodological papers;
reviews papers;
discursive analysis of costs/benefits;
partial evaluation studies, such as cost analyses; efficacy or effectiveness evaluations;
policy papers;
cost of treatment/burden of illness papers;
letters;
editorials;
notes.

(Bibliographic details of methodological papers, costing studies, and reviews articles are included in the Database)

2.2 Not a relevant topic:

- e.g., diseases/interventions/forms of organisation of health care not relevant to the NHS.

APPENDIX 5

Guidance for Writing Critical Abstracts for the

NHS Economic Evaluation Database

(These guidelines have been developed by Alessandra Vanoli, Mike Drummond and Trevor Sheldon, and are currently used by the commissioned health economists who are contributing to the production of structured critical abstracts for the NHS Economic Evaluation Database).

In order to appreciate the potential value of economic evaluations, it is important to critically appraise each study and not just accept the author's analysis. The CRD aims to make available information on appraisal of economic evaluations in a user-friendly format to ensure that the NHS Economic Evaluation Database is of maximum use to the potential audience (health care professionals, managers, policy makers, researchers and academics).

A critical analysis is easier if the evaluation of each study is undertaken systematically, following guidelines based on criteria for judging the quality of the studies. Therefore, the CRD has developed a detailed abstract structure and a rigorous system of supervision and quality assurance. An extensive checklist has been written as a guide for those producing the abstracts for the NHS Economic Evaluation Database.

The aim of the abstract is to provide a structure for summarising the study; to facilitate an understanding of the methods used as well as the assessment of its quality; to allow comparison across studies; to highlight any features of special interest. Comment fields contain summaries of key features which affect the usefulness of the evaluation and give an independent view on its conclusions and implications.

The structure of the abstract allows separate consideration of the quality of evidence of clinical effectiveness and the economic component. It also distinguishes between economic evaluations carried out alongside a single effectiveness study, those based on a review or synthesis of more than one study, and those in which the estimates of effectiveness are based on opinion. Where the estimates of effectiveness are based on a study published elsewhere, and insufficient details are provided in the report of the economic evaluation, the relevant paper is retrieved and examined. The quality of the effectiveness study, review or model is assessed as well as the relevance of the costs to the treatments.

A schematic summary of the abstract fields is given on page 36. The fields containing bibliographic details and other technical details - with the headings written in italics - are filled in by the CRD information officer. The non-italic fields, providing a summary and a critical appraisal of the study, are filled in by the abstractor. The contents of these fields are described below.

In producing the abstract of the study, the abstractor follows the "prompts" (marked with a dot) and the relevant explanation notes provided in the Guidance. Very rarely will it be possible to find enough information in an article relevant to all the prompts. In fact, the abstract structure has been elaborated to be very general and usable for a broad collection of different studies. If the information required is not given in the study, the abstractor leaves the fields blank except where the prompts are marked by an asterisk. In this case the abstractor reports either the lack of information (writing for example that the details are not stated), or the negative answer (writing for example that 'no sensitivity analysis was carried out'). In filling in the fields the abstractor has to write at least one complete sentence. If the abstractor is uncertain about the contents to be included in some fields, he/she leaves them blank, indicating "unclear" or unsure".

The abstractor gets a copy of the paper and a record template on disk to complete. The bibliographic details of the paper are filled in on the template by Susan Mottram (information officer). When the abstractor has finished the abstract, he/she returns the template disc to Margaret Anderton (database secretary). Then, the disk is assigned to another abstractor to check it for quality. After the abstract has been finally checked by Alessandra Vanoli, CRD/CHE health economist, it is approved by an editorial meeting then imported into the production database. If the abstract is considered not accurate enough, the original abstractor is asked to revise it.

In filling in the abstract structure provided on disk the abstractors may need to discuss computer/technical problems. They may also want to communicate some particular areas of health care interventions in which they would like to abstract papers. In these cases they should contact Margaret at CRD (tel. 01904-434558; E-mail: maa7@york.ac.uk). If they want to discuss methodological issues, linked for example to the use of the abstract structure, they should contact Alessandra, Tel. 01904-434564/4558; E-mail: av100@york.ac.uk).

At the time of publishing, the payment is £40 for writing each abstract, which has to be returned within one month of dispatch from CRD. £30 will be paid if the abstractors return the abstract between one and two months after dispatch from CRD. Unless a prior agreement has been made, abstracts not completed within two months will not be paid for and the paper will be assigned to another abstractor. £20 will be paid for checking an abstract written by someone else.

We recommend that each abstractor should produce, to keep in practice and maintain skills, at least 4/5 reviews and check 4/5 other reviews per two month period.

Contents of the abstract structure for the NHS Economic Evaluation Database

Accession number
Addition date
Edit date
CRD status
Record status
CRD reviewer
Author(s)
Title
Source information
Journal volume
Publisher
ISBN
Series information
Pages
Date of publication
Publication type
Language of publication
English summary available
Correspondence address
Health technology
Disease
Type of intervention
Hypothesis/study question
Economic study type
Study population
Setting
Dates to which data relate
Source of effectiveness data
Modelling
Link between effectiveness and cost data (for case A - single study - only)

(Case A: Single study)
Study sample
Study design
Analysis of effectiveness
Effectiveness results
Clinical conclusions

(Case B: Review/synthesis of studies)
Outcomes assessed in the review
Study designs and other criteria for inclusion in the review
Sources searched to identify primary studies
Criteria used to ensure the validity of primary studies
Methods used to judge relevance and validity, and for extracting data
Number of primary studies included
Method of combination of primary studies
Investigation of differences between primary studies
Results of the review

(Case C: Estimates of effectiveness based on opinion)
Methods used to derive estimates of effectiveness
Estimates of effectiveness and key assumptions

Measure of benefits used in the economic analysis
Direct costs
Indirect costs
Currency
Statistical analysis of costs
Sensitivity analysis
Estimated benefits used in the economic analysis
Cost results
Synthesis of costs and benefits
Author's conclusions
CRD commentary
Implications of the study
Other publications of related interest
Subject index terms
Country codes
Source of funding
Copyright comments

Field	Description
1. SUBJECT OF STUDY	
1.1 Health technology	•Describe the health technology(s) studied by name and type.[1] *
1.2 Disease (This field is filled in by CRD information staff.)	•To identify the disease field, choose one - or more - of the following broad terms:[2] Bacterial and fungal diseases Behavioural and mental disorders Virus diseases Parasitic diseases Neoplasms Musculoskeletal diseases Digestive system diseases Stomatognathic diseases Respiratory tract diseases Otorhinolaryngologic diseases Nervous system diseases Eye diseases Urologic and male genital diseases Female genital diseases and pregnancy complications Cardiovascular diseases Hemic and lymphatic diseases Neonatal diseases and abnormalities Skin and connective tissue diseases Nutritional and metabolic diseases Endocrine diseases Immunologic diseases

[1]The Office of Technology Assessment (1978) defined as a health technology "...the drugs, devices, and medical and surgical procedures used in medical care, and the organisational and supportive systems within which such care is provided." However, the definition used here is broader. We consider health technology to be any method used to promote health, prevent, diagnose or treat disease, or improve rehabilitation and long term care, including self-medication and self-help, or complementary medicines. In this field the abstractor should specify in detail such methods investigated in the study.

