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The effectiveness and cost-effectiveness of ultrasound locating devices for central venous access: a systematic review and economic evaluation

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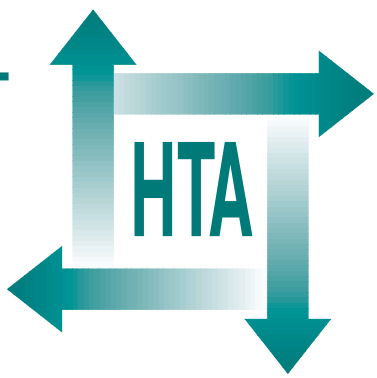

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Contents

List of abbreviations

CI	confidence interval
CPR	cardiopulmonary resuscitation
CVA	central venous access
CVC	central venous catheter
CVL	central venous line
2-D/3-D	two-/three-dimensional
df	degrees of freedom
FV	femoral vein
HDU	high-dependency unit
ICU	intensive care unit
IJV	internal jugular vein
NICE	National Institute for Clinical Excellence
PICC	peripherally inserted central catheter
RCT	randomised controlled trial
SV	subclavian vein
ULD	ultrasonic locating device
US	ultrasound

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

Background

Approximately 200,000 central venous access (CVA) procedures are performed annually in the NHS.

CVA has traditionally been achieved by the landmark method of passing the needle along the anticipated line of the relevant vein using surface anatomical landmarks and the expected relationship of the vein to its palpable companion artery. While experienced operators can achieve relatively high success rates with the landmark method with few complications, such as arterial puncture and pneumothorax, failure rates in the literature have been reported to be as high as 35%.

The experience of radiologists suggests that CVA can be achieved quickly, with low failure and complication rates, using ultrasonic locating devices (ULD). There are two types: ultrasound (US) probes generating a two-dimensional (2-D) grey-scale image; and Doppler® US generating an audible sound from flowing venous blood. In practice the 2-D US is used in preference to Doppler US. A crude estimate of the cost of promoting 2-D US in the NHS is £29 million in the first year, reducing in following years.

Objectives

- To investigate the clinical and cost-effectiveness of ULD.

Methods

Major bibliographic databases were searched up to October 2001 for references on ULDs and central venous lines. Randomised controlled trials (RCTs) were targeted. Only studies with the following features were included:

- 2-D US or Doppler US compared with the landmark method or a surgical cut-down procedure
- study populations requiring the placement of central venous lines
- measuring outcomes such as the number of failed catheter placements, number of catheter placement complications, risk of failure on the first catheter placement attempt, number of attempts to successful catheterisation, number of seconds to successful catheterisation, rate of success after failure by the alternate method (where a crossover design was incorporated).

A systematic review of economic analyses was also undertaken.

Results

Review of clinical effectiveness

Twenty RCTs of variable methodological quality were identified. Sample sizes were generally small. A total of 13 studies addressed 2-D US versus landmark procedures. Eight studies addressed internal jugular vein (IJV) venepuncture, one subclavian vein (SV) insertions, and one femoral vein (FV) insertions: all ten of these were in adults. Two studies analysed IJV insertions in infants. One reported neither the age of the population nor the insertion site. Six studies addressed Doppler US versus landmark, all in adults. In three of these studies, the insertion site was the IJV while in two it was the SV. One RCT had four arms, comparing Doppler US and landmark for insertion in both the IJV and the SV. Only one very small study compared 2-D US, Doppler US and landmark for the venepuncture of infants through the IJV.

The trial evidence suggests that 2-D US is significantly better than landmark for all five outcome variables measured for insertions into the IJV in adults. The results also favour 2-D US for insertions into the SV and FV in adults, although based on only one RCT each. For the three infant studies addressing insertion into the IJV, the results again suggest that 2-D US has a statistically significant beneficial effect.

For Doppler US, only insertions into the IJV in adults, reported in four RCTs, indicated improved failure and complication rates over landmark. The other three Doppler US RCTs for SV insertions in adults and IJV insertions in

children provide little support for Doppler over landmark methods. For clinically experienced operators, proficient with the landmark method, Doppler US increased the number of failed catheter placements in attempts to catheterise the SV. The extent to which it is possible to generalise from these results for Doppler US is unclear.

Economic analysis

No studies were identified from the systematic review of economic analyses.

A spreadsheet decision-analytic model was carried out to assess cost-effectiveness. Because Doppler US is less common than 2-D US and the effectiveness evidence suggests Doppler is less effective compared with 2-D US, 2-D US compared with landmark was the focus. Costing analysis indicates that the marginal cost of using US for CVA is less than £10 per procedure. It is sensitive to assumptions about machine usage. The base scenario assumes that a machine is used for 15 procedures each week. Other base scenario assumptions are deliberately cautious about the potential economic costs and benefits of US.

Economic modelling results indicate that using 2-D US in CVA is likely to save NHS resources as well as improve failure and complication rates. For every 1000 procedures undertaken, a resource saving of £2000 has been suggested to result. Sensitivity analysis indicates that the results of modelling appear to be robust and that the resource saving result is likely to hold for the three main insertion sites, and for both adults and children. The modelling results are most sensitive to US machine usage assumptions implying that purchased machines should be used sufficiently often to make them economically efficient.

Conclusions

There is evidence for the effectiveness and cost-effectiveness of 2-D US-guided CVA, particularly via the IJV in adults and children. However, some important implications of possible wider use of 2-D US for CVA are clearly identifiable.

Implications for the NHS

There are significant training implications if the US-guided procedure is to be advocated. Economic modelling indicates that training schemes would need to be set up in a cost-effective way in order to ensure that the US procedure is itself cost-effective. Training of medical and nursing staff would need to be coordinated and agreed among professional bodies.

In emergency situations, where a line needs to be inserted without delay, landmark insertions may still be appropriate. It is important that training in US-guided access allows operators to remain skilled in the landmark methods.

If machines were purchased to guide IJV insertions, policy-makers would need to consider how US should be used for CVA for non-IJV insertions where evidence is more limited. If SV insertions were to be performed without US when machines are available, this could lead to avoidable complications, with medico-legal implications. If 2-D US were not to be recommended for SV insertions, a compromise policy of advocating US for patency checking and vessel localisation might be applicable. The possible implications of more widespread use of US for operators already skilled in the use of landmark methods, also needs to be considered. Again the compromise policy may be applicable.

Recommendations for research

No RCT evidence was found for the effectiveness of using US for peripherally inserted central catheters or for US versus surgical cut-down. The possible economic and clinical implications of CVA by nurse operators in the NHS may be another useful area for further research, given that feasibility has already been demonstrated.

Chapter 1
Introduction

Aim of the review

Central venous access (CVA) including catheter insertion, is routinely practised in a variety of emergency and elective situations and for a variety of clinical reasons. Traditionally the venepuncture procedure for CVA has been done using blind 'landmark' methods to locate and guide needle insertion into the target vessel. Occasionally, though more rarely, a surgical 'cut-down' procedure has been used to achieve CVA.

This rapid review investigates the effectiveness and cost-effectiveness of using ultrasound locating devices (ULDs) for the venepuncture procedure. The report focuses on the use of 2-dimentional (2-D) real-time grey-scale ultrasound (US) imaging as an alternative to the traditional landmark method.

Background

The underlying need for CVA

CVA, including catheter insertion, is routinely practised in emergency and elective situations for haemodynamic monitoring, delivery of blood products and drugs (e.g. chemotherapy and antibiotics), haemodialysis, total parenteral nutrition, and management of perioperative fluids. Patients needing CVA include cancer patients, dialysis patients, patients admitted to intensive care units (ICUs) and high-dependency units (HDUs), and patients undergoing coronary and other major surgery. Given that no routine data are collected, it is difficult to estimate how many catheters are placed each year in the NHS, although in a paper published in 1994 it was estimated that there are around 200,000 CVA procedures performed in the NHS each year.[1]

Central venous catheters (CVCs) are inserted in a wide range of settings within a hospital by a diverse group of doctors including radiologists, anaesthetists, nephrologists, oncologists, surgeons and general medical doctors. Nurse specialists in the USA and increasingly in the UK are also undertaking catheter insertions.[2] The range of settings includes operating theatres, emergency rooms, nephrology, oncology and other wards, radiology departments, ICUs and HDUs.

CVA can be achieved using various puncture sites on the human body but most commonly using the internal jugular vein (IJV), the subclavian vein (SV), femoral vein (FV), or upper limb veins (using peripherally inserted central catheters (PICCs)). The choice of access route depends on multiple factors including the reason for CVA, the anticipated duration of access, the sites available and the available skills.

If high flow rates are needed through a CVC then a large diameter catheter is needed, which precludes access from the small peripheral veins of the arm. High flow rates are needed for patients requiring large volumes of blood products and those undergoing haemodialysis. The large veins that may be accessed are the FV, SV and jugular vein. Although good data are not available nationally to breakdown the number of procedures by site of access, it is likely that the majority of CVA procedures are attempted initially by the IJV. Some clinicians use the SV route by preference, although the IJV is generally considered to be technically easier and to have a lower complication rate. FV access is used infrequently as there is a higher risk of catheter infection as the catheter tracks through the groin area and also a greater risk of catheter-related venous thrombosis.

When the anticipated duration of CVA is short then non-tunnelled lines are used where there is no subcutaneous tunnel and the catheter exits the skin through the same site that the vein is punctured. Infection and accidental line withdrawal are important risks of long-term venous access. To minimise these risks a tunnelled line may be used. CVA is achieved in the same way as for non-tunnelled lines. However, the catheter passes through a subcutaneous tunnel from the point of venous access to exit the skin several centimetres away. The subcutaneous portion of the catheter contains a cuff of synthetic material that causes local scarring, which both holds the catheter in place and reduces the risk of bacteria passing from the skin surface to the bloodstream.

The first step in establishing percutaneous venous access is safe puncture of a central vein (venepuncture). This may be achieved by passing the needle along the anticipated line of the relevant vein using surface anatomical landmarks and by knowing the expected anatomical relationship of the vein to its palpable, companion artery, in the case of the IJV. This 'landmark technique' has been the traditional approach to venepuncture. Surgical 'cut-down' is a more invasive and alternative method for gaining CVA, although this technique is rarely used. This report is primarily concerned with examining the most effective and cost-effective way of achieving successful and safe venepuncture during the placement of central venous lines (CVLs).

Venepuncture complications

It is not always possible to achieve a successful catheter placement using the chosen puncture site. Anatomical relationships are variable and variant anatomy will result in failure when the operator passes the puncture needle in a direction that the vein does not follow. A long-term complication of CVA is vein thrombosis. Many patients undergoing CVA procedures will have had multiple previous episodes of central catheterisation. If the relevant vein has thrombosed then the landmark method will fail irrespective of the anatomical course of this thrombosed vein.

Each pass of a needle during the venepuncture procedure carries with it the risk of complications. Successful access at the first attempt is clearly the ideal for minimising the risk of complications. In the case of a thrombosed vein, for example, an operator may make numerous needle passes before realising that access is not possible at the chosen puncture site. Each pass of the needle increases the risk of complication as well as delaying subsequent catheter placement. Failure or delayed CVA may delay important treatments in ill patients.

The complication rate from these procedures varies. The complications of CVA procedures range from minor issues to uncommon but possibly fatal haemorrhage. The most common complications are arterial puncture, arteriovenous fistula, pneumothorax, nerve injury and multiple unsuccessful attempts with delayed treatment. The risks and the consequences of complications vary substantially across patients and patient groups. For example, infants, obese patients, and patients with short necks are more difficult to puncture. Also, patients with clotting problems, ventilated patients, and cardiac patients undergoing emergency pacing procedures may suffer more serious consequences (including death) from a venepuncture complication. A recent report of the National Confidential Enquiry into Perioperative Deaths indicates that in a survey of over 3000 CVA procedures undertaken in the NHS, one death occurred as a result of a procedure-induced pneumothorax.[3] It is particularly important that the risks of failed insertion and complications are minimised. Having said this, any procedure undertaken in resource intensive surroundings like theatres and ICU/HDU make it important, from both a clinical and a resource point of view, that venepuncture for CVA is achieved as quickly and as safely as possible.

Current service provision

The preceding discussion highlights the difficulties of deriving estimates of the number of CVC placed annually within the NHS. Based on sales figures from appropriate catheter suppliers, one of our expert advisers has estimated the number of central venous catheterisations for a teaching trust in Liverpool to be in the region of 1500 per annum. This figure includes all tunnelled Hickman and dialysis lines, temporary CVA lines, and PICCs. A similarly derived estimate for the Sheffield Teaching Hospitals NHS Trust is over 3700 catheters per annum.

Data are not readily available to break down these figures for different speciality groups, sites of access, and insertion technique employed. The Sheffield Teaching Hospitals NHS Trust has estimated that their own figures imply that 46% of the total is accounted for by cardiac surgery and coronary ICU, 32% by general ICU/HDU units, and 8% for renal patients. In major renal centres such as Leeds, the proportion of catheter placements might be expected to be higher for renal patients. Better data are available from the USA where it is recorded that of 835,003 CVC insertions in 1999, 80% were temporary non-tunnelled lines and 20% were tunnelled permanent lines.[4] Radiologists inserted 15% of temporary and 20% of tunnelled lines in 1999. Surgeons placed the majority (72%) of tunnelled lines. Anaesthesiology (36%) and surgery (24%) were the major speciality groups inserting non-tunnelled CVCs.

Although there are likely to be some differences in these percentages in England and Wales, it is highly probable that anaesthetists and surgeons, as in the USA, insert the majority of non-tunnelled lines. It is also probable that surgeons and anaesthetists insert the majority of tunnelled lines.

It is difficult to estimate the cost of venepuncture in CVL placement because of the paucity of costing data in this area. The disposable equipment, such as the needle used in the procedure will cost pence rather than pounds. The major cost of the procedure will be the time resource for the operator to achieve successful venepuncture. This will normally be only a few minutes, although failed insertions can take up to three-quarters of an hour.[5,6] In an expensive ICU unit and using a highly qualified operator for example, the opportunity cost of a difficult insertion will be considerably more than a successful venepuncture achieved with the first pass of the venepuncture needle. Complications induced by the venepuncture may have only minor resource implications. Alternatively, a serious complication such as pneumothorax in a high-risk patient who then needs to be hospitalised for a number of days for treatment and monitoring can use hundreds or even thousands of pounds worth of resources.

