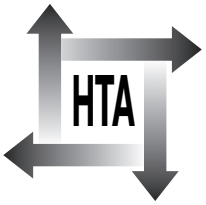
Health Technology Assessment 2008; Vol. 12: No. 23

A prospective randomised comparison of minor surgery in primary and secondary care. The MiSTIC trial

S George, P Pockney, J Primrose, H Smith, P Little, H Kinley, R Kneebone, A Lowy, B Leppard, N Jayatilleke and C McCabe

May 2008

Health Technology Assessment
NHS R&D HTA Programme
www.hta.ac.uk



How to obtain copies of this and other HTA Programme reports.
An electronic version of this publication, in Adobe Acrobat format, is available for downloading free of charge for personal use from the HTA website (http://www.hta.ac.uk). A fully searchable CD-ROM is also available (see below).

Printed copies of HTA monographs cost £20 each (post and packing free in the UK) to both public **and** private sector purchasers from our Despatch Agents.

Non-UK purchasers will have to pay a small fee for post and packing. For European countries the cost is £2 per monograph and for the rest of the world £3 per monograph.

You can order HTA monographs from our Despatch Agents:

– fax (with **credit card** or **official purchase order**)
– post (with **credit card** or **official purchase order** or **cheque**)
– phone during office hours (**credit card** only).

Additionally the HTA website allows you **either** to pay securely by credit card **or** to print out your order and then post or fax it.

Contact details are as follows:

HTA Despatch
c/o Direct Mail Works Ltd
4 Oakwood Business Centre
Downley, HAVANT PO9 2NP, UK

Email: orders@hta.ac.uk
Tel: 02392 492 000
Fax: 02392 478 555
Fax from outside the UK: +44 2392 478 555

NHS libraries can subscribe free of charge. Public libraries can subscribe at a very reduced cost of £100 for each volume (normally comprising 30–40 titles). The commercial subscription rate is £300 per volume. Please see our website for details. Subscriptions can only be purchased for the current or forthcoming volume.

Payment methods

Paying by cheque
If you pay by cheque, the cheque must be in **pounds sterling**, made payable to *Direct Mail Works Ltd* and drawn on a bank with a UK address.

Paying by credit card
The following cards are accepted by phone, fax, post or via the website ordering pages: Delta, Eurocard, Mastercard, Solo, Switch and Visa. We advise against sending credit card details in a plain email.

Paying by official purchase order
You can post or fax these, but they must be from public bodies (i.e. NHS or universities) within the UK. We cannot at present accept purchase orders from commercial companies or from outside the UK.

How do I get a copy of *HTA on CD*?

Please use the form on the HTA website (www.hta.ac.uk/htacd.htm). Or contact Direct Mail Works (see contact details above) by email, post, fax or phone. *HTA on CD* is currently free of charge worldwide.

The website also provides information about the HTA Programme and lists the membership of the various committees.

A prospective randomised comparison of minor surgery in primary and secondary care. The MiSTIC trial

S George,[1*] P Pockney,[2] J Primrose,[2] H Smith,[3] P Little,[4] H Kinley,[2] R Kneebone,[5] A Lowy,[6] B Leppard,[7] N Jayatilleke[1] and C McCabe[8]

[1] Public Health Sciences and Medical Statistics, University of Southampton School of Medicine, UK
[2] University Surgery, University of Southampton School of Medicine, UK
[3] Brighton and Sussex Medical School, Brighton, UK
[4] Primary Medical Care, University of Southampton School of Medicine, Southampton, UK
[5] Department of Biosurgery and Technology, Imperial College London, UK
[6] Swiss Institute for Applied Cancer Research, Bern, Switzerland
[7] Southampton University Hospitals NHS Trust, UK
[8] Institute of Health Sciences and Public Health Research, University of Leeds, UK

* Corresponding author

Declared competing interests of authors: none

Published May 2008

This report should be referenced as follows:

George S, Pockney P, Primrose J, Smith H, Little P, Kinley H, *et al*. A prospective randomised comparison of minor surgery in primary and secondary care. The MiSTIC trial. *Health Technol Assess* 2008;**12**(23).

Health Technology Assessment is indexed and abstracted in *Index Medicus*/MEDLINE, *Excerpta Medica*/EMBASE and *Science Citation Index Expanded (SciSearch®)* and *Current Contents®*/Clinical Medicine.

NIHR Health Technology Assessment Programme

The Health Technology Assessment (HTA) Programme, part of the National Institute for Health Research (NIHR), was set up in 1993. It produces high-quality research information on the effectiveness, costs and broader impact of health technologies for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined as all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care.

The research findings from the HTA Programme directly influence decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee (NSC). HTA findings also help to improve the quality of clinical practice in the NHS indirectly in that they form a key component of the 'National Knowledge Service'.

The HTA Programme is needs-led in that it fills gaps in the evidence needed by the NHS. There are three routes to the start of projects.

First is the commissioned route. Suggestions for research are actively sought from people working in the NHS, the public and consumer groups and professional bodies such as royal colleges and NHS trusts. These suggestions are carefully prioritised by panels of independent experts (including NHS service users). The HTA Programme then commissions the research by competitive tender.

Secondly, the HTA Programme provides grants for clinical trials for researchers who identify research questions. These are assessed for importance to patients and the NHS, and scientific rigour.

Thirdly, through its Technology Assessment Report (TAR) call-off contract, the HTA Programme commissions bespoke reports, principally for NICE, but also for other policy-makers. TARs bring together evidence on the value of specific technologies.

Some HTA research projects, including TARs, may take only months, others need several years. They can cost from as little as £40,000 to over £1 million, and may involve synthesising existing evidence, undertaking a trial, or other research collecting new data to answer a research problem.

The final reports from HTA projects are peer-reviewed by a number of independent expert referees before publication in the widely read journal series *Health Technology Assessment*.

Criteria for inclusion in the HTA journal series

Reports are published in the HTA journal series if (1) they have resulted from work for the HTA Programme, and (2) they are of a sufficiently high scientific quality as assessed by the referees and editors.

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

The research reported in this issue of the journal was commissioned by the HTA Programme as project number 95/25/03. The contractual start date was in May 1999. The draft report began editorial review in April 2004 and was accepted for publication in April 2007. As the funder, by devising a commissioning brief, the HTA Programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

The views expressed in this publication are those of the authors and not necessarily those of the HTA Programme or the Department of Health.

ISSN 1366-5278

Published by Gray Publishing, Tunbridge Wells, Kent, on behalf of NCCHTA.
Printed on acid-free paper in the UK by St Edmundsbury Press Ltd, Bury St Edmunds, Suffolk.

Abstract

A prospective randomised comparison of minor surgery in primary and secondary care. The MiSTIC trial

S George,[1*] P Pockney,[2] J Primrose,[2] H Smith,[3] P Little,[4] H Kinley,[2] R Kneebone,[5] A Lowy,[6] B Leppard,[7] N Jayatilleke[1] and C McCabe[8]

[1] Public Health Sciences and Medical Statistics, University of Southampton School of Medicine, UK
[2] University Surgery, University of Southampton School of Medicine, UK
[3] Brighton and Sussex Medical School, Brighton, UK
[4] Primary Medical Care, University of Southampton School of Medicine, Southampton, UK
[5] Department of Biosurgery and Technology, Imperial College London, UK
[6] Swiss Institute for Applied Cancer Research, Bern, Switzerland
[7] Southampton University Hospitals NHS Trust, UK
[8] Institute of Health Sciences and Public Health Research, University of Leeds, UK
* Corresponding author

Objective: To determine whether there is equivalence in the competence of GPs and hospital doctors to perform a range of elective minor surgical procedures, in terms of the safety, quality and cost of care.
Design: A prospective randomised controlled equivalence trial was undertaken in consenting patients presenting at general practices and needing minor surgery.
Setting: The study was conducted in the south of England.
Participants: Consenting patients presenting at general practices who needed minor surgery in specified categories for whom the recruiting doctor felt able to offer treatment or to be able to refer to a colleague in primary care.
Interventions: On presentation to their GP, patients were randomised to either treatment within primary care or treatment at their local hospital. Evaluation was by assessment of clinical quality and safety of outcome, supplemented by examination of patient satisfaction and cost-effectiveness.
Main outcome measures: Two independent observers assessed surgical quality by blinded assessment of wound appearance, between 6 and 8 weeks postsurgery, from photographs of wounds. Other measures included satisfaction with care, safety of surgery in terms of recognition of and appropriate treatment of skin malignancies, and resource use and implications.
Results: The 568 patients recruited (284 primary care, 284 hospital) were randomised by 82 GPs. In total, 637 skin procedures plus 17 ingrowing toenail procedures were performed (313 primary care, 341 hospital) by 65 GPs and 60 hospital doctors. Surgical quality was assessed for 273 (87%) primary care and 316 (93%) hospital lesions. Mean visual analogue scale score in hospital was significantly higher than that in primary care [mean difference = 5.46 on 100-point scale; 95% confidence interval (CI) 0.925 to 9.99], but the clinical importance of the difference was uncertain. Hospital doctors were better at achieving complete excision of malignancies, with a difference that approached statistical significance [7/16 GP (44%) versus 15/20 hospital (75%), $\chi^2 = 3.65$, $p = 0.056$]. The proportion of patients with post-operative complications was similar in both groups. The mean cost for hospital-based minor surgery was £1222.24 and for primary care £449.74. Using postoperative complications as an outcome, both effectiveness and costs of the alternative interventions are uncertain. Using completeness of excision of malignancy as an outcome, hospital minor surgery becomes more cost-effective. The 705 skin procedures undertaken in this trial generated 491 lesions with a traceable histology report: 36 lesions (7%) from 33 individuals were malignant or premalignant. Chance-corrected agreement (kappa) between GP diagnosis of malignancy and histology was 0.45 (95% CI 0.36 to 0.54) for lesions and 0.41 (95% CI 0.32 to 0.51) for individuals affected by malignancy. Sensitivity of GPs for detection of malignant lesions was 66.7% (95% CI 50.3 to 79.8) for lesions and 63.6% (95% CI 46.7 to 77.8) for individuals affected by malignancy.

Conclusions: The quality of minor surgery carried out in general practice is not as high as that carried out in hospital, using surgical quality as the primary outcome, although the difference is not large. Patients are more satisfied if their procedure is performed in primary care, largely because of convenience. However, there are clear deficiencies in GPs' ability to recognise malignant lesions, and there may be differences in completeness of excision when compared with hospital doctors. The safety of patients is of paramount importance and this study does not demonstrate that minor surgery carried out in primary care is safe as it is currently practised. There are several alternative models of minor surgery provision worthy of consideration, including ones based in primary care that require all excised tissue to be sent for histological examination, or that require further training of GPs to undertake the necessary work. The results of this study suggest that a hospital-based service is more cost-effective. It must be concluded that it is unsafe to leave minor surgery in the hands of doctors who have never been trained to do it. Further work is required to determine GPs' management of a range of skin conditions (including potentially life-threatening malignancies), rather than just their recognition of them. Further economic modelling work is required to look at the potential costs of training sufficient numbers of GPs and GPs with special interests to meet the demand for minor surgery safely in primary care, and of the alternative of transferring minor surgery large-scale to the hospital sector. Different models of provision need thorough testing before widespread introduction.

Contents

List of abbreviations vii

Executive summary ix

1 Introduction 1
Background 1
Historical context 1
Unresolved issues 2

2 Objective and aims of the study 3
Objective 3
Aims 3

3 Methods 5
Design 5
Protocol revision 7
Assessment of quality of surgery 7
Patient satisfaction 8
Pathological diagnosis 8
Analysis 8
Training of GPs and quality of surgery 9
Participants 9
Financial issues 10
Patient route through the trial 11
Randomisation 11
Blinding 11
Patient withdrawal protocol 11
Record-keeping 12

4 Results: quality of surgery and patient satisfaction 13
Potential recruitment population 13
Types of lesion presenting and procedure undertaken 13
VAS scores of quality of surgery 13
Categorical quality scores 13
Patient satisfaction 15
Patient access to care 15
Later complications of surgery 15
Pathology reports 15
Completeness of excision of malignant lesions 15
Training of GPs and results in terms of quality of surgery 16

5 Economic analysis of trial 17
Cost of minor surgery 17
Incremental cost-effectiveness ratio 17
Sensitivity analysis 17
Discounting 18
Results 18

6 Comparison of GP diagnosis and histopathology of lesions, and performance regarding recognition of malignant lesions 21
Data 21
Analysis 21
Results 22
Agreement between GP diagnosis and histology 23
Test characteristics of GPs in detecting skin malignancy 23
Recognition of a malignancy and completeness of excision 24

7 Discussion 25
Conclusions 26
Recommended research 26

Acknowledgements 27

References 29

Appendix 1 Wound assessment tool 31

Appendix 2 Patient Satisfaction Questionnaire 33

Appendix 3 CONSORT statement for MiSTIC trial 37

Health Technology Assessment reports published to date 39

Health Technology Assessment Programme 55

List of abbreviations

CEAC	cost-effectiveness acceptability curve
CI	confidence interval
CONSORT	Consolidated Standards of Reporting Trials
df	degrees of freedom
ICER	incremental cost-effectiveness ratio
IQR	interquartile range
ITT	intention-to-treat
MiSTIC	Minor Surgery Trial In the Community
NA	not applicable
OR	odds ratio
SD	standard deviation
SUHT	Southampton University Hospitals Trust
VAS	visual analogue scale
WReN	Wessex Research Network

All abbreviations that have been used in this report are listed here unless the abbreviation is well known (e.g. NHS), or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices in which case the abbreviation is defined in the figure legend or at the end of the table.

Executive summary

Objectives

The objective of this study was to determine whether there is equivalence in the competence of GPs and hospital doctors to perform a range of elective minor surgical procedures, in terms of the safety, quality and cost of care.

The aims were:

- to conduct a randomised controlled equivalence trial of minor surgery in two settings
- to collect data on quality of surgery, patient satisfaction, patient safety and cost of procedure in two settings
- to review data from this trial and from other sources in order to consider future direction and future research in this area.

Methods

Design

This prospective randomised controlled equivalence trial was undertaken in consenting patients presenting at general practices and needing minor surgery.

Setting

The study was conducted in the south of England. At the time of this trial, minor surgery provision was provided mainly via a fee for service contract with general medical practitioners, with some serious pathology treated in hospital.

Participants

Participants were consenting patients presenting at general practices. They all needed minor surgery in specified categories and the recruiting doctor felt able to offer treatment or to be able to refer to a colleague in primary care.

Interventions

Patients were randomised, on presentation to their GP, to either treatment within primary care or treatment at their local hospital. Evaluation was by assessment of clinical quality and safety of outcome, supplemented by examination of patient satisfaction and cost-effectiveness.

Main outcome measures

The primary measure was surgical quality assessed by blinded assessment of wound appearance, between 6 and 8 weeks postsurgery, by two independent observers, using photographs of wounds. Secondary measures included satisfaction with care, which was obtained by means of a patient questionnaire; safety of surgery in terms of recognition of and appropriate treatment of skin malignancies, obtained by an examination of histological material supplied and cross-referencing with referral forms from GPs; and resource use and implications.

Results

In total, 568 patients were recruited (284 primary care, 284 hospital) and randomised by 82 GPs. Altogether, 637 skin procedures plus 17 ingrowing toenail procedures were performed (313 primary care, 341 hospital) by 65 GPs and 60 hospital doctors. Surgical quality was assessed for 273 (87%) primary care and 316 (93%) hospital lesions. Mean visual analogue scale score in hospital was significantly higher than that in primary care [mean difference = 5.46 on 100-point scale; 95% confidence interval (CI) 0.925 to 9.99], but the clinical importance of the difference was uncertain. Patients tended to be more satisfied with procedures in primary care and to report less inconvenience from their procedure. Hospital doctors were better at achieving complete excision of malignancies, with a difference that approached statistical significance [7/16 GP (44%) versus 15/20 hospital (75%), $\chi^2 = 3.65$, $p = 0.056$]. The proportion of patients with post-operative complications was similar in both groups. The mean cost for hospital-based minor surgery was £1222.24 and for primary care £449.74. Using postoperative complications as an outcome, both effectiveness and costs of the alternative interventions are uncertain. Using completeness of excision of malignancy as an outcome, hospital minor surgery becomes more cost-effective.

The 705 skin procedures undertaken in this trial generated 491 lesions with a traceable histology report: 36 lesions (7%) from 33 individuals were

malignant or premalignant. Chance-corrected agreement (kappa) between GP diagnosis of malignancy and histology was 0.45 (95% CI 0.36 to 0.54) for lesions and 0.41 (95% CI 0.32 to 0.51) for individuals affected by malignancy. Sensitivity of GPs for detection of malignant lesions was 66.7% (95% CI 50.3 to 79.8) for lesions and 63.6% (95% CI 46.7 to 77.8) for individuals affected by malignancy.

Conclusions

The quality of minor surgery carried out in general practice is not as high as that carried out in hospital, using surgical quality as the primary outcome, although the difference is not large. Patients are more satisfied if their procedure is performed in primary care, however, largely because of advantages in terms of convenience. However, there are clear deficiencies in the ability of GPs to recognise malignant lesions, and there may be differences in completeness of excision when compared with hospital doctors.

The safety of patients is of paramount importance and this study does not demonstrate that minor surgery carried out in primary care is safe as it is currently practised. There are several alternative models of minor surgery provision worthy of consideration, including ones based in primary care that require all excised tissue to be sent for histological examination, or that require further training of GPs to undertake the necessary work. The results of this study suggest that a hospital-based service is more cost-effective, but at the moment there is not the capacity in hospitals to take on the workload of minor surgery, and it would likely be unpopular with patients if it were to happen. It must be concluded that it is unsafe to leave minor surgery in the hands of doctors who have never been trained to do it. If the capacity to undertake the work is present in primary care, then the increased costs associated with training doctors to do it must be borne.

Suggestions for further research

Further work is required to determine GPs' management of a range of skin conditions (including potentially life-threatening malignancies), rather than just their recognition of them. Further economic modelling work is required to look at the potential costs of training sufficient numbers of GPs and GPs with special interests to meet the demand for minor surgery safely in primary care, and of the alternative of transferring minor surgery large-scale to the hospital sector. Different models of provision need thorough testing before widespread introduction.

Chapter 1
Introduction

Background

Minor surgery has formed part of general practice (family practice) throughout its history. Indeed, in the UK, GPs' clinics and facilities are normally referred to as their 'surgeries'. However, the range of procedures performed, the facilities and resources available, the training structures and requirements of the practising doctor, and the contractual arrangements that pertain to the doctor vary widely between and within different healthcare systems around the developed world. This study concentrates on the situation in the UK, except where the literature suggests issues that may be as relevant in their country of origin as here.

Historical context

Minor surgery offered by GPs within the NHS declined during the period from 1948, the date of inception of the NHS, to the mid-1980s.[1] This decline was ascribed to two main causes: first, the limiting contractual arrangements based on a capitation system that existed between independent GPs and commissioning health authorities; and, second, the perceived wish of patients to be treated by specialists. There was no financial incentive for GPs to undertake minor surgery, most patients were referred to secondary care (hospitals) for procedures that were provided there free of charge to the patient, and consequently the range and number of surgical procedures performed in general practice declined sharply. A few enthusiasts maintained the tradition, funded by ad hoc arrangements with their local health authorities.[2–4]

The 1990 contract for GPs in England and Wales specified an item-of-service payment for minor surgical procedures, which replaced an element of per capita funding and contributed to target income.[5] The money that was directed at this initiative did not increase the total that GPs could earn, therefore, but it introduced a new incentive to perform minor surgery that reflected the prevailing political agenda of the times. The stated aim of the reforms was, in part, to try to transfer some procedures that were being performed in secondary care to primary care. This reflected the needs of the government to reduce the political pressure that long waiting lists for hospital services were generating. It was also a reaction to several publications advocating primary care surgery as being more cost-effective, equal in quality to hospital care, and better received by patients than hospital care for some procedures. The widely held belief was that most GPs had acquired sufficient skills in minor surgical techniques during their hospital-based prequalification and postqualification training to allow them to perform a variety of procedures safely, conveniently and cost-effectively for patients.[2,6,7]

The contract specified that in order to be able to offer minor surgery sessions a GP had to be included on the health authority's minor surgery list. A GP was able to treat his or her own patients or those of partners or group members. The types of surgical procedure for which claims could be made under the new contract are listed in *Table 1*.

This part of the 1990 contract changes was cautiously welcomed by GPs and generated debate about equipment, training and quality control.[8–13]

Within 5 years of the contract being launched, around 90% of GP principals in England and Wales were accredited by their local health authority as providers of minor surgery, and were claiming for the maximum number (60) of remunerable procedures per annum. This activity forms the vast bulk of GP-performed minor surgery in routine practice, and has therefore attracted the most attention from investigators over the years since.[14–16]

Of note in *Table 1* is that two categories of procedure for which claims could be made include procedures that do not utilise traditional surgical techniques: injections (largely of joints and around joints) and cautery (or cryosurgery). As discussed later in this report, this had implications for both the conduct of the trial and the development of GP minor surgery over the course of the 1990s.

TABLE 1 *Minor surgery procedures defined in the 1990 contract*

Category	Includes
Injections	Intra-articular Periarticular Varicose veins Haemorrhoids
Aspirations	Joints Cysts Bursae Hydroceles
Incisions	Abcesses Cysts Thrombosed piles
Excisions	Sebaceous cysts Lipomas Skin lesions for histology Intradermal naevi, papillomata Dermatofibromata and similar conditions Warts Removal of toenails
Curette, cautery and cryocautery	Warts and verrucae Other skin lesions
Other	Ligation of varicose veins Removal of foreign bodies Nasal cautery

Unresolved issues

Since the introduction of the 1990 contract, there has been a significant increase in the volume of minor surgery performed in primary care, but little to suggest that care has been transferred from secondary care to the GP's premises.[15] There has also been at times fierce debate about the quality and appropriateness of management decisions and clinical practices in general practice, focusing around two issues. First is the accuracy of clinical diagnosis and consequent need for histological confirmation of diagnosis. Associated with this is the second issue, the technical quality of surgery performed, discussed most often in terms of incomplete excision of malignant or premalignant conditions.[14,17–28] These debates are still unresolved, owing to the absence of firm evidence to support either view. What evidence there is comprises descriptions of personal case series from general practice, and audits of completely or incompletely excised lesions reported by pathologists, with or without accurate diagnoses being recorded on the pathologist's request form.

Leese and colleagues examined the effect of the minor surgery contract in 1995.[29] In their conclusion they state, 'There are many issues which are … still of concern and of these, lack of appropriate skills and expertise are foremost … In effect, the issues of quality and cost effectiveness have not been sufficiently addressed.'

This study attempts to address these issues.

Chapter 2

Objective and aims of the study

Objective

The objective of this study was to determine whether there is equivalence in the competence of GPs and hospital doctors to perform a range of elective minor surgical procedures, in terms of the safety, quality and cost of care.

Aims

The aims were:

- To conduct a randomised controlled equivalence trial of minor surgery in two settings.
- To collect data on quality of surgery, patient satisfaction, patient safety and cost of procedure in two settings.
- To consider data from this trial and from other sources, to consider the implications for policy and to make recommendations for future research in this area.

Chapter 3
Methods

Design

Project structure

This study comprised a randomised, controlled equivalence trial comparing the quality of minor surgery performed by GPs and hospital doctors (surgeons and dermatologists). The primary outcome measure was clinical quality and safety of minor surgery, with secondary outcome measures of patient satisfaction and cost-effectiveness. This trial was designed to test the hypothesis that there is equivalence in the competence of GPs and surgeons to perform a range of elective minor surgical procedures. An equivalence trial has the primary objective of showing that the response to two or more treatments differs by an amount that is clinically unimportant. This is usually demonstrated by showing that the true treatment difference is likely to lie between a lower and an upper equivalence limit of clinically acceptable difference.[30,31] An equivalence design was decided upon because of the situation pertaining when this trial was designed, because of a lack of observational evidence that would have allowed either an expected difference in performance in one set of practitioners over the other, or the direction of that difference, to be specified.

Figure 1 shows a range of possible results for an equivalence trial, with confidence intervals around each result. It should be noted that it is quite possible to have results where the two treatments being compared are, statistically, significantly different from each other (all results except for the central result), but are either still equivalent in clinical importance (the two results to either side of the central result) or are uncertain in importance [the two results overlapping the equivalence limits (marked –δ and +δ)]. Only the two outermost results in *Figure 1* are both significant and clinically important. This makes the interpretation of equivalence trials different from that of straightforward treatment trials, but in some ways more honest: many treatment difference trials are reported as showing 'significant differences' without comment being made on the clinical importance of results.

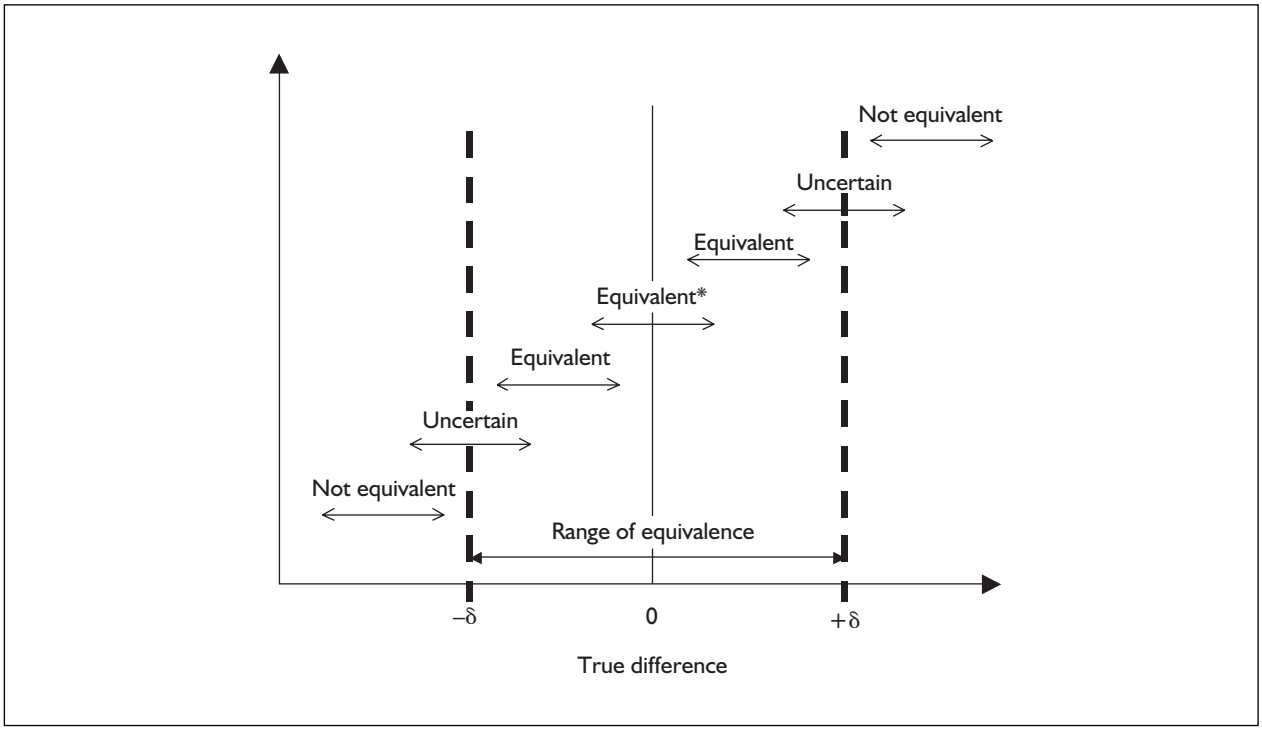


FIGURE 1 *Equivalence trial: possible results*

Setting

The trial was performed in South Hampshire, the geographical area lying between the New Forest and Portsmouth and surrounding Southampton.

Participants and inclusion criteria

All patients with one of a range of conditions amenable to minor surgery, who presented to one of the GPs participating in the trial and who were considered suitable for treatment by an individual GP or one of their partners, were invited to participate in the trial. The trial recruited patients over 2 years (2000–2002), from more than 40 practices throughout two health authority areas.