[2]This field takes the broad subject headings used in Medical Subject Headings (MeSH) to provide an access route into the database. It allows, for example, the retrieval of all economic valuations of cancer treatment. MeSH is the indexing language chosen for the database because it is internationally known, comprehensive and extensively updated each year. It is also used by other databases being produced as part of the ISS namely the Project Register System and the Cochrane Database of Systematic Reviews and has been adopted by CRD for the sake of consistency.

Injury, occupational diseases and poisoning
Symptoms and general pathology
Therapeutics
Techniques and equipment
Health care: Residence characteristics
Health care: Socio-economic factors
Health care: Health promotion
Health care: Emergency medical services
Health care: Health policy
Health care: Patient care management
Health care: Primary health care
Other organisational issues of health care

1.3 Type of intervention

- Report the intervention type in broad terms, using, for example, one - or more - of the following:*****

Primary prevention;[3]
Secondary prevention;[4]
Screening;
Diagnosis;
Treatment;
Rehabilitation;
Palliative care;
Other (specify).

1.4 Hypothesis/study question

- Summarise the general objective of the study.*****
- Specify the hypothesis/question(s) posed.
- State whether any alternative health technology was explicitly stated as a comparator.*****
- If any, report the alternative health technology(s).
- Report, if any, the justification given for the choice of the alternative technology.*

[3] Primary prevention includes interventions addressed to prevent a disease in people with no obvious disease even though they may have risk factors (e.g. routine immunisation of healthy children; therapy to prevent deep vein thrombosis after hip replacement; exercise to prevent the first heart attack).
[4] Secondary prevention involves identification and treatment of persons who have already developed a disease, in order to prevent worsening or repeat events (e.g. aspirin to prevent the recurrence of heart attacks).

2. KEY ELEMENTS OF STUDY

2.1 Economic study type

•To define the study type, choose one or more of the following:[5] *****

Cost-effectiveness analysis;[6]
Cost-utility analysis;[7]
Cost-benefit analysis.[8]

2.2 Study population

•Outline the main characteristics of the patient population studied; e.g. age, sex, health status, socio-economic status, occupation, etc.*****

2.3 Setting

•Specify the practice setting (e.g. community, primary care, institution).*****

•Quote the country(s) (e.g. UK) or specific place (e.g. Sheffield) in which the economic study was carried out.*****

2.4 Dates to which data relate

Report the years during which the data was collected, for:

•Effectiveness analysis.*****

•Resources used, such as equipment, manpower, medicines, etc. (if different for different components of intervention, report separately).*****

•Prices used.*****

---

[5]It may happen that the author defines the study type incorrectly. In this case the abstractor should write the correct definition and should justify his/her correction in the commentary field.

[6] Cost-effectiveness analysis is the term given to any analysis where the health outcomes are expressed in natural units (e.g. life-years gained, death avoided, heart attacks avoided). Studies with multiple outcome measures (sometimes called cost-consequences analyses) are also included in this category. In addition, cost-minimisation analyses, where it is assumed (based on either previous research or opinion) or it is shown within the economic analysis, that the alternatives have identical outcomes, are also included as a special case of cost-effectiveness analysis.

[7]In cost-utility analysis the benefits are measured in utility units or utility-weighted life-years (such as QALYs). The final result is expressed, as a cost/utility ratio for each programme compared.

[8]Cost-benefit analysis measures costs and benefits in monetary terms, and the final result is expressed as a net monetary gain (or loss) or as a cost/benefit ratio. Studies are not regarded here as cost-benefit analyses if the savings of resources are considered as benefits (outcomes), even if the authors define them as cost-benefits analyses. Probably in these studies there was an estimate of an effectiveness outcome (e.g. number of cases of disease prevented) which allowed the calculation of the resource savings. Therefore, these studies should be classified as cost-effectiveness analyses. A methodologically correct cost-benefits analysis is that in which the (final) outcomes of effectiveness are expressed in monetary terms, using approaches such as 'willingness-to-pay' or 'human capital'.

2.5 Source of effectiveness data

•State whether the evidence/estimate for final outcomes was: [9]

i) derived from a single study (case A);

ii) based on a review/synthesis of previously completed studies (case B);

iii) not based on any studies:[10] estimates of effectiveness based on opinion (case C).*****

2.6 Modelling

•State whether a model was used in estimating benefits/costs.[11]

2.7 Link between effectiveness and cost data

(This field has to be filled in for case A - single study - only).

•State whether the costing was undertaken on the same patient sample as that used in the effectiveness study.*****

•State whether the costing (i.e. the collection of resource data) was undertaken prospectively (alongside the effectiveness study) or retrospectively (after the effectiveness results were known).*****

---

[9] The estimates of effectiveness may be based on more than one of these options (e.g. cases 'A' and 'B', when the clinical evidence for the intervention was derived from a case series and that for the comparator was based on a review of the literature). In this case the abstractor should fill in more than one section only if such estimates of clinical outcomes were strictly relevant for the economic analysis.

[10]The effectiveness estimates may reflect the author(s)' assumptions, or the analysis may be based on an estimation of what the different level of benefits should be, given the costs, in order to make an intervention cost-effective. In the first case the abstractor should choose the option 'C' and fill in the corresponding fields in section 3. In the second case, the abstractor should not fill in the fields included in section 3, and should go to the fields relevant for the valuation of benefits, i.e. "4.1 Measure of benefits" and "4.6 Sensitivity analysis".

[11]Modelling studies are increasingly employed in developing economic evaluations. They may be useful when information which cannot be directly inferred from the collected clinical/economic data, or when few data are available (e.g. in the case of new technologies), or when experimental and observational investigations are difficult or unethical to conduct. For example, using decision analytic techniques (such as decision trees, Markov models, simulation models) it is possible to compare alternative strategies having long term implications by defining their possible outcomes and the probability and utility of each outcome.

3. DETAILS ABOUT CLINICAL EVIDENCE[12] [13]

A. Single study

A.3.1 Study sample

Provide details such as sample selection; sample/trial size; power calculation; [14] refusal to participate. More specifically:

- Summarise the method of sample selection (e.g., outline, if any, the sample randomization method).
- State whether there is evidence that the initial study sample is appropriate for the clinical study question.[15]
- State whether power calculations determined the sample size.[16] *****
- Report the trial/study size. Distinguish between the number of subjects (e.g. patients, doctors, health care provider units) overall, in the intervention group, and in the control group.*****
- Report the percentage of subjects invited to participate who refused.
- Report the percentage of subjects excluded for any reasons from the initial sample.

A.3.2 Study design

- Define the type of study as:*****
  Randomized controlled trial;[17]
  Nonrandomized trial with concurrent controls;[18]
  Nonrandomized trial with historical controls;[19]
  Cohort study;[20]

---

[12]It is possible that the paper reporting the economic appraisal may not give sufficient details of the clinical study. In this case it is necessary to get the related papers which describe the clinical evaluation.

[13] Abstractor should note that the clinical analysis can provide information on both the effectiveness and use of resources. In this section only the clinical outcomes should be reported. Any information about the implications on the use of resources should be reported in fields “4.2 Direct costs”, “4.3 Indirect costs”, “5.2 Cost results”, and “5.3 Synthesis of costs and benefits”, as appropriate.

