RAPID REVIEWS FOR THE HTA PROGRAMME

A. **This protocol is provisional and subject to change**

B. **Details of review team**

The review will be conducted by the School of Health and Related Research (ScHARR) Rapid Review Group based at the University of Sheffield.

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C. Title: The clinical and cost-effectiveness of ultrasound locating devices for placing central venous lines.

D. **Clarification of research question and scope**

The scope of the question as currently defined is broad. CVLs are inserted in patients for a whole host of clinical reasons including short-term analysis of patients admitted to intensive care units to long term haemodialysis and administration of drugs for patients with cancer and AIDS. The review will assess the clinical and economic consequences of CVL placement using ultrasound guidance compared with standard placement for key clinical indications. This analysis will be condition specific if a more generic analysis is deemed inappropriate. An overview of both current and ongoing research evidence will be presented.

More specifically the review aims to:

i. Compare complications rates from insertion of CVL using ultrasound versus standard placement methods.
ii. Assess any consequent clinical, quality of life, and patient satisfaction implications of any differences in complication rates identified in (i).
iii. Model the marginal economic costs and benefits of ultrasound versus standard CVL placement.
iv. Assess the implications of increased use of ultrasound for placement of CVLs on radiology departments in the NHS.

Early research for this review has identified that a key issue in the placement of CVLs is the possible increased use of trained nurse operators complementing or replacing the role traditionally played by clinicians (surgical, medical and radiological staff). This operator issue has been subjected to research as part of the HTA CLIP trial (in press)[1]. It is proposed that this review should include an analysis of the cost and benefit implications of using nurse operators for CVL placement using blind and ultrasound guided techniques.

Report Methods

Search strategy

Searches using the following databases will be undertaken; Medline, Embase, Science Citation Index (SCI), Cochrane Library, NHS CRD DARE, NHS EED and HTA, OHE HEED and PubMED. Language limits will not be used unless the number of 'hits' necessitates a narrowing of the search. The search will aim to identify studies that evaluate ultrasonic guided placement of central venous lines. Search strategies will include the terms central venous line, CVL, central venous catheter, CVC, Hickman, ultrasound/image guidance, Doppler.

Expectations at this stage of the research are that there will be a relatively small evidence base in the literature. If this is the case then the search results will not be restricted by publication type or by study design. Studies identified, which do not meet the review inclusion criteria, may be important in identifying further relevant papers and current research. Current research registers will be searched and relevant professional and research organisations will be contacted. Citation searches of included studies will be undertaken using the SCI citation search facility. The reference list of included studies and of sponsor submissions will also be checked.

Inclusion and exclusion criteria

Studies conducted on human (adults and children) subjects only will be included. CVLs are used for a variety of patient conditions including cancer, HIV/AIDS, and patients treated in intensive care units, so no single condition can be defined for inclusion at this stage. Main outcome measures will include complication rates (eg catheter tip misplacement, pneumothorax, arterial puncture, haematoma, infection, and failed insertion), and economic cost and outcome related terms. Comparator interventions will include standard (non-ultrasonic) placement methods including blind and surgical placement. Provision of service and nurse training will also be included as they are key

issues in CVL placement in the NHS. RCTs comparing the two technologies will be the gold standard although other study designs will be included if evidence from RCTs is insufficient. An independent reviewer will select studies for inclusion with guidance from clinical experts.

Data extraction strategy
Data will be extracted, using standardised forms, by one reviewer, and checked by a second, with any disagreements being resolved by discussion.

Quality assessment strategy
Published papers will be assessed according to the accepted hierarchy of evidence, whereby systematic reviews of randomised controlled trials are taken to be the most authoritative forms of evidence, with uncontrolled observational studies the least authoritative. A detailed description of the methodology of all included studies will be provided. Scoring systems such as Jadad for RCTs may be used as appropriate.

Methods of analysis/synthesis
The precise methods of any analysis and synthesis will be determined by the availability and volume of appropriate studies reported in the literature. Meta analysis will be undertaken where appropriate. It is particularly difficult to be more precise before reviewing the literature because CVLs are inserted for a variety of clinical and non-clinical reasons and in a number of medical and surgical specialties. Synthesis of published results may therefore not be appropriate.