As discussed in Chapter 1, there are six categories of treatment attracting payment. Of these, two differ markedly from the others. The first is cautery, activity within which is largely composed of treatment for cutaneous warts, and for which a recent systematic review confirmed little evidence of benefit.[32] The evidence used in this review, albeit not yet synthesised, was available in 1999/2000, when the study design was being finalised. In an equivalence trial it is possible for two treatments to be judged as equivalent in terms of effectiveness, and yet for both to be equally ineffective. This clearly compromises the interpretation of the trial result. On this basis it was decided to exclude this category of treatment from inclusion.

The second treatment category differing markedly from the others is injections, which is mainly concerned with the treatment of painful joints. Including joint injections in this trial was considered, but it was concluded that outcome measures for this category would be different from those for the other categories of treatment included and, moreover, would be specific to each joint treated. A preliminary search of the literature showed that for many joints these measures did not exist in validated form, if at all. Inclusion of joint injections would have rendered both design and interpretation of the trial very complex, therefore, and it was agreed with the HTA Programme that this category of treatment should not form part of the trial. All other categories of treatment, however, could be judged in terms of a common set of outcome measures. Included within the trial, therefore, are surgical excisions, incisions, ablations and aspirations of skin and subcutaneous lesions, injection of varicose veins, and banding of haemorrhoids.

Interventions

In formal terms the interventions were structurally rather than clinically different, and comprised elective minor surgery for the conditions described above, delivered in either a primary care or a secondary care setting. In the primary care setting the intervention could be delivered either by the patient's own GP or by referral to a colleague within primary care. In secondary care the interventions were delivered by either surgeons or dermatologists at a variety of grades. Both interventions mimicked the situation pertaining in real life as much as possible, except for the fact that specially organised clinics were set up in the hospital arm (see below for explanation).

Sample size and outcome measures

Quality of treatment was initially defined as the absence of complications resulting from the surgery. The design of an equivalence trial and its sample size depend heavily on the expectations of the outcomes that will be achieved. There was very little in the literature regarding the complication rates that could reasonably be expected for minor operations conducted in general practice. The best available was from O'Cathain and colleagues, who conducted a non-randomised comparison of minor operations conducted in GP practices and hospitals in Rotherham in 1989.[33] They found no statistical difference in indicators of complications such as wound infection rates and other complications between the GP and hospital arms of the study. The overall rate of wound infections and other complications was 11.4% in the hospital group. This was used as the expected rate of complications for the initial sample size calculations in the present study, with a 50% each way (±5.7%) range of equivalence.

Using the formula proposed by Makuch and Simon, and specifying 5% significance and 90% power for sample sizes, a sample size of 653 patients in each arm was obtained.[30] This was considered to be a large, but achievable, recruitment target for this study. The number of GPs taking part in the study was expected to be large, as the project group had ready access to the local primary care research network of GPs [Wessex Research Network (WReN): 190 of these GPs had already expressed an interest in taking part in a study of this kind]. As each GP was believed to have up to 60 eligible patients per annum who could potentially be randomised into the trial, recruiting slightly over 1300 patients did not appear overambitious.

Secondary outcome measures were defined initially as quality of surgery, patient satisfaction and cost-effectiveness.

Protocol revision

Upon starting recruitment it quickly became obvious that the overall complication rate was not as high as that experienced by O'Cathain and colleagues in their study.[33] Details of the complications suffered by patients were collected in the questionnaire developed for this study to assess the patient experience with the treatment process. The initial estimate, based on the first 50 questionnaires received from patients, was a complication rate of less than 5%, although clearly this was an estimate with wide confidence intervals. Using the same 50% each-way equivalence limits, however, this would have inflated the required sample size to 1596 in each arm, or 3192 patients in total. Whereas the original estimate of 1306 patients needing to be randomised had seemed achievable, more than doubling that estimate did not, and the researchers decided to investigate powering the trial using other outcome measures.

Since the trial hypothesis was that there is equivalence in the competence of GPs and surgeons to perform a range of elective minor surgical procedures, the choice of outcome measure to replace complications of treatment had to remain within the sphere of operator competence. This ruled out patient satisfaction and cost, leaving wound scoring scales as the next best alternative.

Two tools are found in emergency medicine literature from the USA. Quinn and Wells describe the use and reliability of both a simple visual analogue score (VAS) and a categorical scale for the assessment of traumatic wounds, showing that both produce good interobserver and intraobserver reliability when assessing wounds using photographs.[34] Their categorical scale (*Table 2*) has been shown to produce results that show strong correlation with patients' views of their wounds.[35] Although these scales and measures were developed for assessing repairs to traumatic lacerations, they have also been validated for use in elective wounds[36] and it was decided to use them henceforward as primary outcome measures; they were in any case already in use as secondary outcome measures. This change in protocol was discussed with and approved by the commissioning body, the NHS HTA Programme.

The VAS has a potential score from 0 to 100 in a continuous distribution. The increased power afforded by using a continuous measure to power the trial, rather than an ordinally distributed one which would require non-parametric analysis, meant that it was the obvious choice to recalculate sample size. The mean VAS for those patients who had returned questionnaires by the time of recalculation was 50.7 [standard deviation (SD) 17.3]. Using the formula provided by Machin and colleagues[31] for calculating sample sizes for equivalence studies utilising outcome measures with continuous distributions, and specifying 5% significance and 90% power, a sample size of 245 patients in each arm (490 in total) was obtained, with 10% each way limits of equivalence (i.e. 50.7 $\pm$ 5.07).[31] This appeared achievable, and the trial continued using this revised sample size.

Assessment of quality of surgery

Assessment of the wound was undertaken between 6 and 8 weeks postsurgery by two blinded independent reviewers using digital photographs of each wound. This was a pragmatic time interval. The appearance of wounds has been shown to be reliably correlated at 3 months and 1 year, whereas the appearance at 5–10 days does not correlate with 1-year appearance.[37] However, 3 months was felt to be too long an interval to allow accurate recall of subjective impressions that the patients were to be asked about in the assessment of satisfaction, and might also have led to an unacceptably large loss to follow-up rate in the study. A time of 6–8 weeks postsurgery was felt to be an acceptable compromise. Digital photographs were taken of each wound by the trial nurse (some

TABLE 2 *Criterion-based score system for assessing wounds*

Distortion of skin around the scar	Score 0 if present	Score 1 if not present
Width of the scar	Score 0 if > 2 mm	Score 1 if < 2 mm
Step across scar	Score 0 if present	Score 1 if not present
Edge inversion	Score 0 if present	Score 1 if not present
Inflammation/discharge	Score 0 if present	Score 1 if not present
Overall result	Score 0 if not acceptable	Score 1 if acceptable
Total score	< 6 = suboptimal healing	6 = optimal healing

patients had more than one procedure undertaken) using a Nikon D1 digital single-lens reflex camera. It was planned that four photographs would be taken of each wound: one was taken from enough distance to allow the reviewers to orientate themselves to which part of the body had been treated; three close-up pictures were then taken, one perpendicular to the wound, one obliquely to the wound and a final picture was taken with the camera at a fixed distance from the wound. This series of photos was designed to allow the reviewer to assess the wounds using both the VAS and the categorical scale.

Photographs were judged separately by two observers, one a consultant surgeon, and one a GP with surgical training. They were both blind to the arm of the trial, and neither of them undertook any of the trial surgery. The photographs were presented to the reviewers in a specially written form program based on a Microsoft Access database, allowing simple completion (Appendix 1). The assessors judged each set of photographs using both wound scoring scales (VAS and categorical) at the same time. Their scores were combined for analysis.

Patient satisfaction

No satisfactory measure of patient satisfaction existed for this group of patients that had been validated and that contained questions on all the areas upon which data were to be gathered, and it was decided to construct a questionnaire specifically for the purpose as part of an MSc project.[38] A search of the literature and two group interviews with minor surgical patients generated a comprehensive list of issues to be covered within the questionnaire. From these issues items with Likert responses were formed. The literature, patient and expert opinion contributed to face and content validity. The final questionnaire used in the study forms Appendix 2.

Pathological diagnosis

Pathological diagnosis was considered important as the issue of appropriate treatment of both benign and malignant lesions was much debated in the early years after the introduction of the fee-for-service payments for minor surgery. The authors attempted to obtain a pathology report for every operation if there was one available, a detailed search being made. All the histology services for the hospitals and GP practices participating in the study were provided by three pathology departments (Southampton University Hospitals, Salisbury District Hospital and Portsmouth Hospitals). The majority of the reports came from Southampton University Hospitals Trust (SUHT) and were obtained directly from the results service within the hospital. Those from the other centres were obtained via the GPs involved. Where missing, the individual patient records were searched at the GP practice and the hospital results service approached. Only when this process was exhausted was it assumed that a specimen had not been sent. This process was repeated several times after completion of recruitment and initial follow-up had been completed. The referring diagnosis was compared with the final report, the pathologist's report taken as being correct. For malignant lesions, completeness of excision was noted.

Analysis

As well as the effect of the trial arm upon outcome, individual operator effects have to be taken into account in both arms of the trial, and so does the effect of patients having more than one lesion removed during the trial. The resulting data set is hierarchical in nature, therefore, with three levels for variables measuring quality of surgery at lesion level (trial arm, operator, lesion) and two levels for questionnaire variables (trial arm, operator).

The primary outcome (VAS) is a continuous variable. A clinically important difference in VAS score was defined as 10% of the overall mean VAS score either way from zero (no difference). This clinically important difference was used to define an upper and a lower equivalence limit around zero. If the 95% confidence interval (CI) around the observed difference in VAS score lay completely *above* the *upper* equivalence limit, or completely *below* the *lower* equivalence limit, then the performance of the operators in the two arms was to be judged non-equivalent: if it lay entirely *between* the two equivalence limits it was to be judged equivalent: if it *straddled either* equivalence limit, the result was to be judged uncertain. The mean difference and 95% confidence intervals around it were calculated using the MIXED procedure in SPSS 14.0, with trial arm specified as a fixed effect, and operator and patient (to account for multiple lesions) as random effects. This was a per-protocol analysis, this being an equivalence trial.

For other trial outcomes no prior hypothesis was made to enable generation of equivalence limits.

Outcomes are therefore reported simply as mean differences (or differences in proportions) and confidence intervals. For these outcomes intention-to-treat (ITT) analysis was undertaken, making a worst case assumption for each missing data item. For the categorical quality scale the proportion in each trial arm achieving maximum score from both assessors on quality scale (i.e. 12/12) was calculated, as was the mean score for each trial arm on a scale comprised of adding both assessors' assessments together for each case. Scales derived from questionnaire items were treated in a similar fashion to assessed quality scales. Certain items (e.g. median distance travelled to surgery) were not amenable to multilevel adjustment and have been reported as they stand.

Training of GPs and quality of surgery

To try to estimate the effect of training on GPs' abilities to undertake minor surgery an analysis was also undertaken comparing the VAS scores from scars resulting from those who had received formal 'in-post' surgical training and those who had not. Details of amount of training undergone by GPs in surgical techniques were collected in a separate questionnaire survey. A questionnaire was distributed to all GPs in South Hampshire asking for details of jobs undertaken in surgery, dermatology or obstetrics and gynaecology, possession of FRCS (Fellow of the Royal College of Surgeons) or equivalent [e.g. Member of the Royal College of Obstetricians and Gynaecologists (MRCOG)] and attendance at other training courses. The results of the whole survey are largely not pertinent to the trial or its interpretation, and will not be presented in full. For the purposes of this analysis results of individual questions were combined to give a classification in in-post or informal training undergone. This classification was then applied to operators in the trial and their results in terms of surgical quality were compared.

Participants

General practitioners

It was originally planned to recruit members of the WReN to take part in the project. When this study was undertaken, WReN was an active organisation, primarily of GPs, promoting and developing both research ideas and projects in primary care in the Wessex region of the NHS (Dorset, Hampshire, the Isle of Wight and Wiltshire). However, for logistic regions, it was not possible to use this network in the way envisaged because of the organisation of hospital services in the region. The project had to be limited to the areas in which there was ready access to a hospital service for providing minor surgery to patients randomised to the hospital arm of the study. It proved impossible to persuade some hospital trusts of the benefits to them of entering the trial at all, and it was equally impossible to persuade others that they should treat patients randomised to the hospital arm but who were resident in other catchment areas. This resulted in setting the catchment area for the trial as (initially) the bulk of the Southampton and South West Hampshire health authority area. This was subsequently extended to the western areas of the Portsmouth and South East Hampshire health authority.

Hospitals

Recruiting hospitals to take part in the study was difficult. When the initial application was made to the HTA to conduct the study, the relevant senior managers in the principal hospital trust (SUHT) had agreed to support the study. However, there was a long gap between initial application for the grant and starting the project (3 years). During this time the funding arrangements for research within the NHS evolved rapidly following the adoption of the principles described by Culyer.[39] This review of research funding mechanisms assigned research costs, service costs and treatment costs to three separate fund-holding bodies. Definitions provided in the review were not tight enough, and this led to inevitable differences in interpretation. Lack of agreement on what constituted 'service' and 'treatment' costs, and what differentiated one from another, led to protracted discussions with SUHT, the likely major host for the hospital arm of the trial. The issue centred on the requirement to set up a special operating list for the purposes of the trial. This was necessitated by the very long hospital waiting lists for minor surgery for non-malignant skin lesions at Southampton, which would have meant that most, if not all, patients randomised to this arm would not have had a procedure undertaken within the timespan of the trial, had they been assigned to routine hospital care. Although this would have provided a definitive result as to the feasibility of undertaking all minor surgery in a hospital setting (at least under current financial constraints), it would not have answered questions relating to quality or patient experience of actually having surgery. Altogether, these delays

necessitated a 6-month extension to contract, which was agreed by the HTA.

These same problems came to the fore when attempts were made to extend the trial recruitment area to Portsmouth in 2000/01. At that time, the dermatology and general surgery consultants in Portsmouth who specialised in treating skin lesions had a waiting time of 11 months for low-grade skin cancer surgery, and had stopped offering any service for non-malignant skin lesions. In addition, internal funding arrangements for pathology services in Portsmouth meant that each lesion sent for pathological analysis would be more expensive to the clinical budgets of the operating consultants than in Southampton. Portsmouth Hospitals Trust was also in receipt of a far smaller Service Increment for Teaching and Research (SIFT-R: the research funding grant given to hospital trusts) allocation as a trust than that given to SUHT, as a result of the teaching hospital status granted to Southampton.

These problems were not as acute in the Southampton Community Health Services Trust, which runs most of the smaller scale hospitals in the Southampton district. Their waiting lists were shorter, and generally there was less pressure on each list. The overall numbers predicted to need treatment in the community trust facilities were also much smaller, only 20% of the total number of patients recruited to the hospital arm of the study. Once the practicalities had been decided of how to make appointments in the units involved, there were no significant further problems in supporting the trial in these locations. Similarly, these problems were not an issue when the armed services hospital at Haslar in Gosport was approached. Here, the practical difficulty of predicting when consultant surgeons or their teams would be available to perform procedures was more important.

The hospitals and trusts that agreed to take part in the study, finally, were the Southampton University Hospitals NHS Trust, the Southampton Community Health Services NHS Trust, and the Royal Hospital Haslar, Gosport. The community trust made available facilities at Romsey Hospital, Lymington Hospital, The Fenwick Hospital, Lyndhurst Hospital and Hythe Hospital. The university hospitals trust made available facilities at the Royal South Hants Hospital. The study was supported directly by the use of staff from academic and NHS staff in general surgery, dermatology and pathology, within all of the trusts and institutions mentioned. In terms of numbers of hospital doctors directly involved, 59 performed procedures for the study.

Recruitment

Recruitment of patients to the trial was by GPs in their surgeries on an opportunistic basis. It was necessary initially to approach GPs to ask them to participate in the trial. All GPs in the area were contacted by letter, this being followed by a letter to their practice manager. The intention was to arrange a direct presentation with the GPs about the reasons for the study and the practical arrangements for taking part in it.

Financial issues

The challenges of negotiating Culyer funding were not the only financial issues to impact upon this trial. As described, GPs receive payment for their minor surgery activity. In the Southampton and South West Hampshire health authority area more than 90% of GPs were registered as providers of minor surgery. They were entitled to claim £25.65 for each procedure undertaken, up to a total of 60 procedures per annum (1999/2000 rates), a total of £1539 per year. Theoretically, therefore, a GP could lose a significant amount of money by taking part in the trial; if the demand for minor surgery from their patients in a year amounted to only the 60 patients on whom they would have been entitled to claim, approximately 30 would be sent to hospital for their treatment. They would not be able to claim the fee for these patients, thus losing £769.50 in fees for their practice.

In order to remove this disincentive to take part, a means had to be found to compensate the GPs for their potential loss of earnings. However, the internal rules for the NHS and for supporting clinical research meant that it was not possible simply to pay the fee for patients randomised to hospital to the GP from trial funds. A compromise was found such that GPs received a payment to cover their costs in taking part in the study; principally, the time that it took them to complete the minimal paperwork for the recruited patients. This allowed for a payment of £21.75 per patient recruited to the GP. This was funded by additional monies allocated from the National Co-ordinating Committee for the HTA Programme. This sum ensured that the GPs would receive slightly more if they recruited patients to the study than if they simply operated on them themselves, without there being such a large financial inducement that patients would be recruited who did not need operations.

Patient route through the trial

The trial process was designed to be simple and efficient for both GP and patient. GPs were given a ringbinder file with information and instructions about the trial and, within each, a number of recruitment packs. The packs contained the paperwork required to complete the recruitment of each patient, this was: a reminder of the inclusion/exclusion criteria for the study, an information leaflet for the patient, a recruitment pro forma and a sealed envelope containing the randomisation allocation to hospital or GP treatment.

When a patient presented to a participating GP with a condition suitable for randomisation, the GP asked for their informed consent for recruitment to the trial. If consent was obtained, randomisation to one or other arm of the study was performed by means of opening a sealed envelope which contained a card containing details of trial arm. Details of the patient, their diagnosis and randomisation were then faxed to the trial office. If they were randomised to hospital, the trial office arranged for treatment at an appropriate venue; if they were randomised to general practice, the GP was responsible for notifying the trial office of the date for the procedure. A special treatment list was provided by SUHT to allow rapid treatment of trial patients in the hospital sector. This clinic mimicked normal hospital service in all respects other than the time taken to be treated in it. All patients randomised to the hospital arm of the study were seen and treated within 21 days of entering the study, unless the patient opted for a later appointment. The trial office arranged and conducted all follow-up related to the trial, usually meeting the patient at a time convenient to them, in their own home, in their GP practice or in another convenient place, to enable photography and for the patient to complete the patient satisfaction questionnaire.

Randomisation

A computer-generated sequence of random allocation to hospital or general practice was obtained from the Public Health Sciences and Medical Statistics Group at the University of Southampton. The numbers were randomised in blocks of six, a detail that was withheld from the GPs using the envelopes. A series of envelopes was made up, each with a sequential number on the outside, and a sticker with 'Hospital' or 'GP' placed inside. The envelopes were manila, and therefore it was not possible to read the allocation without opening the envelope.

The envelopes were put in sequence into the patient recruitment packs given to the GPs. Thus each GP would have, in the ringbinder, ten packs with envelope numbers that ran consecutively. Once a patient was recruited to the trial and had signed the consent form, the randomisation number was recorded by the GP on the recruitment pro forma and the GP then opened the envelope. They then recorded the treatment allocation onto the pro forma, sent this to the trial office and, if the patient was randomised to general practice, proceeded with making the arrangements for the procedure to be carried out.

The randomisation number was checked against a list kept in the trial office, to confirm that the reported randomisation was that which would be expected from that envelope, and that envelopes were being used in sequence by GPs. This system worked well during the trial. On one occasion the randomisation was not what was expected from the envelope numbers. After having checked with the GP concerned that they had been used in the correct order, the error was found to have been with putting the wrong randomisation stickers in the envelopes in that batch. That batch of recruitment packs was withdrawn from the GP involved, and a new one issued. There were no further problems of this sort with the process of randomisation.

Blinding

Clearly, it was not possible to blind patients to which arm of the trial they had been allocated. However, blinding of the two independent observers undertaking assessment of wounds was undertaken. Since all photographs of wounds were taken some 6–8 weeks after surgery, and often in the patient's own home, it was not possible to tell from them where treatment had been undertaken.

Patient withdrawal protocol

A patient could be withdrawn from the study for a number of reasons:

- At all stages within the study, the patients themselves could elect to withdraw from the trial, without compromising their ongoing care with the doctors involved in treating them.

- Patients could also be withdrawn if the condition with which they had presented had resolved, or they no longer wanted it treated.
- More complex rules had to be established for the study for lesions or conditions where the decision to treat by surgery might be questioned by the doctor asked to perform the surgery. There were two situations where this could occur. The first was where a patient was randomised to treatment in general practice, within a practice where one or two partners performed the minor operation for their colleagues. Although appropriately recruited by another GP, the operating GP had the right to decline to treat, usually on the basis that the lesion was sited in a more difficult area, for example the face or over a joint, and that therefore they were not happy to proceed. The second situation was when a patient had been randomised to hospital for treatment, and the opinion of the hospital doctor concerned was that the lesion had been misdiagnosed in general practice and needed either more radical treatment than could be offered in the clinic or day theatre concerned, or other investigation before treatment.

Record-keeping

The mainstay of the record-keeping for this study was a database written in Microsoft Access 2000 for this study. It incorporated reports that allowed tracking of patients through the study; generating due lists of operations that were pending, follow-up appointments that were pending and lists of outstanding paperwork. It also enabled monitoring of recruitment rates and sites, comparison with actual and expected randomisation, and dropout rates from the study. Most importantly, it allowed digital storage of photographs and assessment of wounds. The database and photographs were maintained on University of Southampton mainframe computers, behind electronic firewalls allowing limited access with passwords. This proved a secure and confidential way of maintaining the records. The paper record for the study was minimised, consisting of a patient recruitment pro forma, a consent form, an operation summary and, when applicable, a copy of the pathology report for each procedure. These were kept in the secure trials office in the University Department of Surgery within Southampton General Hospital.

Chapter 4

Results: quality of surgery and patient satisfaction

Potential recruitment population

It is important for the completeness of the Consolidated Standards of Reporting Trials (CONSORT) statement for a trial of this sort that an estimate is made for the total number of patients that could potentially have been recruited. From the data obtained from GPs throughout the area presented elsewhere in this report, the numbers of patients can be estimated that are treated with eligible procedures. GPs in Southampton and Portsmouth area health authorities perform an average of 20.12 (SD 28.9) excisions per year.

In total, 170 GPs agreed to take part in the study, of whom 82 referred at least one patient, although the number of patients contributed varied widely, ranging from a single patient (n = 16) to a maximum of 28 patients (with 41 lesions between them). The trial recruited for 2 years, but not all practices were active recruiters throughout this time. A reasonable estimate would be that they recruited for an average of 1 year.

Using these figures for 170 GPs gives an estimate of 3420 eligible patients. Repeating the calculation using only 82 GPs, the number who actually recruited any patients, gives an estimate of 1695. A pragmatic average of 2500 was made for the total number of eligible patients that might have been recruited to the study.

Recruitment

Eighty-two GPs referred one or more patients to this study: 568 patients were recruited to the trial (284 primary care, 284 hospital). The basic demography of the participants and pathology of lesions as judged by referring GPs are given in *Table 3*. The arms are similar in age, gender distribution and diagnosis. A CONSORT diagram appears in Appendix 3. Twenty-three cases in the primary care arm and 26 in the hospital arm did not attend for surgery or were excluded because they were unsuitable for surgery in primary care or ineligible to enter the trial.

Types of lesion presenting and procedure undertaken

Altogether, referrals were received for 705 lesions. There is evidence that 637 skin procedures plus 17 ingrowing toenail procedures were performed, based on the presence of photographs of the operation scar, completed questionnaires, histological samples or documentation (313 primary care, 341 hospital). Of those not receiving surgery one case died before surgery, in 17 cases the lesion resolved (e.g. 'fell off') or required only reassurance, in eight the lesion or subject was either judged unsuitable for surgery in general practice or was ineligible for the trial (three of these were referred urgently to hospital specialist surgery), and in 26 cases 'did not attend' is all that is recorded. In 589 cases assessable pictures resulted [273 primary care (87%), 316 hospital (93%)]. Sixty-five GPs undertook surgery in the primary care arm of the trial and 60 hospital surgeons or dermatologists in the hospital arm. Excisions of skin lesions were the most numerous procedures undertaken, the remaining categories making up less than 10% of the total.

VAS scores of quality of surgery

The overall VAS score across all trial subjects was 59.8, generating 10% each-way equivalence limits of ± 5.98. The VAS score in the hospital arm was 61.22, and in the primary care arm 55.76 (mean difference 5.46, 95% CI 0.925 to 9.990). *Figure 2* shows a graphical representation of the result and makes it clear that while there is a statistically significant difference in VAS scores, it is an uncertain result rather than a non-equivalent one.

Categorical quality scores

In the hospital group 66/341 lesions (19.4%) achieved a maximum score on the categorical scale, compared with 40/313 (12.8%) in the primary care group [odds ratio (OR) 1.64, 95% CI 0.997 to 2.69].

TABLE 3 *Demography of trial participants, and number of lesions referred (number where procedure performed) into the trial as diagnosed by referring doctor, by trial arm*

	Hospital group (*n* = 284)	**Primary care group (*n* = 284)**
Mean age (years)	47.8	49.7
Number (%) of females	159 (56%)	150 (53%)
Total lesions referred (procedure performed)	369 (341)	336 (313)
Unknown/non-specific description	7 (7)	7 (7)
Eczema/dermatitis	0	0
Granuloma	5 (4)	3 (2)
Solar elastosis	0	0
Ingrowing toenail	10 (9)	8 (8)
Sebaceous gland hyperplasia	0	1 (1)
Skin tag, fibroepithelial polyp, skin polyp	21 (20)	37 (35)
Chondrodermatitis nodularis helices	0	0
Viral warts	5 (5)	7 (7)
Scars including keloid	1 (1)	1 (1)
Benign tumours including neurofibroma	14 (13)	18 (17)
Lipoma	9 (7)	10 (10)
Cysts including epidermoids	95 (90)	62 (53)
Lentigo	0	0
Seborrhoeic keratosis, seborrhoeic wart, basal cell papilloma	85 (79)	63 (53)
Melanocytic naevus	78 (72)	81 (78)
Solar keratosis	2 (2)	2 (2)
Cutaneous horn	0	1 (1)
Bowen's disease	1 (1)	0
Basal cell carcinoma	25 (21)	26 (24)
Keratoacanthoma	3 (3)	1 (1)
Squamous cell carcinoma	4 (3)	4 (4)
Malignant melanoma	1 (1)	3 (1)
Missing diagnosis/not referred by GP	3 (3)	1 (0)

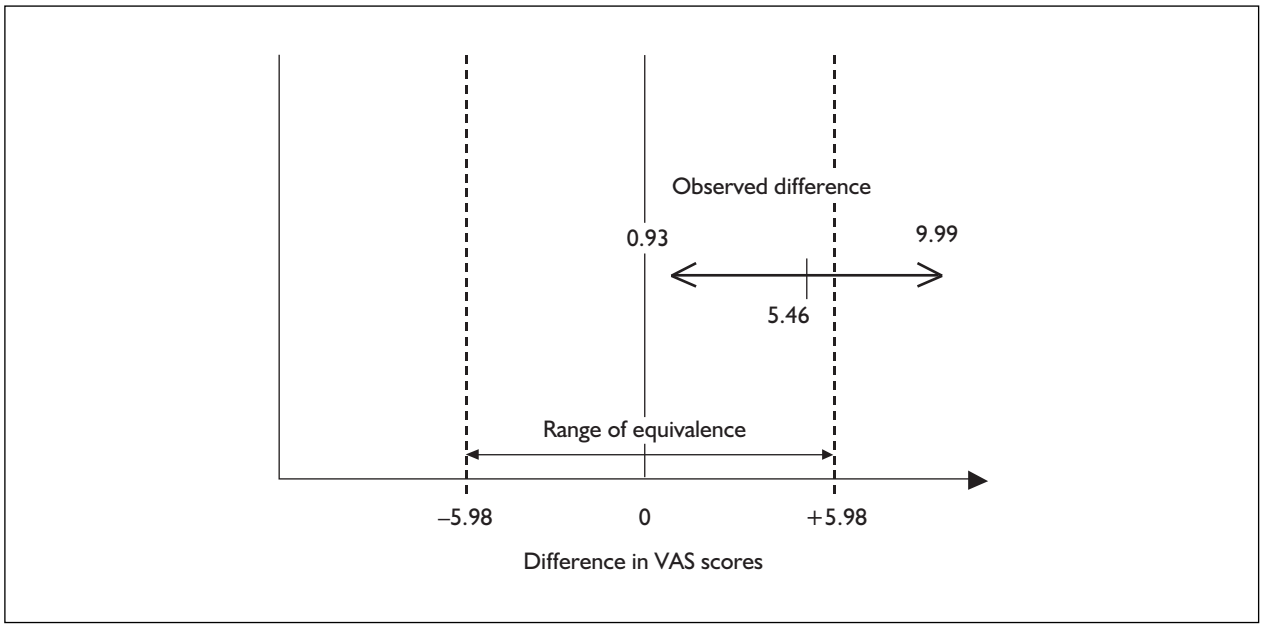


FIGURE 2 *Pictorial representation of VAS score results showing observed difference with 95% CIs and equivalence range*

Patient satisfaction

A total of 467 subjects returned questionnaires (228 GP arm, 239 hospital arm), although not all subjects answered all questions. *Table 4* presents patient satisfaction scores for five domains (with number of items in domain) and eight individual items in each trial arm. All scores have a maximum range from 1 to 5. For all scores a low score reflects greater patient satisfaction. There are few significant differences between arms, except in matters relating to convenience and knowing the doctor, where the primary care arm has lower scores than the hospital arm. The hospital arm scored better on provision of information following the operation.