Description of the new intervention

US has traditionally been the domain of radiologists and ultrasonographers. Radiologists use US to guide percutaneous procedures at multiple sites such as the kidneys, liver, arterial and venous circulation, pleural cavity, gallbladder, joints and bowel. This expertise is applied to CVA procedures where there are large series that record 100% success for right internal jugular access with no clinically important complications.[7] One of the largest series from the interventional radiology literature records a 99.4% initial success rate in deployment of tunnelled central lines with no major complications in a group of 880 consecutive patients.[8] CVA in all these patients was achieved with real-time US guidance.

The previous discussion has shown the diverse clinical indications requiring venepuncture for CVC placement and the numerous sites where the procedure is undertaken both within the hospital and on the human body. Portable US machines now exist with the functionality for high-quality imaging and can be used in theatres, ICU/HDU suites, and at the bedside on the hospital ward, as well as in the radiology suite. It is now standard practice for radiologists to use US imaging to guide the venepuncture procedure in CVC placement. However, radiologists do not perform the majority of central access procedures. Anaesthetists, renal physicians, surgeons and cardiologists all regularly establish CVA. Some of these doctors already use some form of US localisation. In principle, and with adequate training for the operator, it is theoretically possible that US-guided venepuncture be used for all of the clinical scenarios discussed above.

The US image can be used to confirm the anatomy and patency of the vein (the state of being freely open or exposed). It has been reported that the sensitivity and specificity of ULD for detecting thrombosed vessels for example is 100%.[9] Having established these, the US machine can be dispensed with at the time of venous puncture.[10] Most radiologists, however, would go on to use the US to guide the venous puncture in real time.

Two main types of US have been used for this procedure in recent years: audio-guided Doppler® US and 2-D image US.

Audio-guided Doppler US

Continuous-wave Doppler US may be used to generate an audible sound from flowing venous blood. The audio-guided technique relies on the Doppler principle, which is the frequency shift that occurs when an US pulse is reflected by a moving object. The reflectors in veins are moving red blood cells and the frequency shift that occurs when US is reflected from veins in a breathing patient results in a characteristic pattern of sound that can be used to localise a vein and differentiate the vein from its companion artery. If the vein is localised then its site can be marked to assist percutaneous puncture. This technique can be used with reusable hand-held continuous wave pencil-like Doppler probes and also with single-use needles that contain a US crystal at their tip. Neither of these techniques is widely used.

2-D image US

The most commonly used ULD is a US probe linked to a US machine to provide real-time grey-scale imaging of the anatomy (*Figure 1*). A grey-scale image is generated by a US probe and machine. Superficial structures such as the jugular veins are best seen with US frequencies in the range 5–10 MHz. A real-time image allows the operator to identify the vein and distinguish the vein from its companion artery. The vein does not pulsate, if patent is compressible and is of more variable shape than its companion artery.

Some experience of US anatomy is necessary to reliably interpret US images. For example, cervical lymph nodes in patients with lymphoma, who often need venous access, can look remarkably like a vein on a single cross-sectional image of the neck. Many US machines incorporate a

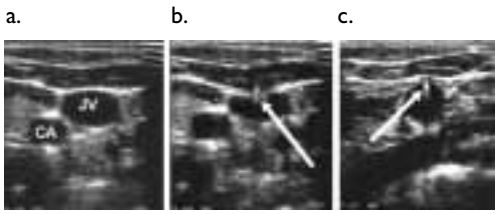

FIGURE 1 *2-D US images of the IJV being punctured by needle. (a) shows a transverse image of the neck and the relative positions of the IJV to be punctured and the carotid artery to be avoided; (b) shows the needle indenting the anterior wall of the vein; (c) illustrates the needle tip safely in the jugular vein*

Doppler facility with the ability to generate grey-scale images. This dual-mode or duplex scanning allows the operator to image the vein and confirm with certainty that this is not an artery by the additional use of Doppler US. In practice, this additional functionality is rarely needed.

The US image is generated by a series of crystals in the US probe, which transmit and receive US waves. When this is understood, the operator can image the vein and know which part of the probe is generating the image of the vein. Thus, if the vein is directly in the middle of the image a needle passed through the skin where the middle of the probe contacts the skin will travel in the direction of the vein. Some US probes incorporate a needle guide either as an integral part of the probe or as a removable attachment. The needle guide controls the movement of the needle in a predetermined and defined path in the image plane. The US machine plots the line of the needle on the monitor and as the needle is now fixed in one plane, an initial 3-D problem is reduced to a 2-D one.

Some US imaging equipment is dedicated solely to superficial imaging of the neck. These machines are cheaper than newer portable machines but the image quality of the dedicated machines is inferior. As well as providing better image quality the newer portable machines open up other possibilities for the wider use of medical US. A machine with additional functionality on an ICU may, with training, allow for US-guided drainage of pleural effusions, rapid diagnosis of cardiac tamponade, aspiration of ascites and other procedures. This will have implications for the cost-effectiveness of US-guided CVL placement.

Real-time scanning during needle passage is a skill that is not universal and has the potential to cause complications in the hands of untrained operators. Ideally the operator should hold the probe in a sterile cover in one hand and pass the puncture needle using the other hand guided by the US image. Some series record this as involving two people – one to hold the probe and the other to pass the needle.[11] This two-operator technique is cumbersome, unnecessary when experienced, adds to the expense of the procedure and compromises the potential of US-guided access in emergency situations.

Resource implications

The purchase cost of these portable machines currently varies between £7000 and £15,000.[12] The additional disposables necessary for the US-guided procedure cost less than £1 per procedure. Estimates made in this report indicate that the additional cost of using US equipment for the CVA procedure is likely to be less than £10 per procedure. This is discussed further in chapter 3.

What is less clear is how many machines need to be purchased if US were to be adopted as standard practice for CVA across the NHS in England and Wales. This will depend on both the extent of the policy recommendations, and the current supply of suitable portable US machines in NHS trusts.

In order to provide a ballpark estimate of the possible costs of a policy to adopt widespread use of US for CVA, a crude estimate of the possible capital and training costs implications has been calculated. Such an analysis carries many caveats. A Department of Health website quoting hospital activity statistics[13] indicates that there are approximately 2000 operating theatres (excluding dedicated day-case theatres) in England. The data are disaggregated to trust level analysis. Assuming one US machine for every three theatres, the estimated number of machines required by each trust has been estimated (rounding up or down to the nearest whole number) and aggregated to 660 machines for England as a whole.

The health service financial database[14] indicates that there are 193 English trusts (teaching, acute, and small to large multi-service units) and 16 Welsh trusts. Pro rata, this implies a total of 715 machines required for England and Wales operating theatres. Assuming three additional machines per trust to service ICU/HDU, accident and emergency, and ward use implies a total of 1342 machines. Costing each machine at £11,000 gives a total machine cost of approximately £15 million. Bulk purchasing by the NHS should mean that machines can be purchased at a reduced cost.

One manufacturer has indicated that this £15 million estimate could be reduced to £9 million. The availability of existing machines also implies that the £15 million is an overestimate. Additional ward and specialist (e.g. renal) unit requirements may mean this figure is an underestimate.

Training costs are the other major resource requirement. Again only a ballpark figure carrying many caveats is presented for indicative purposes. It is assumed (for illustrative purposes only) that a consultant radiologist/anaesthetist/surgeon has half of their time allocated to training relevant trust staff in the year following possible policy implementation. Assuming a consultant staff cost of £134,000,[15] the estimated training cost is £14 million for England and Wales in year 1 of implementation. In subsequent years this cost might be expected to fall as skills are cascaded downwards and the trained become trainers. This cost estimate does not include the trainee's time, or any capital cost requirement for training laboratories and dummies.

Thus, for the year following an assumed policy implementation, a crude estimate of capital and training costs is £29 million. This figure is clearly indicative only and carries many caveats.

Anecdotal evidence gathered during the preparation of this report indicates that the current availability of suitable machines varies from trust to trust. The Sheffield Teaching Hospitals trust, for example, has only one machine that is used occasionally by an anaesthetist. In Leeds, on the other hand, some 12 or so machines are available for use in their theatre and ICU/HDU suites. The resource implications of wider adoption of US for CVC placement will clearly vary significantly by trust.

Other uses

It is often stated that US assists only with the venous puncture and does not help with guide-wire introduction. This is not so in experienced hands, where the guide-wire can be imaged in the jugular vein and US at the root of the neck can be used to confirm that the wire has passed into the brachiocephalic vein and not the SV. US also confirms that the wire has not passed through the posterior wall of the jugular vein into the carotid artery, which is potentially the beginning of the rare complication of an arterio-venous fistula. This additional use of US is not difficult to learn. US is not used during the introduction of the dilators and sheaths prior to line introduction and the hazards that are relevant to these stages are not avoided with US but may be avoided by the use of fluoroscopy. Traditional US techniques have not been used to assess the position of the line tip and this is achieved either with fluoroscopy at the time of insertion or with a post-procedural chest radiograph.

This report only concerns itself with the evidence for the effectiveness and cost-effectiveness of using US in the venepuncture part of CVC placement.

Chapter 2

Effectiveness

Methods for reviewing effectiveness

Search strategy

The search aimed to identify references related to ULDs and CVLs. The searches were conducted in September and October 2001.

Fifteen electronic bibliographic databases were searched, covering biomedical, science, social science, health economic and grey literature (including current research). A list of databases is provided in appendix 1.

In addition, the reference lists of relevant articles were checked and various health services research-related resources were consulted via the Internet. These included health economics and health technology assessment organisations, guideline-producing agencies, generic research and trials registers, and specialist sites. A list of these additional sources is given in appendix 1.

The sponsor submissions were handsearched for any new potential randomised controlled trial (RCT) citations.

A combination of free-text and thesaurus terms was used. CVL search terms (e.g. catheterisation, central venous/central venous line, PICC, venous cannulation, central venous catheter, pulmonary artery flotation, central line insertion, Hickman line) were combined with 'ultrasound' terms (e.g. ultrasonics, ultrasonography, imaged guidance, ultrasound, Doppler). Copies of the search strategies used in the major databases are included in appendix 1.

Where possible (e.g. in the smaller databases), searches were not restricted by publication type or study design. However, methodological filters aimed at identifying guidelines, systematic reviews, clinical trials, economic evaluations, and quality of life studies, were used in MEDLINE (refer to appendix 1 for details of the filters used). Date and language restrictions were not used.

Inclusion and exclusion criteria

Only studies of the clinical effectiveness of using US or Doppler US for locating devices for the placement of CVLs were included. Studies were confined to those including patient populations requiring placement of CVLs. In terms of comparators, only studies assessing 2-D US/Doppler US against the landmark method, or the surgical cut-down procedure were included. Only studies with one or more of the following outcomes were included:

- number of failed catheter placements
- number of catheter placement complications
- risk of failure on the first catheter placement attempt
- number of attempts to successful catheterisation
- number of seconds to successful catheterisation
- rate of success after failure by the alternate method (where a crossover design was incorporated).

The abstracts of potentially relevant citations were reviewed. After examining the full manuscripts of all potentially relevant abstracts, those deemed to be potential RCTs relating directly to the scope question were obtained (i.e. the effectiveness of ULD against the landmark method or surgical cut-down procedure with respect to CVA).

All non-English language papers were excluded, as were trials with a quasi-random design. Trials that dealt with the use of US for vessel localisation, but not for insertion, were dealt with separately from those that dealt with both.

Data extraction strategy

Data extraction was undertaken by one researcher and checked by another. Disagreement was resolved by consensus. Data on the number of catheters and/or the number of patients were abstracted the way they were reported, as were data about mechanical complications. The numbers of patients with complications were pooled for purposes of meta-analysis; where known, the individual complications were reported (see appendix 2). Catheters were the unit of analysis when data were pooled (i.e. the number of catheter placements rather than the number of patients were recorded).

Quality assessment strategy

RCTs were not rated according to the validated quality scale devised by Jadad and others.[16]

This is because the Jadad system relies heavily on blinding without allowing for the fact that blinding is not possible in trials of certain interventions (ULDs being a case in point). Instead, a component approach[17] was adopted to assess trial quality. This took into account six individual quality domains and their associated biases.

First, the number of patient characteristics reported out of five key variables was recorded: the greater number, the greater the external validity of the study. Following the approach taken by Randolph and co-workers,[18] the selected variables were:

- age
- sex
- diagnoses
- coagulopathy, and
- body surface area or height weight ratio.

The last two are commonly associated with risk assessment in the insertion of CVCs. Second, the standardisation of the insertion method was recorded, a factor affecting the internal statistical validity of the trial. Third, the method of randomisation was recorded, where reported, to assess the potential for bias. Fourth and fifth, the number of post-randomisation exclusions was recorded, as well as whether or not intention-to-treat analysis was performed. These last two factors were included to reflect the potential presence of attrition bias.

Data analysis

Data analysis was performed using the Cochrane Collaboration's Review Manager 4.1 software package. Data to estimate the relative risk and associated 95% confidence intervals (CIs) across studies using the random effects model were combined. Statistical heterogeneity (major differences between studies in the estimates of apparent effects of the interventions) was tested for to assess whether the observed variance in effect size between studies is greater than that expected to occur by chance. Using the null hypothesis that the relative risks were the same across studies, the *p*-value for the heterogeneity test indicates the statistical significance of the differences in study results. The significance of this *p*-statistic in the test for heterogeneity, is that the pooling of studies that are shown to be heterogeneous can lead to the reporting of insignificant *p*-values for the outcome variable of interest, when this *p*-value may actually be significant for homogeneous subsets of the pooled studies. A significant outcome variable *p*-value, combined with a significant heterogeneity test *p*-value result, implies that the outcome variable is statistically significant despite the presence of heterogeneity.

Results

Quantity and quality of research available

Number of studies identified and excluded

Twenty-seven RCTs were identified, which evaluated the clinical effectiveness of using US/Doppler US versus the landmark method in the context of CVA. Three were excluded on the grounds that the method of allocation was unclear and the trials were not described as randomised.[19–21] Two quasi-randomised trials, which used alternate or sequential designs, were excluded.[22,23] No additional studies were identified from the sponsor submissions.

Number and type of studies included

There were 20 prospective, randomised trials (including two abstracts[24,25]), as well as one meta-analysis,[18] assessing 2-D US-guided vessel localisation followed by 2-D US-guided venepuncture versus a control, three of which[26–28] incorporated a crossover element (see appendix 2, *Table 10*). The abstracts have been included in the data extraction, but excluded from the meta-analyses. The authors felt it unnecessary to look for further evidence on this central issue. There were also two prospective, randomised trials concerned with Doppler US-guided vessel localisation followed by blind venepuncture.[29,30] These are discussed below (see *ULDs for vessel location followed by blind venepuncture*).