[14]Power of a test is the ability of a test to detect the effect of an intervention if it truly exists. In statistical terms, it is the probability of detecting a true effect as statistically significant (or the probability of avoiding Type II error).

[15]In other words, report if and how the author fully justified the choice of the patient sample with respect to the characteristics of the disease and/or treatment under investigation and with respect to the generalisability of the findings.

[16]The clinical study should report the determination of the sample size that would enable the detection of any clinically important effect as statistically significant. If the clinical trial had too few patients, then the power of the trial may have been too low to detect a treatment effect.

[17]The Randomized Controlled Trial (RCT) is an experimental study in which the participants are randomly assigned to an intervention or a control group (it may also be reported by the author’s as a randomized clinical trial). Studies not using truly random and concealed approaches may introduce bias.

[18]This is an experimental study in which the assignment of patients to treatment and control groups was not random, and the investigators observed the control group at the same time as the treatment group. This includes what are sometimes referred to as quasi-experimental studies.

[19]In this trial the control group is chosen from a group of patients who were observed at some previous time.

Case-control study;[21]
Before-and-after study;[22]
Case series;[23]
Single case report (anecdote);[24]
Other (specify).

- State whether the study was single or multi centre. Please give details (e.g. number of centres or number of sites).
- Report the duration of follow-up of the treatment cohort.*
- If an experimental study, report the subject allocation method, choosing for example:

Unit of randomization;[25]
Method of random allocation,[26] including blinding of allocation if done;
Block randomization;[27]
Stratified allocation;[28]
Haphazard or other nonrandom allocation;[29]
Other (specify).

- Quote the loss to follow up[30] (may state the reasons for withdrawals). For example in an experimental study report: % Overall; % in Intervention Group; % in Control group.*

---

[20]A cohort study is an observational study in which a group is followed-up over time to observe changes in health. Outcomes are then related to exposure to a risk factor or an intervention. It may be undertaken prospectively or retrospectively. In a prospective study the investigator does not know the outcomes when the study is planned at the onset. In contrast, in a retrospective study the investigator selects groups of patients after treatment or exposure to risk factors. Observational studies may give biased estimates of treatment effects because treated and untreated groups may not be sufficiently comparable.

[21]In a case-control study, people with a disease or outcome are selected and their exposure to a treatment or risk factor compared to a group of people who do not have the disease or outcome (controls). This study is retrospective, and is used particularly when the outcome of interest is rare. Case-control studies are particularly susceptible to a number of potential biases.

[22] This is a study design where a group of individuals is studied before and after an intervention, with no comparison or control group. It is often hard to attribute a change to the intervention, due to spontaneous changes in the condition or other changes that may have been occurred over the course of the study.

[23]This is an uncontrolled observational study of a series of consecutive patients who receive a particular intervention and the relative outcomes are observed. It can be prospective or retrospective and may take the form of a cohort study.

[24]This is also called "Case study". This is an uncontrolled observational study in which intervention and outcome are analysed for a single patient. This study can be prospective or retrospective.

[25]For example: person, clinician, unit, area, etc.

[26]With true random allocation each study participant has the same probability of being assigned to the experimental or to the control group.

[27]Block randomization is a modification of random allocation, in which subjects are allocated in small blocks. The subjects in the first block are randomly assigned to the groups, and so on for the other blocks, until the final sample size is achieved. This is carried out to try and ensure comparability between groups.

[28]Stratified allocation is similar to the stratified selection. The aim is to ensure that the groups do not differ too significantly with respect to the stratification variables.

[29]This is a non random allocation of the subjects.

[30]"Loss to follow up" describes the participants who were initially included in the study but did not complete the observation period. It is also known as withdrawal or drop out rate.

•Specify the blinding method for assessment of outcomes, if any. For example: Patient; Clinician; Assessor of patients' outcome. [31]

A.3.3 Analysis of effectiveness

•State whether the analysis of the clinical study was based on: 1) intention to treat; or 2) treatment completers only; or 3) not stated. [32] *****

•Report the primary health outcomes used in the analysis (e.g. CHD deaths, quality of life, side-effects) [33]*****, and specify any particular instruments used to valuate these data (e.g. quality of life questionnaire).

•State if, at analysis, groups were shown comparable in age, sex and prognostic features or if there was adjustment for confounding variables.[34] List, if any, the confounding variables.

A.3.4 Effectiveness results

•Summarise the results of the trial or study, including the side or adverse effects (give quantitative results when reported). *****

•Quote the 95% confidence interval[35] and p-values[36] of primary outcomes.*****

A.3.5 Clinical conclusions

•Summarise the clinical conclusions derived from the evaluation of intervention (this may not be given in the economic study).

---

[31]If the method is double-blinding, neither the person doing the assessment nor the study participant may identify the intervention. Blinded assessment in cases where outcome measurement involves some subjectivity or judgement can help reduce bias.

[32]The analysis is called "intention to treat" if the effectiveness results are based on all the original participants in the treatment or comparison groups as originally allocated, including the withdrawals. In contrast, in the "treatment completers" analysis, the effectiveness results are only based on the patient sample who completed the observation period. This may introduce bias due to non-random drop out.

[33] In some studies, the principal difference between health technologies is in terms of the incidence and severity of side-effects. This should not mislead the abstractor to report that there was not an effectiveness analysis. Side-effects are negative clinical benefits and should be reported in this field. The impact of side-effects on the use of resources should be reported by the abstractors in field "4.2 Direct costs" (or eventually in field "4.3 Indirect costs") and in fields "5.2 Cost results" and "5.3 Synthesis of costs and benefits", as appropriate.

[34]A confounding variable is correlated with the outcome and the probability of receiving a treatment or exposure, so biasing estimates of the association between treatment and outcome.

[35]The confidence interval is the plausible range of values above and below the point estimate of a treatment effect, that is likely to include the true value of the treatment effect. A confidence interval of 95% means that there is a probability of 95% that the confidence interval calculated from a specific study includes the true value of a treatment effect. If the interval includes a null treatment effect, the null hypothesis cannot be rejected.

[36]In hypothesis testing, the p-value is the probability that an observed difference between the control and the intervention groups was due to chance alone if the null hypothesis (no difference) is true. Conventionally, if "p" is less than 0.01 or 0.05, the null hypothesis is rejected.

B. Review/synthesis of previous published studies (if the economic study uses data from more than one review/synthesis, give an entry for each).

B.3.1 Outcomes assessed in the review

•Report the outcomes chosen by the author and determined by the assessments made in the primary studies

B.3.2 Study designs and other criteria for inclusion in the review

•List the particular study designs included in the review as described by the author*****.

•State any other inclusion or exclusion criteria, such as age, disease state, outcome measurement, duration of follow up, measure of quality of studies.[37] *****

B.3.3 Sources searched to identify primary studies

•List the sources searched by the author(s).[38] Example: Medline,[39] other databases, unpublished data, journal references, personal communication.*****

B.3.4 Criteria used to ensure the validity of primary studies

•Specify the criteria used to assess the validity of the primary studies. For example: concealment of randomisation; blind assessment; low drop out rates, etc.*****

B.3.5 Methods used to judge relevance and validity, and for extracting data[40]

•Specify the judgement criteria applied by the author(s) for assessing the validity of the primary studies. For example:*****

Single reviewer;
Single blind reviewer;[41]
Two reviewers;
Not stated.