Patient access to care

Table 4 also presents questionnaire-derived items related to access to care, which all favour treatment in primary care.

Later complications of surgery

Table 5 shows questionnaire-derived results for problems following surgery. Although postoperative wound infection was significantly lower in the hospital arm there was no difference found in the overall problem rate following surgery.

Pathology reports

Overall, 491/637 skin procedures (77%) generated a traced pathology report. Only 213/305 (70%) of GP skin procedures produced a pathology report, compared with 278/332 (84%) in the hospital arm [$\chi^2 = 17.38$, degrees of freedom (df) = 1, $p < 0.001$].

Completeness of excision of malignant lesions

Completeness of excision was achieved in 15/20 malignancies (75%) in the hospital arm and 7/16

TABLE 4 *Patient satisfaction scores with mean differences and 95% CIs for the two trial arms using ITT analysis and the MIXED procedure in SPSS 14.0: ITT analysis*

Domain (number of questionnaire items)	Hospital group (n = 258)	Primary care group (n = 261)	Mean difference (95% CI)
Care and courtesy[a] (4)	1.872	1.921	–0.049 (–0.322 to 0.225)
Satisfaction with wound[a] (3)	3.062	3.099	–0.037 (–0.273 to 0.198)
Privacy and comfort[a] (2)	2.327	2.466	–0.138 (–0.39911 to 0.123)
Feeling that procedure was rushed[a] (2)	2.184	2.150	+0.034 (–0.228 to 0.296)
Worry that lesion was more serious than stated[a] (2)	2.050	2.182	–0.132 (–0.348 to 0.084)
Ease of making appointment (1)	2.261	2.058	+0.203 (–0.055 to 0.461)
Pain during operation (1)	2.517	2.371	+0.146 (–0.153 to 0.445)
Not kept waiting (1)	2.741	2.244	+0.496 (0.177 to 0.816)
Information following operation (1)	1.951	2.204	–0.253 (–0.478 to –0.028)
Confident to have similar operation in the future (1)	1.968	1.998	–0.030 (–0.309 to 0.249)
Importance of meeting doctor in the past (1)	3.249	2.694	+0.556 (0.290 to 0.822)
Pain in week after operation (1)	2.807	2.696	+0.111 (–0.153 to 0.375)
Wound irritating (1)	2.448	2.464	–0.016 (–0.286 to 0.255)
Items not adjusted for clustering by operator			
Median distance travelled to have procedure done (miles) (1)	5	2	+3 (3 to 4.25)
Median time waited after arrival and before treatment (minutes) (1)	45	10	+35 (35 to 50)
Median time taken in total (minutes) (1)	135	60	+75 (60 to 90)
Trouble parking if came by car (1)	58/214 (22.5%) (44 NA)	39/220 (14.9%) (41 NA)	9.4% (1.5 to 17.1)

A low score reflects greater patient satisfaction.
NA, not applicable.
[a] Domain.

TABLE 5 *Number (%) of respondents to questionnaire reporting complications of surgery in each arm, with ORs (95% CIs) calculated using logistic regression analysis adjusted for clustering by operator in Stata 9.0: ITT analysis*

	Hospital group (*n* = 258)	GP Group (*n* = 261)	OR (95% CI)
Wound infection	31 (12.0)	50 (19.2)	0.58 (0.36 to 0.91)
Discomfort	62 (24.0)	58 (22.2)	1.11 (0.70 to 1.75)
Bleeding	52 (20.2)	64 (24.5)	0.78 (0.54 to 1.12)
Allergy	26 (10.1)	38 (14.6)	0.66 (0.39 to 1.12)
Other problem	53 (20.5)	70 (26.8)	0.71 (0.48 to 1.04)
No problems	116 (45.0)	123 (47.1)	0.91 (0.62 to 1.33)

(44%) in the primary care arm of the trial ($\chi^2 = 3.65$, df = 1, $p = 0.056$). However, two of the three cases referred for specialist surgery in this trial were malignant in character upon arrival at hospital. If the assumption is made that they received adequate excision from specialist surgical intervention, this would result in revised figures of 17/22 (77%) completely excised in the hospital arm and 7/16 (44%) in the primary care arm of the trial ($\chi^2 = 4.47$, df = 1, $p = 0.034$).

Training of GPs and results in terms of quality of surgery

Of the 65 GPs who undertook procedures in this trial 48 (74%) returned the questionnaire; together they carried out 278 of the 337 GP procedures (82%). None possessed FRCS or equivalent. Twenty-six (54%) had worked for 6 months or more in a surgical or equivalent post (158 procedures) and the remainder had informal or no specific training (120 procedures). *Table 6* compares VAS scores in the two groups.

Clearly, the result, that those in the 'informal' groups score better than those in the 'in-post' group, is the opposite of what might be expected. The obvious explanation is selection bias (i.e. that those with more surgical experience are prepared to tackle more complex procedures), but without the benefit of a scoring system to allow procedures to be graded by complexity it was not possible to investigate this further. Consequently, no further analysis was undertaken comparing these groups.

TABLE 6 *Comparison of VAS result in GP operators according to level of surgical experience*

	In-post group (*n* = 158)	Informal group (*n* = 120)	Mean difference	95% CI for difference
Mean VAS score	52.02	60.46	–8.44	–0.426 to –16.457

Chapter 5

Economic analysis of trial

Two cost-effectiveness analyses are reported. The first uses the original primary outcome measure: absence of problems following surgery. The second uses the completeness of excision of malignancies removed.

Cost of minor surgery

Patient-level resource-use data were not collected alongside the MiSTIC trial, and in order to produce a cost-effectiveness analysis it was necessary to attach costs to each patient in the hospital and GP arms of the trial. To do this, two cost distributions were simulated, using the NHS reference costs for minor surgery in hospitals and primary care, respectively. Following convention, it was assumed that the costs were log-normally distributed. The NHS reference costs report the mean and interquartile range (IQR).[40] It is possible to extract the standard deviation from the IQR (*Table 7*). The mean and the standard deviation are sufficient to parameterise the log-normal distribution. The distributions are shown in *Figure 3*.

Monte Carlo simulation was then used to generate samples of costs. One-thousand simulations were generated for GP and hospital minor surgery costs. SPSS was then used to select randomly the appropriate number of cost observations from each sample and allocate a cost to each subject in each arm of the trial. The Monte Carlo simulations were generated using the Crystal Ball Add-in for Microsoft Excel.[41]

This process of generating costs draws on the between-centre variation in costs, which is described by the NHS reference costs, rather than the within-centre variation in costs that is normally captured in sample cost data. Its use for this evaluation can be thought of in terms of randomly sampling trusts from across the NHS to provide the care.

TABLE 7 *Costs of hospital and GP-based minor surgery*

	Mean cost (£)	SD
Hospital-based minor surgery	1222.24	23.24
GP-based minor surgery	449.74	47.74

Incremental cost-effectiveness ratio

The primary result of cost-effectiveness analysis is the incremental cost-effectiveness ratio (ICER). This is calculated as the difference in the mean effect in each group divided by the difference in mean cost in each group.

Sensitivity analysis

It is now good practice to address explicitly the uncertainty regarding the true population values of the cost and effect parameters.[42] Although one-way sensitivity analyses may provide some insight into the potential importance of this uncertainty, probabilistic sensitivity analysis is the most appropriate method of incorporating the uncertainty across all the parameters into the

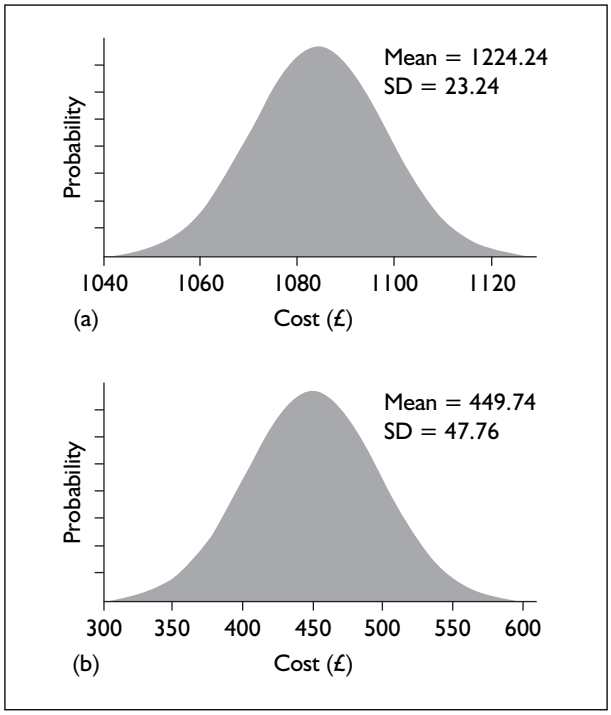


FIGURE 3 *Sampling distributions for (a) hospital and (b) GP minor surgery costs*

results of an economic evaluation.[43] Conventional frequentist analysis often uses the confidence interval to characterise uncertainty. However, a 95% confidence interval does not give you a range within which you are 95% certain the true value lies. Rather, it tells you that if you were to repeat the experiment 100 times and calculate the confidence interval on each occasion, in 95 of those analyses the true value would lie within the calculated range and on five occasions it would not. It provides no information about whether the result you are analysing is one of the 95 or one of the five. In contrast to this, the Bayesian approach to characterising uncertainty, which is taken here, gives the degree of belief or probability that something is true.

The bootstrap was used to construct probability distributions for the population mean costs and outcomes for patients treated in hospital or by GPs.[44] The basic idea of the bootstrap involves repeated random sampling with replacement from the original data sets to produce random samples of the same size as the original sample, each of which provides an estimate of the parameters of interest.[45] In this case, it was used for mean costs and mean effects. 'With replacement' means that any observation can be sampled more than once in each bootstrap sample.

Incremental costs and outcomes were calculated for each bootstrapped simulation and plotted on the incremental cost-effectiveness plane.[46] This was repeated 10,000 times, and these 10,000 simulation results used to construct a cost-effectiveness acceptability curve (CEAC).[47] A CEAC plots the probability that an intervention is cost-effective as the decision-maker's willingness to pay for an additional unit of effect increases. In this analysis the CEAC plots the probability that hospital-based minor surgery is cost-effective compared with GP-based minor surgery, as the decision-maker's willingness to pay to avoid a missed diagnosis of malignancy increases.

Discounting

All events considered in this evaluation occurred within 1 year and therefore, by convention, discounting was not required.

Results

The mean cost (SD) for hospital-based minor surgery was £1222.24 (£23.24) and for primary care £449.74 (£47.74). The mean difference in effect between the hospital and GP surgery in terms of the patient-reported 'no problems following the operation' outcome was 0.0135 in favour of hospital surgery. The mean cost difference between hospital and GP surgery was £770.77.

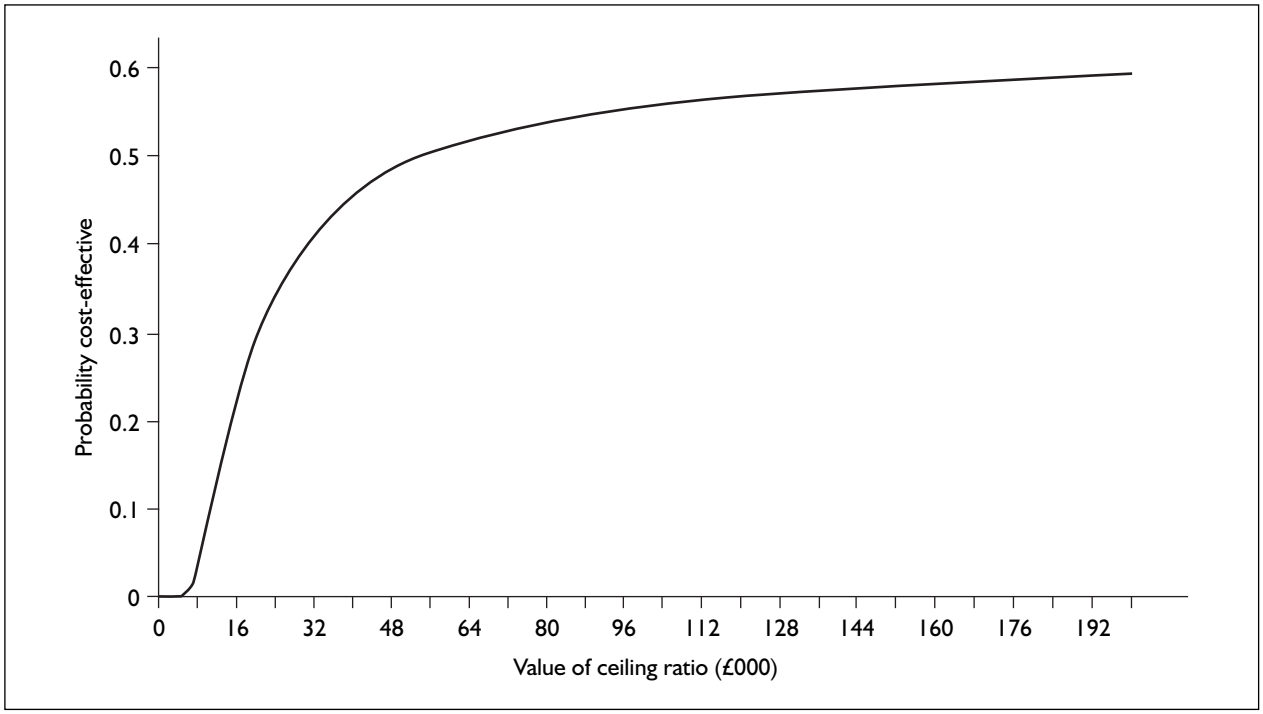


FIGURE 4 *CEAC for hospital minor surgery versus primary care minor surgery: no problems after surgery outcome*

The expected ICER was £13,558 per additional 'no problems following operation' for hospital surgery versus primary care surgery (SD 631,878). *Figure 4* plots the CEAC for hospital versus primary care surgery. The vertical axis indicates the probability that hospital minor surgery is cost-effective. There is no plausible willingness to pay for which primary care is expected to be cost-effective. However, there remains a large amount of uncertainty around both the expected difference in costs and outcomes using this measure of effect.

At £33,800, the mean ICER per additional complete excision is high, as is the standard deviation (697,170). The uncertainty around the ICER is clustered around the origin, meaning that the ICER is not very stable, and small changes in either the incremental costs or effects will lead to large shifts in the ICER. The CEAC is well behaved and easy to interpret (*Figure 5*). As the value of an incomplete excision avoided approaches £13,000, the probability that hospital surgery is cost-effective becomes stable at around 90%. Given the potential health consequences of an incomplete excision of, say, a malignant melanoma, this appears a cost-effective option.

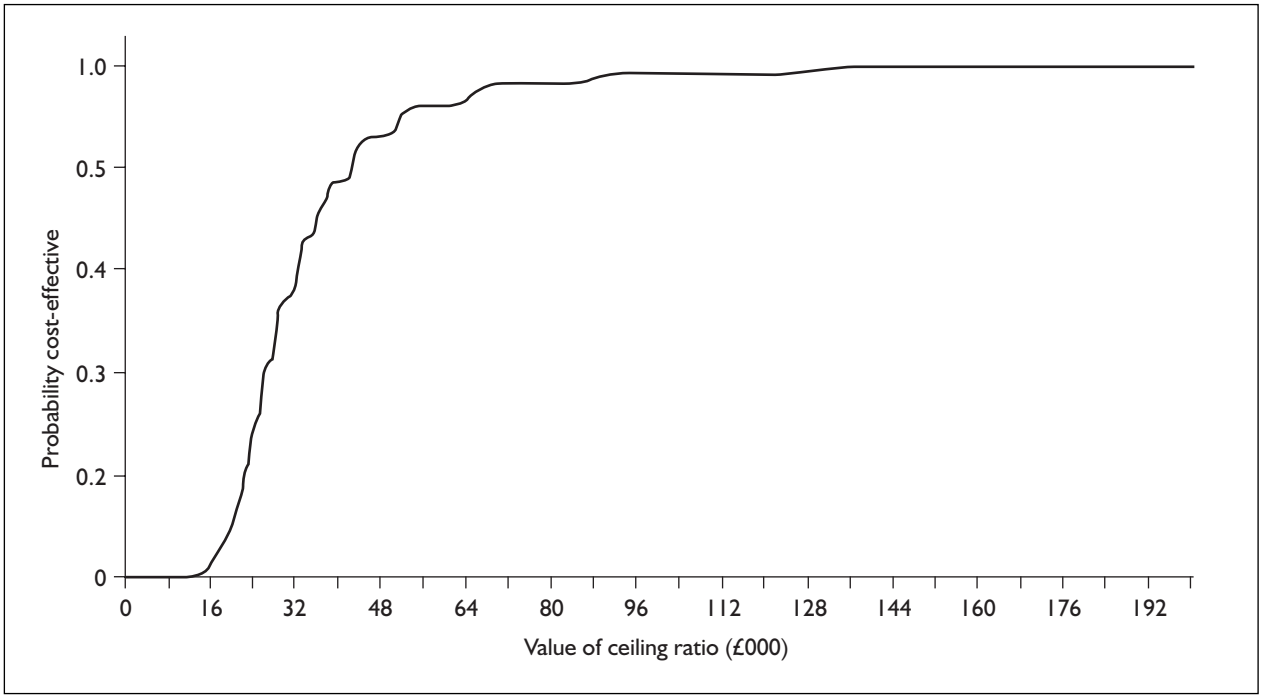


FIGURE 5 *CEAC for hospital minor surgery versus primary care minor surgery: complete excision of malignancy outcome*

Chapter 6

Comparison of GP diagnosis and histopathology of lesions, and performance regarding recognition of malignant lesions

This study was not powered to investigate pathological outcomes, and the resource to allow proper follow-up of clinical outcomes (e.g. survival following diagnosis of malignant melanoma) was not available. However, many procedures in this trial resulted in a pathology specimen being sent, and the decision was made to investigate the nature of lesions sent for pathology, the accuracy of their diagnosis and the completeness of excision of malignant lesions.

Data

All patients recruited to the MiSTIC trial had a GP referral form indicating a working diagnosis for the lesion concerned. Details from these were entered into a database, along with the histological diagnosis found on the histology form pertaining to the sample, where one was found. There were many diagnoses on the referral forms and pathology reports, and they were divided into 23 categories for analysis, using a classification derived from *Rook's textbook of dermatology*, Sixth edition.[48] The categories arrived at are shown in *Table 8*.

Analysis

Chance-corrected inter-rater reliability was measured using Cohen's kappa in Stata 8.0 (Stata Corp.). A kappa value greater than 0.75 is considered excellent agreement beyond chance, values below 0.40 represent poor agreement, and values between 0.40 and 0.75 represent fair to good agreement.[49] An initial comparison between GP diagnosis and histological diagnosis was undertaken across 22 of the 23 categories (ingrowing toenails were excluded from this analysis). For cases where a procedure was known to have been performed but where no histology report was recovered a sensitivity analysis was undertaken assuming, first, no agreement over missing cases and, second, complete agreement over missing cases. The 22 categories were then collapsed into two categories, benign and malignant, and kappa was recalculated. The 'malignant' category comprised three malignancies (malignant melanoma, squamous cell carcinoma and basal cell carcinoma) and one premalignant condition (Bowen's disease). Using this dichotomous categorisation the sensitivity, specificity and positive predictive value for GPs'

TABLE 8 *Categories used to classify diagnoses by histology*

Category	Type of skin lesion	Category	Type of skin lesion
1	Unknown	13	Cysts including epidermoids
2	Eczema/dermatitis	14	Lentigo
3	Granuloma	15	Seborrhoeic keratosis, basal cell papilloma
4	Solar elastosis	16	Naevi
5	Ingrowing toenail	17	Solar keratosis
6	Sebaceous gland hyperplasia	18	Cutaneous horn
7	Skin tags, fibroepithelial polyp, skin polyp	19[a]	Bowen's disease
8	Chondrodermatitis nodularis helices	20[a]	Basal cell carcinoma
9	Viral warts	21	Keratoacanthoma
10	Scars including keloids	22[a]	Squamous cell carcinoma
11	Benign tumours including neurofibroma	23[a]	Malignant melanoma
12	Lipoma		

[a] Malignant.

recognition of skin malignancies were calculated with 95% confidence intervals. Lack of any estimate of malignancy among missing cases rendered it difficult to make assumptions that would have allowed a sensitivity analysis on the dichotomised data, and this was consequently not done.

In the group of malignancies where surgery was undertaken by the GP, cross-tabulation was used to examine whether recognition of the lesion as malignant had an effect on completeness of excision.

Results

Of 705 lesions referred into the original study, 654 can be shown to have been subject to a procedure, 17 of these being ingrowing toenails in which histology is not usually performed, and which were excluded from analysis. Overall, 491 of the 637 skin procedures (77%) generated a traceable pathology report. *Table 9* shows numbers of these cases by histological category as described by GPs, and number in each category where a histological sample was found by trial arm. In one case there was no referral from the GP, the procedure having been performed at the request of a patient with multiple lesions and in whom that lesion had not been mentioned in the referral. This lesion was excluded, leaving 490 for further analysis. The table demonstrates that the deficit in samples does not follow a random pattern; while it might be expected that skin tags would be underrepresented, shortfalls in other categories (e.g. basal cell papillomata, melanocytic naevi) are more worthy of concern.

TABLE 9 *Number of cases as described by GPs on the referral form, numbers where a procedure can be shown to have been performed and numbers of those where a histological sample was found, by trial arm*

GP description	Total with GP diagnosis	Total operated on	Histological sample found	
			Hospital group	Primary care group
Lesions analysed				
1. Unknown/non-specific description	14	14	6/7	7/7
2. Eczema/dermatitis	0	0	0/0	0/0
3. Granuloma	8	6	4/4	2/2
4. Solar elastosis	0	0	0/0	0/0
6. Sebaceous gland hyperplasia	1	1	0/0	1/1
7. Skin tag, fibroepithelial polyp, skin polyp	58	55	14/20	10/35
8. Chondrodermatitis nodularis helices	0	0	0/0	0/0
9. Viral warts	12	12	5/5	7/7
10. Scars including keloid	2	2	1/1	1/1
11. Benign tumours including neurofibroma	32	30	13/13	12/17
12. Lipoma	19	17	6/7	4/10
13. Trichilemmal cysts and epidermoids	157	143	74/90	30/53
14. Lentigo	0	0	0/0	0/0
15. Seborrhoeic keratosis, seborrhoeic wart, basal cell papilloma	148	138	57/79	43/59
16. Melanocytic naevus	159	150	66/72	62/78
17. Solar keratosis	4	4	2/2	2/2
18. Cutaneous horn	1	1	0/0	1/1
19. Bowen's disease	1	1	1/1	0/0
20. Basal cell carcinoma	51	45	21/21	23/24
21. Keratoacanthoma	4	4	3/3	1/1
22. Squamous cell carcinoma	8	7	3/3	4/4
23. Malignant melanoma	4	4	1/1	3/3
Total	683	634	277/329	213/305
Lesions not analysed				
5. Ingrowing toenail	18	17	0/9	0/8
No procedure undertaken or referred elsewhere		51	28	23
Not referred by GP	2	1	1/1	0/0
No data on referral form	2	2	0/2	0/0
Grand total	705	654	369	336

Table 10 shows the numbers of cases where a histological sample was found as described by GPs and as classified by histological examination (ingrowing toenails are excluded).

Agreement between GP diagnosis and histology

An overall kappa statistic of 0.42 (95% CI 0.38 to 0.45) was obtained across the whole data set using the 22-category classification (ingrowing toenails excluded). This represents moderate agreement between GP diagnosis and histological findings, but is at the lower boundary of the moderate category. The sensitivity analysis for missing data improved kappa to 0.55 (95% CI 0.51 to 0.58) if complete agreement between GP diagnosis and histology was assumed for missing cases, but it fell to 0.31 (95% CI 0.28 to 0.33) if complete disagreement was assumed.

In an attempt to improve the level of agreement, both GP referral diagnosis and histological diagnosis were collapsed into a malignant/benign classification and the analysis was redone. This resulted in a kappa of 0.45 (95% CI 0.36 to 0.54). Even at its upper 95% confidence interval, therefore, agreement is moderate at best.

Four of the lesions (all basal cell carcinomas) were diagnosed, correctly, in the same individual. Similarly, many individuals had several benign ones. The figures can be recomputed, therefore, to reflect individuals correctly diagnosed rather than lesions, but it becomes impossible to calculate a kappa across all 22 categories as in some cases individuals had a mixture of benign and malignant lesions. Rather, they can be classified by whether or not they were judged to have one or more malignant lesions. The resulting kappa statistic, calculated on 423 individuals, is 0.41 (0.32 to 0.51). Again, even at the upper level of statistical confidence, agreement is 'moderate' at best.

Test characteristics of GPs in detecting skin malignancy

The results above can be expressed as 2×2 tables and test characteristics computed. *Table 11* shows the data for individual lesions, with test characteristics computed in the footnote, and

TABLE 10 *Comparison of numbers (%) in each histological category as described by GPs and as classified by histological examination (ingrowing toenails not shown)*

	GP diagnosis	Histological diagnosis
1. Unknown/nonsense description	13 (2.6)	0
2. Eczema/dermatitis	0	2 (0.4)
3. Granuloma	6 (1.2)	12 (2.4)
4. Solar elastosis	0	9 (1.8)
6. Sebaceous gland hyperplasia	1 (0.2)	1 (0.2)
7. Skin tag, fibro-epithelial polyp, skin polyp	24 (4.7)	27 (5.3)
8. Chondrodermatitis nodularis helices	0	1 (0.2)
9. Viral warts	12 (2.4)	15 (2.9)
10. Scars including keloid	2 (0.4)	1 (0.2)
11. Benign tumours including neurofibroma	25 (4.9)	64 (12.6)
12. Lipoma	10 (2.0)	11 (2.2)
13. Cysts including epidermoids	104 (20.4)	72 (14.1)
14. Lentigo	0	7 (1.4)
15. Seborrhoeic keratosis, seborrhoeic wart, basal cell papilloma	100 (19.6)	93 (18.5)
16. Melanocytic naevus	128 (25.1)	134 (26.3)
17. Solar keratosis	4 (0.8)	4 (0.8)
18. Cutaneous horn	1 (0.2)	0
19. Bowen's disease	1 (0.2)	3 (0.6)
20. Basal cell carcinoma	44 (8.6)	26 (5.1)
21. Keratoacanthoma	4 (0.8)	1 (0.2)
22. Squamous cell carcinoma	7 (1.4)	5 (1.0)
23. Malignant melanoma	4 (0.8)	2 (0.4)
Total	490	490

Note that figures in the second column are not a subset of figures in the first column.