In each included trial, the comparator was the landmark method, except for one[31] where the comparator was blind venepuncture preceded by ULD-guided vessel localisation; there were no trials which compared the use of ULD against surgical cut-down for the clinically effective placement of CVCs. In each case, the unit of analysis was the catheter placement (as opposed to the individual patient; an individual receiving two placements would be recorded twice), but the sample size varied enormously. Eight studies recorded the placement of under 50 catheters and only two studies recorded the placement of over 200 catheters.[26,32]

There were 20 RCTs evaluating US guidance or Doppler US guidance for placement of CVCs. Seven evaluated Doppler US guidance against landmark method, twelve evaluated US guidance

against landmark method and one evaluated both Doppler US and US guidance against a control as well as each other (see appendix 2, *Table 11*).

The Doppler US guidance methods included:

- the SMART® Needle Doppler[5,26,27,33,34] with the 14 MHz continuous-wave probe in the needle (Peripheral Systems Group, Mountain View, CA, USA)
- pulsed (4 MHz)[6,32] and continuous-wave[32] transducers (Vermon SA, Tours, France).

The non-Doppler US guidance methods included:

- the Site Rite® 7.5 MHz[5,35,36] or 9 MHz[37] transducers (Dymax Corporation, Pittsburgh, PA, USA) (another trial[10] also used a Dymax portable, 2-D US 7.5 MHz transducer, but the model name was not reported)
- the Sonos 100 7.5 MHz[38] and Sonos 500 5 MHz[36] 2-D US transducers, and the 7702A 5 MHz real-time 2-D US[28] and an unspecified 2-D, 5 MHz surface US transducer[39] (all Hewlett-Packard, Andover, MA, USA)
- 650 CL. 7.5 MHz real-time US probe (Aloka, Tokyo, Japan)
- the SDR[40] (Phillips, Eindhoven, The Netherlands), with 7.5 MHz probe
- the CS9100 (Picker International (now Marconi) Medical Systems, Highland Heights, OH, USA)
- the SSA 270A[11] 5 MHz transducer (Toshiba, Tokyo, Japan).

Two further trials that used a 5 MHz 2-D real-time US transducer[24] and a 7.5 MHz probe did not specify the manufacture or model of the devices.

It should be noted that one trial[36] used both the Site Rite 7.5 MHz and Sonos 500 5.0 MHz in the same US arm of the trial without distinguishing on which patients each was used. Another[5] used the SMART Needle Doppler in one arm, the Site Rite 7.5 MHz in the second and the landmark method in the third.

Catheter size was specified in only seven studies but, even from those, it is clear that a variety of gauge-measurements were in use between and even within[39] trials. The use of fluoroscopy was not recorded for any trial. Only two studies[5,35] reported the use of a needle guide.

Table 1 indicates the type of operator undertaking the trial procedures. The range of experience, both with respect to the medical career and use of the intervention, differed greatly from study to study. Six studies described the operators as having up to 5 years postgraduate experience,[25,27,35,37,38,41] eight as having more than 5 years,[5,10,26,28,32–34,39] and two as varying in experience.[6,31] Four trials did not record the career experience of the operator.[11,24,36,40]

TABLE 1 *Frequency of trial by type of operator*

Operator	Frequency	Reference
Anaesthetist	7	5, 10, 32, 33, 34, 37, 39
Medical staff	4	25
Radiologist	1	40
Unclear	9	28

In terms of experience in the use of the ULD, only one study[39] made a claim of expertise for the operator, although this was not quantified. One study[32] acknowledged that its lone operator had no experience prior to the trial, as one purpose of the trial was to gauge the learning curve. In three studies,[27,37,41] the operators were inexperienced both with ULD guidance **and** with the landmark method. In a further six studies,[6,25,26,34,35,38] the operators were inexperienced with ULD guidance and did not refer to their relative experience with the landmark method. Where this inexperience was defined, it was only in one study[35] where the operator had cannulated more than ten (but less than 30) patients with the ULD. Four more studies[6,34,37,38,41] recorded less than ten 2-D US-guided cannulations prior to the trial, and in one of these,[6] the operators only had to demonstrate one successful cannulation, using the ULD, prior to the trial. Nine studies did not record the operators' ULD experience.[5,10,11,24,28,31,33,36,40]

Few of the studies were clear about where the cannulation took place within the hospital. Six, took place on the ICU/trauma unit.[24,27,28,32,35,38] Two took place in emergency rooms,[25,41] In the seven studies involving patients scheduled for cardiac surgery, cannulation is most likely to have taken place on the way into theatre.[5,10,33,34,36,37,39] Only three seem likely to have taken place on wards or in clinics.[11,26,40]

Table 2 illustrates the frequency of trial by insertion site. None of the trials addressed the placement of PICCs or ports.

Patient characteristics differed from trial to trial (appendix 2, *Table 10, Table 13*). Most of the studies were concerned with catheter insertion in adults,

TABLE 2 *Frequency of trial by insertion site*

Insertion site	Frequency	Reference
IJV (right side)	5	34
IJV (both sides)	2	39
IJV (side not reported)	7	28
SV (both sides)	2	35
SV (side not reported)	1	26
IJV and SV	1	6
FV (both sides)	1	41
Not specified	1	25

only three trials[5,10,37] recording patient populations of infants or neonates. All the latter cases involved patients about to undergo cardiac surgery. In the adult trials, four studies[33,34,36,39] involved patients scheduled for cardiovascular/cardiothoracic surgery; five studies[24,28,32,35,38] concerned patients in ICU; two studied patients undergoing dialysis;[6,31] one studied patients in ICU or on dialysis;[27] two looked at patients in the emergency room;[25,41] one looked at patients receiving chemotherapy;[26] one at patients undergoing transjugular liver biopsy;[41] and one[11] merely described cannulation as 'routine'.

Three trials[26,27,40] deliberately targeted high-risk patients with coagulopathies or obesity, factors associated with increased risk for failure or complication with respect to catheter insertion; low-risk patients were excluded in these trials. Two trials[6,32] deliberately excluded patients for whom CVA was high risk, because of coagulopathies or obesity, and included only low-risk patients. Only one trial[26] recorded including patients with a history of surgery or radiotherapy in the area, also associated with increased risk for failure or complication. Three trials[10,32,39] reported deliberately excluding patients with these factors.

The studies were of varying quality (see *Quality assessment strategy*, above). With reference to the number of patient variables (age, sex, diagnoses, coagulopathy and body surface area or height weight ratio), only one study[32] recorded all five key variables. Five studies[26,27,33,36,40] recorded four variables, three[24,39,41] recorded three, one[38] recorded two, five recorded one,[5,10,31,34,37] and five[6,11,25,28,35] recorded none of the variables. All of the studies except the two abstracts[24,25] had clearly standardised the catheter insertion method. Eleven studies did not report the randomisation method.[10,11,24,25,27,28,33,34,36,38,40] All the other studies reported truly random allocation methods (computer-generated numbers, random tables, lot). Only two studies[33,35] reported post-randomisation exclusions. Neither undertook intention-to-treat analysis, and the systematic differences between comparison groups, in terms of withdrawals or exclusions of participants from the study sample, suggests the results were affected by 'attrition bias'.[42] Attrition bias arises because of inadequacies in accounting for losses of participants due to drop-outs or exclusions, leading to missing data in the results. The statistical validity of a report displaying attrition bias is questionable. Only in one of the abstracts[24] was it unclear whether intention-to-treat analysis had taken place or not. There was no apparent attrition bias in any of the other reports.

Discussion of results

The choice of outcome measures varied between trials. We selected the following for record (where available), in line with the scoped question of the review and the existing meta-analysis:[18]

- failure rate
- time to successful placement
- number of attempts before successful placement
- complication rate, and
- rate of success after failure by the alternate method.

Definitions of placement failure differed greatly from study to study. Failure was variably defined as inability to place the catheter after 15,[41] six,[28,40] four,[33] three,[27,35] or two[26] passes of the needle (i.e. skin punctures). In one trial, inability to insert the line after seven attempts or 45 minutes both constituted failure.[37] In another study, failure was defined as placement not being achieved after five attempts, or after encountering arterial puncture or haematoma.[5] One further trial set a 30-minute time limit for placement.[6] In ten trials, there was no definition of placement failure.[10,11,24,25,31,32,34,36,38,39] In one of these studies it was reported that one patient had 15 insertion attempts and two more had six and ten attempts, respectively, before stopping due to arterial puncture.[36]

While a number of trials investigated the effects of 2-D US/Doppler US rescue after catheterisation failure in the control group,[6,31,35,40] only three trials incorporated a true crossover element.[26–28] In two of the latter,[26,27] Doppler US was more effective than the landmark method as a rescue measure, but in neither was this result statistically significant. In the other trial,[28] there were no failures in the US group and, therefore, no crossover to landmark method; all the landmark method failures were successfully catheterised using 2-D US.

In the seventeen studies where time factors for a successful catheterisation were recorded they were measured in a variety of ways. Two studies[31,36] measured the time from anaesthesia to venepuncture. Four studies[5,10,37,38] measured the time from the initial skin puncture to syringe aspiration of venous blood. Two studies[27,39] measured the time from initial skin puncture to the placement of the guide-wire. One study[33] measured the time from the injection of local anaesthetic to the insertion of the cannula into the IJV. One study[41] recorded the time from the point at which the US machine was turned on and in position at the bedside, two femoral line catheterisation kits were open, the groins had been swabbed with povidone–iodine, and sterile gloves were on the investigator to the point at which a flash of blood was obtained (and also to when a functional catheter placement was achieved). Six studies did not make explicit what the recorded time interval represented.[11]

Assessment of effectiveness

Trial data for five of the six outcome measurements were combined in the Cochrane Collaborations Review Manager 4.1: the results are displayed in appendix 3. No meta-analysis of crossover success was attempted because there were only four studies to pool, which were diverse in terms of interventions, populations and outcomes.

Unlike in the meta-analysis by Randolph and co-workers[18] the results of studies assessing 2-D US were not pooled with those considering Doppler US: the use of these different machines involves qualitatively different forms of attentive engagement and, therefore, a different kind of practical mastery on the part of the operator. Results are pooled using entry site as a distinguishing variable.

In the following sections, statistical heterogeneity is not statistically significant unless stated otherwise.

The effects of 2-D US

IJV (adults)

In terms of the effect of 2-D US guidance on the number of failed catheter placements (appendix 3, *Figure 4*), the pooled effect size of 0.14 represents an 86% reduction in the risk of failed catheter placements. This result is highly significant ($p = 0.00001$).[11,28,31,36,38,39,40] In terms of the effect on the number of catheter placement complications (appendix 3, *Figure 5*), the pooled effect size of 0.43 represents a 57% reduction in the risk of catheter placement complications. This result is statistically significant at the 2% level ($p = 0.02$).[11,31,36,38,39,40]

Assessing the effect of 2-D US guidance on the risk of failure on the first catheter placement attempt (appendix 3, *Figure 6*), the pooled effect size of 0.59 represents a 41% reduction, statistically significant at the 1% level ($p = 0.009$) despite significant heterogeneity at the 8% level. The forrest plot indicates that all four studies favour 2-D US.[28,31,36,38]

In terms of the effect on the number of attempts to successful catheterisation (appendix 3, *Figure 7*), it took, on average, 1.5 fewer attempts to successfully catheterise a patient using 2-D US guidance, statistically significant at the 1% level ($p = 0.004$) despite significant heterogeneity at the 1% level. The forrest plot indicates that all three studies strongly favour 2-D US.[36,39,40]

Assessing the effect on the number of seconds to successful catheterisation (appendix 6, *Figure 8*), the effect size is small (2-D US-guided catheterisation is 20.47 seconds faster) and not statistically significant ($p = 0.7$). However, there is significant heterogeneity at the 1% level indicating that it may not be appropriate to pool these results. While four trials were significantly faster with 2-D US guidance, it took (on average, 240 seconds) longer in the fifth trial.[40] Unlike other trials in which time to success was an outcome, this study by Soyer and co-workers included the time taken to set up the ULD in the outcome measurement (see *Discussion of results*, above). Set-up time will always be a part of the procedure, but it need not be the operator's time that is used in finding and preparing the machine. When this study is removed from the meta-analysis (appendix 3, *Figure 9*), heterogeneity is no longer significant ($p = 0.52$). The pooled result shows that catheterisation is, on average, 69 seconds faster with the ULD than with the landmark method, and is highly statistically significant ($p < 0.00001$).[31,36,38,39]

SV (adults)

There was only one study that analysed the effect of 2-D US on SV catheterisation.[35] In terms of the effect of 2-D US guidance on the number of failed catheter placements (appendix 3, *Figure 4*), the effect size of 0.14 represents an 86% reduction in the risk of failed catheter placements, statistically significant above the 1% level ($p = 0.006$). Assessing the effect of 2-D US guidance on the number of catheter placement complications (appendix 3, *Figure 5*), the effect size of 0.10 represents a 90% reduction in the risk of catheter placement

complications, statistically significant at the 2% level ($p = 0.02$). These results are statistically significant, despite the trial's small sample size.

The findings are less clear for the catheterisation of the SV than for the IJV. The relative experience of operators may be a factor here. In the single trial investigating SV access, the operators were relatively inexperienced in the landmark method and 2-D US guidance.[35] This trial produced a failure rate of 15/27 (55%) lines using the landmark method and a 2/25 (8%) failure rate for the 2-D US technique. Extracted data from more experienced operators using Doppler US/landmark method for SV access[6,26,32] yielded a 9–19% failure rate for the landmark method. Experienced operators would certainly have a lower failure rate using the landmark method, than those in the study by Gualtieri and co-workers.[35] Therefore it remains to be established that US is a safe and effective way of achieving SV access.

FV (adults)

There was only one study that analysed the effect of US on FV catheterisation.[41] In terms of the effect of US guidance on the number of failed catheter placements (appendix 3, *Figure 4*), the effect size of 0.29 represents a 71% reduction in the risk of failed catheter placements. This result is significant at the 9% level ($p = 0.09$). The operators also took, on average, 2.7 fewer attempts to catheterise patients using 2-D US-guidance (appendix 3, *Figure 7*), statistically significant at the 4% level ($p = 0.04$). However, there was little effect on the number of seconds to successful catheterisation, which was, on average, just 3.2 seconds faster ($p = 0.9$; appendix 3, *Figure 8*).