Methods for estimating qualify of life, costs and cost-effectiveness and/or cost/QALY
At this stage in the research, it is equally difficult to be precise about the appropriate economic analysis to be undertaken. The choice to use ultrasonic imaging in CVL placement will rarely save lives, but may reduce complications rates from blind placement. The appropriate analyses are likely to be cost-consequence, cost-effectiveness (where effectiveness accounts for specific or general complication rates, or possibly lives saved), or cost-minimisation analysis, where costs of complications avoided are included in the analysis. Cost-utility analysis, where cost per QALY is assessed is unlikely to be appropriate in this clinical context. Insertion of Hickman lines per se does not lead to improved health outcomes for patients. Their use with chemotherapy or blood products will improve patient quality of life. There will be short-term effects on quality of life if use of ultrasound significantly reduces complication rates such as infection and pneumothorax. The review will report and use any published estimates of changes in quality of life for patients. It is anticipated that the economic analysis will include an analysis of the implications of increased use of nurse operators for ultrasonic guided and standard placement of CVLs.

Sensitivity analysis will be undertaken with the objective of identifying variables that produce the greatest uncertainties in the economic analysis presented. Sensitivity analysis will identify whether available information and evidence is sufficient for the purposes of commissioning decisions or whether further evidence would be of value to commissioners.

E. Handling the company submission(s)

A critique of economic analyses submitted by the manufacturers will be provided. Any economic model produced by ScHARR will be independent of models presented in the industry submission. Any differences between ScHARR and industry based models will be justified. Any 'commercial in confidence' data taken from the company submission and used in the independent review will be highlighted using underlining in the HTA report, (followed by an indication of the relevant company name e.g. in brackets) so that the NICE secretariat can negotiate, (before and during the Institute's consultation process) with industry, the subsequent inclusion of such data in the HTA monograph publication or subsequent peer-review publications.

F. Project Management

a. **Timetable/milestones** - submission of:

Draft protocol: July 30 2001

Progress report: November 2 2001

Draft final report: January 24 2002

b. **Competing Interests**
None of the authors has any financial interests in the companies producing the technologies being assessed in this report.

c. **External reviewers** :
The rapid review will be subject to external peer review by at least two experts. These reviewers will be chosen according to academic seniority and content expertise and will be agreed with NCCHTA. We recognise that the NICE secretariat and Appraisal Committee will undertake methodological review, but if the rapid review encounters particularly challenging methodological issues we will organise independent methodological reviews. External expert reviewers will see a complete and near final draft of the rapid review and will understand that their role is part of external quality assurance. Where the review contains data that is regarded as 'commercial in confidence' we will require peer reviewers to sign a copy of the NICE Confidentiality Acknowledgement and Undertaking. We will return peer reviewers' signed copies to NCCHTA. Comments from external reviewers and our responses to these will be made available to NCCHTA in strict confidence for editorial review and approval.

G. Appendices

Background

It has been estimated that around 200,000 central venous catheters (CVCs) are placed in NHS patients annually[2]. The total annual cost to the NHS of this activity is conservatively estimated at £80 million. CVLs are placed for a variety of reasons but most commonly for the delivery of total parenteral nutrition (TPN). The range of indications for CVLs has expanded over recent years including both hospital and ambulatory use for TPN, long term chemotherapy, and haemodialysis. Demand for CVCs is increasing as supply of treatments for leukaemia, solid tumours, AIDS, and infection expands.

Over recent years radiologists have developed techniques to guide the placement of CVLs. Protagonists of the use the ultrasonic technologies argue that complication rates (catheter tip misplacement, pneumothorax, arterial punctures, infections, failed insertions etc) which result from the use of standard placement techniques will be reduced. As well as being beneficial for patients and patient care, costs of averted treatment for complications will be reduced. On the other hand, increased use of ultrasound will have implications for the demand on ultrasonic equipment and radiologists, and therefore capacity within radiology departments will almost certainly need to expand or prices will be driven upwards. The relative economic costs and benefits using ultrasound guidance for CVL placement compared with standard placement techniques therefore need quantifying.

One solution to addressing the potential problem of limited radiology department capacity is to increase the transference of skills for placement of CVLs from clinicians to trained nurses. The acceptability and capacity for this skill transference to take place, including an analysis of the implications for nurse training should be undertaken. Many of these issues are being researched by the HTA CLIP trial, which at the time of writing is close to publication

Reference List

1. Boland A, Fitzsimmons L, Haycox A, and Bagust A. A randomised controlled trial to evaluate the clinical and cost-effectiveness of Hickman line insertions in adult cancer patients. HTA . 2001.
Ref Type: In Press

2. Elliot TSJ, Faroqui MH, Armstrong RF, Hanson GC. Guidelines for good practice in central venous catheterization. *Journal of Hospital Infection* 1994;**28**:163-76.