---

[37]The quality of a study can be judged on the basis of its validity. The validity of a study is generally expressed as: a) "internal validity", i.e. in a particular setting the results of a study describe the true causal relation between the intervention and the outcome. The internal validity can be influenced by different factors, for example the patient selection bias and other confounding biases; b) "external validity", i.e. the generalisability of the results of the study to other settings.

[38]Systematic searches of literature sources, such as electronic databases and hard copy information, should be undertaken to ensure that the selection of studies included in the review is unbiased and comprehensive.

[39]Medline is a bibliographic database which contains citations for articles published from health and biomedical journal. It is the most used Medical Literature Analysis and Retrieval System's (MEDLARS) database, managed by the US National Library of Medicine (NLM).

[40]Decisions regarding the relevance, the validity and the data extracted from the primary studies might be subjective. Their reliability improves if decisions are made by more than one independent reviewer, according to clearly defined and appropriate criteria.

[41]In this case the reviewer does not know relevant bibliographic information (such as the periodical's and the author's name) which could bias the judgement.

•Specify the methods used to extract data from the primary studies, using for example:

Individual data, i.e. the original/raw data in individual studies;
Summary statistics from each study;
Graphs summarising results from each study;
Other (define).

B.3.6 Number of primary studies included

•Report the number of primary studies included in the review, and the types of studies (if more than one type).*****

B.3.7 Method of combination of primary studies

•If carried out, specify the methods used to combine the results of the individual primary studies. For example:*****

Meta-analysis;[42]
Narrative method;[43]
Other (define);
Not done.

•In the case of a statistical meta-analytical technique, outline how the results were combined, and if they were, for instance, weighted according to the sample size and variability.

•In the case of narrative reviews, report any weighting scheme the author(s) used to reach the conclusions.

B.3.8 Investigation of differences between primary studies

•State whether the author investigated the differences between the primary studies, focusing attention for example on the differences in participants, exposures or interventions, outcome measures, study designs, etc.[44] *****

•State whether the author provided an explanation of differences between individual studies;[45] including results of statistical tests of

[42]Meta-analysis is a systematic method of analysis which combines results from independent studies using statistical techniques. The results are weighted according to the sample size or variability, and are sometimes weighted by study quality. The aims are mainly: to obtain a pooled estimate of an overall "true treatment effect", reporting standard errors and confidence intervals; to obtain improved estimate of the outcome of a specific intervention which has been analysed in a class of studies. It is also known as “data synthesis” or “quantitative overview”.

[43]Narrative reviews should state how different studies contributed to the final conclusions.

[44]Special attention should be paid when the differences between study results are only attributed to one explanation without considering other explanations adequately.

[45]There are sometimes significant differences between the results of the primary studies, as indicated by a test of heterogeneity (or homogeneity). A review may investigate how differences in the interventions, participants, outcomes or study designs affect the estimate of the effectiveness of the technology.

homogeneity[46] (e.g. significant, not significant, not done, not applicable).

•State whether the author investigated how these differences affect the estimate of the effectiveness of the technology.

B.3.9 Results of the review

•Summarise the author(s) findings from combining primary studies, including actual data, odds ratios,[47] confidence intervals.*****

C. Estimates of effectiveness based on opinion.

C.3.1 Methods used to derive estimates of effectiveness

• Report the methods used to derive estimates of effectiveness. E.g. consensus, experts' opinion, authors' assumptions.

C.3.2 Estimates of effectiveness and key assumptions

• Report the estimates of effectiveness of health technology and key assumptions used in producing them.

[46]There exist in the literature different formulas to calculate such tests. Generally, they are based on the calculation of a statistic regarding the sum of the weighted difference existing between the summary effect measure and the effect resulting from each study. The statistic is distributed as a chi-square, with degrees of freedom equal to the number of studies minus one. The hypothesis of homogeneity is rejected if the p-value is less than some critical values. Test of homogeneity however, have low power. So the critical values used should be higher than is conventional for hypothesis testing. Visual inspection of the variability of results may be more informative.

[47]The odds ratio measures a treatment effect comparing the odds of a certain outcome in the treatment group with that in the control group. If the outcome is not too frequent then the odds ratio is similar to the relative risk.

4. ECONOMIC ANALYSIS

4.1 Measure of benefits used in the economic analysis[48]

- Specify which outcome measure was used in the economic analysis, using for example:*
  - Heart attack avoided;
  - Lives Saved;
  - Life-Years gained;
  - Quality-Adjusted-Life-Years gained (QALYs);[49]
  - Healthy-Years Equivalent (HYEs);[50]
  - Monetary benefits (in Cost-benefit analysis only).[51]
- Report, if any, the type of model adopted and why it was used.[52]
- Report the basic method of valuation of health states.[53] For example can be one or more of:*
  - Generic valuation matrix, (e.g. Rosser classification);
  - Direct measurement;
  - Author's assumption.
- Report whose, and how many (i.e. number of these people used to elicit values) values were used to assess the health states. For example, use one or more of the following:*
  - Author;
  - Clinician;

---

[48] When the authors assumed or showed within the study that the alternative strategies produce identical benefits, the abstractor should report in this field a sentence like the following: 'Since the effectiveness analysis showed no difference in effectiveness/clinical benefit between the intervention and comparator, the economic analysis was based on the difference in costs only'. Then, the abstractor should write 'Not applicable' both in field "5.1 Estimated benefits used in the economic analysis" and in field "5.3 Synthesis of costs and benefits".

[49] QALY measures the duration of life discounted by some fraction between 0 and 1 which estimates the quality of life during the period. It represents the equivalence of being alive for a certain proportion of a year in perfect health. It is also known as "well years", "well life expectancy", "health life-years" and "years of healthy life".

[50] This is a measure of health-related quality of life. It is the hypothetical number of years spent in perfect health which could be considered equivalent to the actual number of years spent in a defined imperfect health state. It differs from QALY because not only is it based on the individual's preferences for the duration of life, but also on the individual's preferences for the states of health. QALYs and HYEs are used to measure the benefits in cost-utility analysis, where single or multiple effects are not common to both alternatives.

[51] Savings of resources should not be considered as benefits used in the economic analysis, whatever the economic study type may be. Therefore, abstractors should distinguish between saving of resources (sometimes defined by the authors as an economic benefit) and benefits used in the economic analysis. In the first case the data relate to the negative incremental costs (e.g. due to averted treatments), and must be reported in the cost fields. In the second case, the benefits relate to the intermediate or final health outcome.

[52] For example, decision tree to estimate expected life-years/QALYs of the alternatives; Markov model to extrapolate outcome results from the short-term to the long-term, or from one setting to another; regression model.

[53] When applicable, please use this and the following prompts to provide details about any methods used to extrapolate effectiveness data.

Patient;
Relative;
Society;
Other health worker;
Literature.

- Specify when they were valued.[54]
- Specify how they were valued. For example: postal or telephone survey, interview.
- Report the valuation tool used. For example:*

Standard gamble;[55]
Time trade-off;[56]
Other (specify).