It is difficult to generalise from the results of the single available RCT on FV access.[41] The patients in this trial were undergoing cardiopulmonary resuscitation (CPR) and therefore would be unlikely to have a femoral arterial pulse, the most commonly used anatomical marker during FV access with the landmark method. Therefore, it is hardly surprising that, in this situation, US has a significant effect. While this in itself represents a strong argument for the presence of ULDs in the emergency room,[43] the majority of FV lines will not be inserted under these conditions; therefore it seems inappropriate to place a great significance on this study.

However, supporting evidence comes from another trial, which was not included in this review due to its sequential protocol (i.e. it was not an RCT).[20] The study involved operators who were experienced in the landmark method (but not in the use of 2-D US), working in non-emergency conditions, catheterising 66 patients (28 2-D US versus 38 landmark method) scheduled for acute dialysis. Cannulation of the FV was achieved in all patients (100%) using US and in 34 patients (89.5%) using the landmark-guided technique. The vein was entered on the first attempt in 92.9% of patients using US and in 55.3% using the landmark method technique ($p < 0.05$). Average access time (skin to vein) was similar but total procedure time was 45.1 ± 18.8 seconds by the US approach and 79.4 ± 61.7 seconds by the landmark method approach ($p < 0.05$). Using US, puncture of the femoral artery occurred in 7.1% of patients, and haematoma in 0%. Using external landmark technique, puncture of the femoral artery occurred in 15.8% of patients, and haematoma in 2.6%.

IJV (infants)

Only three trials studied the effect of 2-D US guidance on the catheterisations of infants, all of which concerned the cannulation of the IJV.[5,10,37] In appendix 3, *Figure 10,* the pooled outcome effect of 0.15 represents an 85% reduction in the risk of failed catheter placements, statistically significant at the 1% level ($p = 0.01$). In appendix 3, *Figure 11,* the pooled outcome effect of 0.27 represents a 73% reduction in the risk of catheter placement complications, statistically significant at the 3% level ($p = 0.03$).[5,10,37] In appendix 3, *Figure 12,* the number of attempts to successful catheterisation was reduced by an average of 2, a highly significant result, statistically ($p < 0.00001$).[37] In appendix 3, *Figure 13,* the pooled effect of 2-D US-guidance is that successful cannulation is achieved, on average 349 seconds quicker than with the landmark method though this result is only statistically significant at the 13% level.[5,10,37]

The effects of Doppler US

IJV (adults)

Measuring the effect of Doppler US guidance in respect of number of failed catheter placements (appendix 3, *Figure 14*), the pooled effect size of 0.39 represents a 61% reduction in the risk of failed catheter placements, statistically significant at the 3% level ($p = 0.03$).[6,27,33,34] In terms of the effect on the number of catheter placement complications (appendix 3, *Figure 15*), the pooled effect size of 0.43 represents a 57% reduction in the risk of catheter placement complications, statistically significant at the

6% level ($p = 0.06$).[27,33,34] In terms of the effect on the risk of failure on the first catheter placement attempt (appendix 3, *Figure 16*), the pooled effect size of 0.57 represents a 43% reduction in the risk of failed catheter placements, statistically significant at the 1% level ($p = 0.01$).

In terms of the effect of Doppler US guidance on the number of attempts to successful catheterisation (appendix 3, *Figure 17*), the effect size of the pooled studies was an average of 0.59 fewer attempts to catheterise patients, a statistically non-significant result ($p = 0.4$). There is, however, significant heterogeneity at the 7% level ($p = 0.07$), indicating that it may not be appropriate to combine the individual studies. Considered individually, Gratz and co-workers[33] shows a statistically significant effect size (1.4 fewer attempts on average; $p = 0.037$) but Branger and co-workers[6] demonstrated only a small effect. Both of these studies have small sample sizes with weak statistical power.

It took, on average, 35 seconds longer to successfully catheterise patients using Doppler US guidance than it did with the landmark method (appendix 3, *Figure 18*), a non-significant effect ($p = 0.4$).[6,27,33,34] Individually, most of the studies favour the landmark method, aside from one study[34] where one arm was composed of patients who were 'difficult' to catheterise (e.g. because of obesity).

SV (adults)

In terms of the effect of Doppler US guidance on the number of failed catheter placements (appendix 3, *Figure 14*), the pooled effect size of 1.48 represents a significant **increase** in the risk of failed catheter placements at the 3% level ($p = 0.03$), which is to say that the landmark method was preferable to the Doppler US guidance technique.[26] In appendix 3, *Figure 15,* the pooled effect size of 0.57 represents a 43% fall in the risk of catheter placement complication. This result is not statistically significant ($p = 0.5$).

Only one study[32] recorded the effect of Doppler US guidance on the risk of failure on the first catheter placement (appendix 3, *Figure 16*). The effect size of 1.04 represents slight increase in the risk of catheter placement complications through the use of Doppler US, although this result is not statistically significant ($p = 0.8$).

Only one study recorded the effect of Doppler US guidance on the number of attempts to successful catheterisation (appendix 3, *Figure 17*). On average, it took 0.4 fewer attempts to successfully catheterise patients using Doppler US, a highly statistically significant result ($p = 0.0002$).[6] The same study was the only one to record the effect of Doppler US guidance on the number of seconds to successful catheterisation (appendix 3, *Figure 18*). Doppler US guidance was significantly (on average 209 seconds) slower than the landmark method ($p < 0.00001$).[6]

The operators in two of these trials[26,32] were considerably more experienced in landmark-guided cannulation than they were with Doppler, but both studies had relatively large populations and neither noted a significant training effect. Doppler US guidance appears not to be an effective alternative to the landmark method for SV insertion in adults.

IJV (infants)

Only one trial studied the effect of Doppler US on infants.[5] The sample size of this study is small making it difficult to demonstrate statistical power. The study found that Doppler US increased the risk of failed catheter placements (appendix 3, *Figure 19*) but not significantly so ($p = 0.8$). The intervention slightly decreased the risk of a catheter placement complication (appendix 3, *Figure 20*) but, again, not significantly so ($p = 0.8$). It took an average of 138 seconds longer for operators to catheterise the patient using Doppler US (appendix 3, *Figure 21*) but, once more, this outcome was not held to be statistically significant ($p = 0.3$).

Related issues

Several issues were not addressed by the included RCTs. First, the effectiveness of ULDs for vessel location followed by blind venepuncture; second, the suitability of US for detecting the vessel patency and variant anatomy; third, the effectiveness of 2-D US against the landmark method for the placement of PICCs; and, fourth, the effectiveness of ULDs versus surgical cut-down procedure for CVA. The literature was systematically searched for RCTs on these subjects: where none were available, the best available evidence has been systematically retrieved and reviewed.

ULDs for vessel location followed by blind venepuncture

All of the trials discussed hitherto were concerned with the use of ULDs for not only the location of blood vessels, but also the guidance

of venepuncture. Two RCTs investigated the use of Doppler US to locate the vessel before blind catheter insertion.

The first trial,[29] was a large RCT, in which 821 patients (411 Doppler US versus 410 landmark method) underwent SV catheterisation in non-emergency conditions. The operators (physicians) had a wide range of experience in landmark-guided catheterisation, but all had relatively little with the use of Doppler US. There was no benefit to the use of Doppler US, either in terms of the failure rate or complications.

The other study,[30] was a smaller RCT in which operators (of unknown speciality and experience) catheterised 43 patients (22 Doppler US versus 21 landmark method) via the right IJV, prior to cardiovascular surgery. The only outcome recorded was the rate of success on the first attempt: 77.3% with Doppler and 28.6% without.

In summary, there is no evidence that it is more clinically effective to use Doppler US for vessel location, prior to blind venepuncture of the SV, than it is to use the landmark method for the whole procedure. There is evidence that such a procedure would be effective prior to the cannulation of the IJV.

ULDs for the assessment of vessel patency and vessel location

Successful use of the anatomic landmark approach to catheterisation requires that the vein be 'patent' and normal, both in size and in its expected position.[44] Patency refers to the state of the vessel being present with no evidence of thrombosis. The literature recognises central venous catheterisation as a significant risk factor in the formation of a thrombus of the IJV, SV or FV,[45] so that it becomes increasingly likely with repeated procedures (for instance, in the case of chemotherapy patients).

A case series by Caridi and co-workers,[44] which used 2-D US guidance to assess the patency and physiology of patients scheduled for CVA via the right IJV, also provided a table reviewing the result of this and other studies.[10,19,46] Across the studies, US diagnosed between 9% and 20% of patients as having either a variant anatomy or thrombosed veins, which would have compromised access using landmark techniques.

No comparable studies were found for the detection of thrombosis/variant anatomy in the SV or FV.

PICCs

Only one comparative study detailed the efficacy of ultrasonography in peripheral venous cannulation.[47] In this retrospective sequential study, the same nurse catheterised a diverse population of 431 patients using the landmark method and 326 patients using ultrasonography. The US approach required 42% fewer attempts to successful catheterisation and demonstrated a 26% greater chance of successful cannulation on the first attempt.

US versus surgical cut-down procedure

No papers were found comparing 2-D US alone with the surgical cut-down procedure. Only one paper was found comparing image guidance with both surgical cut-down procedure and the landmark method.[48] However, this study was performed in a radiology suite and, unlike the studies discussed hitherto also employed fluoroscopy. The success and infection rates of radiological placement were similar to those of surgical placement. Radiological placement required fewer attempts.

Conclusion

Table 3 summarises the results of the meta-analyses for 2-D US for both adults and children. In the case of adult IJV insertion there is very strong statistical evidence that US-guided CVA is more effective for all five outcome variables analysed. Measured by the number of trials, the evidence base for SV and FV insertions is not as strong as for IJV, however, the results are still statistically significant in favour of US for failed insertions and for complication rates where measured.

For the three infant studies (relatively small sample sizes) investigating insertions into the IJV, the results again suggest that US has statistically significant effects over the landmark method. The exception is the seconds to success outcome variable, which is only significant at the 13% level, although the significant heterogeneity test may mean that it is inappropriate to pool these results and that pooling may be masking a significant effect for this variable.

Table 4 summarises the results of the meta-analyses for Doppler US. In general, the results are far less favourable for Doppler US. For IJV insertions US has statistically significant improved effects in terms of failure to insert and immediate complications. Number of attempts and time to success favours the landmark method though the result is

TABLE 3 *Summary of significance of outcome measures for 2-D US*

	IJV		SV		FV	
	Effect size (95% CI)	***p***	**Effect size (95% CI)**	***p***	**Effect size (95% CI)**	***p***
US (adults)						
Relative risk of failed catheter placement	0.14 (0.06 to 0.33)	0.00001	0.14 (0.04 to 0.57)	0.006	0.29 (0.07 to 1.21)	0.09
Relative risk of catheter placement complication	0.43 (0.22 to 0.87)	0.02	0.10 (0.01 to 0.71)	0.02	N/A	N/A
Relative risk of failure on the first placement attempt	0.59 (0.39 to 0.88)	0.009	N/A	N/A	N/A	N/A
Mean no. of attempts to successful catheterisation	–1.50 (–2.53 to –0.47)	0.004	N/A	N/A	–2.70 (–5.26 to –0.14)	0.04
Mean no. of seconds to successful catheterisation*	–20.47 (–124.27 to 83.33)*	0.7*	N/A	N/A	N/A	N/A
Mean no. of seconds to successful catheterisation	–69.33 (–92.36 to –46.31)	< 0.00001	N/A	N/A	–3.20 (–43.27 to 36.87)	0.88
US (infants)						
Relative risk of failed catheter placement	0.15 (0.03 to 0.64)	0.01	N/A	N/A	N/A	N/A
Relative risk of catheter placement complication	0.27 (0.08 to 0.91)	0.03	N/A	N/A	N/A	N/A
Relative risk of failure on the first placement attempt	N/A	N/A	N/A	N/A	N/A	N/A
Mean no. of attempts to successful catheterisation	–2.00 (–2.82 to –1.18)	< 0.00001	N/A	N/A	N/A	N/A
Mean no. of seconds to successful catheterisation	–349.38 (–801.89 to 103.13)	0.13	N/A	N/A	N/A	N/A

All outcomes favoured 2-D US

* *Outcome prior to the removal of the study by Soyer* et al. *(see text)*

N/A, data not available

TABLE 4 *Summary of significance of outcome measures for Doppler US*

	IJV		SV		FV	
	Effect size (95% CI)	***p***	**Effect size (95% CI)**	***p***	**Effect size (95% CI)**	***p***
Doppler US (adults)						
Relative risk of failed catheter placement	0.39 (0.17 to 0.92)	0.03	1.48 (1.03 to 2.14)*	0.03*	N/A	N/A
Relative risk of catheter placement complication	0.43 (0.17 to 1.05)	0.06	0.57 (0.11 to 2.88)	0.5	N/A	N/A
Relative risk of failure on the first placement attempt	0.57 (0.37 to 0.88)	0.01	1.04 (0.76 to 1.43)*	0.8*	N/A	N/A
Mean no. of attempts to successful catheterisation	–0.59 (–1.82 to 0.65)	0.35	–0.4 (–0.61 to –0.19)	0.0002	N/A	N/A
Mean no. of seconds to successful catheterisation	34.86 (–54.49 to 124.21)*	0.44*	209.00 (175.48 to 242.52)*	< 0.00001*	N/A	N/A
Doppler US (infants)						
No. of failed catheter placements	1.23 (0.30 to 5.11)*	0.77*	N/A	N/A	N/A	N/A
No. of catheter placement complications	0.82 (0.16 to 4.20)	0.81	N/A	N/A	N/A	N/A
Risk of failure on the first catheter placement attempt	N/A	N/A	N/A	N/A	N/A	N/A
No. of attempts to successful catheterisation	N/A	N/A	N/A	N/A	N/A	N/A
No. of seconds to successful catheterisation	138.00 (–114.72 to 390.72)*	0.28*	N/A	N/A	N/A	N/A

* *Outcome favours the landmark method (all other results favour Doppler US)*

not statistically significant; however, significant heterogeneity tests cast doubt on the pooling of these results. The study results imply that Doppler is less effective than landmark for SV insertions.

Only one small study for Doppler IJV insertions was found and was too small to achieve statistical significance. No studies on the FV were reported for adults or children for Doppler versus landmark.