TABLE 11 *Benign and malignant skin lesions as judged by histology and by GP diagnosis*

	Histology malignant	Histology benign	Total
GP diagnosis malignant	24	36	60
GP diagnosis benign	12	416	428
Total	36	452	488
Sensitivity = 66.7% (52.9 to 78.00), specificity = 92.0% (89.7 to 93.9), positive predictive value = 40% (30.2 to 50.6), negative predictive value = 97.2% (95.6 to 98.2).			

TABLE 12 *Individuals by whether they were judged to have a malignant skin lesion as assessed by histology and by GP diagnosis*

	Histology malignant	Histology benign	Total
Malignant diagnosis by GP	21	35	56
No malignant diagnosis by GP	12	355	367
Total	33	390	423
Sensitivity = 63.6% (49.3 to 75.9), specificity = 91.0% (88.3 to 93.1), positive predictive value = 37.5% (27.6 to 48.5), negative predictive value = 96.7% (94.8 to 98.0).			

Table 12 is the analogous table for individuals affected with malignancy. The results do not differ by a great deal between the two analyses. They indicate that, in this population, GPs failed to recognise one-third of the skin malignancies, or slightly more than one-third of the patients with malignancies. Taking statistical uncertainty into account, the upper 95% confidence interval indicates that they miss no less than one in five. Neither of the malignant melanomas included here was diagnosed by the GP concerned: one was described as a 'dermatofibroma' and the other given a general description as 'red lesion'.

Recognition of a malignancy and completeness of excision

To investigate whether recognition of malignancy improved completeness of excision, the 16 malignancies where surgery was undertaken by the GP were assessed. Six out of the 11 where the malignancy had been recognised resulted in a complete excision (55%) compared with one of the five (20%) where malignancy had not been recognised. However, the association was not statistically significant (Fisher's exact test $p = 0.31$).

Chapter 7
Discussion

Patients are generally happier with minor surgery carried out in primary care rather than hospital and, while higher quality surgical results were achieved in the hospital arm of the trial, their clinical importance is unclear. The perceived advantages in terms of the convenience of having surgery in a local facility must be the main positive influence on increased satisfaction with the process of minor surgery, as it is clear that postoperative problems are not. However, the fact that special surgical lists were organised in the hospital arm to avoid excessive waiting for procedures might mean that hospital treatment appears more attractive than it might really be, and that the true difference may be greater than that observed. Although confined to one geographical area of the UK, the trial was population based and undertaken by a large number of practitioners in both arms, and recruitment was from a wide variety of general practices; therefore, the authors believe the results to be generalisable.

Ideally, patient-level resource utilisation and costs data would have been collected as part of the primary study, but in the absence of these data a cost data set was simulated using the cost data reported in the NHS reference cost data sets for primary and secondary care. The range of simulated values reflects the large uncertainty around the true mean cost of minor surgery in both hospital and primary care. However, many of the costs of minor surgery, from an NHS perspective, are similar in both settings: procedures in both arms were booked, typically, at 30-minute intervals within formal lists of three to four patients, and if the time allocated to each case is not fully utilised the usefulness of the intervening time in undertaking other healthcare activities is uncertain. Likewise, a pack with the necessary items for minor surgery was a requirement in both arms of the trial, and can be assumed to be equivalent. The cost differences seen are likely to be primarily attributable to differences in allocation of staffing and overhead costs in primary and secondary care.

Based on patient satisfaction, and notwithstanding small differences in surgical quality, the authors believe it is necessary to continue providing most minor surgery in primary care. However, there are potentially worrying differences between primary care and hospital doctors in the treatment of malignancies which it may be unwise to dismiss as being due to chance. Hospital doctors send a higher proportion of skin lesions for pathological examination, and upon examination more malignant lesions are found to have been removed adequately in hospital. The difference is unlikely to be due to case-mix in the two study arms, which was very similar. In addition, using the outcome 'complete excision of malignancy', hospital minor surgery appears more effective and, acknowledging uncertainty about willingness to pay, the authors believe may be cost-effective.

Not all malignant lesions are clinically obvious at presentation, and some have potentially serious adverse outcomes if missed. In this study GPs missed one-third of malignancies, including both of the malignant melanomas. Coupled with the results of the trial it is clear that the major challenge of providing minor surgery in primary care is the potential for missed diagnosis of serious skin malignancies.

So why is this? The 1990 contract was based on the premise that doctors in practice were not using skills in minor surgery that they had acquired in medical school. However, changes in the content of medical school curricula, coupled with increased public expectations of certain procedures only being carried out by 'qualified' doctors, mean that in most UK medical schools minor surgery skills are no longer the province of the medical student nor, increasingly, of the junior doctor. The 1990 contract gave GPs a financial incentive to perform procedures, therefore, for which many of them had received little training. Perhaps it is the case that most treatment could be carried out in primary care, provided that GPs received further training in the diagnosis and management of skin lesions. A recently published trial shows that a dermatology service operated by two GPs with special interests gave results clinically indistinguishable from those obtained at a hospital outpatient clinic, although minor surgery did not form a part of the work

undertaken.[50] However, the general practice service was considerably more expensive than its hospital equivalent.[51]

Conclusions

Patients like the service in general practice and, while the quality of minor surgery in primary care is not as high as that in hospital, the difference is not large. However, there are possible differences between primary care and hospital doctors in the recognition and treatment of malignant lesions which mean that care needs to be taken in the development of primary care-based minor surgery. The incidence of skin malignancies is increasing, and a major limiting factor in refocusing minor surgical care into the hospital sector is limited capacity, both in terms of physical clinic and operating theatre space and in terms of medical and support staff to undertake the procedures.[52] Recently, it has been announced that more surgical services are to be moved into primary care, and similar issues will apply as do here.[53] Resolution of this dilemma is not a simple matter and will extend beyond the traditional testing of two alternative interventions. The solution in this case may be not to avoid primary care minor surgery, but to improve its quality.

Recommended research

Areas for further, future study include the following:

- Further work is required to determine GPs' management of a range of skin conditions (including potentially life-threatening malignancies), rather than just their recognition of them.
- Further economic modelling work is required to look at the potential costs of training sufficient numbers of GPs and GPs with special interests (GPSIs) to meet the demand for minor surgery safely in primary care, and of the alternative of transferring minor surgery large-scale to the hospital sector.
- A series of models of different service configurations should be tested to identify the optimum service specification. Given more capacity, one such model might include community provision of services by specialist dermatologists; this might prove a safe option which is also popular with the public. Such a service might not necessarily require treatment of all cases by the dermatologist concerned; diagnosis may suffice. Another might involve testing a system in which the submission of samples resected in primary care for histological examination was made mandatory (or at least encouraged).

Acknowledgements

This research was funded by the NHS R&D HTA Programme. The views expressed in this report are those of the authors and not necessarily those of the NHS R&D HTA Programme. Any errors are the responsibility of the authors.

Contribution of authors

Steve George (Reader in Public Health), John Primrose (Professor of Surgery), Helen Smith (Professor of Primary Care), Paul Little (Professor of Primary Care) and Adam Lowy (Epidemiologist) designed the study and obtained funding. Pete Pockney (Research Fellow), Helen Kinley (Researcher), SG, JP, HS and PL coordinated the trial on a day-to-day basis and collected data. HK developed the patient satisfaction questionnaire with help from PL, PP and SG. JP and Roger Kneebone (Senior Lecturer in Surgical Education) assessed the quality of outcome. SG, PP, JP, RK and AL carried out an initial analysis, and SG and PP a final analysis, of the trial data. The economic evaluation was undertaken by Chris McCabe (Professor of Heath Economics). PP, Nishmali Jayatilleke (medical student) and SG prepared the data for analysis of histology with help from Barbara Leppard (Consultant Dermatologist). PP and NJ analysed the histological data with help from SG. SG, PP and JP wrote the report with help from all authors.

References

1. Wall DW. Beware the pitfalls. *Physician* 1987;**6**: 71–2.
2. Brown JS. Minor operations in general practice. *BMJ* 1979;**i**:1609–10.
3. Jackson AD. Treatment of skin cancers in general practice. *Br J Gen Pract* 1991;**41**:213.
4. Menon NK. Minor surgery in general practice. *Practitioner* 1986;**230**:917–19.
5. Department of Health and the Welsh Office. *General practice in the National Health Service, the 1990 contract. The government's program for changes to general practitioners' terms and conditions of service and remunerative systems*. London: HMSO; 1989.
6. Coid DR. General practitioner minor surgery facilitated by a Fife District General Hospital. Evaluation of a pilot project. *Health Bull* (*Edinb*) 1990;**48**:132–6.
7. Coopers and Lybrand Associates. *The cost effectiveness of general practice. A general medical services discussion document*. London: British Medical Association; 1983.
8. Berry DP, Harding KG. Potential pitfalls of minor surgery in general practice. *Br J Gen Pract* 1993; **43**:358–9.
9. Chew CA, Black CN. Training for the new contract. *Br J Gen Pract* 1991;**41**:35–6.
10. Kneebone RL. Training general practitioners in minor surgery. *Br J Gen Pract* 1994;**44**:103–4.
11. Milne R. Minor surgery in general practice. *Br J Gen Pract* 1990;**40**:175–6.
12. Pringle M, Hasler J, De Marco P. Training for minor surgery in general practice during preregistration surgical posts. *BMJ* 1991; **302**:830–2.
13. Thompson AM, Park KG, Kelly DR, MacNamara I, Munro A. Training for minor surgery in general practice: is it adequate? *J R Coll Surg Edinb* 1997; **42**:89–91.
14. Brown PA, Kernohan NM, Smart LM, Savargaonkar P, Atkinson P, Robinson S, *et al*. Skin lesion removal: practice by general practitioners in Grampian Region before and after April 1990. *Scott Med J* 1992;**37**:144–6.
15. Lowy A, Brazier J, Fall M, Thomas K, Jones N, Williams BT. Minor surgery by general practitioners under the 1990 contract: effects on hospital workload. *BMJ* 1993;**307**:413–17.
16. Morrison JM, Murray TS. Survey of minor surgery in general practice in the west of Scotland. *Br J Surg* 1993;**80**:202–4.
17. Brazier J, Lowy A. Performance of skin biopsies by general practitioners. *BMJ* 1991;**303**:1472.
18. Bricknell MC. Skin biopsies of pigmented skin lesions performed by general practitioners and hospital specialists. *Br J Gen Pract* 1993;**43**: 199–201.
19. Bull AD, Silcocks PB, Start RD, Kennedy A. Performance of skin biopsies by general practitioners. *BMJ* 1991;**303**:1373.
20. Cox NH, Wagstaff R, Popple AW. Using clinicopathological analysis of general practitioner skin surgery to determine educational requirements and guidelines. *BMJ* 1992;**304**:93–6.
21. Cross P. Is histological examination of tissue removed by GPs always necessary? Even specialists get the clinical diagnosis wrong. *BMJ* 1998; **316**:778.
22. Khorshid SM, Pinney E, Bishop JA. Melanoma excision by general practitioners in north-east Thames region, England. *Br J Dermatol* 1998;**138**: 412–17.
23. Kirby B, Harrison P, Blewitt R. Is histological examination of tissue removed by GPs always necessary. More skin carcinomas might be detected with routine histological examination. *BMJ* 1998;**316**:779.
24. Lowy A, Willis D, Abrams K. Is histological examination of tissue removed by general practitioners always necessary? Before and after comparison of detection rates of serious skin lesions. *BMJ* 1997;**315**:406–8.
25. Lowy A, Abrams K, Willis D. Is histological examination of tissue removed by general practitioners always necessary? *BMJ* 1998;**316**:779.
26. McWilliam LJ, Knox F, Wilkinson N, Oogarah P. Performance of skin biopsies by general practitioners. *BMJ* 1991;**303**:1177–9.
27. Paraskevopoulos JA, Hosking SW, Johnson AG. Do all minor excised lesions require histological examination? Discussion paper. *J R Soc Med* 1988;**81**:583–4.
28. Suvarna SK, Shortland JR, Smith JH. Is histological examination of tissue removed by GPs always necessary? Over 10 days two important lesions were sent to histopathologists in Sheffield. *BMJ* 1998;**316**:778–9.

29. Leese B, Taylor C, Bosanquet N. *A stitch in time? Minor surgery in general practice*. York: University of York; 1995.

30. Makuch R, Simon R. Sample size requirements for evaluating a conservative therapy. *Cancer Treat Rep* 1978;**62**:1037–40.

31. Machin D, Campbell MJ, Fayers P, Pinol A. *Sample size tables for clinical studies*. 2nd ed. Oxford: Blackwell; 1997.

32. Gibbs S, Harvey I, Sterling J, Stark R. Local treatments for cutaneous warts: systematic review. *BMJ* 2002;**325**:461.

33. O'Cathain A, Brazier JE, Milner PC, Fall M. Cost effectiveness of minor surgery in general practice: a prospective comparison with hospital practice. *Br J Gen Pract* 1992;**42**:13–17.

34. Quinn JV, Wells GA. An assessment of clinical wound evaluation scales. *Acad Emerg Med* 1998; **5**:583–6.

35. Singer AJ, Church AL, Forrestal K, Werblud M, Valentine SM, Hollander JE. Comparison of patient satisfaction and practitioner satisfaction with wound appearance after traumatic wound repair. *Acad Emerg Med* 1997;**4**:133–7.

36. Singer AJ, Quinn JV, Thode HC Jr, Hollander JE. Determinants of poor outcome after laceration and surgical incision repair. *Plast Reconstr Surg* 2002;**110**:429–35.

37. Quinn J, Wells G, Sutcliffe T, Jarmuske M, Maw J, Stiell I, *et al*. Tissue adhesive versus suture wound repair at 1 year: randomized clinical trial correlating early, 3-month, and 1-year cosmetic outcome. *Ann Emerg Med* 1998;**32**:645–9.

38. Kinley H. The development of a questionnaire to measure patient satisfaction with the process and outcome of minor surgery. MSc project, University of Southampton; 2002. URL: http://www.som.soton.ac.uk/research/cancersciences/Research_Groups/Surgery/Kinley%20Thesis.pdf

39. Culyer A, NHS Research and Development Task Force. *Supporting research and development in the NHS*. London: HMSO; 1994.

40. Department of Health. *NHS reference costs 2005*. London: Department of Health; 2005. URL: http://www.dh.gov.uk/PolicyAndGuidance/OrganisationPolicy/FinanceAndPlanning/NHSReferenceCosts/fs/en

41. *Crystal Ball* [computer program]. Version 7.0. Denver, Colorado: Decisioneering; 2000.

42. Gold MR. *Cost-effectiveness in health and medicine*. New York: Oxford University Press; 1996.

43. National Institute for Clinical Excellence. *Guide to the methods of technology appraisal*. London: National Institute for Clinical Excellence; 2004. URL: http://www.nice.org.uk/pdf/TAP_Methods.pdf

44. Chaudhary MA, Stearns SC. Estimating confidence intervals for cost-effectiveness ratios: an example from a randomized trial. *Stat Med* 1996;**15**: 1447–58.

45. Efron B. *An introduction to the bootstrap*. New York: Chapman & Hall; 1993.

46. Briggs A, Fenn P. Confidence intervals or surfaces? Uncertainty on the cost-effectiveness plane. *Health Econ* 1998;**7**:723–40.

47. van Hout BA, Al MJ, Gordon GS, Rutten FF. Costs, effects and C/E-ratios alongside a clinical trial. *Health Econ* 1994;**3**:309–19.

48. Champion RH, Burton JL, Burns DA, Breathnach SM. *Rook/Wilkinson/Ebling textbook of dermatology*. 6th ed. Oxford: Blackwell Scientific; 1998.

49. Fleiss JL. *Measurement of inter-rater agreement. Statistical methods for rates and proportions*. 2nd ed. New York: Wiley; 1981.

50. Salisbury C, Noble A, Horrocks S, Crosby Z, Harrison V, Coast J, *et al*. Evaluation of a general practitioner with special interest service for dermatology: randomised controlled trial. *BMJ* 2005;**331**:1441–6.

51. Coast J, Noble S, Noble A, Horrocks S, Asim O, Peters TJ, *et al*. Economic evaluation of a general practitioner with special interests led dermatology service in primary care. *BMJ*;**331**: 1444–9.

52. Diffey BL. The future incidence of cutaneous melanoma within the UK. *Br J Dermatol* 2004; **151**:868–72.

53. Department of Health. *Our health, our care, our say: a new direction for community services*. London: Stationery Office; 2006.

Appendix 1

Wound assessment tool

Figure 6 is a photograph of the screen with which the assessors marked the photographs of the wounds. By clicking on the 'open photo' buttons above and to the right of each photograph, the operator could view a full-screen version of the picture. There were no details of either who the patient was or the trial arm of the patient anywhere in the database file sent to the assessors.

When marked, the program automatically returned a file with the scores to the trial office, where it was automatically inserted into the master database. There was no manual transcription of scores.

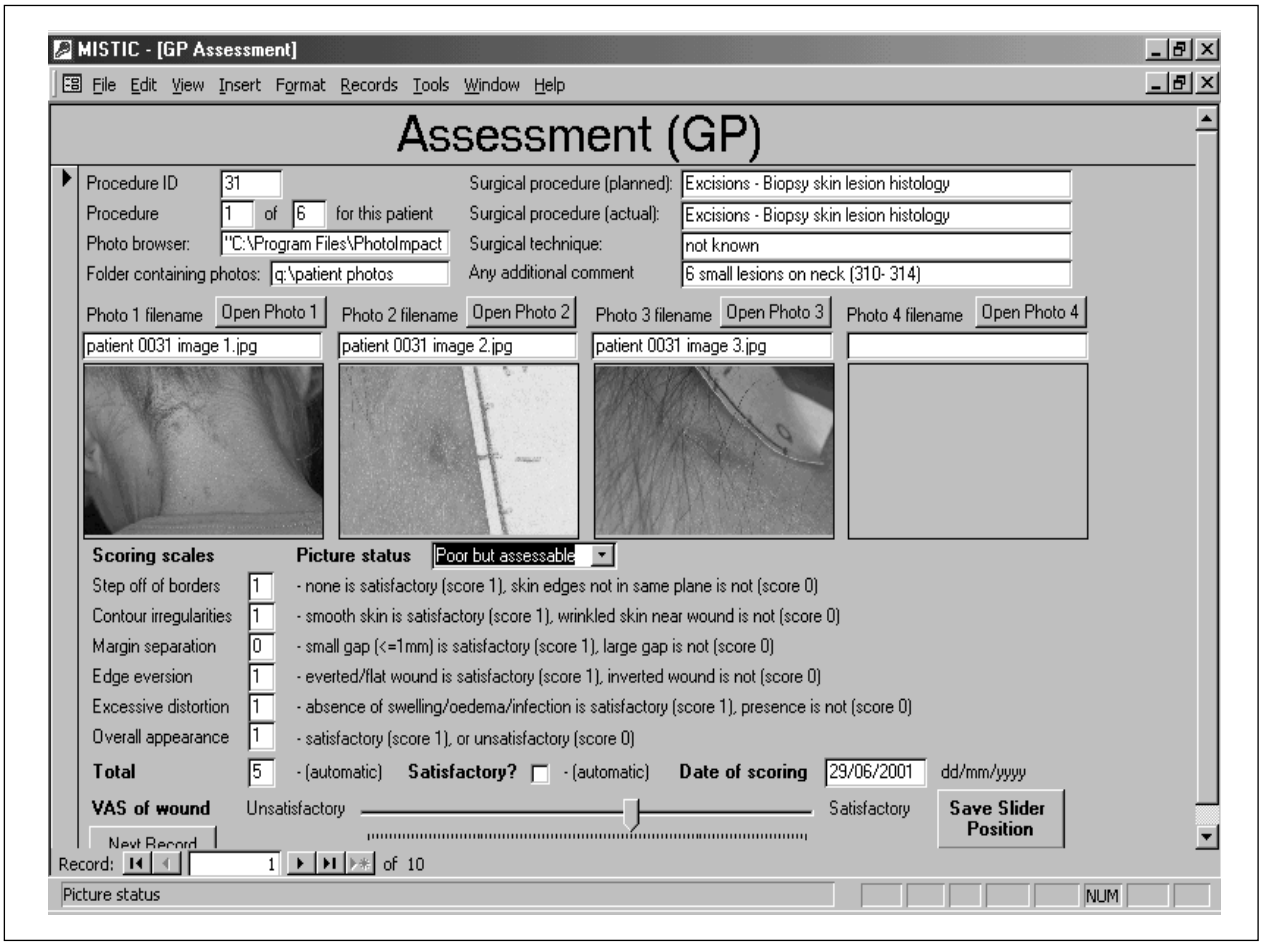


FIGURE 6 *Screenshot of wound assessment tool*

Appendix 2

Patient Satisfaction Questionnaire

Study No:
Site:
Date:

Minor Surgery Study – Patient Satisfaction Questionnaire

Thank you for agreeing to take part in our study of minor surgery. We would be interested to hear your experiences and what happened when you went to have your minor operation, why you had it done and what happened afterwards. Your answers will be treated as completely confidential.

Most of the questionnaire asks you to tick a box ☐ to indicate your degree of agreement with a statement.

For example, if you like to eat ice-cream you might strongly agree (or agree) with the following statement:

	Strongly agree	**Agree**	**Neutral**	**Disagree**	**Strongly disagree**
I like to eat ice-cream.	☐	☐	☐	☐	☐

On the other hand you may not like to eat ice-cream, in which case you may strongly disagree (or disagree) with the following statement.

	Strongly agree	**Agree**	**Neutral**	**Disagree**	**Strongly disagree**
I like to eat ice-cream.	☐	☐	☐	☐	☐

The neutral box means you neither agree nor disagree with the statement.

If you would like to, please feel free to add comments on the back of this form.

Thank you.

I had my minor operation because:

	Strongly agree	Agree	Neutral	Disagree	Strongly disagree
1. The problem needing the operation looked unsightly.	☐	☐	☐	☐	☐
2. The problem needing the operation was painful.	☐	☐	☐	☐	☐
3. The problem needing the operation was irritating me, for example by itching or rubbing on my clothes.	☐	☐	☐	☐	☐
4. I was worried that it might be something serious.	☐	☐	☐	☐	☐
5. My doctor advised me to have the operation.	☐	☐	☐	☐	☐

6. Other reason why I had it done: .....

I would now like to ask you what happened when you came for your minor operation.

	Strongly agree	Agree	Neutral	Disagree	Strongly disagree
7. I found it easy to get an appointment for the operation at a convenient time.	☐	☐	☐	☐	☐
8. When I arrived to have my operation I had a clear idea of what was going to happen.	☐	☐	☐	☐	☐
9. After I arrived for my operation I was able to wait in as much privacy as I would have liked.	☐	☐	☐	☐	☐
10. After I arrived for my operation I was able to wait in as much comfort as I would have liked.	☐	☐	☐	☐	☐
11. I felt I needed more time to discuss what to expect after the operation.	☐	☐	☐	☐	☐
12. The doctor doing the operation explained clearly what he was going to do.	☐	☐	☐	☐	☐
13. I had every confidence in the doctor doing the operation.	☐	☐	☐	☐	☐
14. The doctor doing my operation spent enough time with me and didn't hurry me.	☐	☐	☐	☐	☐
15. I experienced more pain than I expected during the operation.	☐	☐	☐	☐	☐
16. When I arrived for the operation I was not kept waiting very long to have it done.	☐	☐	☐	☐	☐
17. I felt the doctor was rushed during my operation.	☐	☐	☐	☐	☐
18. When I had my operation I felt I didn't have enough time with the doctor to discuss things and ask all the questions I wanted to.	☐	☐	☐	☐	☐
19. I felt I was treated with care and courtesy.	☐	☐	☐	☐	☐

And now I would like to ask you what happened after your minor operation.

	Strongly agree	Agree	Neutral	Disagree	Strongly disagree
20. After my operation I was told what to do if I had any problems (for example bleeding or soreness).	☐	☐	☐	☐	☐
21. I am satisfied with the way the wound looks now.	☐	☐	☐	☐	☐
22. Should the need arise I would be confident to undergo a similar operation in the future.	☐	☐	☐	☐	☐
23. I think it is important that patients having an operation have met the doctor doing it in the past.	☐	☐	☐	☐	☐
24. When I first discussed my operation with my doctor (GP) I was not aware that they were able to carry out this type of operation.	☐	☐	☐	☐	☐

25. Had you met the doctor doing the operation in the past?
    - ☐ No
    - ☐ Yes – details: .....
    - ☐ Not sure

26. Did you have to take time away from paid employment in order to have your operation?
    - ☐ No
    - ☐ Yes – details: .....
    - ☐ Not applicable

27. Did you take any time away from paid employment in the days following your operation?
    - ☐ No
    - ☐ Yes – number of days: .....
    - ☐ Not applicable

28. Approximately how far did you have to travel from home or work to the place where you had your operation?

    ..... miles

29. If you came by car did you have trouble parking?
    - ☐ No
    - ☐ Yes – details: .....
    - ☐ Not applicable (e.g. travelled by public transport)

30. When you arrived for your operation about how long were you kept waiting before you had it done?

    ..... hrs ..... mins

31. Altogether about how much time did you spend in travelling, waiting for your operation, having your operation and returning home?

    ..... hrs ..... mins

Did you experience any problems after your operation? (Please comment if appropriate).

[32]☐ wound infection
[33]☐ discomfort greater than I expected
[34]☐ bleeding
[35]☐ an allergy
[36]☐ something else, please explain: .....
[37]☐ none of these

38. Since the operation have you been in contact with your GP? (Please tick all that apply).
☐ No, not regarding the operation.
☐ Yes – for the results of the operation.
☐ Yes – I was concerned about my wound. Please specify: .....

Please could you tick a box to indicate whether you agree or disagree with the following statements.

	Strongly agree	**Agree**	**Neutral**	**Disagree**	**Strongly disagree**
39. I am reassured that there is nothing serious to worry about.	☐	☐	☐	☐	☐
40. I think my scar looks unsightly.	☐	☐	☐	☐	☐
41. In the week following the operation the wound was painful.	☐	☐	☐	☐	☐
42 The wound is irritating me, for example by itching or rubbing on my clothes.	☐	☐	☐	☐	☐
43. I am still worried it might have been something serious.	☐	☐	☐	☐	☐

44. The appearance of the wound now is:
☐ much better than I expected
☐ better than I expected
☐ about what I expected
☐ worse than I expected
☐ much worse than I expected
☐ not applicable (for example, unable to see it)

45. If you needed another similar minor operation in the future, would you prefer to have this carried out:
☐ In a local hospital by a hospital doctor?
☐ By your GP in his surgery?
☐ Don't mind, either?
☐ Not sure?

46. If a friend or relative asked your opinion about having a similar minor operation at the place where you have just had yours, would you recommend it to them?
☐ No
☐ Yes
☐ Not sure

Thank you for your time in filling out this questionnaire.

If you would like to add any other comments about your experience that you feel are important please feel free to do so on the back of this form.

Please return the questionnaire in the enclosed FREEPOST envelope.