4.2 Direct costs[57]

Provide details of methods used (include discounting) [58] distinguishing, where possible, between costs and quantities of the resources:

- State whether costs were discounted.[59] *
- State whether quantities/costs were reported separately.*
- Specify which quantities/costs were measured. For example: health care costs due to added years of life, capital costs, overhead costs, operating costs, costs of complications.
- Report the quantity/cost boundary adopted, specifying whose direct costs were included in the analysis. [60] *

For example:
Hospital;[61]

---

[54]For example: at baseline, at 1 month, at three months from the intervention.

[55]Standard gamble is a method to measure utility directly. It is based on the fundamental von Neumann-Morgenstern axioms of expected utility theory. The subject is asked to make a trade-off between the certainty to have a cronic disease for a certain period of time, and a gamble. The gamble has the following alternatives: good health for the same above period and death.

[56]In time trade-off, the utility value is measured by finding the point at which the respondent is indifferent between two health states for different lengths of time. For chronic states, the choice is between the index health state for time t and perfect health for a shorter time, both followed by death. For temporary states, the choice is between the index health state for time t and a worse health state for a shorter time, both followed by the same specified outcome.

[57]Direct costs include fixed and operating costs incurred during the development and the implementation of a health care programme, carried out within or outside the health care sector (e.g. health professional's time, equipment and capital costs, etc.). Direct costs may also include the costs borne by patients and their families, such as out-of pocket expenditures. See also footnotes 61 to 65.

[58]Discounting of costs is important because money available today has a higher value than the same amount of money available in the future. Discounting future health benefits reflects individual positive time preference but is more controversial. The rate of discount for costs is typically 2 to 6% per annum.

[59]Where costs were not discounted, the abstractor must answer the question in cases when discounting would have been appropriate.

[60] Health care is provided through various programmes and institutions and the costs can be borne by a wide range of groups including patients and their families. The boundaries are often imprecise and the authors' judgement on the viewpoint they adopted might be inappropriate. Therefore, the abstractor is not asked to report the study perspective as defined by the authors, but he/she has to list whose direct costs were included. The user of the database can then infer the perspective of the study from this information.

Health service;[62]
Other agencies;[63]
Patient;[64]
Relatives;
Others (define).[65]

- State if the estimation of the quantities was one or more of the following: i) a guess; ii) based on actual data, i.e. based for example on one unit of analysis or a sampling technique or on published information from other studies (e.g. clinical trial); iii) derived using modelling studies.[66]
- State if the estimation of the costs was one or more of the following: i) a guess; ii) based on actual data, i.e. based for example on one unit of analysis or a sampling technique or on published information from other studies (e.g. clinical trial) or standard prices; iii) derived using modelling studies.[67]
- Report the source of quantity/cost data.
- Specify when the quantity of resources was measured. (range of years quoted if necessary). For example: trial date.
- Specify the date(s) the price data refer to.*
- State whether costs were reflated and report the method used.
- State whether the study reported any difference between marginal costs and average costs.[68]

---

[61] This includes a hospital or any other institutions providing outpatient and in-patient services. It might be private or public. Costs may relate to surgical and diagnostic procedures, nursing care, acquisition and administration of drugs, hotel, etc.

[62]The abstractor should chose this option if a broad range of resources for providing health care services has been considered in the study. These may relate for example to more than one of the following: provider institution for outpatient and in-patient services (e.g. hospital, tertiary care centre), general practice, non-hospital laboratories costs, dentist services and any other ambulatory care, nursing home costs, acquisition and administration of drugs outside the hospital, professional health services provided by single physician (e.g. specialists, consultants) outside the hospital; any other medical costs, such as those related to the implementation of vaccination programmes.

[63]This option refers to the case where the study analysed costs of agencies providing social care (non-medical direct costs), such as residential care, voluntary services, and social services.

[64] These are non-health care sector costs borne by the patients and/or their families for visitation, travel, goods and services purchased in the market by the consumers, e.g. therapeutic appliances, optical equipment, hearing devices. Abstractors should note that the lost income from work is not included in this category since this is considered to be an indirect cost.

[65] For example, other societal costs different from the patients/relative costs previously described may have been included in the economic evaluation.

[66] The abstractor should provide a brief description, reporting the type of model and its use, for example: decision tree to estimate expected quantity/costs of the alternatives; Markov model to generate quantities/costs (e.g. to extrapolate costs from the short-term to the long-term, or from one setting to another); regression model.

[67] See footnote 66.

[68] Incremental cost and marginal cost are two different concepts, although the terms are often used interchangeably. Incremental cost is the difference in costs found between two programmes (i.e. intervention

- State whether the author established that some cost components were excluded because they were common to both alternatives.
- State whether any adjustments were made to the observed costs to correct, for example, for protocol driven costs or learning effects for new technologies.

and comparator). Marginal cost is the difference in cost due to the expansion or contraction of a programme (e.g. increase of one day the length of stay). They coincide only when the expanded (or contracted) programme is considered as the alternative option.

4.3 Indirect costs[69]

Provide details of methods used (include discounting)[70]distinguishing, where possible, between costs and quantities.

- State whether the costs were discounted.[71] *****
- State whether quantities/costs were reported separately.*****
- Specify which quantities/costs were measured (for example, production gains/losses).
- Report the quantity/cost boundary. For example:*****
  Patient;
  Relative;
  Others (define);
- State if the estimation of the quantities was one or more of the following: i) a guess; ii) based on actual data, i.e. based for example on one unit of analysis or a sampling technique or on published information from other studies (e.g. clinical trial); iii) derived using modelling studies.[72]
- State if the estimation of the costs was one or more of the following: i) a guess; ii) based on actual data, i.e. based for example on one unit of analysis or a sampling technique or on published information from other studies (e.g. clinical trial) or standard prices; iii) derived using modelling studies.[73]
- Report the source of quantity/cost data.
- Specify when the quantity of resources was measured (range of years quoted if necessary). For example: trial date.
- Specify the date(s) the price data refer to.*****
- State whether costs were reflated and report the method used.

4.4 Currency

- Quote the currency as reported in original study. For example: US $, Yen.
- State whether a conversion was done.

[69]Indirect costs are the costs of lost productivity due to a disease, for example the time lost from work.
[70]See footnote 58.
[71]See footnote 59.
[72] See footnote 66.
[73]Ibid.

4.5 Statistical analysis of quantities/costs

- State whether the author(s) treated the costs in a stochastic way, and if so, how.
- State whether a statistical test was carried out.[74]
- Specify which method was used.

4.6 Sensitivity analysis

- State whether a sensitivity analysis of benefits/costs was carried out and specify the parameters (e.g. discount rate, estimates of effectiveness or cost data, etc.).[75] *
- Specify which areas of uncertainty were investigated. Choose one or more of the following:
  - Variability in data;[76]
  - Generalisability of results;[77]
  - Extrapolation from primary data source to make the results more comprehensive;[78]
  - Analytical methods;[79]
  - Other (specify).
- Specify the method used. Choose one or more of the following:*
  - One-way simple sensitivity analysis;[80]
  - Multi-way simple sensitivity analysis;[81] [82]
  - Threshold analysis;[83]
  - Analysis of extremes;[84]

---

[74]When the input data collected for a prospective economic evaluation are measured as random variables - i.e. the resource data are sampled - a statistical test may have been calculated to estimate confidence intervals.