Chapter 3
Economic analysis

Existing economics evidence

A systematic search of electronic databases including the economic evaluation databases NHS Economic Evaluation Database (EED) and the Office of Health Economics Health Economic Evaluation Database (HEED) have been conducted as discussed in chapter 2. These searches have been supplemented by strategies designed to find economic evaluations. The literature search failed to reveal any economic or US costing papers for CVL insertion. Furthermore, none of the industry submissions found any published economic evaluations, nor attempted to present any themselves. Two of the industry submissions have identified a paper by Neuman and co-workers,[49] but this paper is not relevant in the context of this report, as it assesses the cost-effectiveness of PICCs compared with venepuncture at other insertion sites. There is no economic evaluation of US in the Neuman paper. In view of the lack of published evidence, the costs and benefits of US versus landmark venepuncture in CVA is assessed in this report using an economic model. A simple decision-analysis approach has been taken using Microsoft Excel™.

Methods for economic analysis

Estimation of net benefits

The benefits of US for needle insertion in CVA include fewer failed insertions, fewer complications, and faster venepuncture, thereby improving subsequent catheter insertion rates. This implies clinical and comfort benefits for patients. It has been reported that the sensitivity and specificity of US for detecting thrombosed vessels for example is 100%.[9] A thrombosed vein cannot be used for venous access and this can be determined using US.

The clinical effectiveness review indicates that use of US for CVA requires fewer needle passes compared with the landmark method (appendix 3, *Figure 7*). The benefits of this are twofold. First, access will be quicker with comfort benefits for the patient and need for fewer staff time resources. Additionally, complication rates (primarily failed insertion, arterial puncture, haematoma and pneumothorax) have been shown to be correlated with the number of needle pass attempts required before successful insertion.[36] Therefore, if US results in fewer needle passes before successful puncture then complication rates will be reduced with both clinical and resource benefits for patients and trusts. Furthermore, the literature provides evidence that where failure to gain access to vessels using landmark method has been observed, the subsequent use of US has resulted in first-time successful puncture.[28,36] The resource advantages may be substantial, particularly as the majority of insertions are performed in high-cost theatre and ICU environments, where delays may have significant cost and clinical implications. Quicker and safer access is clearly beneficial in terms of patient anxiety and comfort, as well as preventing delays in subsequent treatment and reduced risks of further complications. In extreme cases, the complications of venepuncture can be fatal,[36] and so it is possible that reduced complication rates will prevent deaths.

Estimation of net costs

The costs of using US for venepuncture in CVA include purchase costs, maintenance contract costs, the costs of training operators, and the costs of disposable equipment. The first three of these resource categories require assumptions about machine usage.

Purchase cost

Costs for purchase of a portable US machine range from about £7000 to £15,000 depending on specification. For capital equipment such as US machines, it is necessary to estimate life expectancy and to annualise costs using discounting rates. Because technology improves over time and machines become obsolete relatively quickly, it has been assumed that a machine purchased today will be replaced with a scrap value of zero in 3 years' time. Using a 6% discounting assumption, the annualised cost for an £11,000 machine is, for example, £3882.

The cost of the procedure can be estimated by making assumptions about the number of times

TABLE 5 *Purchase costs per procedure*

Times used per week	Purchase cost		
	£7,000	£11,000	£15,000
1	£47.51	£74.66	£101.81
10	£4.75	£7.47	£10.18
20	£2.38	£3.73	£5.09

that a machine is used. *Table 5* presents some procedure purchase cost estimates, varying both the purchase cost itself, and the number of times that the US machine is used each week.

Table 5 illustrates the sensitivity of the procedure purchase cost to changes in the two input assumptions. The estimated cost is particularly sensitive to the usage assumption, illustrating that the cost-effectiveness of US for CVA will be dependent on purchased machine being used sufficiently often in cost-effective procedures. The above analysis does not necessarily assume that the US machine is purchased solely for use in CVL placement. US machines can be legitimately used for purposes other than those being investigated in this report (e.g. pleural drainage). Using it for other purposes would mean a legitimate reduction in costs incurred for the CVL venepuncture. Doubling the use of the machine for any purpose would halve the US estimated costs.

Maintenance costs

An expert advisor has indicated an annual maintenance charge of £1350 per annum for one of their machines in Liverpool; however, a Site Rite machine costing £7500 at the Royal Hallamshire Hospital in Sheffield carries no maintenance contract with it. The procedure cost for the maintenance charge is calculated in the same way as was the purchase costs in *Table 5*, so that the unit cost is dependent on usage. Assuming, for example, a maintenance charge of £1350 per annum, and ten procedures per week per machine, implies an estimated maintenance cost of £2.60 per insertion.

Training costs

The costs of a training scheme will be highly dependent on how a scheme is set up, including which, and how many operators are to be trained, by whom, and how many times the trainee will put their US skills into practice. The calculation of costs at procedure level also requires an assumption about the remaining working life of the trainee. For example, training costs per insertion will be higher for intensive training courses provided by highly qualified radiologists or anaesthetists, where the trainee is highly qualified, with few working years left and, unlikely to use their new skills much on a weekly basis.

Making the assumption that a consultant radiologist incurs an annual cost of £134,300 (including salary cost, on-costs, overheads, and educational/general training costs) and it is assumed that they are employed for half of their time to run such a programme, then assuming 20 trainees per annum (approximately one every 2 working weeks) implies a cost per trainee of £3357. Alternatively, assuming that a consultant radiologist trains a consultant anaesthetist for ten half-hour supervised insertions, including the salary costs of both the trainer and trainee, the training cost estimate is £1090 per trainee.

Table 6 presents estimates of the discounted (6%) training costs per US procedure for a range of assumptions about the cost per trainee, working years remaining, and number of procedures undertaken by the trained operator per week.

Using this broad range of assumptions, cost estimates vary from as little as £0.15 to £17 per insertion. Once again the cost estimate is sensitive to the number of procedures undertaken per week by the trained operator.

TABLE 6 *Estimates of discounted training costs per US procedure*

Venepunctures per week	Remaining working life (years)	Discounted training costs per procedure (£)	
		£1090	£3357
1	5	5.42	16.71
	40	1.52	4.68
5	5	1.08	3.34
	40	0.30	0.94
10	5	0.54	1.67
	40	0.15	0.47

Disposables

Use of the US machine requires gel and a disposable cover. These costs have been estimated at £0.67 per CVL insertion by one of the expert advisors to this report.

Cost-effectiveness

In view of the absence of published economic evaluations in the literature, a simple decision-analysis model has been constructed in order to derive initial estimates of the cost-effectiveness of US for venepuncture in CVA. Where possible we have used evidence from the RCTs reported in the review of clinical effectiveness in chapter 2. Modelling assumptions are made explicit in the text and are tested using sensitivity analysis.

The model

Given the numerous different types of operator, insertion sites and hospital locations, where this procedure can be undertaken, a number of alternative models were considered. In view of the fact that most CVLs are inserted using the IJV in theatre and ICU environments, the decision was made to present a theatre-based IJV model. The implications for other insertion sites and bedside ward-based insertions are discussed. Also, given that real-time grey-scale 2-D is the technology being considered for wider use in this report, the model analyses this technology in contrast to the Doppler audio technology.

The model thus contains a theoretical cohort of 1000 adult patients undergoing surgery and in whom the risk of complications is considered to be low to moderate. Thus, infants and adult patients considered more difficult to puncture, such as obese or short-necked patients are not explicitly modelled. In developing the model we have chosen to present a conservative model in terms of possible US benefits. So, for example, we assume that the operator is experienced in the use of the landmark method venepuncture method, thereby presenting relatively conservative failure and complication rates for the landmark method arm of the model. The implications of the model results for other scenarios and higher-risk patients are discussed.

The structure of the decision-tree model is presented in *Figure 2* and illustrates identical structure (shape) of the US and landmark

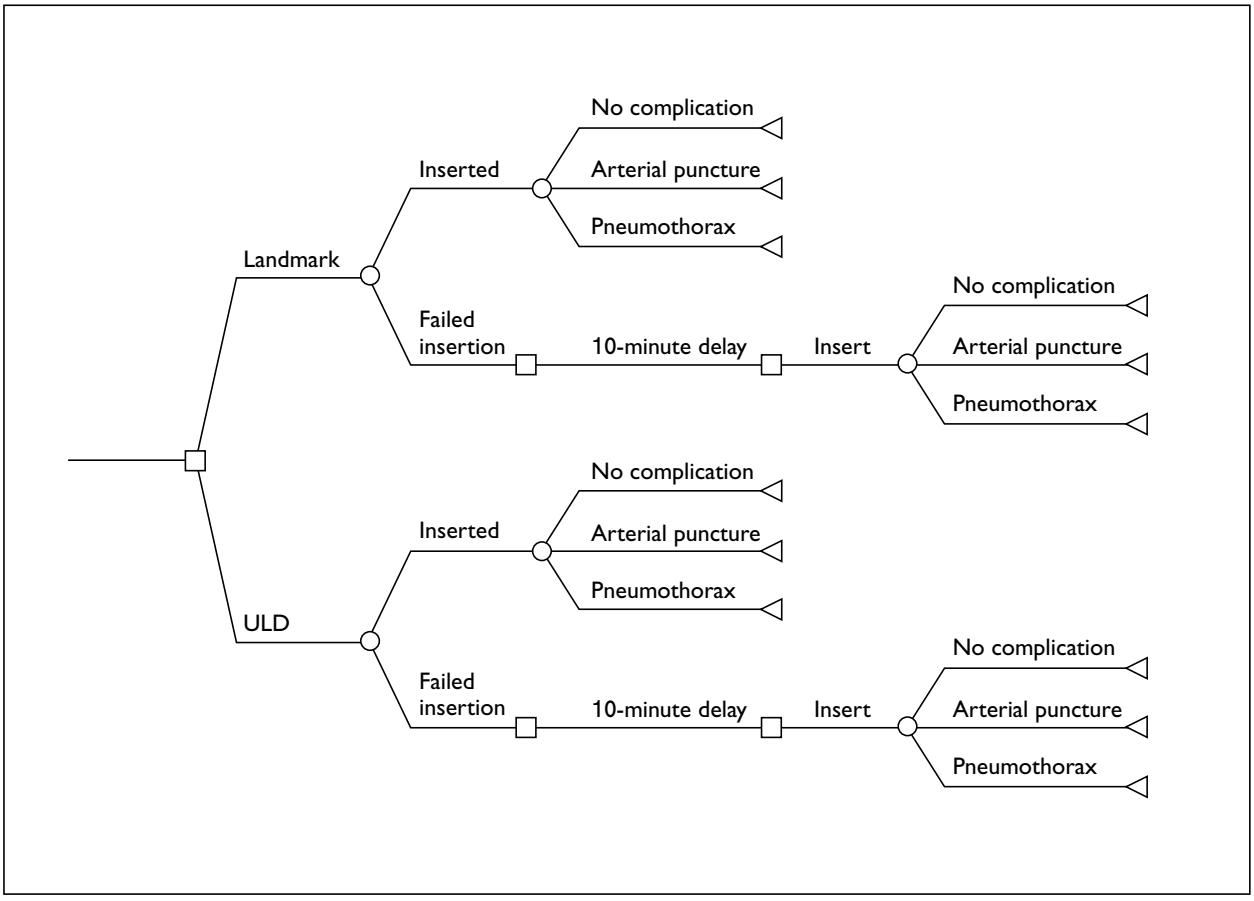

FIGURE 2 *Decision tree*

sub-trees. It is the probabilities attached to the chance node events and the subsequent costs and chances of complications that distinguish the two policy arms of the model.

The first sub-tree of the model depicts how a proportion of patients will fail to have a successful needle insertion while the remainder have a successful insertion either with or without immediate complications. The only complications considered in the model are arterial puncture and pneumothorax. The model assumes that successful punctures take the same time to achieve for both approaches. There is strong evidence from the review of clinical effectiveness that that US requires fewer needle passes to achieve successful venepuncture than does landmark method (appendix 3, *Figure 7*). It might therefore be expected that time to successful puncture from the time of attempting the first needle pass will be faster using US. This is supported by the review of clinical evidence. Excluding the paper by Soyer and co-workers[40] in which the preparation time for the US machine has been included in timings, the US-guided venepuncture is achieved 70 seconds faster ($p < 0.00001$) than using landmark method (appendix 3, *Figure 9*). Including the non-significant results for the FV analysis, the average time for successful insertion is still 59 seconds faster using US ($p < 0.001$). These timings do not include the additional time necessary for failed catheter insertions, which are more common using landmark method. Although minimal, the additional time necessary to set up the US machine needs to be offset against the time to achieve successful needle puncture as indicated by Soyer and co-workers.[40]

In the case of a failed venepuncture at the initial insertion site, the operator (at consultant level) is assumed to have spent 10 minutes trying to insert prior to failure and changing insertion site before achieving successful insertion. Given reported evidence that failure takes between 5 and 10 minutes,[36] and given that some time will be needed to drape and prepare the new insertion site before insertion can be attempted at a new site, our assumption seems reasonable. Some operators spend about 30–45 minutes trying to achieve successful insertion.[6,37]

The model assumes 100% success at the second insertion site. We also assume no new line equipment for the second insertion attempt. New lines may be necessary in reality[35] and will carry resource implications.

The model assumes that the operating theatre is staffed by a consultant surgeon, assisted by a senior house officer and an E-grade theatre nurse. A consultant anaesthetist, assisted by a medical technical officer (grade 2/3) is also assumed present for the operation. Hourly staff cost estimates are given in *Table 7*. The 10-minute delay for the failed procedures is assumed to incur a cost equivalent to 10 minutes for each of these theatre staff, and 10 minutes of theatre time estimated at £125 per hour.

TABLE 7 *Staff costs per hour*

Theatre staff and time*	Costs per hour (£)	Reference
Consultant surgeon	106	15
Consultant anaesthetist	106	15
Senior house officer	35	15
Medical technical officer	31	50
E-grade theatre nurse	31	15
Theatre suite	125	Based on 51

* *Staff costs include, overheads, on-costs and education costs*

Event probabilities

The papers presenting the results of RCTs and reviewed in this report are used to populate the model for risk of failure and complications. Given the scenario to be modelled, papers for IJV insertion in adults excluding emergency (CPR) and high-risk patients were selected. Also, papers reporting results for inexperienced operators and those using Doppler US were set aside. This exclusion process reduced the number of papers to be used to populate the model with risk probabilities to three.[28,36,39]

Fourteen (9%) failures out of 160 landmark attempts were recorded in the three RCTs compared with 3/149 (2%) failures using real-time imaging US. Nine per cent and 2% failure rates are therefore assumed in the model.

The paper by Mallory and co-workers[28] does not report non-failure complication rates and so could not be used to derive complication parameter estimates for the model. The remaining two RCTs reported complication rates for arterial puncture. Seventeen arterial punctures were reported for 143 landmark attempts (12%), compared with four in 137 (3%), using US. None of the selected papers reported pneumothorax complications.