Appendix 3

CONSORT statement for MiSTIC trial

Paper section and topic	Item	Description	Reported on page(s)
Title and Abstract	1	How participants were allocated to interventions	i, iii
Introduction	2	Scientific background and explanation of rationale	1, 2
Methods			
Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected	6
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered	6
Objectives	5	Specific objectives and hypotheses	3
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements	6–9
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules	6
Randomisation – sequence generation	8	Method used to generate the random allocation sequence, including details of any restriction	11
Randomisation – allocation concealment	9	Method used to implement the random allocation sequence, clarifying whether the sequence was concealed until interventions were assigned	11
Randomisation – implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups	11
Blinding (masking)	11	Whether or not participants, those administering the interventions and those assessing the outcomes were blinded to group assignment	8, 11–12
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); methods for additional analyses, such as subgroup analyses and adjusted analyses	8–9
Results	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol and analysed for the primary outcome. Describe protocol deviations from study as planned, together with reasons	11, 13
Participant flow			
Recruitment	14	Dates defining the periods of recruitment and follow-up	6
Baseline data	15	Baseline demographic and clinical characteristics of each group	13–16
Numbers analysed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by 'intention-to-treat'. State the results in absolute numbers	9, 13–16
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision	13–24
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those prespecified and those exploratory	NA
Adverse events	19	All important adverse events or side-effects in each intervention group	NA
Discussion			
Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes	25, 26
Generalisability	21	Generalisability (external validity) of the trial findings	25
Overall evidence	22	General interpretation of the results in the context of current evidence	25, 26

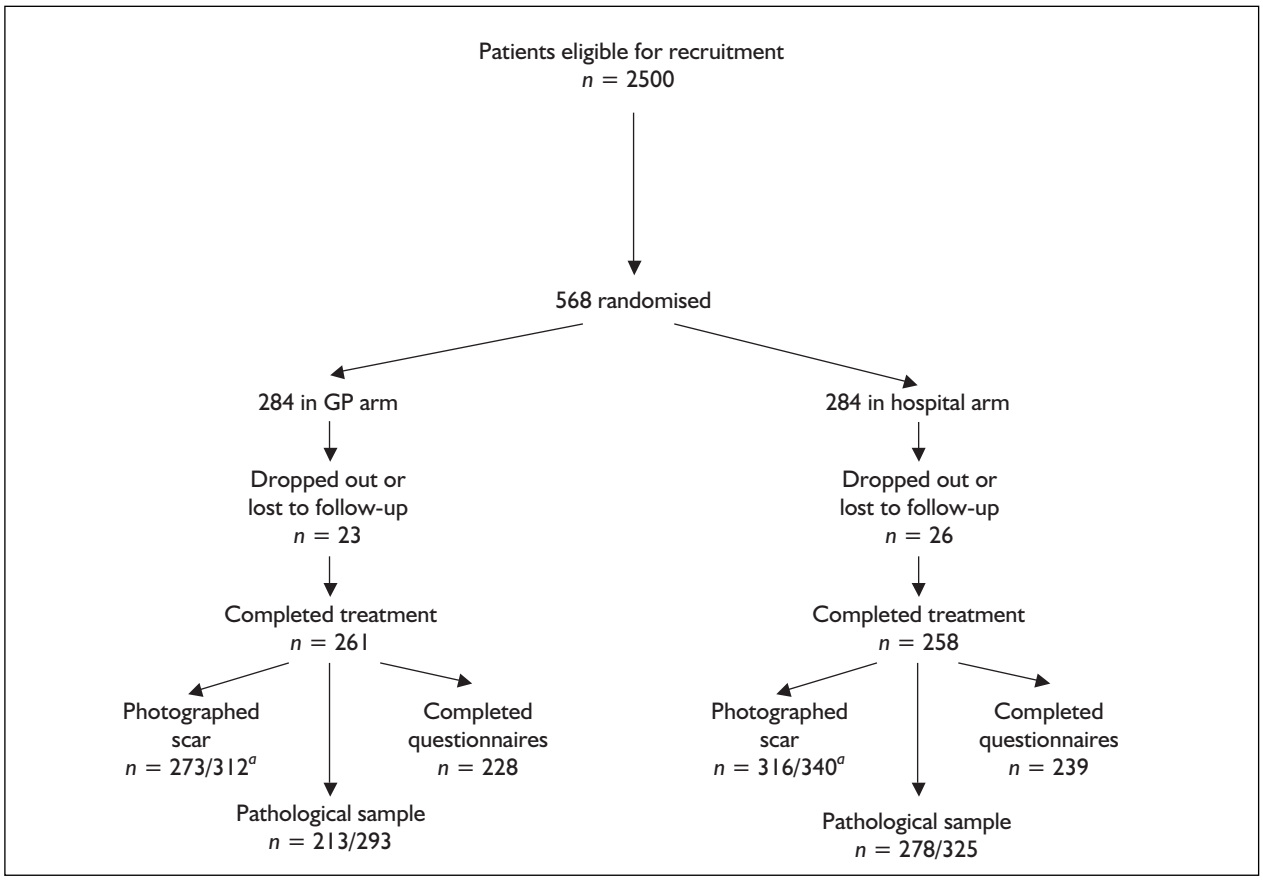


FIGURE 7 *Flow diagram for MiSTIC trial. ([a]Includes ingrowing toenails).*

Health Technology Assessment reports published to date

Volume 1, 1997

No. 1
Home parenteral nutrition: a systematic review.
By Richards DM, Deeks JJ, Sheldon TA, Shaffer JL.

No. 2
Diagnosis, management and screening of early localised prostate cancer.
A review by Selley S, Donovan J, Faulkner A, Coast J, Gillatt D.

No. 3
The diagnosis, management, treatment and costs of prostate cancer in England and Wales.
A review by Chamberlain J, Melia J, Moss S, Brown J.

No. 4
Screening for fragile X syndrome.
A review by Murray J, Cuckle H, Taylor G, Hewison J.

No. 5
A review of near patient testing in primary care.
By Hobbs FDR, Delaney BC, Fitzmaurice DA, Wilson S, Hyde CJ, Thorpe GH, *et al*.

No. 6
Systematic review of outpatient services for chronic pain control.
By McQuay HJ, Moore RA, Eccleston C, Morley S, de C Williams AC.

No. 7
Neonatal screening for inborn errors of metabolism: cost, yield and outcome.
A review by Pollitt RJ, Green A, McCabe CJ, Booth A, Cooper NJ, Leonard JV, *et al*.

No. 8
Preschool vision screening.
A review by Snowdon SK, Stewart-Brown SL.

No. 9
Implications of socio-cultural contexts for the ethics of clinical trials.
A review by Ashcroft RE, Chadwick DW, Clark SRL, Edwards RHT, Frith L, Hutton JL.

No. 10
A critical review of the role of neonatal hearing screening in the detection of congenital hearing impairment.
By Davis A, Bamford J, Wilson I, Ramkalawan T, Forshaw M, Wright S.

No. 11
Newborn screening for inborn errors of metabolism: a systematic review.
By Seymour CA, Thomason MJ, Chalmers RA, Addison GM, Bain MD, Cockburn F, *et al*.

No. 12
Routine preoperative testing: a systematic review of the evidence.
By Munro J, Booth A, Nicholl J.

No. 13
Systematic review of the effectiveness of laxatives in the elderly.
By Petticrew M, Watt I, Sheldon T.

No. 14
When and how to assess fast-changing technologies: a comparative study of medical applications of four generic technologies.
A review by Mowatt G, Bower DJ, Brebner JA, Cairns JA, Grant AM, McKee L.

Volume 2, 1998

No. 1
Antenatal screening for Down's syndrome.
A review by Wald NJ, Kennard A, Hackshaw A, McGuire A.

No. 2
Screening for ovarian cancer: a systematic review.
By Bell R, Petticrew M, Luengo S, Sheldon TA.

No. 3
Consensus development methods, and their use in clinical guideline development.
A review by Murphy MK, Black NA, Lamping DL, McKee CM, Sanderson CFB, Askham J, *et al*.

No. 4
A cost–utility analysis of interferon beta for multiple sclerosis.
By Parkin D, McNamee P, Jacoby A, Miller P, Thomas S, Bates D.

No. 5
Effectiveness and efficiency of methods of dialysis therapy for end-stage renal disease: systematic reviews.
By MacLeod A, Grant A, Donaldson C, Khan I, Campbell M, Daly C, *et al*.

No. 6
Effectiveness of hip prostheses in primary total hip replacement: a critical review of evidence and an economic model.
By Faulkner A, Kennedy LG, Baxter K, Donovan J, Wilkinson M, Bevan G.

No. 7
Antimicrobial prophylaxis in colorectal surgery: a systematic review of randomised controlled trials.
By Song F, Glenny AM.

No. 8
Bone marrow and peripheral blood stem cell transplantation for malignancy.
A review by Johnson PWM, Simnett SJ, Sweetenham JW, Morgan GJ, Stewart LA.

No. 9
Screening for speech and language delay: a systematic review of the literature.
By Law J, Boyle J, Harris F, Harkness A, Nye C.

No. 10
Resource allocation for chronic stable angina: a systematic review of effectiveness, costs and cost-effectiveness of alternative interventions.
By Sculpher MJ, Petticrew M, Kelland JL, Elliott RA, Holdright DR, Buxton MJ.

No. 11
Detection, adherence and control of hypertension for the prevention of stroke: a systematic review.
By Ebrahim S.

No. 12
Postoperative analgesia and vomiting, with special reference to day-case surgery: a systematic review.
By McQuay HJ, Moore RA.

No. 13
Choosing between randomised and nonrandomised studies: a systematic review.
By Britton A, McKee M, Black N, McPherson K, Sanderson C, Bain C.

No. 14
Evaluating patient-based outcome measures for use in clinical trials.
A review by Fitzpatrick R, Davey C, Buxton MJ, Jones DR.

No. 15
Ethical issues in the design and conduct of randomised controlled trials.
A review by Edwards SJL, Lilford RJ, Braunholtz DA, Jackson JC, Hewison J, Thornton J.

No. 16
Qualitative research methods in health technology assessment: a review of the literature.
By Murphy E, Dingwall R, Greatbatch D, Parker S, Watson P.

No. 17
The costs and benefits of paramedic skills in pre-hospital trauma care.
By Nicholl J, Hughes S, Dixon S, Turner J, Yates D.

No. 18
Systematic review of endoscopic ultrasound in gastro-oesophageal cancer.
By Harris KM, Kelly S, Berry E, Hutton J, Roderick P, Cullingworth J, *et al*.

No. 19
Systematic reviews of trials and other studies.
By Sutton AJ, Abrams KR, Jones DR, Sheldon TA, Song F.

No. 20
Primary total hip replacement surgery: a systematic review of outcomes and modelling of cost-effectiveness associated with different prostheses.
A review by Fitzpatrick R, Shortall E, Sculpher M, Murray D, Morris R, Lodge M, *et al*.

Volume 3, 1999

No. 1
Informed decision making: an annotated bibliography and systematic review.
By Bekker H, Thornton JG, Airey CM, Connelly JB, Hewison J, Robinson MB, *et al*.

No. 2
Handling uncertainty when performing economic evaluation of healthcare interventions.
A review by Briggs AH, Gray AM.

No. 3
The role of expectancies in the placebo effect and their use in the delivery of health care: a systematic review.
By Crow R, Gage H, Hampson S, Hart J, Kimber A, Thomas H.

No. 4
A randomised controlled trial of different approaches to universal antenatal HIV testing: uptake and acceptability. Annex: Antenatal HIV testing – assessment of a routine voluntary approach.
By Simpson WM, Johnstone FD, Boyd FM, Goldberg DJ, Hart GJ, Gormley SM, *et al*.

No. 5
Methods for evaluating area-wide and organisation-based interventions in health and health care: a systematic review.
By Ukoumunne OC, Gulliford MC, Chinn S, Sterne JAC, Burney PGJ.

No. 6
Assessing the costs of healthcare technologies in clinical trials.
A review by Johnston K, Buxton MJ, Jones DR, Fitzpatrick R.

No. 7
Cooperatives and their primary care emergency centres: organisation and impact.
By Hallam L, Henthorne K.

No. 8
Screening for cystic fibrosis.
A review by Murray J, Cuckle H, Taylor G, Littlewood J, Hewison J.

No. 9
A review of the use of health status measures in economic evaluation.
By Brazier J, Deverill M, Green C, Harper R, Booth A.

No. 10
Methods for the analysis of quality-of-life and survival data in health technology assessment.
A review by Billingham LJ, Abrams KR, Jones DR.

No. 11
Antenatal and neonatal haemoglobinopathy screening in the UK: review and economic analysis.
By Zeuner D, Ades AE, Karnon J, Brown J, Dezateux C, Anionwu EN.

No. 12
Assessing the quality of reports of randomised trials: implications for the conduct of meta-analyses.
A review by Moher D, Cook DJ, Jadad AR, Tugwell P, Moher M, Jones A, *et al*.

No. 13
'Early warning systems' for identifying new healthcare technologies.
By Robert G, Stevens A, Gabbay J.

No. 14
A systematic review of the role of human papillomavirus testing within a cervical screening programme.
By Cuzick J, Sasieni P, Davies P, Adams J, Normand C, Frater A, *et al*.

No. 15
Near patient testing in diabetes clinics: appraising the costs and outcomes.
By Grieve R, Beech R, Vincent J, Mazurkiewicz J.

No. 16
Positron emission tomography: establishing priorities for health technology assessment.
A review by Robert G, Milne R.

No. 17 (Pt 1)
The debridement of chronic wounds: a systematic review.
By Bradley M, Cullum N, Sheldon T.

No. 17 (Pt 2)
Systematic reviews of wound care management: (2) Dressings and topical agents used in the healing of chronic wounds.
By Bradley M, Cullum N, Nelson EA, Petticrew M, Sheldon T, Torgerson D.

No. 18
A systematic literature review of spiral and electron beam computed tomography: with particular reference to clinical applications in hepatic lesions, pulmonary embolus and coronary artery disease.
By Berry E, Kelly S, Hutton J, Harris KM, Roderick P, Boyce JC, *et al*.

No. 19
What role for statins? A review and economic model.
By Ebrahim S, Davey Smith G, McCabe C, Payne N, Pickin M, Sheldon TA, *et al*.

No. 20
Factors that limit the quality, number and progress of randomised controlled trials.
A review by Prescott RJ, Counsell CE, Gillespie WJ, Grant AM, Russell IT, Kiauka S, *et al*.

No. 21
Antimicrobial prophylaxis in total hip replacement: a systematic review.
By Glenny AM, Song F.

No. 22
Health promoting schools and health promotion in schools: two systematic reviews.
By Lister-Sharp D, Chapman S, Stewart-Brown S, Sowden A.

No. 23
Economic evaluation of a primary care-based education programme for patients with osteoarthritis of the knee.
A review by Lord J, Victor C, Littlejohns P, Ross FM, Axford JS.

Volume 4, 2000

No. 1
The estimation of marginal time preference in a UK-wide sample (TEMPUS) project.
A review by Cairns JA, van der Pol MM.

No. 2
Geriatric rehabilitation following fractures in older people: a systematic review.
By Cameron I, Crotty M, Currie C, Finnegan T, Gillespie L, Gillespie W, *et al*.

No. 3
Screening for sickle cell disease and thalassaemia: a systematic review with supplementary research.
By Davies SC, Cronin E, Gill M, Greengross P, Hickman M, Normand C.

No. 4
Community provision of hearing aids and related audiology services.
A review by Reeves DJ, Alborz A, Hickson FS, Bamford JM.

No. 5
False-negative results in screening programmes: systematic review of impact and implications.
By Petticrew MP, Sowden AJ, Lister-Sharp D, Wright K.

No. 6
Costs and benefits of community postnatal support workers: a randomised controlled trial.
By Morrell CJ, Spiby H, Stewart P, Walters S, Morgan A.

No. 7
Implantable contraceptives (subdermal implants and hormonally impregnated intrauterine systems) versus other forms of reversible contraceptives: two systematic reviews to assess relative effectiveness, acceptability, tolerability and cost-effectiveness.
By French RS, Cowan FM, Mansour DJA, Morris S, Procter T, Hughes D, *et al*.

No. 8
An introduction to statistical methods for health technology assessment.
A review by White SJ, Ashby D, Brown PJ.

No. 9
Disease-modifying drugs for multiple sclerosis: a rapid and systematic review.
By Clegg A, Bryant J, Milne R.

No. 10
Publication and related biases.
A review by Song F, Eastwood AJ, Gilbody S, Duley L, Sutton AJ.

No. 11
Cost and outcome implications of the organisation of vascular services.
By Michaels J, Brazier J, Palfreyman S, Shackley P, Slack R.

No. 12
Monitoring blood glucose control in diabetes mellitus: a systematic review.
By Coster S, Gulliford MC, Seed PT, Powrie JK, Swaminathan R.

No. 13
The effectiveness of domiciliary health visiting: a systematic review of international studies and a selective review of the British literature.
By Elkan R, Kendrick D, Hewitt M, Robinson JJA, Tolley K, Blair M, *et al*.

No. 14
The determinants of screening uptake and interventions for increasing uptake: a systematic review.
By Jepson R, Clegg A, Forbes C, Lewis R, Sowden A, Kleijnen J.

No. 15
The effectiveness and cost-effectiveness of prophylactic removal of wisdom teeth.
A rapid review by Song F, O'Meara S, Wilson P, Golder S, Kleijnen J.

No. 16
Ultrasound screening in pregnancy: a systematic review of the clinical effectiveness, cost-effectiveness and women's views.
By Bricker L, Garcia J, Henderson J, Mugford M, Neilson J, Roberts T, *et al*.

No. 17
A rapid and systematic review of the effectiveness and cost-effectiveness of the taxanes used in the treatment of advanced breast and ovarian cancer.
By Lister-Sharp D, McDonagh MS, Khan KS, Kleijnen J.

No. 18
Liquid-based cytology in cervical screening: a rapid and systematic review.
By Payne N, Chilcott J, McGoogan E.

No. 19
Randomised controlled trial of non-directive counselling, cognitive–behaviour therapy and usual general practitioner care in the management of depression as well as mixed anxiety and depression in primary care.
By King M, Sibbald B, Ward E, Bower P, Lloyd M, Gabbay M, *et al*.

No. 20
Routine referral for radiography of patients presenting with low back pain: is patients' outcome influenced by GPs' referral for plain radiography?
By Kerry S, Hilton S, Patel S, Dundas D, Rink E, Lord J.

No. 21
Systematic reviews of wound care management: (3) antimicrobial agents for chronic wounds; (4) diabetic foot ulceration.
By O'Meara S, Cullum N, Majid M, Sheldon T.

No. 22
Using routine data to complement and enhance the results of randomised controlled trials.
By Lewsey JD, Leyland AH, Murray GD, Boddy FA.

No. 23
Coronary artery stents in the treatment of ischaemic heart disease: a rapid and systematic review.
By Meads C, Cummins C, Jolly K, Stevens A, Burls A, Hyde C.

No. 24
Outcome measures for adult critical care: a systematic review.
By Hayes JA, Black NA, Jenkinson C, Young JD, Rowan KM, Daly K, *et al*.

No. 25
A systematic review to evaluate the effectiveness of interventions to promote the initiation of breastfeeding.
By Fairbank L, O'Meara S, Renfrew MJ, Woolridge M, Sowden AJ, Lister-Sharp D.

No. 26
Implantable cardioverter defibrillators: arrhythmias. A rapid and systematic review.
By Parkes J, Bryant J, Milne R.

No. 27
Treatments for fatigue in multiple sclerosis: a rapid and systematic review.
By Brañas P, Jordan R, Fry-Smith A, Burls A, Hyde C.

No. 28
Early asthma prophylaxis, natural history, skeletal development and economy (EASE): a pilot randomised controlled trial.
By Baxter-Jones ADG, Helms PJ, Russell G, Grant A, Ross S, Cairns JA, *et al*.

No. 29
Screening for hypercholesterolaemia versus case finding for familial hypercholesterolaemia: a systematic review and cost-effectiveness analysis.
By Marks D, Wonderling D, Thorogood M, Lambert H, Humphries SE, Neil HAW.

No. 30
A rapid and systematic review of the clinical effectiveness and cost-effectiveness of glycoprotein IIb/IIIa antagonists in the medical management of unstable angina.
By McDonagh MS, Bachmann LM, Golder S, Kleijnen J, ter Riet G.

No. 31
A randomised controlled trial of prehospital intravenous fluid replacement therapy in serious trauma.
By Turner J, Nicholl J, Webber L, Cox H, Dixon S, Yates D.

No. 32
Intrathecal pumps for giving opioids in chronic pain: a systematic review.
By Williams JE, Louw G, Towlerton G.

No. 33
Combination therapy (interferon alfa and ribavirin) in the treatment of chronic hepatitis C: a rapid and systematic review.
By Shepherd J, Waugh N, Hewitson P.

No. 34
A systematic review of comparisons of effect sizes derived from randomised and non-randomised studies.
By MacLehose RR, Reeves BC, Harvey IM, Sheldon TA, Russell IT, Black AMS.

No. 35
Intravascular ultrasound-guided interventions in coronary artery disease: a systematic literature review, with decision-analytic modelling, of outcomes and cost-effectiveness.
By Berry E, Kelly S, Hutton J, Lindsay HSJ, Blaxill JM, Evans JA, *et al*.

No. 36
A randomised controlled trial to evaluate the effectiveness and cost-effectiveness of counselling patients with chronic depression.
By Simpson S, Corney R, Fitzgerald P, Beecham J.

No. 37
Systematic review of treatments for atopic eczema.
By Hoare C, Li Wan Po A, Williams H.

No. 38
Bayesian methods in health technology assessment: a review.
By Spiegelhalter DJ, Myles JP, Jones DR, Abrams KR.

No. 39
The management of dyspepsia: a systematic review.
By Delaney B, Moayyedi P, Deeks J, Innes M, Soo S, Barton P, *et al*.

No. 40
A systematic review of treatments for severe psoriasis.
By Griffiths CEM, Clark CM, Chalmers RJG, Li Wan Po A, Williams HC.

Volume 5, 2001

No. 1
Clinical and cost-effectiveness of donepezil, rivastigmine and galantamine for Alzheimer's disease: a rapid and systematic review.
By Clegg A, Bryant J, Nicholson T, McIntyre L, De Broe S, Gerard K, *et al*.

No. 2
The clinical effectiveness and cost-effectiveness of riluzole for motor neurone disease: a rapid and systematic review.
By Stewart A, Sandercock J, Bryan S, Hyde C, Barton PM, Fry-Smith A, *et al*.

No. 3
Equity and the economic evaluation of healthcare.
By Sassi F, Archard L, Le Grand J.

No. 4
Quality-of-life measures in chronic diseases of childhood.
By Eiser C, Morse R.

No. 5
Eliciting public preferences for healthcare: a systematic review of techniques.
By Ryan M, Scott DA, Reeves C, Bate A, van Teijlingen ER, Russell EM, *et al*.

No. 6
General health status measures for people with cognitive impairment: learning disability and acquired brain injury.
By Riemsma RP, Forbes CA, Glanville JM, Eastwood AJ, Kleijnen J.

No. 7
An assessment of screening strategies for fragile X syndrome in the UK.
By Pembrey ME, Barnicoat AJ, Carmichael B, Bobrow M, Turner G.

No. 8
Issues in methodological research: perspectives from researchers and commissioners.
By Lilford RJ, Richardson A, Stevens A, Fitzpatrick R, Edwards S, Rock F, *et al*.

No. 9
Systematic reviews of wound care management: (5) beds; (6) compression; (7) laser therapy, therapeutic ultrasound, electrotherapy and electromagnetic therapy.
By Cullum N, Nelson EA, Flemming K, Sheldon T.

No. 10
Effects of educational and psychosocial interventions for adolescents with diabetes mellitus: a systematic review.
By Hampson SE, Skinner TC, Hart J, Storey L, Gage H, Foxcroft D, *et al*.

No. 11
Effectiveness of autologous chondrocyte transplantation for hyaline cartilage defects in knees: a rapid and systematic review.
By Jobanputra P, Parry D, Fry-Smith A, Burls A.

No. 12
Statistical assessment of the learning curves of health technologies.
By Ramsay CR, Grant AM, Wallace SA, Garthwaite PH, Monk AF, Russell IT.

No. 13
The effectiveness and cost-effectiveness of temozolomide for the treatment of recurrent malignant glioma: a rapid and systematic review.
By Dinnes J, Cave C, Huang S, Major K, Milne R.

No. 14
A rapid and systematic review of the clinical effectiveness and cost-effectiveness of debriding agents in treating surgical wounds healing by secondary intention.
By Lewis R, Whiting P, ter Riet G, O'Meara S, Glanville J.

No. 15
Home treatment for mental health problems: a systematic review.
By Burns T, Knapp M, Catty J, Healey A, Henderson J, Watt H, *et al*.

No. 16
How to develop cost-conscious guidelines.
By Eccles M, Mason J.

No. 17
The role of specialist nurses in multiple sclerosis: a rapid and systematic review.
By De Broe S, Christopher F, Waugh N.

No. 18
A rapid and systematic review of the clinical effectiveness and cost-effectiveness of orlistat in the management of obesity.
By O'Meara S, Riemsma R, Shirran L, Mather L, ter Riet G.

No. 19
The clinical effectiveness and cost-effectiveness of pioglitazone for type 2 diabetes mellitus: a rapid and systematic review.
By Chilcott J, Wight J, Lloyd Jones M, Tappenden P.

No. 20
Extended scope of nursing practice: a multicentre randomised controlled trial of appropriately trained nurses and preregistration house officers in pre-operative assessment in elective general surgery.
By Kinley H, Czoski-Murray C, George S, McCabe C, Primrose J, Reilly C, *et al*.

No. 21
Systematic reviews of the effectiveness of day care for people with severe mental disorders: (1) Acute day hospital versus admission; (2) Vocational rehabilitation; (3) Day hospital versus outpatient care.
By Marshall M, Crowther R, Almaraz-Serrano A, Creed F, Sledge W, Kluiter H, *et al*.

No. 22
The measurement and monitoring of surgical adverse events.
By Bruce J, Russell EM, Mollison J, Krukowski ZH.

No. 23
Action research: a systematic review and guidance for assessment.
By Waterman H, Tillen D, Dickson R, de Koning K.

No. 24
A rapid and systematic review of the clinical effectiveness and cost-effectiveness of gemcitabine for the treatment of pancreatic cancer.
By Ward S, Morris E, Bansback N, Calvert N, Crellin A, Forman D, *et al*.

No. 25
A rapid and systematic review of the evidence for the clinical effectiveness and cost-effectiveness of irinotecan, oxaliplatin and raltitrexed for the treatment of advanced colorectal cancer.
By Lloyd Jones M, Hummel S, Bansback N, Orr B, Seymour M.

No. 26
Comparison of the effectiveness of inhaler devices in asthma and chronic obstructive airways disease: a systematic review of the literature.
By Brocklebank D, Ram F, Wright J, Barry P, Cates C, Davies L, *et al*.

No. 27
The cost-effectiveness of magnetic resonance imaging for investigation of the knee joint.
By Bryan S, Weatherburn G, Bungay H, Hatrick C, Salas C, Parry D, *et al*.

No. 28
A rapid and systematic review of the clinical effectiveness and cost-effectiveness of topotecan for ovarian cancer.
By Forbes C, Shirran L, Bagnall A-M, Duffy S, ter Riet G.

No. 29
Superseded by a report published in a later volume.

No. 30
The role of radiography in primary care patients with low back pain of at least 6 weeks duration: a randomised (unblinded) controlled trial.
By Kendrick D, Fielding K, Bentley E, Miller P, Kerslake R, Pringle M.

No. 31
Design and use of questionnaires: a review of best practice applicable to surveys of health service staff and patients.
By McColl E, Jacoby A, Thomas L, Soutter J, Bamford C, Steen N, *et al*.

No. 32
A rapid and systematic review of the clinical effectiveness and cost-effectiveness of paclitaxel, docetaxel, gemcitabine and vinorelbine in non-small-cell lung cancer.
By Clegg A, Scott DA, Sidhu M, Hewitson P, Waugh N.