[75]Sensitivity analysis is a method testing the robustness of the analysis : the deterministic variables for which there is uncertainty (e.g. effectiveness data, discount rate, costs, etc.) are varied over a range and the related changes in the final results are analysed.

[76]When sample data is not available it is not possible to deal with uncertainty using statistical techniques, and other methods, such as the sensitivity analysis, are required.

[77]In this case the uncertainty may concern for example the validity of the effectiveness and cost results for different groups of patients, the applicability of the cost-effectiveness observed in a trial to a routine clinical practice, the possibility of getting similar consequences in different settings (hospitals, regions, countries).

[78]The extrapolation may concern for example: a) the extension of cost-effectiveness results based on intermediate clinical end-points to a model based on final clinical end-points; b) the prolongation of the time horizon of a study.

[79]There exists a certain degree of disagreement about the methods and the instruments of analysis used in the economic evaluation studies (for example the inclusion of indirect costs, the valuation of the consequences of the interventions, etc.).

[80]By this method each parameter is varied individually in order to isolate the consequences of each parameter on the results of the study.

[81]By this method two or more parameter are varied at the same time and the overall effect on the results is valuated (this is sometimes called "scenario analysis").

[82]Simple sensitivity analysis is generally useful in investigating all the areas of uncertainty previously described.

[83]This analysis identifies the critical values of the parameters above or below which the results of a study vary. This method is usually used jointly with the simple sensitivity analysis, and it is generally useful to investigate all the areas of uncertainty described, with the exception of the uncertainty surrounding the analytical methods.

[84]By this method, a base-case analysis based on the best estimates of inputs is considered. Therefore alternative analyses based on extreme estimates ("pessimistic" and "optimistic") are generated. This analysis,

Probabilistic sensitivity analysis;[85]
Other (specify).

which is also known as worst/best case analysis, is generally useful to deal with uncertainty in data variability and extrapolation from primary data source, and may be useful in addressing the issue of the generalisability.

[85]This method of analysis attributes distributions of probabilities to the uncertain variables which are incorporated into evaluation models based on decision analytical techniques (e.g. Monte-carlo simulation). This method can only be used to deal with uncertainty in data input.

5. RESULTS

In the following sub fields quote the results, if any, including figures for quantities/costs, discounted and not discounted.[86]

5.1 Estimated benefits used in the economic analysis

- Report (incremental) benefits using for example: (incremental) lives saved; (incremental) life-years gained and discount rate; (incremental) quality-adjusted-life-years gained and discount rate,[87] etc., including confidence intervals, if any.*****
- Report the duration of benefits from the intervention to the patient used in the economic analysis (e.g. length of follow-up as in clinical study, ten years, life time).
- Report the duration of comparator benefits to the patient used in the economic analysis (example as above).
- State whether the side-effects of treatment were considered in the economic analysis, or they were not relevant.

5.2 Cost results

- Report the total intervention cost and discount rate, recorded in original currency*****.
- Report the total comparator cost and discount rate, recorded in original currency*****.
- Report the result of the currency conversion.
- If calculated, report the incremental quantity/cost (discounted and not discounted figures).
- Report the results of any statistical analysis of costs or confidence intervals.
- Report the duration of intervention quantities/costs used in the economic analysis.
- Report the duration of comparator quantities/costs used in the economic analysis.
- State whether the costs of adverse effects or knock on costs were dealt with in the costing, or not relevant.

[86] If there is more than one discount rate, indicate which discount rate corresponds to which results.
[87] Generally the rate of discount used to convert future benefits into present values is 0 to 6%.

5.3 Synthesis of costs and benefits

- Specify how the estimated benefits and costs were combined.[88]*

  For example:
  Cost/Life Saved and discount rate;
  Cost/Life-Years gained and discount rates of cost and benefits;
  Cost/QALY and discount rates of costs and benefits;
  Net benefit in Cost-benefit analysis;
  Others (define);
  Not combined.[89]
- State whether an incremental analysis was performed.[90]*
- Report the summary findings, quoting currency[91] and year. For example: (incremental) Cost/Life Saved and discount rates;[92] (incremental) Cost/Life-Year gained and cost/benefit discount rates;[93] (incremental) Cost/QALY gained and cost/benefit discount rates.[94]*
- Report the range of the incremental costs/outcomes ratio and the discount rates. For example: incremental Cost/Life Saved and discount rate referring to: baseline and discount rate of costs; lowest value; highest value.
- Report, if any, the most important differences in cost-effectiveness of sub-populations.
- List the sensitive parameters, quoting any influential parameters discovered and figures.

---

[88] In any results, the abstractor should report the relevant discount rate(s). If the same discount rate was used, he/she should report it once.

[89] The abstractor should choose this option when a synthesis of costs and benefits was necessary to reach a conclusion, but the author did not provide it. The abstractor should distinguish this case from that in which a combination was not necessary, because the analysis showed that the intervention yielded positive incremental benefits and negative incremental costs with respect to the comparator. In this case the abstractor should write a sentence like the following: 'A synthesis was not undertaken by the authors since the intervention was the dominant strategy'. Moreover, it may happen that the synthesis was not explicitly reported by the authors, and only the break even points (i.e. points where options appear to be equally cost-effective) of different scenarios derived by sensitivity analysis were reported. This situation is also methodologically correct, although the abstractor could point out in the commentary section that the synthesis could have been reported in a more detailed way.

[90] The calculation of the incremental cost-effectiveness ratio is necessary any time one of the options is more expensive and more effective than the others. Additional costs should be compared by the authors to additional benefits in order to provide an appropriate measure for expressing the final results. The study can record any comments about a given cut-off/critical value. Abstractor should report the lack of the incremental cost-effectiveness ratio in the commentary section.

[91] Report as presented in the original study.

[92] See footnote 88.

[93] Ibid.

[94] Ibid.

- Summarise the author's comments about the sensitive parameters and their range of variation.
- Report the statistical testing results for the sampled data.

6. CONCLUSIONS AND CRITICAL COMMENT

6.1 Author's conclusions

Summarise the author's conclusions.

6.2 CRD Commentary

Provide comments on the quality of: [95]

•Design of the study/review estimating clinical effectiveness, e.g.:

- In the case of clinical evidence based on a single study, did the author provide a justification of choosing to use that particular study rather than others?
- If the clinical evidence was based on a review, did the author undertake a systematic search of the literature to ensure that the selection of studies included in the review is unbiased and comprehensive?[96]
- Was the study design appropriate for the problem considered?
- Was the sample representative for the questions posed?
- Was the trial methodology rigorous?
- Was the analysis based on intention to treat or treatment completers? (Analysis of only treatment completers may bias results.)
- Which health outcome valuation methods were used for variables that were difficult to measure?
- Discuss the internal validity (confounding, bias, unit of analysis error,[97] etc.) and the external validity (applicability to other settings in the UK) of the study.

•Economic analysis, e.g.:

- Was the economic study type appropriate for the problem considered?
- Was the study design, even though simple, sufficient to answer the question(s) posed?

---

[95]To fill in the commentary section, only the main ideas and concepts are required. The following questions/examples may represent a guideline. Copies of this critical commentary will be forwarded to the author of the study.