The results of the SV Doppler RCT reported by Lefrant and co-workers[32] illustrates the increased risk of complications following failed catheterisation. For example, the complication rate rose from 3.2% in the successful group to 21.1% (4/19) in the Doppler group and from 15.4% to 30.8% (4/13) in the landmark group. Our model ignores this phenomenon and simply assumes a constant complication rate irrespective of initial insertion success or failure. This assumption has no implications for our analysis, as we are only concerned with estimating the total number of complications for US versus landmark methods. Adding the modelled probabilities to the decision tree gives the results depicted in *Figure 3*. The end node (triangles) figures represent the number of patients modelled to go down each branch of the sub-trees and the average cost per patient (bracketed) for the respective branch.

Costs

Based on data from a local teaching trust, it is estimated that approximately 1600 central lines are placed in cardiac surgery patients each year in Sheffield. This equates to about 30 lines per week. The model assumes that the theatre machine is used to insert 15 lines per week. Assuming a machine cost of £11,000, (the equivalent of a machine costing £9500 with a maintenance contract cost of £1500) the discounted purchase and maintenance cost is estimated at £4.98 per procedure.

Assuming that the anaesthetist operator was trained by a consultant radiologist during ten supervised half-hour sessions, and assuming that the operator has 20 years' working life remaining, and undertakes only two procedures per week, the discounted training cost per US procedure is estimated at £1.00 per procedure. Adding the purchase and training costs to the disposable equipment costs produces a central scenario estimate of £6.64 per insertion using US. These procedure costs measure only the additional (marginal) cost of using US in the venepuncture procedure. They do not measure the total costs of needle insertion such as the costs of disposable needles and other procedure costs common to both the landmark method and the US procedure.

Cost estimates for arterial puncture and pneumothorax have been taken from the Boland study,[2]

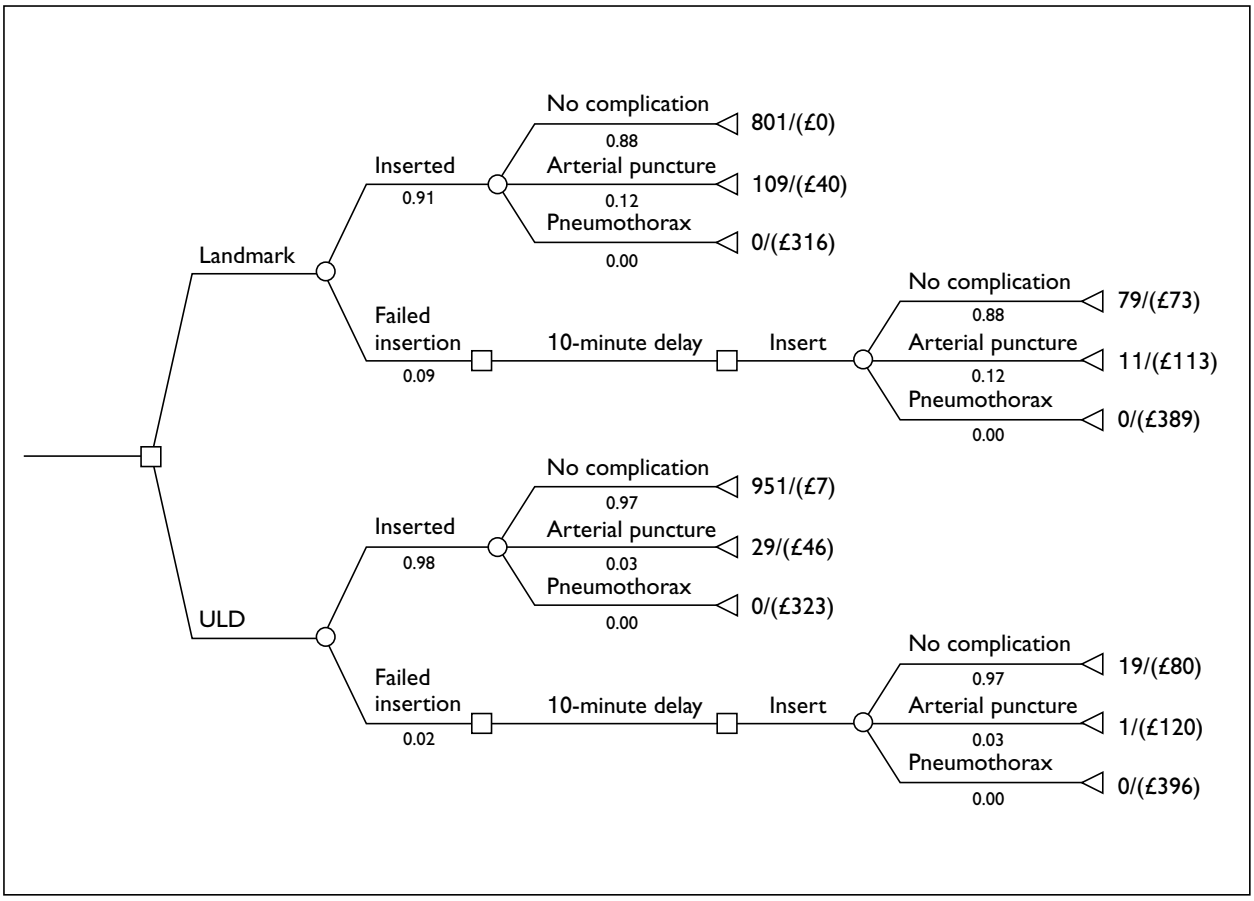

FIGURE 3 *Decision tree populated with risk probabilities*

which estimated average costs of £316 for pneumothorax and £40 for arterial puncture. The complications were costed using patient-specific figures for the whole range of minor and major types of complications that occurred in their study.

Model outputs

The central scenario assumptions result in modelled outputs represented in *Table 8*. The results of modelling show that US not only avoids 90 arterial punctures for every 1000 patients treated, but saves almost £2000, an average of £2 per patient. In other words, the policy to use US for CVA dominates the landmark method by being both more effective and less costly in our modelled scenario.

TABLE 8 *Outputs for central scenario*

	Landmark	ULD
Cost	£11,397	£9,305
Arterial puncture	120	30
Pneumothorax	0	0

Sensitivity analysis

A threshold sensitivity analysis has been undertaken in which we examine by how much key variables need to change before the cost-saving result from the use of US becomes a cost-neutral result. *Table 9* presents the results of the univariate threshold analysis.

TABLE 9 *Univariate threshold sensitivity analysis*

Variable	Baseline value	Threshold value
Failure rate (landmark)	9%	6%
Failure rate (US)	2%	5%
Arterial puncture rate (landmark)	12%	7%
Arterial puncture rate (US)	3%	8%
Cost per US procedure	£6.64	£8.72
Ultrasound machine cost	£11,000	£15,584
Training cost per operator	£1,090	£3,360
Operator procedures per week	2	0.65
US procedures per week	15	10.6
Cost of failure delays	£73	No solution
Cost of arterial puncture	£40	No solution

The cost-saving result for US is robust for a range of parameter estimates. For example the cost of the US machine would have to rise from the assumed £11,000 to over £15,500 to eradicate the cost-saving modelling result. Alternatively the assumed US failure rate of 2% would have to increase to 5% to achieve a cost-neutral result. In only one RCT of puncture of IJV in adults using real-time 2-D US did the US failure rate reach 5% (appendix 3, *Figure 4*), and this is one of the three studies included in our modelled estimate. The arterial puncture complication rate for US would need to increase from the modelled 3% to 8% to negate the cost-saving result.

A cost-neutral result would occur if landmark insertion achieves a failure rate of 6% or an arterial puncture complication rate of 7%. Only one of the adult IJV real-time RCTs reported a failure rate below 6%[36] (appendix 3, *Figure 6*) and again this is one of the three studies used to populate the model.

The modelled result is most sensitive to the cost of the US procedure. The estimated marginal costs of the US procedure only needs to rise from the assumed £6.64 to £8.72 before the US cost-saving result is eradicated. Having said this, it is the usage variables that are most important for cost-effectiveness in this context. *Table 9* shows that the cost-saving result is relatively insensitive to both the purchase cost of the machine and the training cost per operator. However, the cost-saving result is eradicated if the assumed 15 procedures per machine per week are reduced below 10.6, and if the assumed US procedures per week per trained operator falls below 0.65. These results highlight in particular the need for purchased US machines to be used sufficiently for them to be cost-effective.

It should be borne in mind that even if the thresholds presented and discussed above are exceeded, then this means only that the cost-saving dominant result for US would be replaced by a positive cost-effectiveness ratio. The threshold values presented in *Table 9* would have to be exceeded further before a cost-effective conclusion for US would be brought into question.

It should also be borne in mind that the failure and complication risks modelled are favourable to the landmark method in that RCTs using operators already experienced in the landmark method were selected to populate the model. Using the combined failure and complication rate

risks for all the adult IJV trials presented in this report (appendix 3, *Figure 4*) the model indicates a net cost-saving in favour of US of £11,009 and 80 fewer complications per 1000 patients treated. This result gives some indication of the conservative nature of the assumptions used in the modelled scenario presented above.

Discussion

Modelling by definition implies the simplification of reality, and so a number of simplifying assumptions were made in the model presented. In addition to points made above, the following modelling assumptions may be biased against US and in favour of the landmark method.

- The pneumothorax complication rates have been assumed to be zero in the IJV model presented. Despite the evidence from the RCTs, pneumothorax is a risk even in IJV cannulation. Based on the evidence for complications presented in this report, inclusion of pneumothorax rates are likely to further increase the cost-effectiveness of US compared with landmark. On average, the costs of pneumothorax are significantly higher than for arterial puncture (£300 versus £40) as well as being clinically more risky for patients and may contribute to increased mortality.
- The model structure allows for only two complications, namely pneumothorax and arterial puncture. On the basis of both the clinical effectiveness evidence and the modelling results, inclusion of other complications would be likely to favour US further. Death, for example, is an uncommon but possible outcome of insertion complication in high-risk patients (e.g. ventilated patients or patients undergoing a cardiac pacing procedure).
- Delays caused by failure have been limited to 10 minutes. Two papers defined failure as failure to insert after 30 and 45 minutes, respectively.[6,37] Longer delays would further increase the net resource savings for US.
- The model forces success at the second attempt following initial failure to insert catheter. Though uncommon, it may be necessary to attempt insertion at third and subsequent sites with further time resource implications, and the increased likelihood of needing alternative catheters for alternative catheter positions. At least one publication indicates that resources will be consumed for new lines.[35]
- The model assumes that US machines are used only for venepuncture in CVL access. It has been explained in this report that some portable grey-scale 2-D machines can be used to guide other procedures such as pleural drainage (unlikely in a theatre environment). Using purchased US machines for other cost-effective procedures will further reduce the US procedure costs estimated in this report.
- The model assumes a purchase cost for US machines of £11,000. At least one portable machine used in NHS hospitals, and in some of the reported papers can be purchased for £7500 with no maintenance contract costs.
- The US costing assumption includes a 3-year machine life. This is likely to be a conservative estimate.
- The model has not considered possible financial implications of litigation. If patients experience complications following landmark method insertion when US could have been used, and successfully pursue litigation, then further resources implications for the landmark method arm of the model would result.
- The model assumes that successful insertion takes the same time to achieve in both arms of the model. Although only a matter of a minute or two, the evidence suggests that successful insertion is achieved more quickly using US. This will have both resource and clinical benefits.

The following modelling assumptions may be biased against landmark and in favour of the US method.

- Modelling has emphasised the need for machines to be used often to make them cost-effective. This implies that trusts should be careful not to over-purchase. Contrary to this, any treatment delays caused by machines being unavailable because they are being used elsewhere will have time resource, as well as possible clinical implications. This scenario would also increase the risk of litigation costs.
- It is possible that the use of US may increase the risk of infection at the site of insertion if the US machine is not effectively controlled for infection. If so, this will have resource and clinical implications. None of the literature reported infection complication rates.
- The model makes no allowance for additional preparation time when using US. In practice this is minimal but will carry some time resource implications.
- Given the correlation between failure and complication rates, it may be unrealistic to

vary either of these variables independently of the other. As such, the univariate threshold values for these variables may not be as wide as those indicated in the sensitivity analysis.
- Better quality and more versatile US machines will be used more frequently and may need higher maintenance, or have higher replacement cycles than modelled, thus increasing costs.

The model presented is for IJV insertion in adult patient; however it is likely that the modelled results are generalisable to other scenarios. Although there is only one RCT reported for each of the SV and FV insertion sites, both indicate failure rate and complication rate advantages using US (appendix 3, *Figures 4* and *5*). Although the trial sizes are very small, the results still achieve acceptable levels of statistical significance. Furthermore, the risk of the more serious and costly complication of pneumothorax is more common at the SV insertion site. Assuming that US will improve the pneumothorax complication rate in SV insertions, then the model will again indicate a cost-saving result. For example, the literature search found no cases of pneumothorax caused by 2-D US. A paper by Lefrant and co-workers[32] reports a 2% pneumothorax complication rate for the landmark method in the SV. Adding this complication rate to the central-case scenario model (assuming no cases of pneumothorax from US) increases the cost-saving US result from £2000 to over £8000, assuming an average cost per pneumothorax of £316 per case.

In terms of where the insertion procedures is performed, it is not difficult to show that a bedside ward-based treatment scenario will produce similar cost dominant results for the US procedure. Although a ward-based model may involve fewer and less-highly qualified staff than the theatre model presented, less-qualified staff are likely to have higher failure and complication rates. Also, the less critical treatment setting of the ward compared with theatre is likely to mean that operators are more likely to spend longer trying to insert before failure. Time spent locating and obtaining more qualified assistance is likely to be longer for a ward setting.

Infants were excluded from the model. Because of their smaller vessels, CVA in infants is expected to be more difficult than in adults *a priori*. The evidence from the RCT literature presented in this report (appendix 3, *Figures 10* and *11*) imply that the failure and complication rate differences between landmark method and US methods are even greater than those modelled for adults above. Thus, the costs and benefits of US for CVA in infants are likely to be greater than those indicated by the modelling for adults presented above.

Conclusions

Based on a model for IJV insertion in adults, modelling has given a strong indication that the use of US for venepuncture in CVA is likely to save resources as well as improve failure and complication rates. Based on the results of the clinical effectiveness review presented in this report, it is likely that this dominant resource saving result is generalisable to other insertion sites, infants, and bedside ward-based insertions. The evidence base is clearly strongest for the IJV insertion site. No evidence has been reported for PICCs and so no economic analysis has been performed for PICCs.