No. 33
Subgroup analyses in randomised controlled trials: quantifying the risks of false-positives and false-negatives.
By Brookes ST, Whitley E, Peters TJ, Mulheran PA, Egger M, Davey Smith G.

No. 34
Depot antipsychotic medication in the treatment of patients with schizophrenia: (1) Meta-review; (2) Patient and nurse attitudes.
By David AS, Adams C.

No. 35
A systematic review of controlled trials of the effectiveness and cost-effectiveness of brief psychological treatments for depression.
By Churchill R, Hunot V, Corney R, Knapp M, McGuire H, Tylee A, *et al*.

No. 36
Cost analysis of child health surveillance.
By Sanderson D, Wright D, Acton C, Duree D.

Volume 6, 2002

No. 1
A study of the methods used to select review criteria for clinical audit.
By Hearnshaw H, Harker R, Cheater F, Baker R, Grimshaw G.

No. 2
Fludarabine as second-line therapy for B cell chronic lymphocytic leukaemia: a technology assessment.
By Hyde C, Wake B, Bryan S, Barton P, Fry-Smith A, Davenport C, *et al*.

No. 3
Rituximab as third-line treatment for refractory or recurrent Stage III or IV follicular non-Hodgkin's lymphoma: a systematic review and economic evaluation.
By Wake B, Hyde C, Bryan S, Barton P, Song F, Fry-Smith A, *et al*.

No. 4
A systematic review of discharge arrangements for older people.
By Parker SG, Peet SM, McPherson A, Cannaby AM, Baker R, Wilson A, *et al*.

No. 5
The clinical effectiveness and cost-effectiveness of inhaler devices used in the routine management of chronic asthma in older children: a systematic review and economic evaluation.
By Peters J, Stevenson M, Beverley C, Lim J, Smith S.

No. 6
The clinical effectiveness and cost-effectiveness of sibutramine in the management of obesity: a technology assessment.
By O'Meara S, Riemsma R, Shirran L, Mather L, ter Riet G.

No. 7
The cost-effectiveness of magnetic resonance angiography for carotid artery stenosis and peripheral vascular disease: a systematic review.
By Berry E, Kelly S, Westwood ME, Davies LM, Gough MJ, Bamford JM, *et al*.

No. 8
Promoting physical activity in South Asian Muslim women through 'exercise on prescription'.
By Carroll B, Ali N, Azam N.

No. 9
Zanamivir for the treatment of influenza in adults: a systematic review and economic evaluation.
By Burls A, Clark W, Stewart T, Preston C, Bryan S, Jefferson T, *et al*.

No. 10
A review of the natural history and epidemiology of multiple sclerosis: implications for resource allocation and health economic models.
By Richards RG, Sampson FC, Beard SM, Tappenden P.

No. 11
Screening for gestational diabetes: a systematic review and economic evaluation.
By Scott DA, Loveman E, McIntyre L, Waugh N.

No. 12
The clinical effectiveness and cost-effectiveness of surgery for people with morbid obesity: a systematic review and economic evaluation.
By Clegg AJ, Colquitt J, Sidhu MK, Royle P, Loveman E, Walker A.

No. 13
The clinical effectiveness of trastuzumab for breast cancer: a systematic review.
By Lewis R, Bagnall A-M, Forbes C, Shirran E, Duffy S, Kleijnen J, *et al*.

No. 14
The clinical effectiveness and cost-effectiveness of vinorelbine for breast cancer: a systematic review and economic evaluation.
By Lewis R, Bagnall A-M, King S, Woolacott N, Forbes C, Shirran L, *et al*.

No. 15
A systematic review of the effectiveness and cost-effectiveness of metal-on-metal hip resurfacing arthroplasty for treatment of hip disease.
By Vale L, Wyness L, McCormack K, McKenzie L, Brazzelli M, Stearns SC.

No. 16
The clinical effectiveness and cost-effectiveness of bupropion and nicotine replacement therapy for smoking cessation: a systematic review and economic evaluation.
By Woolacott NF, Jones L, Forbes CA, Mather LC, Sowden AJ, Song FJ, *et al*.

No. 17
A systematic review of effectiveness and economic evaluation of new drug treatments for juvenile idiopathic arthritis: etanercept.
By Cummins C, Connock M, Fry-Smith A, Burls A.

No. 18
Clinical effectiveness and cost-effectiveness of growth hormone in children: a systematic review and economic evaluation.
By Bryant J, Cave C, Mihaylova B, Chase D, McIntyre L, Gerard K, *et al*.

No. 19
Clinical effectiveness and cost-effectiveness of growth hormone in adults in relation to impact on quality of life: a systematic review and economic evaluation.
By Bryant J, Loveman E, Chase D, Mihaylova B, Cave C, Gerard K, *et al*.

No. 20
Clinical medication review by a pharmacist of patients on repeat prescriptions in general practice: a randomised controlled trial.
By Zermansky AG, Petty DR, Raynor DK, Lowe CJ, Freementle N, Vail A.

No. 21
The effectiveness of infliximab and etanercept for the treatment of rheumatoid arthritis: a systematic review and economic evaluation.
By Jobanputra P, Barton P, Bryan S, Burls A.

No. 22
A systematic review and economic evaluation of computerised cognitive behaviour therapy for depression and anxiety.
By Kaltenthaler E, Shackley P, Stevens K, Beverley C, Parry G, Chilcott J.

No. 23
A systematic review and economic evaluation of pegylated liposomal doxorubicin hydrochloride for ovarian cancer.
By Forbes C, Wilby J, Richardson G, Sculpher M, Mather L, Reimsma R.

No. 24
A systematic review of the effectiveness of interventions based on a stages-of-change approach to promote individual behaviour change.
By Riemsma RP, Pattenden J, Bridle C, Sowden AJ, Mather L, Watt IS, *et al*.

No. 25
A systematic review update of the clinical effectiveness and cost-effectiveness of glycoprotein IIb/IIIa antagonists.
By Robinson M, Ginnelly L, Sculpher M, Jones L, Riemsma R, Palmer S, *et al*.

No. 26
A systematic review of the effectiveness, cost-effectiveness and barriers to implementation of thrombolytic and neuroprotective therapy for acute ischaemic stroke in the NHS.
By Sandercock P, Berge E, Dennis M, Forbes J, Hand P, Kwan J, *et al*.

No. 27
A randomised controlled crossover trial of nurse practitioner versus doctor-led outpatient care in a bronchiectasis clinic.
By Caine N, Sharples LD, Hollingworth W, French J, Keogan M, Exley A, *et al*.

No. 28
Clinical effectiveness and cost – consequences of selective serotonin reuptake inhibitors in the treatment of sex offenders.
By Adi Y, Ashcroft D, Browne K, Beech A, Fry-Smith A, Hyde C.

No. 29
Treatment of established osteoporosis: a systematic review and cost–utility analysis.
By Kanis JA, Brazier JE, Stevenson M, Calvert NW, Lloyd Jones M.

No. 30
Which anaesthetic agents are cost-effective in day surgery? Literature review, national survey of practice and randomised controlled trial.
By Elliott RA Payne K, Moore JK, Davies LM, Harper NJN, St Leger AS, *et al*.

No. 31
Screening for hepatitis C among injecting drug users and in genitourinary medicine clinics: systematic reviews of effectiveness, modelling study and national survey of current practice.
By Stein K, Dalziel K, Walker A, McIntyre L, Jenkins B, Horne J, *et al*.

No. 32
The measurement of satisfaction with healthcare: implications for practice from a systematic review of the literature.
By Crow R, Gage H, Hampson S, Hart J, Kimber A, Storey L, *et al*.

No. 33
The effectiveness and cost-effectiveness of imatinib in chronic myeloid leukaemia: a systematic review.
By Garside R, Round A, Dalziel K, Stein K, Royle R.

No. 34
A comparative study of hypertonic saline, daily and alternate-day rhDNase in children with cystic fibrosis.
By Suri R, Wallis C, Bush A, Thompson S, Normand C, Flather M, *et al*.

No. 35
A systematic review of the costs and effectiveness of different models of paediatric home care.
By Parker G, Bhakta P, Lovett CA, Paisley S, Olsen R, Turner D, *et al*.

Volume 7, 2003

No. 1
How important are comprehensive literature searches and the assessment of trial quality in systematic reviews? Empirical study.
By Egger M, Jüni P, Bartlett C, Holenstein F, Sterne J.

No. 2
Systematic review of the effectiveness and cost-effectiveness, and economic evaluation, of home versus hospital or satellite unit haemodialysis for people with end-stage renal failure.
By Mowatt G, Vale L, Perez J, Wyness L, Fraser C, MacLeod A, *et al*.

No. 3
Systematic review and economic evaluation of the effectiveness of infliximab for the treatment of Crohn's disease.
By Clark W, Raftery J, Barton P, Song F, Fry-Smith A, Burls A.

No. 4
A review of the clinical effectiveness and cost-effectiveness of routine anti-D prophylaxis for pregnant women who are rhesus negative.
By Chilcott J, Lloyd Jones M, Wight J, Forman K, Wray J, Beverley C, *et al*.

No. 5
Systematic review and evaluation of the use of tumour markers in paediatric oncology: Ewing's sarcoma and neuroblastoma.
By Riley RD, Burchill SA, Abrams KR, Heney D, Lambert PC, Jones DR, *et al*.

No. 6
The cost-effectiveness of screening for *Helicobacter pylori* to reduce mortality and morbidity from gastric cancer and peptic ulcer disease: a discrete-event simulation model.
By Roderick P, Davies R, Raftery J, Crabbe D, Pearce R, Bhandari P, *et al*.

No. 7
The clinical effectiveness and cost-effectiveness of routine dental checks: a systematic review and economic evaluation.
By Davenport C, Elley K, Salas C, Taylor-Weetman CL, Fry-Smith A, Bryan S, *et al*.

No. 8
A multicentre randomised controlled trial assessing the costs and benefits of using structured information and analysis of women's preferences in the management of menorrhagia.
By Kennedy ADM, Sculpher MJ, Coulter A, Dwyer N, Rees M, Horsley S, *et al*.

No. 9
Clinical effectiveness and cost–utility of photodynamic therapy for wet age-related macular degeneration: a systematic review and economic evaluation.
By Meads C, Salas C, Roberts T, Moore D, Fry-Smith A, Hyde C.

No. 10
Evaluation of molecular tests for prenatal diagnosis of chromosome abnormalities.
By Grimshaw GM, Szczepura A, Hultén M, MacDonald F, Nevin NC, Sutton F, *et al*.

No. 11
First and second trimester antenatal screening for Down's syndrome: the results of the Serum, Urine and Ultrasound Screening Study (SURUSS).
By Wald NJ, Rodeck C, Hackshaw AK, Walters J, Chitty L, Mackinson AM.

No. 12
The effectiveness and cost-effectiveness of ultrasound locating devices for central venous access: a systematic review and economic evaluation.
By Calvert N, Hind D, McWilliams RG, Thomas SM, Beverley C, Davidson A.

No. 13
A systematic review of atypical antipsychotics in schizophrenia.
By Bagnall A-M, Jones L, Lewis R, Ginnelly L, Glanville J, Torgerson D, *et al*.

No. 14
Prostate Testing for Cancer and Treatment (ProtecT) feasibility study.
By Donovan J, Hamdy F, Neal D, Peters T, Oliver S, Brindle L, *et al*.

No. 15
Early thrombolysis for the treatment of acute myocardial infarction: a systematic review and economic evaluation.
By Boland A, Dundar Y, Bagust A, Haycox A, Hill R, Mujica Mota R, *et al*.

No. 16
Screening for fragile X syndrome: a literature review and modelling.
By Song FJ, Barton P, Sleightholme V, Yao GL, Fry-Smith A.

No. 17
Systematic review of endoscopic sinus surgery for nasal polyps.
By Dalziel K, Stein K, Round A, Garside R, Royle P.

No. 18
Towards efficient guidelines: how to monitor guideline use in primary care.
By Hutchinson A, McIntosh A, Cox S, Gilbert C.

No. 19
Effectiveness and cost-effectiveness of acute hospital-based spinal cord injuries services: systematic review.
By Bagnall A-M, Jones L, Richardson G, Duffy S, Riemsma R.

No. 20
Prioritisation of health technology assessment. The PATHS model: methods and case studies.
By Townsend J, Buxton M, Harper G.

No. 21
Systematic review of the clinical effectiveness and cost-effectiveness of tension-free vaginal tape for treatment of urinary stress incontinence.
By Cody J, Wyness L, Wallace S, Glazener C, Kilonzo M, Stearns S, *et al*.

No. 22
The clinical and cost-effectiveness of patient education models for diabetes: a systematic review and economic evaluation.
By Loveman E, Cave C, Green C, Royle P, Dunn N, Waugh N.

No. 23
The role of modelling in prioritising and planning clinical trials.
By Chilcott J, Brennan A, Booth A, Karnon J, Tappenden P.

No. 24
Cost–benefit evaluation of routine influenza immunisation in people 65–74 years of age.
By Allsup S, Gosney M, Haycox A, Regan M.

No. 25
The clinical and cost-effectiveness of pulsatile machine perfusion versus cold storage of kidneys for transplantation retrieved from heart-beating and non-heart-beating donors.
By Wight J, Chilcott J, Holmes M, Brewer N.

No. 26
Can randomised trials rely on existing electronic data? A feasibility study to explore the value of routine data in health technology assessment.
By Williams JG, Cheung WY, Cohen DR, Hutchings HA, Longo MF, Russell IT.

No. 27
Evaluating non-randomised intervention studies.
By Deeks JJ, Dinnes J, D'Amico R, Sowden AJ, Sakarovitch C, Song F, *et al*.

No. 28
A randomised controlled trial to assess the impact of a package comprising a patient-orientated, evidence-based self-help guidebook and patient-centred consultations on disease management and satisfaction in inflammatory bowel disease.
By Kennedy A, Nelson E, Reeves D, Richardson G, Roberts C, Robinson A, *et al*.

No. 29
The effectiveness of diagnostic tests for the assessment of shoulder pain due to soft tissue disorders: a systematic review.
By Dinnes J, Loveman E, McIntyre L, Waugh N.

No. 30
The value of digital imaging in diabetic retinopathy.
By Sharp PF, Olson J, Strachan F, Hipwell J, Ludbrook A, O'Donnell M, *et al*.

No. 31
Lowering blood pressure to prevent myocardial infarction and stroke: a new preventive strategy.
By Law M, Wald N, Morris J.

No. 32
Clinical and cost-effectiveness of capecitabine and tegafur with uracil for the treatment of metastatic colorectal cancer: systematic review and economic evaluation.
By Ward S, Kaltenthaler E, Cowan J, Brewer N.

No. 33
Clinical and cost-effectiveness of new and emerging technologies for early localised prostate cancer: a systematic review.
By Hummel S, Paisley S, Morgan A, Currie E, Brewer N.

No. 34
Literature searching for clinical and cost-effectiveness studies used in health technology assessment reports carried out for the National Institute for Clinical Excellence appraisal system.
By Royle P, Waugh N.

No. 35
Systematic review and economic decision modelling for the prevention and treatment of influenza A and B.
By Turner D, Wailoo A, Nicholson K, Cooper N, Sutton A, Abrams K.

No. 36
A randomised controlled trial to evaluate the clinical and cost-effectiveness of Hickman line insertions in adult cancer patients by nurses.
By Boland A, Haycox A, Bagust A, Fitzsimmons L.

No. 37
Redesigning postnatal care: a randomised controlled trial of protocol-based midwifery-led care focused on individual women's physical and psychological health needs.
By MacArthur C, Winter HR, Bick DE, Lilford RJ, Lancashire RJ, Knowles H, *et al*.

No. 38
Estimating implied rates of discount in healthcare decision-making.
By West RR, McNabb R, Thompson AGH, Sheldon TA, Grimley Evans J.

No. 39
Systematic review of isolation policies in the hospital management of methicillin-resistant *Staphylococcus aureus*: a review of the literature with epidemiological and economic modelling.
By Cooper BS, Stone SP, Kibbler CC, Cookson BD, Roberts JA, Medley GF, *et al*.

No. 40
Treatments for spasticity and pain in multiple sclerosis: a systematic review.
By Beard S, Hunn A, Wight J.

No. 41
The inclusion of reports of randomised trials published in languages other than English in systematic reviews.
By Moher D, Pham B, Lawson ML, Klassen TP.

No. 42
The impact of screening on future health-promoting behaviours and health beliefs: a systematic review.
By Bankhead CR, Brett J, Bukach C, Webster P, Stewart-Brown S, Munafo M, *et al*.

Volume 8, 2004

No. 1
What is the best imaging strategy for acute stroke?
By Wardlaw JM, Keir SL, Seymour J, Lewis S, Sandercock PAG, Dennis MS, *et al*.

No. 2
Systematic review and modelling of the investigation of acute and chronic chest pain presenting in primary care.
By Mant J, McManus RJ, Oakes RAL, Delaney BC, Barton PM, Deeks JJ, *et al*.

No. 3
The effectiveness and cost-effectiveness of microwave and thermal balloon endometrial ablation for heavy menstrual bleeding: a systematic review and economic modelling.
By Garside R, Stein K, Wyatt K, Round A, Price A.

No. 4
A systematic review of the role of bisphosphonates in metastatic disease.
By Ross JR, Saunders Y, Edmonds PM, Patel S, Wonderling D, Normand C, *et al*.

No. 5
Systematic review of the clinical effectiveness and cost-effectiveness of capecitabine (Xeloda®) for locally advanced and/or metastatic breast cancer.
By Jones L, Hawkins N, Westwood M, Wright K, Richardson G, Riemsma R.

No. 6
Effectiveness and efficiency of guideline dissemination and implementation strategies.
By Grimshaw JM, Thomas RE, MacLennan G, Fraser C, Ramsay CR, Vale L, *et al*.

No. 7
Clinical effectiveness and costs of the Sugarbaker procedure for the treatment of pseudomyxoma peritonei.
By Bryant J, Clegg AJ, Sidhu MK, Brodin H, Royle P, Davidson P.

No. 8
Psychological treatment for insomnia in the regulation of long-term hypnotic drug use.
By Morgan K, Dixon S, Mathers N, Thompson J, Tomeny M.

No. 9
Improving the evaluation of therapeutic interventions in multiple sclerosis: development of a patient-based measure of outcome.
By Hobart JC, Riazi A, Lamping DL, Fitzpatrick R, Thompson AJ.

No. 10
A systematic review and economic evaluation of magnetic resonance cholangiopancreatography compared with diagnostic endoscopic retrograde cholangiopancreatography.
By Kaltenthaler E, Bravo Vergel Y, Chilcott J, Thomas S, Blakeborough T, Walters SJ, *et al*.

No. 11
The use of modelling to evaluate new drugs for patients with a chronic condition: the case of antibodies against tumour necrosis factor in rheumatoid arthritis.
By Barton P, Jobanputra P, Wilson J, Bryan S, Burls A.

No. 12
Clinical effectiveness and cost-effectiveness of neonatal screening for inborn errors of metabolism using tandem mass spectrometry: a systematic review.
By Pandor A, Eastham J, Beverley C, Chilcott J, Paisley S.

No. 13
Clinical effectiveness and cost-effectiveness of pioglitazone and rosiglitazone in the treatment of type 2 diabetes: a systematic review and economic evaluation.
By Czoski-Murray C, Warren E, Chilcott J, Beverley C, Psyllaki MA, Cowan J.

No. 14
Routine examination of the newborn: the EMREN study. Evaluation of an extension of the midwife role including a randomised controlled trial of appropriately trained midwives and paediatric senior house officers.
By Townsend J, Wolke D, Hayes J, Davé S, Rogers C, Bloomfield L, *et al*.

No. 15
Involving consumers in research and development agenda setting for the NHS: developing an evidence-based approach.
By Oliver S, Clarke-Jones L, Rees R, Milne R, Buchanan P, Gabbay J, *et al*.

No. 16
A multi-centre randomised controlled trial of minimally invasive direct coronary bypass grafting versus percutaneous transluminal coronary angioplasty with stenting for proximal stenosis of the left anterior descending coronary artery.
By Reeves BC, Angelini GD, Bryan AJ, Taylor FC, Cripps T, Spyt TJ, *et al*.

No. 17
Does early magnetic resonance imaging influence management or improve outcome in patients referred to secondary care with low back pain? A pragmatic randomised controlled trial.
By Gilbert FJ, Grant AM, Gillan MGC, Vale L, Scott NW, Campbell MK, *et al*.

No. 18
The clinical and cost-effectiveness of anakinra for the treatment of rheumatoid arthritis in adults: a systematic review and economic analysis.
By Clark W, Jobanputra P, Barton P, Burls A.

No. 19
A rapid and systematic review and economic evaluation of the clinical and cost-effectiveness of newer drugs for treatment of mania associated with bipolar affective disorder.
By Bridle C, Palmer S, Bagnall A-M, Darba J, Duffy S, Sculpher M, *et al*.

No. 20
Liquid-based cytology in cervical screening: an updated rapid and systematic review and economic analysis.
By Karnon J, Peters J, Platt J, Chilcott J, McGoogan E, Brewer N.

No. 21
Systematic review of the long-term effects and economic consequences of treatments for obesity and implications for health improvement.
By Avenell A, Broom J, Brown TJ, Poobalan A, Aucott L, Stearns SC, *et al*.

No. 22
Autoantibody testing in children with newly diagnosed type 1 diabetes mellitus.
By Dretzke J, Cummins C, Sandercock J, Fry-Smith A, Barrett T, Burls A.

No. 23
Clinical effectiveness and cost-effectiveness of prehospital intravenous fluids in trauma patients.
By Dretzke J, Sandercock J, Bayliss S, Burls A.

No. 24
Newer hypnotic drugs for the short-term management of insomnia: a systematic review and economic evaluation.
By Dündar Y, Boland A, Strobl J, Dodd S, Haycox A, Bagust A, *et al*.

No. 25
Development and validation of methods for assessing the quality of diagnostic accuracy studies.
By Whiting P, Rutjes AWS, Dinnes J, Reitsma JB, Bossuyt PMM, Kleijnen J.

No. 26
EVALUATE hysterectomy trial: a multicentre randomised trial comparing abdominal, vaginal and laparoscopic methods of hysterectomy.
By Garry R, Fountain J, Brown J, Manca A, Mason S, Sculpher M, *et al*.

No. 27
Methods for expected value of information analysis in complex health economic models: developments on the health economics of interferon-β and glatiramer acetate for multiple sclerosis.
By Tappenden P, Chilcott JB, Eggington S, Oakley J, McCabe C.

No. 28
Effectiveness and cost-effectiveness of imatinib for first-line treatment of chronic myeloid leukaemia in chronic phase: a systematic review and economic analysis.
By Dalziel K, Round A, Stein K, Garside R, Price A.

No. 29
VenUS I: a randomised controlled trial of two types of bandage for treating venous leg ulcers.
By Iglesias C, Nelson EA, Cullum NA, Torgerson DJ on behalf of the VenUS Team.

No. 30
Systematic review of the effectiveness and cost-effectiveness, and economic evaluation, of myocardial perfusion scintigraphy for the diagnosis and management of angina and myocardial infarction.
By Mowatt G, Vale L, Brazzelli M, Hernandez R, Murray A, Scott N, *et al*.

No. 31
A pilot study on the use of decision theory and value of information analysis as part of the NHS Health Technology Assessment programme.
By Claxton K, Ginnelly L, Sculpher M, Philips Z, Palmer S.

No. 32
The Social Support and Family Health Study: a randomised controlled trial and economic evaluation of two alternative forms of postnatal support for mothers living in disadvantaged inner-city areas.
By Wiggins M, Oakley A, Roberts I, Turner H, Rajan L, Austerberry H, *et al*.

No. 33
Psychosocial aspects of genetic screening of pregnant women and newborns: a systematic review.
By Green JM, Hewison J, Bekker HL, Bryant, Cuckle HS.

No. 34
Evaluation of abnormal uterine bleeding: comparison of three outpatient procedures within cohorts defined by age and menopausal status.
By Critchley HOD, Warner P, Lee AJ, Brechin S, Guise J, Graham B.

No. 35
Coronary artery stents: a rapid systematic review and economic evaluation.
By Hill R, Bagust A, Bakhai A, Dickson R, Dündar Y, Haycox A, *et al*.

No. 36
Review of guidelines for good practice in decision-analytic modelling in health technology assessment.
By Philips Z, Ginnelly L, Sculpher M, Claxton K, Golder S, Riemsma R, *et al*.

No. 37
Rituximab (MabThera®) for aggressive non-Hodgkin's lymphoma: systematic review and economic evaluation.
By Knight C, Hind D, Brewer N, Abbott V.

No. 38
Clinical effectiveness and cost-effectiveness of clopidogrel and modified-release dipyridamole in the secondary prevention of occlusive vascular events: a systematic review and economic evaluation.
By Jones L, Griffin S, Palmer S, Main C, Orton V, Sculpher M, *et al.*

No. 39
Pegylated interferon α-2a and -2b in combination with ribavirin in the treatment of chronic hepatitis C: a systematic review and economic evaluation.
By Shepherd J, Brodin H, Cave C, Waugh N, Price A, Gabbay J.

No. 40
Clopidogrel used in combination with aspirin compared with aspirin alone in the treatment of non-ST-segment-elevation acute coronary syndromes: a systematic review and economic evaluation.
By Main C, Palmer S, Griffin S, Jones L, Orton V, Sculpher M, *et al.*

No. 41
Provision, uptake and cost of cardiac rehabilitation programmes: improving services to under-represented groups.
By Beswick AD, Rees K, Griebsch I, Taylor FC, Burke M, West RR, *et al.*

No. 42
Involving South Asian patients in clinical trials.
By Hussain-Gambles M, Leese B, Atkin K, Brown J, Mason S, Tovey P.

No. 43
Clinical and cost-effectiveness of continuous subcutaneous insulin infusion for diabetes.
By Colquitt JL, Green C, Sidhu MK, Hartwell D, Waugh N.

No. 44
Identification and assessment of ongoing trials in health technology assessment reviews.
By Song FJ, Fry-Smith A, Davenport C, Bayliss S, Adi Y, Wilson JS, *et al*.

No. 45
Systematic review and economic evaluation of a long-acting insulin analogue, insulin glargine
By Warren E, Weatherley-Jones E, Chilcott J, Beverley C.

No. 46
Supplementation of a home-based exercise programme with a class-based programme for people with osteoarthritis of the knees: a randomised controlled trial and health economic analysis.
By McCarthy CJ, Mills PM, Pullen R, Richardson G, Hawkins N, Roberts CR, *et al*.

No. 47
Clinical and cost-effectiveness of once-daily versus more frequent use of same potency topical corticosteroids for atopic eczema: a systematic review and economic evaluation.
By Green C, Colquitt JL, Kirby J, Davidson P, Payne E.

No. 48
Acupuncture of chronic headache disorders in primary care: randomised controlled trial and economic analysis.
By Vickers AJ, Rees RW, Zollman CE, McCarney R, Smith CM, Ellis N, *et al*.

No. 49
Generalisability in economic evaluation studies in healthcare: a review and case studies.
By Sculpher MJ, Pang FS, Manca A, Drummond MF, Golder S, Urdahl H, *et al*.

No. 50
Virtual outreach: a randomised controlled trial and economic evaluation of joint teleconferenced medical consultations.
By Wallace P, Barber J, Clayton W, Currell R, Fleming K, Garner P, *et al*.

Volume 9, 2005

No. 1
Randomised controlled multiple treatment comparison to provide a cost-effectiveness rationale for the selection of antimicrobial therapy in acne.
By Ozolins M, Eady EA, Avery A, Cunliffe WJ, O'Neill C, Simpson NB, *et al*.

No. 2
Do the findings of case series studies vary significantly according to methodological characteristics?
By Dalziel K, Round A, Stein K, Garside R, Castelnuovo E, Payne L.

No. 3
Improving the referral process for familial breast cancer genetic counselling: findings of three randomised controlled trials of two interventions.
By Wilson BJ, Torrance N, Mollison J, Wordsworth S, Gray JR, Haites NE, *et al*.