[96]A comprehensive literature search should include the "grey literature", i.e. both published and unpublished material, such as reports, government agency monographs, discussion papers, conference papers, theses, etc., for which the usual search strategies (e.g. Medline) are not applicable. The inclusion of the grey literature should minimise the risk of publication bias, that is the tendency to publish studies showing positive findings.

[97]In order to avoid the "unit of analysis error", the unit of allocation in an experimental study should be the same as the unit of analysis, i.e. the unit about which the conclusions are drawn.

- Was the prospective used to valuate costs/benefits too restrictive?
- Were the resources costed appropriate for the question posed?[98]
- Was the quantity/cost description adequate?
- Were the methods of estimating the quantities/costs relevant to the NHS?[99]
- Are all common quantities/costs included? (The omission of common cost components can be misleading.)
- Discuss the inclusion/exclusion of adverse/knock-on costs.
- Was the use of modelling techniques appropriate, (e.g. when observational or experimental data were not available or could not be collected)?
- Were there any errors in constructing the model (e.g. invalid path to end nodes; lack of links between variables?)
- Were opportunity-costs[100] issues seriously addressed?[101]

•Synthesis of the study. e.g.:
- Was the analysis directed to investigate a hypothesis/question (hypothesis testing study)[102] or was it a post-hoc analysis?
- Was the representation of the synthesis methodologically adequate?[103]
- Were there any miscalculations of the combinations of estimated benefits and costs?

---

[98]For example: a) Costs that should be excluded are those not relevant to the therapeutic pathway, such as sickness payment and unemployment insurance; b) Direct patient's costs should be included if the question posed is addressing a societal point of view; any double counting should have been avoided; etc.

[99]For example, when the estimation is based on the observation of one or a few providing units outside the NHS, it may be indicative of that unit only and not generalisable to any other providing units.

[100]Since the resources are limited, supporting an effective intervention implies that some other effective treatment (or other welfare programmes) cannot be implemented. The benefits forgone represent the opportunity-cost of the supported intervention.

[101]For example: a) Were opportunity-costs explicitly mentioned? b) Which opportunity-costs were considered? c) Were financial expenditures crudely identified with opportunity-costs? d) Prices are often taken as measures of the marginal opportunity-cost of resources purchased in markets. However prices in the NHS are generally determined by *total cost/quantity* (in the long run they are considered similar to the marginal cost). Did the author consider this issue in discussing opportunity-costs? With what implications for the study? e) Resources often have their most valued alternative use (opportunity-cost) inside the organisation: did such cases arise in the study and were the real opportunity-costs identified? With what implications? f) Opportunity-costs are frequently used where there is incomplete financial information to measure the full effects of the intervention (including costs or benefits associated with externalities): did such cases arise in the study? Were these costs estimated? With what implications?

[102]A hypothesis testing study investigates a hypothesis following interpretation of descriptive studies, or from direct clinical/experimental observation, and the data relevant to test the hypothesis is collected.

[103]Cost-effectiveness ratios, cost-utility ratios and cost-benefit ratios should be based on incremental results. However total costs and total outcomes of the intervention and of the comparator treatments are also useful in order to know the overall level of the expenditures.

- Were there any cost/benefit evaluation omissions from the discussion, or any other omissions? (Such omissions can be, for example, directed to bias the study results in favour of the intervention against the comparator.)
- Were all parameters/assumptions about which there is uncertainty subjected to sensitivity analysis?
- Was the author's justification about the sensitive parameters and their range of variation satisfactory?
- Discuss the side-effects of treatment considered or not considered in the economic analysis.

7. IMPLICATIONS OF THE STUDY

7.1 Implications of the study[104]

- Identify the main implications, when appropriate, for clinical practice, health policy or research.[105]
- State whether there are any equity implications of the study (e.g. any significant distributional implications).

7.2 Other publications of related interest

- Report obvious links with other economic studies in the database, containing information which may clarify, support or expand the results of the study.[106]
- Report possible cross-references to Reviews database/ Cochrane reviews to highlight related studies (e.g. on estimates of clinical effectiveness).

[104] This section has to be interpreted on the basis of local situations and the reader should always refer to the original article. Any feedback from the reader about this point is welcomed and should be forwarded to CRD.

[105] If the abstractor has a knowledge of the area, he/she can briefly indicate any clear implications in this field. However, if the abstractor is not sure, then it is best to indicate that he/she has not enough knowledge of the field. If the study is well conducted and a clear benefit is indicated, the abstractor could state that the study is good, and it implies that a particular intervention is more cost-effective than others. Alternatively, one may say that more research is necessary.

[106] Attention should be paid to differences in methodology (e.g. costing methods) and in settings (e.g. population sample).

BIBLIOGRAPHY

(The following readings constituted useful sources for the preparation of the Guidance for writing critical abstracts for the NHS Economic Evaluation Database).

Birch, S. and Donaldson, C. (1987). Applications of cost-benefit analysis to health care: departures from welfare economic theory. *Journal of Health Economics*, **6**, 211-225.

Birch, S. and Gafni, A. (1992). Cost effectiveness/utility analyses. Do current decision rules lead us to where we want to be? *Journal of Health Economics*, **11**, 279-296.

Birch, S. and Gafni, A. (1993). Changing the problem to fit the solution: Johannesson and Weinstein's (mis)application of economics to real world problems. *Journal of Health Economics*, **12**, 469-476.

Birch, S. and Gafni, A. (1994). Cost-effectiveness ratios: in a league of their own. *Health Policy*, **28**, 133-141.

Briggs, A., Sculpher, M., Buxton, M. (1994). Uncertainty in the economic evaluation of health care technologies: the role of sensitivity analysis. *Health Economics*, **3**, 95-104.

Canadian Coordinating Office for Health Technology Assessment (1994). *Guidelines for economic evaluation of pharmaceuticals: Canada*. Canadian Coordinating Office for Health Technology Assessment, Ottawa.

Chalmers, I. and Haynes, B. (1994). Reporting, updating, and correcting systematic reviews of the effects of health care. *British Medical Journal*, **309**(Oct.), 862-865.

Chalmers, T.C., Celano, P., Sacks, H.S., Smith, H. (1983). Bias in treatment assignment in controlled clinical trials. *The New England Journal of Medicine*, Dec., 1358-1361.

Department of Clinical Epidemiology and Biostatistics, McMaster University Health Sciences Centre (1984). How to read clinical journals: VII. To understand an economic evaluation (part A). *Canadian Medical Association Journal*, **130**(June), 1428-1433.

Department of Health (1994). *DH Register of cost-effectiveness studies*. Department of Health, Economics and Operational Research Division, London.

Drummond, M.F. (1980). *Principles of economic appraisal in health care*. Oxford University Press, Oxford.

Drummond, M. (1994). *Economic analysis alongside controlled trials: an introduction for clinical researchers*. Department of Health.

Drummond, M. and O'Brien, B. (1993). Clinical importance, statistical significance and the assessment of economic and quality-of-life outcomes. *Health Economics*, **2**, 205-212.

Drummond, M., Brandt, A., Luce, B., Rovira, J. (1993). Standardizing methodologies for economic evaluation in health care. *International Journal of Technology Assessment in Health care*, **9**(1), 26-36.