The economic analysis has deliberately concentrated on the favoured real-time US method, which uses grey-scale 2-D imaging as opposed to the Doppler audiological technology. The effectiveness evidence is clearly less favourable for Doppler US and in the case of adult SV insertion, for example, the effectiveness evidence (and by implication the economic evidence) is that landmark method is more effective than Doppler US.

It should be noted that the resources savings indicated by the economic modelling might not manifest themselves as financial savings to the NHS. These resource savings are legitimate opportunity cost savings for staff time, and it is right to include them in an economic analysis. In circumstances where insertion failure causes lengthy delays, theatre lists may have to be curtailed with further resource and clinical implications. The increased use of US for CVA will free up medical and nursing staff time as well as freeing up theatre time and valuable ICU and hospital ward beds. Any financial saving would accrue from reduced need to treat complications.

The model indicates that two of the key factors for achieving the US resource-saving result are that purchased machines are used sufficiently often to justify the costs, and that the required training programme for staff is itself set up in a cost-effective way. Should a policy of wider use of

US for CVA be recommended, it will be important to ensure that machines are utilised sufficiently, but not compromising the need for machines to be available when needed. Lack of availability at the appropriate time will itself cause treatment delays and have resource implications.

Chapter 4

Discussion and conclusions

Implications for other parties

Implications for other parties are few. Reduced risk of complications may reduce the financial risks from possible litigation.

If the increased use of US for CVA leads to fewer complications, then more procedures may be amenable to day-ward and outpatient treatment. This could mean shorter patient length of stay so that relatives and carers need to make fewer hospital visits.

The evidence presented in this report strongly favours the use of US for CVA of the IJV. The evidence for insertion at other sites such as the SV and FV is also positive, but has a poorer evidence base. If machines are purchased to guide IJV insertions, then operators will have to judge whether or not US should be used to guide CVA at the other insertion sites. There may be ethical issues about the use or non-use of US in these situations.

Factors relevant to the NHS

Training

The recommendation to use US-guided CVA will have significant training implications for the NHS. It is not feasible for all access procedures to be performed in radiology departments, nor is it feasible for radiologists to provide a peripatetic service for all procedures. Many procedures are performed on an emergency basis at the bedside in a diverse number of locations and most of these procedures are undertaken by non-radiologists. While some of these operators already use US to guide venous access it is likely that the majority are either sited using percutaneous landmark techniques or by surgical exposure of the vein. A change to US-guided CVC insertion will thus involve a change in practice for the majority of CVA procedures.

Radiology has lagged behind surgery in the development of skills laboratories where techniques are learned and initial errors made at the bench rather than at the bedside. Perhaps not everyone can learn US-guided venous access, but it is highly likely that most individuals who need to can learn these skills. Modelling these anatomical challenges should not be difficult for a training unit. The anatomy of jugular venous access is not complex and can easily be modelled in a skills laboratory. It is not thought difficult to teach the skill of US-guided vein puncture to most individuals. A 90% success rate has been recorded for US-guided FV access in a small series where the investigators received no formal training in US.[41] However, in the absence of suitable training there is the potential for US to make a negative contribution. Having said this, Geddes and co-workers published a study showing that there was no difference in success and complication rates between experienced and inexperienced operators for insertion of haemodialysis cannulae using US guidance – the latter group being defined by having less than 3 years' clinical experience and having inserted fewer than three central venous cannulae.[52] Both groups of operators were taught by one of the experienced group who has previously learned the technique at another centre.

The economic analysis presented in this report highlights the need for training to be set up in a cost-effective way so as not to compromise the cost-effectiveness of the US procedure itself.

De-skilling

Another important training issue is that a potential consequence of the wider availability of US machines for venous access is the development of dependence on US imaging. That is a potential for the de-skilling of operators in landmark insertion. In emergency situations where a line needs to be inserted without delay, landmark insertions may still be appropriate. It is important that training in US-guided access must not allow trainers to dispense with teaching the landmark methods. This issue will need to be addressed by policy-makers and the professional bodies.

Ethics and litigation

The clinical effectiveness evidence presented in this report strongly suggests that the use of US increases the safety of CVA using IJV insertion in adult patients. The quality of the evidence for SV and FV insertions is less good than for IJV, although what RCT evidence there is, is positive

towards the US-guided procedure. If machines are made available to trusts for the IJV procedure, decisions may need to be made about whether it is then ethical to withhold the US option for patients requiring CVA venepuncture using other insertion sites.

If, for example, trusts decide not to use US for SV insertions pending stronger research evidence, as well as decreasing the cost-effectiveness of US for IJV insertions, there is a potential risk that patients experiencing complications following a landmark-guided insertion could decide to pursue litigation.

Guidance implementation

If US-guided CVA were to be recommended as standard practice, a view will need to be taken on whether operators already experienced in the landmark method and with a track record of good success rates should be made to switch to the US-guided method. There is evidence that US is effective for patency checking and vessel localisation reported within (see chapter 2, *ULDs for vessel location followed by blind venepuncture* and *ULDs for the assessment of vessel patency and vessel location*), and also referred to in this review.[9] Any experienced operators reluctant to use US to guide real-time needle insertion, could be directed to use US for patency checking and vessel localisation prior to a landmark venepuncture for example. Policy-makers and the professional bodies will need to give clear guidance on this issue.

Resources

Increased use of US will have short-term resource implications for trusts both in terms of purchase of machines and training of operators. This will mean both short-term and ongoing capital and training investment. The economic analysis presented in this report strongly suggests net resource savings to the NHS using US guidance for CVA. The majority of these savings are likely to be staff time, theatre and ICU/HDU time, and bed resources rather than financial savings.

Discussion

The pertinent question appears to be whether real-time 2-D US imaging is effective and cost-effective compared with landmark insertions for CVA. A wide range of patients, operators, and locations within the hospital experience this procedure. Doppler US is an alternative US technology, which is used less commonly than real-time 2-D US. This trend in practice is supported by effectiveness evidence presented in this report.

The financial implications to the NHS are uncertain given that demand for new machines is unknown. This will depend on the policy recommendations of the National Institute for Clinical Excellence (NICE) and current availability of appropriate machines in the NHS. A ballpark indicative cost of £29 million across the NHS in England and Wales has been estimated if adoption of US for CVA is to be recommended. This cost will diminish over time once machines are in place and as training is cascaded downwards through trusts. Anecdotal evidence suggests that availability and therefore resource implications will vary significantly by NHS trust.

The use of a ULD has been shown to reduce the complications of venous access. However, it is important to recognise that the use of a ULD does not eliminate other potentially fatal complications of venous access, such as air embolus at line introduction, mediastinal venous laceration when large dilators or sheaths are passed, and cardiac tamponade from atrial wall erosion. It should be noted that non-venepuncture complications may be avoided by other radiological technologies such as fluoroscopy during the stages of the procedure after venous access is achieved. This issue is beyond the scope of this report.

Review of evidence for clinical effectiveness

The clinical effectiveness evidence is fairly consistent in pointing to the conclusion that 2-D real-time US imaging leads to fewer catheterisation failures, fewer complications, and requires fewer attempts and less time to achieve successful access. The quantity and quality of evidence is strongest for insertions into the IJV. Few papers address the SV and FV insertion sites, though they too show statistically significant results in favour of real-time US compared with landmark insertions. The evidence for Doppler US is much weaker and possibly negative for insertion sites other than the IJV. No RCT evidence considering the effectiveness of US for PICCs or for US versus surgical cut-down was found. Surgical cut-down is rarely used in practice.

Economic analysis

No published evidence addressing the costs or cost-effectiveness of US in CVA venepuncture

was found in the literature. A simple spreadsheet decision-analysis economic model was used to analyse the cost-effectiveness of real-time 2-D US imaging. This model was populated using RCT effectiveness evidence from the literature, local data, and expert opinion where necessary. The analysis provides a strong argument that the use of US for this procedure, as well as being safer, will achieve net resource savings compared with landmark venepuncture. Sensitivity analysis and other discussion presented in chapter 3 of this report implies that the cost saving and dominant result of the economic model is likely to hold for common insertion sites and for theatre, ICU/HDU and ward scenarios. It is argued that the model was weighted in favour of landmark method, further strengthening the robustness of the model results.

Modelling has indicated that the marginal cost per procedure when using the US machine is about £6. This cost is most sensitive to usage variables. That is, the number of times that a machine is put to use and the number of procedures undertaken by the trained operator. Some of the better machines, although more expensive, have more versatile uses such as guiding pleural drainage procedures. The more a machine is used for cost-effective procedures, the better the cost-effectiveness result for US in the CVA context.

These results highlight the need for machines to be used sufficiently often and for training programmes to be set up in a cost-effective way.

Although not modelled, the surgical cut-down approach to CVA uses high-cost operating theatre and staff resources. The surgical procedure is certain to consume more resources than either the landmark or US approaches, and may carry a higher risk of infection, which can have considerable resource implications.

Implications for the NHS

The financial implications to the NHS are uncertain given that demand for new machines is unknown. This will depend on the policy recommendations of NICE and current availability of appropriate machines in the NHS. Anecdotal evidence suggests that availability and therefore resource implications will vary significantly by NHS trust.

The NHS resource and training implications of a policy to increase the use of US for CVA have been highlighted and will need careful implementation planning and involvement of the professional bodies affected. How this should be done has not been addressed by this report.

Because of the need to undertake landmark venepuncture in emergency situations, when an US machine may not be available, it is important that operators do not become deskilled in the art of the landmark procedure.

Further research

Clearly the existing RCT evidence in this area is weakest (though positive) for insertions into the SV and FV sites. We found no RCT effectiveness for using US for PICCs or compared with surgical cut-down. These areas could be considered for further research; however, this report has indicated the ethical and the economic arguments that put significant question marks over the appropriateness of not using available US machines for insertions at these other sites. If routine cases are chosen the complication rates of procedures in experienced hands is so low (e.g. 1–3%) that a power study of any potential trial would suggest that numbers needed to show statistical significance would run into the thousands. Such trials are very difficult to do without significant external funding to coordinate multiple centres. In the case of more difficult patients or those who have already suffered a complication it is probably unethical to attempt blind puncture again, when we already have an established non-invasive technology available. It is hard to argue against using the machines for all insertion sites even if only for checking vessel patency and localisation prior to needle insertion, if not to guide the needle insertion in real-time. The cost-effectiveness of using US in the context of checking patency and vessel localisation prior to a non-US-guided venepuncture has not been addressed in this report.

There is evidence that nursing staff are increasingly being trained to insert CVLs.[2] The Manchester study undertaken by Boland and co-workers[2] has demonstrated that nurses can safely insert Hickman catheters in cancer patients using landmark method and image guidance using fluoroscopy. This service development, which can free up the relatively expensive time of junior and senior doctors alike, has not been addressed in this report. The possible economic and clinical implications of nurse operators in the NHS may be a useful area for further research.

One paper found in the literature search investigated the cost-effectiveness of PICCs compared with insertions at other puncture sites. This paper was not reviewed in this report as it did not address US and was therefore beyond the scope of the report. Its implications may need to be researched further.

Any future trials must be of sufficient size to ensure statistical power and should collate information on resource use as well as clinical effectiveness data.

Conclusions

This report has presented evidence on the effectiveness and cost-effectiveness for using US guidance in the venepuncture element of the CVA procedure.

The effectiveness evidence gives strong statistical evidence that 2-D real-time US is more effective than the landmark method in the venepuncture procedure for CVA in both adults and children. This is true for IJV insertions in particular, but also for SV and FV insertions, although the number of trials for the latter two sites is small. The evidence for Doppler US is weak, if not negative except for IJV insertions in adults.

No publications were found by the literature search reporting the cost-effectiveness of the procedure under review. Modelling has provided strong evidence that the use of US during CVA will not only reduce complications but is likely to save resources. Resource savings will manifest themselves primarily as savings in operator and theatre time and freeing up of ward beds rather than in cash savings. Sensitivity analysis implies that the resource saving assumption is likely to hold for the IJV, SV and FV insertion sites, for high-cost environments in theatres, but also on the wards, and for children as well as adults. The modelling results indicate that the cost-effectiveness of US is responsive to usage assumptions, so that it is important that US machines are used sufficiently often for cost-effective procedures once purchased.

The main implications for the NHS surround training and de-skilling of those who undertake CVA, and what guidance is to be issued for insertions at sites other than the IJV.

The evidence for the effectiveness of US insertion sites other than the IJV is positive, though less strong in terms of the quantity and quality of the trial evidence. It may be considered unethical or lacking in common sense to withhold the use of available machines that will certainly help operators to determine the location and patency of target vessels.

The training implications of a policy to increase the use of US for CVA have been highlighted and will need careful implementation planning and involvement of the professional bodies affected. Any training programme must itself be cost-effective. The need to ensure that operators do not become deskilled in landmark venepuncture has been highlighted.

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All responsibility for the contents of the report remains with the authors.

Contributions of authors

Neill Calvert (Research Fellow) carried out the economic analysis and is responsible for the full report as lead author.

Daniel Hind (Research Associate) carried out the review of the effectiveness of the technology.

Richard McWilliams (Consultant Radiologist) carried out the review of the background information.

Steve Thomas (Consultant Radiologist) provided specialist advice and clinical guidance in the modelling work.

Catherine Beverley (Information Officer) undertook the electronic literature searches.

Andrew Davidson (Consultant Anaesthetist) provided clinical advice.