No. 4
Randomised evaluation of alternative electrosurgical modalities to treat bladder outflow obstruction in men with benign prostatic hyperplasia.
By Fowler C, McAllister W, Plail R, Karim O, Yang Q.

No. 5
A pragmatic randomised controlled trial of the cost-effectiveness of palliative therapies for patients with inoperable oesophageal cancer.
By Shenfine J, McNamee P, Steen N, Bond J, Griffin SM.

No. 6
Impact of computer-aided detection prompts on the sensitivity and specificity of screening mammography.
By Taylor P, Champness J, Given-Wilson R, Johnston K, Potts H.

No. 7
Issues in data monitoring and interim analysis of trials.
By Grant AM, Altman DG, Babiker AB, Campbell MK, Clemens FJ, Darbyshire JH, *et al*.

No. 8
Lay public's understanding of equipoise and randomisation in randomised controlled trials.
By Robinson EJ, Kerr CEP, Stevens AJ, Lilford RJ, Braunholtz DA, Edwards SJ, *et al*.

No. 9
Clinical and cost-effectiveness of electroconvulsive therapy for depressive illness, schizophrenia, catatonia and mania: systematic reviews and economic modelling studies.
By Greenhalgh J, Knight C, Hind D, Beverley C, Walters S.

No. 10
Measurement of health-related quality of life for people with dementia: development of a new instrument (DEMQOL) and an evaluation of current methodology.
By Smith SC, Lamping DL, Banerjee S, Harwood R, Foley B, Smith P, *et al*.

No. 11
Clinical effectiveness and cost-effectiveness of drotrecogin alfa (activated) (Xigris®) for the treatment of severe sepsis in adults: a systematic review and economic evaluation.
By Green C, Dinnes J, Takeda A, Shepherd J, Hartwell D, Cave C, *et al*.

No. 12
A methodological review of how heterogeneity has been examined in systematic reviews of diagnostic test accuracy.
By Dinnes J, Deeks J, Kirby J, Roderick P.

No. 13
Cervical screening programmes: can automation help? Evidence from systematic reviews, an economic analysis and a simulation modelling exercise applied to the UK.
By Willis BH, Barton P, Pearmain P, Bryan S, Hyde C.

No. 14
Laparoscopic surgery for inguinal hernia repair: systematic review of effectiveness and economic evaluation.
By McCormack K, Wake B, Perez J, Fraser C, Cook J, McIntosh E, *et al*.

No. 15
Clinical effectiveness, tolerability and cost-effectiveness of newer drugs for epilepsy in adults: a systematic review and economic evaluation.
By Wilby J, Kainth A, Hawkins N, Epstein D, McIntosh H, McDaid C, *et al*.

No. 16
A randomised controlled trial to compare the cost-effectiveness of tricyclic antidepressants, selective serotonin reuptake inhibitors and lofepramine.
By Peveler R, Kendrick T, Buxton M, Longworth L, Baldwin D, Moore M, *et al*.

No. 17
Clinical effectiveness and cost-effectiveness of immediate angioplasty for acute myocardial infarction: systematic review and economic evaluation.
By Hartwell D, Colquitt J, Loveman E, Clegg AJ, Brodin H, Waugh N, *et al*.

No. 18
A randomised controlled comparison of alternative strategies in stroke care.
By Kalra L, Evans A, Perez I, Knapp M, Swift C, Donaldson N.

No. 19
The investigation and analysis of critical incidents and adverse events in healthcare.
By Woloshynowych M, Rogers S, Taylor-Adams S, Vincent C.

No. 20
Potential use of routine databases in health technology assessment.
By Raftery J, Roderick P, Stevens A.

No. 21
Clinical and cost-effectiveness of newer immunosuppressive regimens in renal transplantation: a systematic review and modelling study.
By Woodroffe R, Yao GL, Meads C, Bayliss S, Ready A, Raftery J, *et al*.

No. 22
A systematic review and economic evaluation of alendronate, etidronate, risedronate, raloxifene and teriparatide for the prevention and treatment of postmenopausal osteoporosis.
By Stevenson M, Lloyd Jones M, De Nigris E, Brewer N, Davis S, Oakley J.

No. 23
A systematic review to examine the impact of psycho-educational interventions on health outcomes and costs in adults and children with difficult asthma.
By Smith JR, Mugford M, Holland R, Candy B, Noble MJ, Harrison BDW, *et al*.

No. 24
An evaluation of the costs, effectiveness and quality of renal replacement therapy provision in renal satellite units in England and Wales.
By Roderick P, Nicholson T, Armitage A, Mehta R, Mullee M, Gerard K, *et al*.

No. 25
Imatinib for the treatment of patients with unresectable and/or metastatic gastrointestinal stromal tumours: systematic review and economic evaluation.
By Wilson J, Connock M, Song F, Yao G, Fry-Smith A, Raftery J, *et al*.

No. 26
Indirect comparisons of competing interventions.
By Glenny AM, Altman DG, Song F, Sakarovitch C, Deeks JJ, D'Amico R, *et al*.

No. 27
Cost-effectiveness of alternative strategies for the initial medical management of non-ST elevation acute coronary syndrome: systematic review and decision-analytical modelling.
By Robinson M, Palmer S, Sculpher M, Philips Z, Ginnelly L, Bowens A, *et al*.

No. 28
Outcomes of electrically stimulated gracilis neosphincter surgery.
By Tillin T, Chambers M, Feldman R.

No. 29
The effectiveness and cost-effectiveness of pimecrolimus and tacrolimus for atopic eczema: a systematic review and economic evaluation.
By Garside R, Stein K, Castelnuovo E, Pitt M, Ashcroft D, Dimmock P, *et al*.

No. 30
Systematic review on urine albumin testing for early detection of diabetic complications.
By Newman DJ, Mattock MB, Dawnay ABS, Kerry S, McGuire A, Yaqoob M, *et al*.

No. 31
Randomised controlled trial of the cost-effectiveness of water-based therapy for lower limb osteoarthritis.
By Cochrane T, Davey RC, Matthes Edwards SM.

No. 32
Longer term clinical and economic benefits of offering acupuncture care to patients with chronic low back pain.
By Thomas KJ, MacPherson H, Ratcliffe J, Thorpe L, Brazier J, Campbell M, *et al*.

No. 33
Cost-effectiveness and safety of epidural steroids in the management of sciatica.
By Price C, Arden N, Coglan L, Rogers P.

No. 34
The British Rheumatoid Outcome Study Group (BROSG) randomised controlled trial to compare the effectiveness and cost-effectiveness of aggressive versus symptomatic therapy in established rheumatoid arthritis.
By Symmons D, Tricker K, Roberts C, Davies L, Dawes P, Scott DL.

No. 35
Conceptual framework and systematic review of the effects of participants' and professionals' preferences in randomised controlled trials.
By King M, Nazareth I, Lampe F, Bower P, Chandler M, Morou M, *et al*.

No. 36
The clinical and cost-effectiveness of implantable cardioverter defibrillators: a systematic review.
By Bryant J, Brodin H, Loveman E, Payne E, Clegg A.

No. 37
A trial of problem-solving by community mental health nurses for anxiety, depression and life difficulties among general practice patients. The CPN-GP study.
By Kendrick T, Simons L, Mynors-Wallis L, Gray A, Lathlean J, Pickering R, *et al*.

No. 38
The causes and effects of socio-demographic exclusions from clinical trials.
By Bartlett C, Doyal L, Ebrahim S, Davey P, Bachmann M, Egger M, *et al*.

No. 39
Is hydrotherapy cost-effective? A randomised controlled trial of combined hydrotherapy programmes compared with physiotherapy land techniques in children with juvenile idiopathic arthritis.
By Epps H, Ginnelly L, Utley M, Southwood T, Gallivan S, Sculpher M, *et al*.

No. 40
A randomised controlled trial and cost-effectiveness study of systematic screening (targeted and total population screening) versus routine practice for the detection of atrial fibrillation in people aged 65 and over. The SAFE study.
By Hobbs FDR, Fitzmaurice DA, Mant J, Murray E, Jowett S, Bryan S, *et al*.

No. 41
Displaced intracapsular hip fractures in fit, older people: a randomised comparison of reduction and fixation, bipolar hemiarthroplasty and total hip arthroplasty.
By Keating JF, Grant A, Masson M, Scott NW, Forbes JF.

No. 42
Long-term outcome of cognitive behaviour therapy clinical trials in central Scotland.
By Durham RC, Chambers JA, Power KG, Sharp DM, Macdonald RR, Major KA, *et al*.

No. 43
The effectiveness and cost-effectiveness of dual-chamber pacemakers compared with single-chamber pacemakers for bradycardia due to atrioventricular block or sick sinus syndrome: systematic review and economic evaluation.
By Castelnuovo E, Stein K, Pitt M, Garside R, Payne E.

No. 44
Newborn screening for congenital heart defects: a systematic review and cost-effectiveness analysis.
By Knowles R, Griebsch I, Dezateux C, Brown J, Bull C, Wren C.

No. 45
The clinical and cost-effectiveness of left ventricular assist devices for end-stage heart failure: a systematic review and economic evaluation.
By Clegg AJ, Scott DA, Loveman E, Colquitt J, Hutchinson J, Royle P, *et al*.

No. 46
The effectiveness of the Heidelberg Retina Tomograph and laser diagnostic glaucoma scanning system (GDx) in detecting and monitoring glaucoma.
By Kwartz AJ, Henson DB, Harper RA, Spencer AF, McLeod D.

No. 47
Clinical and cost-effectiveness of autologous chondrocyte implantation for cartilage defects in knee joints: systematic review and economic evaluation.
By Clar C, Cummins E, McIntyre L, Thomas S, Lamb J, Bain L, *et al*.

No. 48
Systematic review of effectiveness of different treatments for childhood retinoblastoma.
By McDaid C, Hartley S, Bagnall A-M, Ritchie G, Light K, Riemsma R.

No. 49
Towards evidence-based guidelines for the prevention of venous thromboembolism: systematic reviews of mechanical methods, oral anticoagulation, dextran and regional anaesthesia as thromboprophylaxis.
By Roderick P, Ferris G, Wilson K, Halls H, Jackson D, Collins R, *et al*.

No. 50
The effectiveness and cost-effectiveness of parent training/education programmes for the treatment of conduct disorder, including oppositional defiant disorder, in children.
By Dretzke J, Frew E, Davenport C, Barlow J, Stewart-Brown S, Sandercock J, *et al*.

Volume 10, 2006

No. 1
The clinical and cost-effectiveness of donepezil, rivastigmine, galantamine and memantine for Alzheimer's disease.
By Loveman E, Green C, Kirby J, Takeda A, Picot J, Payne E, *et al*.

No. 2
FOOD: a multicentre randomised trial evaluating feeding policies in patients admitted to hospital with a recent stroke.
By Dennis M, Lewis S, Cranswick G, Forbes J.

No. 3
The clinical effectiveness and cost-effectiveness of computed tomography screening for lung cancer: systematic reviews.
By Black C, Bagust A, Boland A, Walker S, McLeod C, De Verteuil R, *et al*.

No. 4
A systematic review of the effectiveness and cost-effectiveness of neuroimaging assessments used to visualise the seizure focus in people with refractory epilepsy being considered for surgery.
By Whiting P, Gupta R, Burch J, Mujica Mota RE, Wright K, Marson A, *et al*.

No. 5
Comparison of conference abstracts and presentations with full-text articles in the health technology assessments of rapidly evolving technologies.
By Dundar Y, Dodd S, Dickson R, Walley T, Haycox A, Williamson PR.

No. 6
Systematic review and evaluation of methods of assessing urinary incontinence.
By Martin JL, Williams KS, Abrams KR, Turner DA, Sutton AJ, Chapple C, *et al*.

No. 7
The clinical effectiveness and cost-effectiveness of newer drugs for children with epilepsy. A systematic review.
By Connock M, Frew E, Evans B-W, Bryan S, Cummins C, Fry-Smith A, *et al*.

No. 8
Surveillance of Barrett's oesophagus: exploring the uncertainty through systematic review, expert workshop and economic modelling.
By Garside R, Pitt M, Somerville M, Stein K, Price A, Gilbert N.

No. 9
Topotecan, pegylated liposomal doxorubicin hydrochloride and paclitaxel for second-line or subsequent treatment of advanced ovarian cancer: a systematic review and economic evaluation.
By Main C, Bojke L, Griffin S, Norman G, Barbieri M, Mather L, *et al*.

No. 10
Evaluation of molecular techniques in prediction and diagnosis of cytomegalovirus disease in immunocompromised patients.
By Szczepura A, Westmoreland D, Vinogradova Y, Fox J, Clark M.

No. 11
Screening for thrombophilia in high-risk situations: systematic review and cost-effectiveness analysis. The Thrombosis: Risk and Economic Assessment of Thrombophilia Screening (TREATS) study.
By Wu O, Robertson L, Twaddle S, Lowe GDO, Clark P, Greaves M, *et al*.

No. 12
A series of systematic reviews to inform a decision analysis for sampling and treating infected diabetic foot ulcers.
By Nelson EA, O'Meara S, Craig D, Iglesias C, Golder S, Dalton J, *et al*.

No. 13
Randomised clinical trial, observational study and assessment of cost-effectiveness of the treatment of varicose veins (REACTIV trial).
By Michaels JA, Campbell WB, Brazier JE, MacIntyre JB, Palfreyman SJ, Ratcliffe J, *et al*.

No. 14
The cost-effectiveness of screening for oral cancer in primary care.
By Speight PM, Palmer S, Moles DR, Downer MC, Smith DH, Henriksson M *et al*.

No. 15
Measurement of the clinical and cost-effectiveness of non-invasive diagnostic testing strategies for deep vein thrombosis.
By Goodacre S, Sampson F, Stevenson M, Wailoo A, Sutton A, Thomas S, *et al*.

No. 16
Systematic review of the effectiveness and cost-effectiveness of HealOzone® for the treatment of occlusal pit/fissure caries and root caries.
By Brazzelli M, McKenzie L, Fielding S, Fraser C, Clarkson J, Kilonzo M, *et al*.

No. 17
Randomised controlled trials of conventional antipsychotic versus new atypical drugs, and new atypical drugs versus clozapine, in people with schizophrenia responding poorly to, or intolerant of, current drug treatment.
By Lewis SW, Davies L, Jones PB, Barnes TRE, Murray RM, Kerwin R, *et al*.

No. 18
Diagnostic tests and algorithms used in the investigation of haematuria: systematic reviews and economic evaluation.
By Rodgers M, Nixon J, Hempel S, Aho T, Kelly J, Neal D, *et al*.

No. 19
Cognitive behavioural therapy in addition to antispasmodic therapy for irritable bowel syndrome in primary care: randomised controlled trial.
By Kennedy TM, Chalder T, McCrone P, Darnley S, Knapp M, Jones RH, *et al*.

No. 20
A systematic review of the clinical effectiveness and cost-effectiveness of enzyme replacement therapies for Fabry's disease and mucopolysaccharidosis type 1.
By Connock M, Juarez-Garcia A, Frew E, Mans A, Dretzke J, Fry-Smith A, *et al*.

No. 21
Health benefits of antiviral therapy for mild chronic hepatitis C: randomised controlled trial and economic evaluation.
By Wright M, Grieve R, Roberts J, Main J, Thomas HC on behalf of the UK Mild Hepatitis C Trial Investigators.

No. 22
Pressure relieving support surfaces: a randomised evaluation.
By Nixon J, Nelson EA, Cranny G, Iglesias CP, Hawkins K, Cullum NA, *et al*.

No. 23
A systematic review and economic model of the effectiveness and cost-effectiveness of methylphenidate, dexamfetamine and atomoxetine for the treatment of attention deficit hyperactivity disorder in children and adolescents.
By King S, Griffin S, Hodges Z, Weatherly H, Asseburg C, Richardson G, *et al*.

No. 24
The clinical effectiveness and cost-effectiveness of enzyme replacement therapy for Gaucher's disease: a systematic review.
By Connock M, Burls A, Frew E, Fry-Smith A, Juarez-Garcia A, McCabe C, *et al*.

No. 25
Effectiveness and cost-effectiveness of salicylic acid and cryotherapy for cutaneous warts. An economic decision model.
By Thomas KS, Keogh-Brown MR, Chalmers JR, Fordham RJ, Holland RC, Armstrong SJ, *et al*.

No. 26
A systematic literature review of the effectiveness of non-pharmacological interventions to prevent wandering in dementia and evaluation of the ethical implications and acceptability of their use.
By Robinson L, Hutchings D, Corner L, Beyer F, Dickinson H, Vanoli A, *et al*.

No. 27
A review of the evidence on the effects and costs of implantable cardioverter defibrillator therapy in different patient groups, and modelling of cost-effectiveness and cost–utility for these groups in a UK context.
By Buxton M, Caine N, Chase D, Connelly D, Grace A, Jackson C, *et al*.

No. 28
Adefovir dipivoxil and pegylated interferon alfa-2a for the treatment of chronic hepatitis B: a systematic review and economic evaluation.
By Shepherd J, Jones J, Takeda A, Davidson P, Price A.

No. 29
An evaluation of the clinical and cost-effectiveness of pulmonary artery catheters in patient management in intensive care: a systematic review and a randomised controlled trial.
By Harvey S, Stevens K, Harrison D, Young D, Brampton W, McCabe C, *et al*.

No. 30
Accurate, practical and cost-effective assessment of carotid stenosis in the UK.
By Wardlaw JM, Chappell FM, Stevenson M, De Nigris E, Thomas S, Gillard J, *et al*.

No. 31
Etanercept and infliximab for the treatment of psoriatic arthritis: a systematic review and economic evaluation.
By Woolacott N, Bravo Vergel Y, Hawkins N, Kainth A, Khadjesari Z, Misso K, *et al*.

No. 32
The cost-effectiveness of testing for hepatitis C in former injecting drug users.
By Castelnuovo E, Thompson-Coon J, Pitt M, Cramp M, Siebert U, Price A, *et al*.

No. 33
Computerised cognitive behaviour therapy for depression and anxiety update: a systematic review and economic evaluation.
By Kaltenthaler E, Brazier J, De Nigris E, Tumur I, Ferriter M, Beverley C, *et al*.

No. 34
Cost-effectiveness of using prognostic information to select women with breast cancer for adjuvant systemic therapy.
By Williams C, Brunskill S, Altman D, Briggs A, Campbell H, Clarke M, *et al*.

No. 35
Psychological therapies including dialectical behaviour therapy for borderline personality disorder: a systematic review and preliminary economic evaluation.
By Brazier J, Tumur I, Holmes M, Ferriter M, Parry G, Dent-Brown K, *et al*.

No. 36
Clinical effectiveness and cost-effectiveness of tests for the diagnosis and investigation of urinary tract infection in children: a systematic review and economic model.
By Whiting P, Westwood M, Bojke L, Palmer S, Richardson G, Cooper J, *et al*.

No. 37
Cognitive behavioural therapy in chronic fatigue syndrome: a randomised controlled trial of an outpatient group programme.
By O'Dowd H, Gladwell P, Rogers CA, Hollinghurst S, Gregory A.

No. 38
A comparison of the cost-effectiveness of five strategies for the prevention of non-steroidal anti-inflammatory drug-induced gastrointestinal toxicity: a systematic review with economic modelling.
By Brown TJ, Hooper L, Elliott RA, Payne K, Webb R, Roberts C, *et al*.

No. 39
The effectiveness and cost-effectiveness of computed tomography screening for coronary artery disease: systematic review.
By Waugh N, Black C, Walker S, McIntyre L, Cummins E, Hillis G.

No. 40
What are the clinical outcome and cost-effectiveness of endoscopy undertaken by nurses when compared with doctors? A Multi-Institution Nurse Endoscopy Trial (MINuET).
By Williams J, Russell I, Durai D, Cheung W-Y, Farrin A, Bloor K, *et al*.

No. 41
The clinical and cost-effectiveness of oxaliplatin and capecitabine for the adjuvant treatment of colon cancer: systematic review and economic evaluation.
By Pandor A, Eggington S, Paisley S, Tappenden P, Sutcliffe P.

No. 42
A systematic review of the effectiveness of adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis in adults and an economic evaluation of their cost-effectiveness.
By Chen Y-F, Jobanputra P, Barton P, Jowett S, Bryan S, Clark W, *et al*.

No. 43
Telemedicine in dermatology: a randomised controlled trial.
By Bowns IR, Collins K, Walters SJ, McDonagh AJG.

No. 44
Cost-effectiveness of cell salvage and alternative methods of minimising perioperative allogeneic blood transfusion: a systematic review and economic model.
By Davies L, Brown TJ, Haynes S, Payne K, Elliott RA, McCollum C.

No. 45
Clinical effectiveness and cost-effectiveness of laparoscopic surgery for colorectal cancer: systematic reviews and economic evaluation.
By Murray A, Lourenco T, de Verteuil R, Hernandez R, Fraser C, McKinley A, *et al*.

No. 46
Etanercept and efalizumab for the treatment of psoriasis: a systematic review.
By Woolacott N, Hawkins N, Mason A, Kainth A, Khadjesari Z, Bravo Vergel Y, *et al*.

No. 47
Systematic reviews of clinical decision tools for acute abdominal pain.
By Liu JLY, Wyatt JC, Deeks JJ, Clamp S, Keen J, Verde P, *et al*.

No. 48
Evaluation of the ventricular assist device programme in the UK.
By Sharples L, Buxton M, Caine N, Cafferty F, Demiris N, Dyer M, *et al*.

No. 49
A systematic review and economic model of the clinical and cost-effectiveness of immunosuppressive therapy for renal transplantation in children.
By Yao G, Albon E, Adi Y, Milford D, Bayliss S, Ready A, *et al*.

No. 50
Amniocentesis results: investigation of anxiety. The ARIA trial.
By Hewison J, Nixon J, Fountain J, Cocks K, Jones C, Mason G, *et al*.

Volume 11, 2007

No. 1
Pemetrexed disodium for the treatment of malignant pleural mesothelioma: a systematic review and economic evaluation.
By Dundar Y, Bagust A, Dickson R, Dodd S, Green J, Haycox A, *et al*.

No. 2
A systematic review and economic model of the clinical effectiveness and cost-effectiveness of docetaxel in combination with prednisone or prednisolone for the treatment of hormone-refractory metastatic prostate cancer.
By Collins R, Fenwick E, Trowman R, Perard R, Norman G, Light K, *et al*.

No. 3
A systematic review of rapid diagnostic tests for the detection of tuberculosis infection.
By Dinnes J, Deeks J, Kunst H, Gibson A, Cummins E, Waugh N, *et al*.

No. 4
The clinical effectiveness and cost-effectiveness of strontium ranelate for the prevention of osteoporotic fragility fractures in postmenopausal women.
By Stevenson M, Davis S, Lloyd-Jones M, Beverley C.

No. 5
A systematic review of quantitative and qualitative research on the role and effectiveness of written information available to patients about individual medicines.
By Raynor DK, Blenkinsopp A, Knapp P, Grime J, Nicolson DJ, Pollock K, *et al*.

No. 6
Oral naltrexone as a treatment for relapse prevention in formerly opioid-dependent drug users: a systematic review and economic evaluation.
By Adi Y, Juarez-Garcia A, Wang D, Jowett S, Frew E, Day E, *et al*.

No. 7
Glucocorticoid-induced osteoporosis: a systematic review and cost–utility analysis.
By Kanis JA, Stevenson M, McCloskey EV, Davis S, Lloyd-Jones M.

No. 8
Epidemiological, social, diagnostic and economic evaluation of population screening for genital chlamydial infection.
By Low N, McCarthy A, Macleod J, Salisbury C, Campbell R, Roberts TE, *et al*.

No. 9
Methadone and buprenorphine for the management of opioid dependence: a systematic review and economic evaluation.
By Connock M, Juarez-Garcia A, Jowett S, Frew E, Liu Z, Taylor RJ, *et al*.

No. 10
Exercise Evaluation Randomised Trial (EXERT): a randomised trial comparing GP referral for leisure centre-based exercise, community-based walking and advice only.
By Isaacs AJ, Critchley JA, See Tai S, Buckingham K, Westley D, Harridge SDR, *et al*.

No. 11
Interferon alfa (pegylated and non-pegylated) and ribavirin for the treatment of mild chronic hepatitis C: a systematic review and economic evaluation.
By Shepherd J, Jones J, Hartwell D, Davidson P, Price A, Waugh N.

No. 12
Systematic review and economic evaluation of bevacizumab and cetuximab for the treatment of metastatic colorectal cancer.
By Tappenden P, Jones R, Paisley S, Carroll C.

No. 13
A systematic review and economic evaluation of epoetin alfa, epoetin beta and darbepoetin alfa in anaemia associated with cancer, especially that attributable to cancer treatment.
By Wilson J, Yao GL, Raftery J, Bohlius J, Brunskill S, Sandercock J, *et al*.

No. 14
A systematic review and economic evaluation of statins for the prevention of coronary events.
By Ward S, Lloyd Jones M, Pandor A, Holmes M, Ara R, Ryan A, *et al*.

No. 15
A systematic review of the effectiveness and cost-effectiveness of different models of community-based respite care for frail older people and their carers.
By Mason A, Weatherly H, Spilsbury K, Arksey H, Golder S, Adamson J, *et al*.

No. 16
Additional therapy for young children with spastic cerebral palsy: a randomised controlled trial.
By Weindling AM, Cunningham CC, Glenn SM, Edwards RT, Reeves DJ.

No. 17
Screening for type 2 diabetes: literature review and economic modelling.
By Waugh N, Scotland G, McNamee P, Gillett M, Brennan A, Goyder E, *et al*.

No. 18
The effectiveness and cost-effectiveness of cinacalcet for secondary hyperparathyroidism in end-stage renal disease patients on dialysis: a systematic review and economic evaluation.
By Garside R, Pitt M, Anderson R, Mealing S, Roome C, Snaith A, *et al*.

No. 19
The clinical effectiveness and cost-effectiveness of gemcitabine for metastatic breast cancer: a systematic review and economic evaluation.
By Takeda AL, Jones J, Loveman E, Tan SC, Clegg AJ.

No. 20
A systematic review of duplex ultrasound, magnetic resonance angiography and computed tomography angiography for the diagnosis and assessment of symptomatic, lower limb peripheral arterial disease.
By Collins R, Cranny G, Burch J, Aguiar-Ibáñez R, Craig D, Wright K, *et al*.

No. 21
The clinical effectiveness and cost-effectiveness of treatments for children with idiopathic steroid-resistant nephrotic syndrome: a systematic review.
By Colquitt JL, Kirby J, Green C, Cooper K, Trompeter RS.

No. 22
A systematic review of the routine monitoring of growth in children of primary school age to identify growth-related conditions.
By Fayter D, Nixon J, Hartley S, Rithalia A, Butler G, Rudolf M, *et al*.

No. 23
Systematic review of the effectiveness of preventing and treating *Staphylococcus aureus* carriage in reducing peritoneal catheter-related infections.
By McCormack K, Rabindranath K, Kilonzo M, Vale L, Fraser C, McIntyre L, *et al*.

No. 24
The clinical effectiveness and cost of repetitive transcranial magnetic stimulation versus electroconvulsive therapy in severe depression: a multicentre pragmatic randomised controlled trial and economic analysis.
By McLoughlin DM, Mogg A, Eranti S, Pluck G, Purvis R, Edwards D, *et al*.

No. 25
A randomised controlled trial and economic evaluation of direct versus indirect and individual versus group modes of speech and language therapy for children with primary language impairment.
By Boyle J, McCartney E, Forbes J, O'Hare A.

No. 26
Hormonal therapies for early breast cancer: systematic review and economic evaluation.
By Hind D, Ward S, De Nigris E, Simpson E, Carroll C, Wyld L.

No. 27
Cardioprotection against the toxic effects of anthracyclines given to children with cancer: a systematic review.
By Bryant J, Picot J, Levitt G, Sullivan I, Baxter L, Clegg A.

No. 28
Adalimumab, etanercept and infliximab for the treatment of ankylosing spondylitis: a systematic review and economic evaluation.
By McLeod C, Bagust A, Boland A, Dagenais P, Dickson R, Dundar Y, *et al*.