Drummond, M.F. and Davies, L. (1991). Economic analysis alongside clinical trials. *International Journal of Technology Assessment in Health Care*, **7**(4), 561-573.

Drummond, M.F., Stoddart, G.L., Torrance, G.W.(1988). *Methods for the economic evaluation of health care programmes.* Oxford University Press, Oxford.

Drummond, M., Torrance, G., Mason, J. (1993). Cost-effectiveness league tables: more harm than good? *Soc. Sci. Med*., **37**(1), 33-40.

Egger M., Davey Smith, G., Song, F., Sheldon, T.A. (1993). Making sense of meta-analysis. *Pharmacoepidemiology and Drug Safety*, **2**, 65-72.

Elixhauser, A., Luce, B.R., Taylor, W.R., Reblando, J. (1993). Health care CBA/CEA: an update on the growth and composition of the literature. *Medical Care*, **31**(7), JS1-JS11.

Eysenk, H.J. (1994). Meta-analysis and its problems. *British Medical Journal*, **309**(Sept.), 789-792.

Gafni, A. and Birch, S. (1993). Searching for a common currency: critical appraisal of the scientific basis underlying European harmonization of the measurement of Health Related Quality of Life (EuroQol). *Health Policy*, **23**, 219-228.

Glick, H., Kinosian, B., Schulman, K. (1994). Decision analytic modelling: some uses in the evaluation of new pharmaceuticals. *Drug Information Journal*, **28**, 691-707.

Goodman, C. (1993). *Literature searching and evidence interpretation for assessing health care practices.* SBU - The Swedish Council on Technology Assessment in Health Care, Stockholm.

Guyatt, G.H., Sackett, D.L., Cook, D.J. (1994). Users' guide to the medical literature: how to use an article about therapy and prevention. A. Are the results of the study valid? *JAMA*, **270**(21), 2598-2601.

Guyatt, G.H., Sackett, D.L., Cook, D.J. (1994). Users' guide to the medical literature: how to use an article about therapy and prevention. What were the results and will they help me in caring for my patients? *JAMA*, **271**(1), 59-63.

Gudex, C., Kind, P., van Dalen, H., Durand, M., Morris, J., Williams, A. (1993*). Comparing scaling methods for health state valuations - Rosser revisited*. York: Centre for Health Economics (Discussion Paper 107).

Haines, A. and Jones, R. (1994). Implementing findings of research. *British Medical Journal*, 308(June), 1488-1492.

Kaplan, R.M., Bush, J.W. Berry, C.C. (1976). Health status: types of validity and the index of well-being. *Health Services Research*, Winter, 478-507.

L'Abbe', K.A., Detsky, A.S., O'Rourke, K. (1987). Meta-analysis in clinical research. *Annals of Internal Medicine*, **107**(August), 224-233.

Laupacis, A., Feeny, D., Detsky, A.S., Tugwell, P.X. (1992). How attractive does a new technology have to be to warrant adoption and utilisation? Tentative guidelines for using clinical and economic evaluations. *Can. Med. Assoc. Journal*, **146**(4), 473-481.

Mason, J. and Drummond, M. (1995). *The DH register of cost-effectiveness studies: a review of study content and quality*. York: Centre for Health Economics (Discussion Paper 128)

Mason, J., Drummond, M., Torrance, J. (1996). Some guidelines on the use of cost effectiveness league tables. *British Medical Journal*, **306**(Feb.), 570-572.

McGuire, A., Henderson, J., Mooney, G. (1988). *The economics of health care.* Routledge and Kegan Paul, London.

Mooney, G.H. (1984). *Economics, medicine and health care.* Wheatsheaf Books, Brighton.

Mulrow, C.D. (1994). Rational for systematic reviews. *British Medical Journal*, **309**(Sept.), 597-599.

O'Brien, B.J. and Drummond, M.F. (1994). Statistical versus quantitative significance in the socioeconomic evaluation of medicines. *PharmacoEconomics*, **5**(5), 389-398.

O'Brien, B., Drummond, M.F., Labelle, R.J., Willan, A. (1994). In search of power and significance: issues in the design and analysis of stochastic cost-effectiveness studies in health care. *Medical Care*, **32**(2), 150-163.

Office of Technology Assessment (1978). *Assessing the efficacy and safety of medical technologies*. Publication No. OTA-H-75. Government Printing Office, Washington.

Oxman, A.D. (1994). Checklist for review articles. *British Medical Journal*, **309**(Sept.), 648-651.

Oxman, A.D. and Guyatt, G.H. (1988). Guidelines for reading literature reviews. *CMAJ*, **138**(April), 697-703.

Oxman, A.D. and Guyatt, G.H. (1991). Validation of an index of the quality of review articles.
J. Clin. Epidemiology, **44**(11), 1271-1278.

Patrick, D.L. and Erickson, P. (1993). *Health status and health policy: allocating resources to health care.* Oxford University Press, New York.

Petitti, D.B. (1994). *Meta-analysis, decision analysis and cost-effectiveness analysis: methods and quantitative synthesis in medicine.* Oxford University Press, New York.
Rutten, F. and Drummond, M. (1994). *Making decisions about health technologies: a cost-effectiveness perspective.* York: Centre for Health Economics (Occasional Paper Series).

Sackett D.L., Haynes R.B., Guyatt. G.H., Tugwell, P. (1991). *Clinical epidemiology.* Little, Brown and Company, Boston.

Sackett, D.L. and Torrance, G.W. (1978). The utility of different health states as perceived by the general public. *J. Chronic Dis*., **31**(11), 697-704.

Sheldon, T.A. (1992). Discounting in health care decision-making: time for a change? *Journal of Public Health Medicine*, **14**(3), 250-256.

Sheldon, T.A. (1996). Problems of using modelling in the economic evaluation of health care. *Health Economics*, **5**(1), 1-11.

Sheldon, T.A., Song, F., Davey Smith, G. (1993). Critical appraisal of the medical literature: how to assess whether health-care interventions do more good than harm. In *Purchasing and providing cost-effective health care* (eds. M.F. Drummond and A. Maynard). Churchill Livingstone, Edinburgh.

Sonnenberg, F.A., Roberts, M.S., Tsevat, J., Wong, J.B., Barry, M., Kent, D.L. (1994). Toward a peer review process for medical decision analysis models. *Medical Care*, **32**(7), JS52-JS64.

Thompson, S.G. and Pocock, S.J. (1991). Can meta-analyses be trusted? *The Lancet*, **338**(Nov.), 1127-1130.

Torrance, G.W., Boyle, M.H., Horwood, S.P. (1982). Application of multi-attribute utility theory to measure social preferences for health states. *Operations Research*, **30**(6), 1043-1069.

Udvarhelyi, I.S., Colditz, G.A., Rai, A., Epstein, A.M. (1992). Cost-effectiveness and cost-benefit analyses in the medical literature: Are the methods being used correctly? *Annals of Internal Medicine*, **116**(3), 234-244.

Van Hout, B.A., Al, M.J., Gordon, G.S., Rutten, F.H. (1994). Costs, effects and C/E-ratio's alongside a clinical trial. *Health Economics*, **3**(5), 309-319.