No. 29
Prenatal screening and treatment strategies to prevent group B streptococcal and other bacterial infections in early infancy: cost-effectiveness and expected value of information analyses.
By Colbourn T, Asseburg C, Bojke L, Philips Z, Claxton K, Ades AE, *et al*.

No. 30
Clinical effectiveness and cost-effectiveness of bone morphogenetic proteins in the non-healing of fractures and spinal fusion: a systematic review.
By Garrison KR, Donell S, Ryder J, Shemilt I, Mugford M, Harvey I, *et al*.

No. 31
A randomised controlled trial of postoperative radiotherapy following breast-conserving surgery in a minimum-risk older population. The PRIME trial.
By Prescott RJ, Kunkler IH, Williams LJ, King CC, Jack W, van der Pol M, *et al*.

No. 32
Current practice, accuracy, effectiveness and cost-effectiveness of the school entry hearing screen.
By Bamford J, Fortnum H, Bristow K, Smith J, Vamvakas G, Davies L, *et al*.

No. 33
The clinical effectiveness and cost-effectiveness of inhaled insulin in diabetes mellitus: a systematic review and economic evaluation.
By Black C, Cummins E, Royle P, Philip S, Waugh N.

No. 34
Surveillance of cirrhosis for hepatocellular carcinoma: systematic review and economic analysis.
By Thompson Coon J, Rogers G, Hewson P, Wright D, Anderson R, Cramp M, *et al*.

No. 35
The Birmingham Rehabilitation Uptake Maximisation Study (BRUM). Home-based compared with hospital-based cardiac rehabilitation in a multi-ethnic population: cost-effectiveness and patient adherence.
By Jolly K, Taylor R, Lip GYH, Greenfield S, Raftery J, Mant J, *et al*.

No. 36
A systematic review of the clinical, public health and cost-effectiveness of rapid diagnostic tests for the detection and identification of bacterial intestinal pathogens in faeces and food.
By Abubakar I, Irvine L, Aldus CF, Wyatt GM, Fordham R, Schelenz S, *et al*.

No. 37
A randomised controlled trial examining the longer-term outcomes of standard versus new antiepileptic drugs. The SANAD trial.
By Marson AG, Appleton R, Baker GA, Chadwick DW, Doughty J, Eaton B, *et al*.

No. 38
Clinical effectiveness and cost-effectiveness of different models of managing long-term oral anticoagulation therapy: a systematic review and economic modelling.
By Connock M, Stevens C, Fry-Smith A, Jowett S, Fitzmaurice D, Moore D, *et al*.

No. 39
A systematic review and economic model of the clinical effectiveness and cost-effectiveness of interventions for preventing relapse in people with bipolar disorder.
By Soares-Weiser K, Bravo Vergel Y, Beynon S, Dunn G, Barbieri M, Duffy S, *et al*.

No. 40
Taxanes for the adjuvant treatment of early breast cancer: systematic review and economic evaluation.
By Ward S, Simpson E, Davis S, Hind D, Rees A, Wilkinson A.

No. 41
The clinical effectiveness and cost-effectiveness of screening for open angle glaucoma: a systematic review and economic evaluation.
By Burr JM, Mowatt G, Hernández R, Siddiqui MAR, Cook J, Lourenco T, *et al*.

No. 42
Acceptability, benefit and costs of early screening for hearing disability: a study of potential screening tests and models.
By Davis A, Smith P, Ferguson M, Stephens D, Gianopoulos I.

No. 43
Contamination in trials of educational interventions.
By Keogh-Brown MR, Bachmann MO, Shepstone L, Hewitt C, Howe A, Ramsay CR, *et al*.

No. 44
Overview of the clinical effectiveness of positron emission tomography imaging in selected cancers.
By Facey K, Bradbury I, Laking G, Payne E.

No. 45
The effectiveness and cost-effectiveness of carmustine implants and temozolomide for the treatment of newly diagnosed high-grade glioma: a systematic review and economic evaluation.
By Garside R, Pitt M, Anderson R, Rogers G, Dyer M, Mealing S, *et al*.

No. 46
Drug-eluting stents: a systematic review and economic evaluation.
By Hill RA, Boland A, Dickson R, Dündar Y, Haycox A, McLeod C, *et al*.

No. 47
The clinical effectiveness and cost-effectiveness of cardiac resynchronisation (biventricular pacing) for heart failure: systematic review and economic model.
By Fox M, Mealing S, Anderson R, Dean J, Stein K, Price A, *et al*.

No. 48
Recruitment to randomised trials: strategies for trial enrolment and participation study. The STEPS study.
By Campbell MK, Snowdon C, Francis D, Elbourne D, McDonald AM, Knight R, *et al*.

No. 49
Cost-effectiveness of functional cardiac testing in the diagnosis and management of coronary artery disease: a randomised controlled trial. The CECaT trial.
By Sharples L, Hughes V, Crean A, Dyer M, Buxton M, Goldsmith K, *et al*.

No. 50
Evaluation of diagnostic tests when there is no gold standard. A review of methods.
By Rutjes AWS, Reitsma JB, Coomarasamy A, Khan KS, Bossuyt PMM.

No. 51
Systematic reviews of the clinical effectiveness and cost-effectiveness of proton pump inhibitors in acute upper gastrointestinal bleeding.
By Leontiadis GI, Sreedharan A, Dorward S, Barton P, Delaney B, Howden CW, *et al*.

No. 52
A review and critique of modelling in prioritising and designing screening programmes.
By Karnon J, Goyder E, Tappenden P, McPhie S, Towers I, Brazier J, *et al*.

No. 53
An assessment of the impact of the NHS Health Technology Assessment Programme.
By Hanney S, Buxton M, Green C, Coulson D, Raftery J.

Volume 12, 2008

No. 1
A systematic review and economic model of switching from non-glycopeptide to glycopeptide antibiotic prophylaxis for surgery.
By Cranny G, Elliott R, Weatherly H, Chambers D, Hawkins N, Myers L, *et al*.

No. 2
'Cut down to quit' with nicotine replacement therapies in smoking cessation: a systematic review of effectiveness and economic analysis.
By Wang D, Connock M, Barton P, Fry-Smith A, Aveyard P, Moore D.

No. 3
A systematic review of the effectiveness of strategies for reducing fracture risk in children with juvenile idiopathic arthritis with additional data on long-term risk of fracture and cost of disease management.
By Thornton J, Ashcroft D, O'Neill T, Elliott R, Adams J, Roberts C, *et al*.

No. 4
Does befriending by trained lay workers improve psychological well-being and quality of life for carers of people with dementia, and at what cost? A randomised controlled trial.
By Charlesworth G, Shepstone L, Wilson E, Thalanany M, Mugford M, Poland F.

No. 5
A multi-centre retrospective cohort study comparing the efficacy, safety and cost-effectiveness of hysterectomy and uterine artery embolisation for the treatment of symptomatic uterine fibroids. The HOPEFUL study.
By Hirst A, Dutton S, Wu O, Briggs A, Edwards C, Waldenmaier L, *et al*.

No. 6
Methods of prediction and prevention of pre-eclampsia: systematic reviews of accuracy and effectiveness literature with economic modelling.
By Meads CA, Cnossen JS, Meher S, Juarez-Garcia A, ter Riet G, Duley L, *et al*.

No. 7
The use of economic evaluations in NHS decision-making: a review and empirical investigation.
By Williams I, McIver S, Moore D, Bryan S.

No. 8
Stapled haemorrhoidectomy (haemorrhoidopexy) for the treatment of haemorrhoids: a systematic review and economic evaluation.
By Burch J, Epstein D, Baba-Akbari A, Weatherly H, Fox D, Golder S, *et al*.

No. 9
The clinical effectiveness of diabetes education models for Type 2 diabetes: a systematic review.
By Loveman E, Frampton GK, Clegg AJ.

No. 10
Payment to healthcare professionals for patient recruitment to trials: systematic review and qualitative study.
By Raftery J, Bryant J, Powell J, Kerr C, Hawker S.

No. 11
Cyclooxygenase-2 selective non-steroidal anti-inflammatory drugs (etodolac, meloxicam, celecoxib, rofecoxib, etoricoxib, valdecoxib and lumiracoxib) for osteoarthritis and rheumatoid arthritis: a systematic review and economic evaluation.
By Chen Y-F, Jobanputra P, Barton P, Bryan S, Fry-Smith A, Harris G, *et al*.

No. 12
The clinical effectiveness and cost-effectiveness of central venous catheters treated with anti-infective agents in preventing bloodstream infections: a systematic review and economic evaluation.
By Hockenhull JC, Dwan K, Boland A, Smith G, Bagust A, Dündar Y, *et al*.

No. 13
Stepped treatment of older adults on laxatives. The STOOL trial.
By Mihaylov S, Stark C, McColl E, Steen N, Vanoli A, Rubin G, *et al*.

No. 14
A randomised controlled trial of cognitive behaviour therapy in adolescents with major depression treated by selective serotonin reuptake inhibitors. The ADAPT trial.
By Goodyer IM, Dubicka B, Wilkinson P, Kelvin R, Roberts C, Byford S, *et al*.

No. 15
The use of irinotecan, oxaliplatin and raltitrexed for the treatment of advanced colorectal cancer: systematic review and economic evaluation.
By Hind D, Tappenden P, Tumur I, Eggington E, Sutcliffe P, Ryan A.

No. 16
Ranibizumab and pegaptanib for the treatment of age-related macular degeneration: a systematic review and economic evaluation.
By Colquitt JL, Jones J, Tan SC, Takeda A, Clegg AJ, Price A.

No. 17
Systematic review of the clinical effectiveness and cost-effectiveness of 64-slice or higher computed tomography angiography as an alternative to invasive coronary angiography in the investigation of coronary artery disease.
By Mowatt G, Cummins E, Waugh N, Walker S, Cook J, Jia X, *et al*.

No. 18
Structural neuroimaging in psychosis: a systematic review and economic evaluation.
By Albon E, Tsourapas A, Frew E, Davenport C, Oyebode F, Bayliss S, *et al*.

No. 19
Systematic review and economic analysis of the comparative effectiveness of different inhaled corticosteroids and their usage with long-acting beta$_2$ agonists for the treatment of chronic asthma in adults and children aged 12 years and over.
By Shepherd J, Rogers G, Anderson R, Main C, Thompson-Coon J, Hartwell D, *et al*.

No. 20
Systematic review and economic analysis of the comparative effectiveness of different inhaled corticosteroids and their usage with long-acting beta$_2$ agonists for the treatment of chronic asthma in children under the age of 12 years.
By Main C, Shepherd J, Anderson R, Rogers G, Thompson-Coon J, Liu Z, *et al*.

No. 21
Ezetimibe for the treatment of hypercholesterolaemia: a systematic review and economic evaluation.
By Ara R, Tumur I, Pandor A, Duenas A, Williams R, Wilkinson A, *et al*.

No. 22
Topical or oral ibuprofen for chronic knee pain in older people. The TOIB study.
By Underwood M, Ashby D, Carnes D, Castelnuovo E, Cross P, Harding G, *et al*.

No. 23
A prospective randomised comparison of minor surgery in primary and secondary care. The MiSTIC trial.
By George S, Pockney P, Primrose J, Smith H, Little P, Kinley H, *et al*.

Health Technology Assessment Programme

Director,
Professor Tom Walley,
Director, NHS HTA Programme,
Department of Pharmacology & Therapeutics,
University of Liverpool

Deputy Director,
Professor Jon Nicholl,
Director, Medical Care Research Unit, University of Sheffield,
School of Health and Related Research

Prioritisation Strategy Group

Members

Chair,
Professor Tom Walley,
Director, NHS HTA Programme,
Department of Pharmacology & Therapeutics,
University of Liverpool

Professor Bruce Campbell,
Consultant Vascular & General Surgeon, Royal Devon & Exeter Hospital

Professor Robin E Ferner,
Consultant Physician and Director, West Midlands Centre for Adverse Drug Reactions,
City Hospital NHS Trust,
Birmingham

Dr Edmund Jessop, Medical Adviser, National Specialist, Commissioning Advisory Group (NSCAG), Department of Health, London

Professor Jon Nicholl, Director, Medical Care Research Unit,
University of Sheffield,
School of Health and Related Research

Dr Ron Zimmern, Director,
Public Health Genetics Unit,
Strangeways Research Laboratories, Cambridge

HTA Commissioning Board

Members

Programme Director,
Professor Tom Walley,
Director, NHS HTA Programme,
Department of Pharmacology & Therapeutics,
University of Liverpool

Chair,
Professor Jon Nicholl,
Director, Medical Care Research Unit, University of Sheffield,
School of Health and Related Research

Deputy Chair,
Dr Andrew Farmer,
University Lecturer in General Practice, Department of Primary Health Care,
University of Oxford

Dr Jeffrey Aronson,
Reader in Clinical Pharmacology, Department of Clinical Pharmacology,
Radcliffe Infirmary, Oxford

Professor Deborah Ashby,
Professor of Medical Statistics,
Department of Environmental and Preventative Medicine,
Queen Mary University of London

Professor Ann Bowling,
Professor of Health Services Research, Primary Care and Population Studies,
University College London

Professor John Cairns,
Professor of Health Economics,
Public Health Policy,
London School of Hygiene and Tropical Medicine,
London

Professor Nicky Cullum,
Director of Centre for Evidence Based Nursing, Department of Health Sciences, University of York

Professor Jon Deeks,
Professor of Health Statistics,
University of Birmingham

Professor Jenny Donovan,
Professor of Social Medicine,
Department of Social Medicine,
University of Bristol

Professor Freddie Hamdy,
Professor of Urology,
University of Sheffield

Professor Allan House,
Professor of Liaison Psychiatry,
University of Leeds

Professor Sallie Lamb, Director,
Warwick Clinical Trials Unit,
University of Warwick

Professor Stuart Logan,
Director of Health & Social Care Research, The Peninsula Medical School, Universities of Exeter & Plymouth

Professor Miranda Mugford,
Professor of Health Economics,
University of East Anglia

Dr Linda Patterson,
Consultant Physician,
Department of Medicine,
Burnley General Hospital

Professor Ian Roberts,
Professor of Epidemiology & Public Health, Intervention Research Unit, London School of Hygiene and Tropical Medicine

Professor Mark Sculpher,
Professor of Health Economics,
Centre for Health Economics,
Institute for Research in the Social Services,
University of York

Professor Kate Thomas,
Professor of Complementary and Alternative Medicine,
University of Leeds

Professor David John Torgerson,
Director of York Trial Unit,
Department of Health Sciences,
University of York

Professor Hywel Williams,
Professor of Dermato-Epidemiology,
University of Nottingham

Current and past membership details of all HTA 'committees' are available from the HTA website (www.hta.ac.uk)

Diagnostic Technologies & Screening Panel

Members

Chair,
Dr Ron Zimmern, Director of the Public Health Genetics Unit, Strangeways Research Laboratories, Cambridge

Ms Norma Armston, Freelance Consumer Advocate, Bolton

Professor Max Bachmann, Professor of Health Care Interfaces, Department of Health Policy and Practice, University of East Anglia

Professor Rudy Bilous Professor of Clinical Medicine & Consultant Physician, The Academic Centre, South Tees Hospitals NHS Trust

Ms Dea Birkett, Service User Representative, London

Dr Paul Cockcroft, Consultant Medical Microbiologist and Clinical Director of Pathology, Department of Clinical Microbiology, St Mary's Hospital, Portsmouth

Professor Adrian K Dixon, Professor of Radiology, University Department of Radiology, University of Cambridge Clinical School

Dr David Elliman, Consultant in Community Child Health, Islington PCT & Great Ormond Street Hospital, London

Professor Glyn Elwyn, Research Chair, Centre for Health Sciences Research, Cardiff University, Department of General Practice, Cardiff

Professor Paul Glasziou, Director, Centre for Evidence-Based Practice, University of Oxford

Dr Jennifer J Kurinczuk, Consultant Clinical Epidemiologist, National Perinatal Epidemiology Unit, Oxford

Dr Susanne M Ludgate, Clinical Director, Medicines & Healthcare Products Regulatory Agency, London

Mr Stephen Pilling, Director, Centre for Outcomes, Research & Effectiveness, Joint Director, National Collaborating Centre for Mental Health, University College London

Mrs Una Rennard, Service User Representative, Oxford

Dr Phil Shackley, Senior Lecturer in Health Economics, Academic Vascular Unit, University of Sheffield

Dr Margaret Somerville, Director of Public Health Learning, Peninsula Medical School, University of Plymouth

Dr Graham Taylor, Scientific Director & Senior Lecturer, Regional DNA Laboratory, The Leeds Teaching Hospitals

Professor Lindsay Wilson Turnbull, Scientific Director, Centre for MR Investigations & YCR Professor of Radiology, University of Hull

Professor Martin J Whittle, Clinical Co-director, National Co-ordinating Centre for Women's and Childhealth

Dr Dennis Wright, Consultant Biochemist & Clinical Director, The North West London Hospitals NHS Trust, Middlesex

Pharmaceuticals Panel

Members

Chair,
Professor Robin Ferner, Consultant Physician and Director, West Midlands Centre for Adverse Drug Reactions, City Hospital NHS Trust, Birmingham

Ms Anne Baileff, Consultant Nurse in First Contact Care, Southampton City Primary Care Trust, University of Southampton

Professor Imti Choonara, Professor in Child Health, Academic Division of Child Health, University of Nottingham

Professor John Geddes, Professor of Epidemiological Psychiatry, University of Oxford

Mrs Barbara Greggains, Non-Executive Director, Greggains Management Ltd

Dr Bill Gutteridge, Medical Adviser, National Specialist Commissioning Advisory Group (NSCAG), London

Mrs Sharon Hart, Consultant Pharmaceutical Adviser, Reading

Dr Jonathan Karnon, Senior Research Fellow, Health Economics and Decision Science, University of Sheffield

Dr Yoon Loke, Senior Lecturer in Clinical Pharmacology, University of East Anglia

Ms Barbara Meredith, Lay Member, Epsom

Dr Andrew Prentice, Senior Lecturer and Consultant Obstetrician & Gynaecologist, Department of Obstetrics & Gynaecology, University of Cambridge

Dr Frances Rotblat, CPMP Delegate, Medicines & Healthcare Products Regulatory Agency, London

Dr Martin Shelly, General Practitioner, Leeds

Mrs Katrina Simister, Assistant Director New Medicines, National Prescribing Centre, Liverpool

Dr Richard Tiner, Medical Director, Medical Department, Association of the British Pharmaceutical Industry, London

Therapeutic Procedures Panel

Members

Chair,
Professor Bruce Campbell, Consultant Vascular and General Surgeon, Department of Surgery, Royal Devon & Exeter Hospital

Dr Mahmood Adil, Deputy Regional Director of Public Health, Department of Health, Manchester

Dr Aileen Clarke, Consultant in Public Health, Public Health Resource Unit, Oxford

Professor Matthew Cooke, Professor of Emergency Medicine, Warwick Emergency Care and Rehabilitation, University of Warwick

Mr Mark Emberton, Senior Lecturer in Oncological Urology, Institute of Urology, University College Hospital

Professor Paul Gregg, Professor of Orthopaedic Surgical Science, Department of General Practice and Primary Care, South Tees Hospital NHS Trust, Middlesbrough

Ms Maryann L Hardy, Lecturer, Division of Radiography, University of Bradford

Dr Simon de Lusignan, Senior Lecturer, Primary Care Informatics, Department of Community Health Sciences, St George's Hospital Medical School, London

Dr Peter Martin, Consultant Neurologist, Addenbrooke's Hospital, Cambridge

Professor Neil McIntosh, Edward Clark Professor of Child Life & Health, Department of Child Life & Health, University of Edinburgh

Professor Jim Neilson, Professor of Obstetrics and Gynaecology, Department of Obstetrics and Gynaecology, University of Liverpool

Dr John C Pounsford, Consultant Physician, Directorate of Medical Services, North Bristol NHS Trust

Dr Karen Roberts, Nurse Consultant, Queen Elizabeth Hospital, Gateshead

Dr Vimal Sharma, Consultant Psychiatrist/Hon. Senior Lecturer, Mental Health Resource Centre, Cheshire and Wirral Partnership NHS Trust, Wallasey

Professor Scott Weich, Professor of Psychiatry, Division of Health in the Community, University of Warwick

Disease Prevention Panel

Members

Chair,
Dr Edmund Jessop, Medical Adviser, National Specialist Commissioning Advisory Group (NSCAG), London

Mrs Sheila Clark, Chief Executive, St James's Hospital, Portsmouth

Mr Richard Copeland, Lead Pharmacist: Clinical Economy/Interface, Wansbeck General Hospital, Northumberland

Dr Elizabeth Fellow-Smith, Medical Director, West London Mental Health Trust, Middlesex

Mr Ian Flack, Director PPI Forum Support, Council of Ethnic Minority Voluntary Sector Organisations, Stratford

Dr John Jackson, General Practitioner, Newcastle upon Tyne

Mrs Veronica James, Chief Officer, Horsham District Age Concern, Horsham

Professor Mike Kelly, Director, Centre for Public Health Excellence, National Institute for Health and Clinical Excellence, London

Professor Yi Mien Koh, Director of Public Health and Medical Director, London NHS (North West London Strategic Health Authority), London

Ms Jeanett Martin, Director of Clinical Leadership & Quality, Lewisham PCT, London

Dr Chris McCall, General Practitioner, Dorset

Dr David Pencheon, Director, Eastern Region Public Health Observatory, Cambridge

Dr Ken Stein, Senior Clinical Lecturer in Public Health, Director, Peninsula Technology Assessment Group, University of Exeter, Exeter

Dr Carol Tannahill, Director, Glasgow Centre for Population Health, Glasgow

Professor Margaret Thorogood, Professor of Epidemiology, University of Warwick, Coventry

Dr Ewan Wilkinson, Consultant in Public Health, Royal Liverpool University Hospital, Liverpool

Expert Advisory Network

Members

Professor Douglas Altman, Professor of Statistics in Medicine, Centre for Statistics in Medicine, University of Oxford

Professor John Bond, Director, Centre for Health Services Research, University of Newcastle upon Tyne, School of Population & Health Sciences, Newcastle upon Tyne

Professor Andrew Bradbury, Professor of Vascular Surgery, Solihull Hospital, Birmingham

Mr Shaun Brogan, Chief Executive, Ridgeway Primary Care Group, Aylesbury

Mrs Stella Burnside OBE, Chief Executive, Regulation and Improvement Authority, Belfast

Ms Tracy Bury, Project Manager, World Confederation for Physical Therapy, London

Professor Iain T Cameron, Professor of Obstetrics and Gynaecology and Head of the School of Medicine, University of Southampton

Dr Christine Clark, Medical Writer & Consultant Pharmacist, Rossendale

Professor Collette Clifford, Professor of Nursing & Head of Research, School of Health Sciences, University of Birmingham, Edgbaston, Birmingham

Professor Barry Cookson, Director, Laboratory of Healthcare Associated Infection, Health Protection Agency, London

Dr Carl Counsell, Clinical Senior Lecturer in Neurology, Department of Medicine & Therapeutics, University of Aberdeen

Professor Howard Cuckle, Professor of Reproductive Epidemiology, Department of Paediatrics, Obstetrics & Gynaecology, University of Leeds

Dr Katherine Darton, Information Unit, MIND – The Mental Health Charity, London

Professor Carol Dezateux, Professor of Paediatric Epidemiology, London

Dr Keith Dodd, Consultant Paediatrician, Derby

Mr John Dunning, Consultant Cardiothoracic Surgeon, Cardiothoracic Surgical Unit, Papworth Hospital NHS Trust, Cambridge

Mr Jonothan Earnshaw, Consultant Vascular Surgeon, Gloucestershire Royal Hospital, Gloucester

Professor Martin Eccles, Professor of Clinical Effectiveness, Centre for Health Services Research, University of Newcastle upon Tyne

Professor Pam Enderby, Professor of Community Rehabilitation, Institute of General Practice and Primary Care, University of Sheffield

Professor Gene Feder, Professor of Primary Care Research & Development, Centre for Health Sciences, Barts & The London Queen Mary's School of Medicine & Dentistry, London

Mr Leonard R Fenwick, Chief Executive, Newcastle upon Tyne Hospitals NHS Trust

Mrs Gillian Fletcher, Antenatal Teacher & Tutor and President, National Childbirth Trust, Henfield

Professor Jayne Franklyn, Professor of Medicine, Department of Medicine, University of Birmingham, Queen Elizabeth Hospital, Edgbaston, Birmingham

Dr Neville Goodman, Consultant Anaesthetist, Southmead Hospital, Bristol

Professor Robert E Hawkins, CRC Professor and Director of Medical Oncology, Christie CRC Research Centre, Christie Hospital NHS Trust, Manchester

Professor Allen Hutchinson, Director of Public Health & Deputy Dean of ScHARR, Department of Public Health, University of Sheffield

Professor Peter Jones, Professor of Psychiatry, University of Cambridge, Cambridge

Professor Stan Kaye, Cancer Research UK Professor of Medical Oncology, Section of Medicine, Royal Marsden Hospital & Institute of Cancer Research, Surrey

Dr Duncan Keeley, General Practitioner (Dr Burch & Ptnrs), The Health Centre, Thame

Dr Donna Lamping, Research Degrees Programme Director & Reader in Psychology, Health Services Research Unit, London School of Hygiene and Tropical Medicine, London

Mr George Levvy, Chief Executive, Motor Neurone Disease Association, Northampton

Professor James Lindesay, Professor of Psychiatry for the Elderly, University of Leicester, Leicester General Hospital

Professor Julian Little, Professor of Human Genome Epidemiology, Department of Epidemiology & Community Medicine, University of Ottawa

Professor Rajan Madhok, Consultant in Public Health, South Manchester Primary Care Trust, Manchester

Professor Alexander Markham, Director, Molecular Medicine Unit, St James's University Hospital, Leeds

Professor Alistaire McGuire, Professor of Health Economics, London School of Economics

Dr Peter Moore, Freelance Science Writer, Ashtead

Dr Andrew Mortimore, Public Health Director, Southampton City Primary Care Trust, Southampton

Dr Sue Moss, Associate Director, Cancer Screening Evaluation Unit, Institute of Cancer Research, Sutton

Mrs Julietta Patnick, Director, NHS Cancer Screening Programmes, Sheffield

Professor Robert Peveler, Professor of Liaison Psychiatry, Royal South Hants Hospital, Southampton

Professor Chris Price, Visiting Professor in Clinical Biochemistry, University of Oxford

Professor William Rosenberg, Professor of Hepatology and Consultant Physician, University of Southampton, Southampton

Professor Peter Sandercock, Professor of Medical Neurology, Department of Clinical Neurosciences, University of Edinburgh

Dr Susan Schonfield, Consultant in Public Health, Hillingdon PCT, Middlesex

Dr Eamonn Sheridan, Consultant in Clinical Genetics, Genetics Department, St James's University Hospital, Leeds

Professor Sarah Stewart-Brown, Professor of Public Health, University of Warwick, Division of Health in the Community Warwick Medical School, LWMS, Coventry

Professor Ala Szczepura, Professor of Health Service Research, Centre for Health Services Studies, University of Warwick

Dr Ross Taylor, Senior Lecturer, Department of General Practice and Primary Care, University of Aberdeen

Mrs Joan Webster, Consumer member, HTA – Expert Advisory Network

Feedback

The HTA Programme and the authors would like to know your views about this report.

The Correspondence Page on the HTA website (http://www.hta.ac.uk) is a convenient way to publish your comments. If you prefer, you can send your comments to the address below, telling us whether you would like us to transfer them to the website.

We look forward to hearing from you.

The National Coordinating Centre for Health Technology Assessment,
Alpha House, Enterprise Road
Southampton Science Park
Chilworth
Southampton SO16 7NS, UK.
Fax: +44 (0) 23 8059 5639 Email: hta@hta.ac.uk
http://www.hta.ac.uk

ISSN 1366-5278