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Appendix 1

Search strategy

Electronic bibliographic databases searched

Biological Abstracts
CCTR (Cochrane Controlled Trials Register)
CDSR (Cochrane Database of Systematic Reviews)
CINAHL
EBM Reviews
EMBASE
HEED
HMIC (Health Information Management Consortium – comprising DH-Data, the King's Fund Database, and Helmis)
MEDLINE
NHS DARE
NHS EED
NHS HTA database
PreMEDLINE
Science Citation Index
Social Sciences Citation Index

Other sources searched

AHRQ (Agency for Healthcare Research and Quality)
Alberta Clinical Guidelines Programme
AltaVista
American College of Cardiology
ARIF (Aggressive Research Intelligence Facility)
Bandolier
CCOHTA (Canadian Coordinating Centre for Health Technology Assessment)
CCT (Current Controlled Trials)
CenterWatch Trials Register
Centre for Clinical Effectiveness, Monash University
Centre for Health Economics, University of York
ClinicalTrials.gov, NIH Clinical Trials Database
COIN/POINT, Department of Health publications databases
Copernic
CRiB (Current Research in Britain)
eGuidelines
Health Evidence Bulletins, Wales
HSTAT (Health Services/Technology Assessment Text, US National Library of Medicine)
INAHTA (International Network of Agencies for Health Technology Assessment) Clearinghouse
Index to Theses
MRC (Medical Research Council) Funded Projects Database
National Guideline Clearinghouse
National Research Register
NCCHTA (National Coordinating Centre for Health Technology Assessment)
NHS CRD (Centre for Reviews and Dissemination), University of York
NHS R&D Programmes
NIH (National Institutes of Health) Consensus Development Programme
North of England Guidelines, University of Newcastle
OMNI (Organising Medical Networked Information)
ReFeR (Research Findings Register)
SBU (Swedish Council for Health Technology Assessment)
ScHARR Library Catalogue
SIGN (Scottish Intercollegiate Guidelines Network)
SumSearch
Trent Working Group on Acute Purchasing
TRIP (Turning Research into Practice) Database
Wessex DEC (Development and Evaluation Committee) Reports
West Midlands DES (Development and Evaluation Services) Reports

Search strategies used

Biological abstracts

1985–2001
SilverPlatter WebSPIRS
Search undertaken October 2001

#1. central venous line* or central line* or hickman line* or central venous catheter* or central vein* catheter*
#2. ultrasound or ultrasonic* or ultrasonograph* or imag* guid* or radiolog*
#3. #1 and #2

CDSR and CCTR

2001 Issue 3
The Cochrane Library, Update Software (CD-ROM version)
Search undertaken September 2001

#1. catheterization-central-venous*:me
#2. central-venous-pressure*:me
#3. (central next venous next line*)
#4. (central next venous next pressure)
#5. (venous or vein*) near (cannulation or access or catheter*)
#6. (pulmonary bext art* next flotation*)
#7. (central next line* next insertion*)
#8. (hickman next line*)
#9. #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8
#10. ultrasonics*:me
#11. ultrasonography*:me
#12. (imag* near guid*)
#13. (ultrasound* or ultrasonic* or doppler)
#14. #10 or #11 or #12 or #13
#15. #9 and #14

CINAHL

1982–2001
Ovid Biomed
Search undertaken October 2001

1. exp catheterization, central venous/
2. exp central venous catheters/
3. central venous pressure/
4. central venous line$.tw
5. central venous pressure.tw
6. ((venous or vein$) adj2 (cannulation or access or catheter$)).tw
7. pulmonary arter$ flotation$.tw
8. central line$ insertion$.tw
9. hickman line$.tw
10. or/1-9
11. exp ultrasonics/
12. exp ultrasonography/
13. (imag$ adj5 guid$).tw
14. (ultrasound or ultrasonic$ or doppler).tw
15. or/11-14
16. 10 and 15

Citation indexes (Science and Social Sciences)

1981–2001
Web of Science
Search undertaken September 2001

Title=(ultrasound* or ultrasonic* or imag* guid* or doppler or ultrasonograph*) and (central venous or venous cannulation or venous catheter* or vein* cannulation or vein* catheter* or pulmonary arter* flotation* or central line* or hickman line*); DocType=All document types; Languages=All languages; Databases=SCI-EXPANDED, SSCI; Timespan=All Years

CRD Databases (NHS DARE, EED, HTA)

CRD website – complete databases
Search undertaken September 2001

ultrasound of ultrasonic or ultrasono or doppler/All fields AND vein or venous or pulmonary artery/All fields AND central or line or hickman/All fields

EMBASE

1980–2001
SilverPlatter WebSPIRS
Search undertaken October 2001

#1. 'central-venous-catheterization' / all subheadings
#2. 'central-venous-pressure' / all subheadings
#3. central venous line*
#4. central venous pressure
#5. (venous or vein*) near2 (cannulation or access or catheter*)
#6. pulmonary arter* flotation*
#7. central line* insertion*
#8. hickman line*
#9. #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8
#10. 'ultrasound-' / all subheadings
#11. explode 'echography-' / all subheadings
#12. imag* near5 guid*
#13. ultrasound* or ultrasonic* or doppler
#14. #10 or #11 or #12 or #13
#15. #9 and #14

HEED (Office of Health Economics Health Economic Evaluation Database)

CD-ROM version
Search undertaken September 2001

Search terms

- (ultrasound or ultrasonic or ultrasonics or image guidance or image guided or doppler or ultrasonography or ultrasonographic)

AND

- (catheter or catheters or catherization or catheterisation or vein or veins or venous or line or lines or pulmonary artery)

Fields searched

- Abstract
- All data
- Article title
- Book title

- Keywords
- Technology assessed

MEDLINE

1966–2001
Ovid Biomed
Search undertaken September 2001

1. catheterization, central venous/
2. central venous line$.tw
3. central venous pressure.tw
4. central venous pressure/
5. ((venous or vein$) adj2 (cannulation or access or catheter$)).tw
6. pulmonary arter$ flotation$.tw
7. central line insertion$.tw
8. hickman line$.tw
9. picc.tw
10. peripheral$ insert$ central catheter$.tw
11. or/1-10
12. exp ultrasonics
13. exp ultrasonography/
14. (imag$ adj5 guid$).tw
15. (ultrasound or ultrasonic$ or doppler).tw
16. or/12-15
17. 11 and 16

Methodological search filters used in Ovid MEDLINE

Guidelines

1. guideline.pt
2. practice guideline.pt
3. exp guidelines/
4. health planning guidelines/
5. or/1-4

Systematic reviews

1. meta-analysis/
2. exp review literature/
3. (meta-analy$ or meta analy$ or metaanaly$).tw
4. meta-analysis.pt
5. review academic.pt
6. review literature.pt
7. letter.pt
8. review of reported cases.pt
9. historical article.pt
10. review multicase.pt
11. or/1-6
12. or/7-10
13. 11 not 12

RCTs

1. randomized controlled trial.pt
2. controlled clinical trial.pt
3. randomized controlled trials/
4. random allocation/
5. double blind method/
6. or/1-5
7. clinical trial.pt
8. exp clinical trials/
9. ((clin$ adj25 trial$)).ti, ab
10. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti, ab
11. placebos/
12. placebos.ti, ab
13. random.ti, ab
14. research design/
15. or/7-14
16. comparative study/
17. exp evaluation studies/
18. follow up studies/
19. (control$ or prospectiv$ or volunteer$)).ti, ab
20. prospective studies/
21. or/16-20
22. 6 or 15 or 21

Economic evaluations

1. economics/
2. exp "costs and cost analysis"/
3. economic value of life/
4. exp economics, hospital/
5. exp economics, medical/
6. economics, nursing/
7. economics, pharmaceutical/
8. exp models, economic/
9. exp "fees and charges"/
10. exp budgets/
11. ec.fs
12. (cost or costs or costed or costly or costing$).tw
13. (economic$ or pharmacoeconomic$ or price$ or pricing).tw
14. or/1-13

Quality of life

1. exp quality of life/
2. quality of life.tw
3. life quality.tw
4. qaly$.tw
5. quality adjusted life year$.tw
6. (sf36 or sf 36 or short form 36).tw
7. (eq5d or eq 5d or euroqol).tw
8. or/1-7

Appendix 2

Data extraction

TABLE 10 *Study characteristics*

Study	Study type	Patient population	Comparator	Sample size	Patients/placements
Alderson *et al.*, 1993[10]	Prospective, randomised, study	Children (< 2 years); pathology not stated; cardiac surgery; risk not stated	Landmark	US = 20 Landmark = 20	40/40
Bold *et al.*, 1998[26]	Prospective, randomised, crossover trial	Adult chemotherapy patients (cancer types not specified); high risk (for failure/complications)	Landmark	Doppler US = 119 Landmark = 121	240/240
Branger *et al.*, 1995[6] (IJV)	Randomised, prospective study	Patients needing haemodialysis, aphresis or parenteral nutrition requiring CVC (pathology not stated); low risk of complications (high-risk patients excluded)	Landmark	Doppler US = 15 Landmark = 15	30/29
Branger *et al.*, 1995[6] (SV)	Randomised, prospective study	Patients needing haemodialysis, aphresis or parenteral nutrition requiring CVC (pathology not stated); low risk of complications (high-risk patients excluded)	Landmark	Doppler US = 50 Landmark = 50	100/98
Gilbert *et al.*, 1995[27]	Prospective, randomised, crossover clinical study	Adult patients (pathology not stated) at high risk from complications (obesity or coagulopathy)	Landmark	Doppler US = 32 Landmark = 44	76/76
Gratz *et al.*, 1994[33]	Prospective, randomised trial	Cardiothoracic/vascular surgery patients (age and pathology not stated)	Landmark	Doppler US = 21 Landmark = 20	41/40
Gualtieri *et al.*, 1995[35]	Prospective, randomised study	Critical care patients (age, pathology and risk not stated) non-emergency procedures	Landmark	US = 25 Landmark = 27	33/53
Hilty *et al.*, 1997[41]	Prospective, randomised, paired subject-controlled clinical trial	Patients (age, pathology and risk not reported) undergoing CPR	Landmark	US = 20 Landmark = 20	20/40
Johnson *et al.*, 1996[24] (abstract)	Randomised prospective study	Critically ill patients	Landmark	US = 33 Landmark = 37	70/70
Lefrant *et al.*, 1998[32]	Prospective, randomised study	Critically ill adults (pathology and risk not stated) non-emergency	Landmark	Doppler US = 143 Landmark = 143	286/286
Mallory *et al.*, 1990[28]	Prospective, randomised trial	Critically ill adult ICU patients, (pathology not stated), high risk and low risk	Landmark	US = 12 Landmark = 17	29/29
Nadig *et al.*, 1998[31]	Prospective, randomised study	Dialysis patients (age, pathologies and risk level not reported)	Blind venepuncture following US-guided vessel location	US = 36 Landmark = 37	65/73
Slama *et al.*, 1997[38]	Prospective, randomised study	Adults in ICU (pathology not reported, no risk assesment)	Landmark	US = 37 Landmark = 42	79/79
Soyer *et al.*, 1993[40]	Prospective, randomised study	Adult patients with liver dysfunction requiring transjugular liver biopsy (no risk assessment)	Landmark	US = 24 Landmark = 23	47/47

continued

***TABLE 10* contd** *Study characteristics*

Study	Study type	Patient population	Comparator	Sample size	Patients/placements
Sulek *et al.*, 2000[39]	Prospective, randomised study	Adults scheduled for abdominal, vascular or cardiothoraic procedures with general anaesthesia and mechanical ventilation (pathology and risk assessment not reported)	Landmark	Right IJV/landmark = 30 Right IJV/US = 30 Left IJV/landmark = 30 Left IJV/US = 30	120/120
Teichgräber *et al.*, 1997[11]	Prospective, randomised trial	Patients undergoing routine catheterisation of the IJV (age, pathology and risk assessment not reported)	Landmark	US = 50 Landmark = 50	100/100
Troianos *et al.*, 1991[36]	Prospective, randomised study	Cardiothoracic surgical patients (age, pathology and risk factor not recorded)	Landmark	US = 77 Landmark = 83	160/160
Verghese *et al.*, 1999[37]	Prospective, randomised study	Infants scheduled for cardiovascular surgery, < 12 months, < 10 kg (pathology and risk assessment not reported)	Landmark	US = 43 Landmark = 52	95/95
Verghese *et al.*, 2000[5]	Prospective, randomised study	45 infants scheduled to undergo IJV cannulation during cardiac surgery	Landmark	Doppler US = 13 US = 16 Landmark = 16	45/45
Vucevic *et al.* 1994[34]	Prospective, randomised study	Cardiac surgery and ICU patients	Landmark	Doppler US = 20 Landmark = 20	40/40
Woody *et al.*, 2001[25] (abstract)	Prospective, randomised trial	Emergency	Landmark	US = 40 Landmark = 43	83/83

TABLE 11 *Therapy details*

Study	ULD type	Catheter size	Needle guide	Insertion point	Study setting	Operator
Alderson *et al.*, 1993[10]	US: portable, 2-D US scanner (Dymax Corporation), mechanical liquid-path 7.5 MHz transducer that allows high resolution	16-G	No	Right IJV	Not reported	Anaesthetist: experienced cardiac anaesthetist
Bold *et al.*, 1998[26]	Doppler US: Smart Needle. 14 MHz continuous-wave Doppler instrument with probe in the needle (Smart Needle)	Not reported	–	SV (side not reported)	Controlled non-emergency conditions	Medic: 18 surgical oncology fellows (postgraduate year 6–10). Instruction in the use of the Smart Needle and demonstrated competence in the use of the Doppler probe
Branger *et al.* 1995[6] (IJV)	Doppler US: Vermon 4 MHz pulsed Doppler system probe with a transducer (audio)	Not reported	–	IJV (side not reported)	Not reported	Unclear: 14 junior postgraduate students with fewer than 5 years' clinical experience and eight senior staff members with more than 5 years' experience, from nephrology, emergency and ICU. Taught the Doppler technique over 2 weeks, achieved at least one venous catheterisation before entering study
Branger *et al.*, 1995[6] (SV)	Doppler US: Vermon 4 MHz pulsed Doppler system probe with a transducer (audio)	Not reported	–	SV (side not reported)	Not reported	Unclear: 14 junior postgraduate students with fewer than 5 years' clinical experience and eight senior staff members with more than 5 years' experience, from nephrology, emergency and ICU. Taught the Doppler technique over 2 weeks, achieved at least one venous catheterisation before entering study
Gilbert *et al.*, 1995[27]	Doppler US: Smart Needle. Audio-guided Doppler US	Not reported	–	IJV (side not reported)	ICU and operating theatre	Unclear: number not reported. Junior house staff relatively inexperienced in using either technique
Gratz *et al.*, 1994[33]	Doppler US: Smart Needle. Doppler US guidance (14.3 MHz probe in needle)	20-gauge	–	IJV (side not reported)	Not reported	Anaesthetist: number not reported. Experienced anesthesiologists
Gualtieri *et al.*, 1995[35]	US: Site Rite. 7.5 MHz real-time, portable battery-operated US transducer (Site Rite)	20–25 cm long	Yes	SV (both sides)	20 bed trauma-surgical-medical-ICU	Unclear: 18 physicians with < 30 procedures

continued

TABLE 11 contd *Therapy details*

Study	ULD type	Catheter size	Needle guide	Insertion point	Study setting	Operator
Hilty *et al.*, 1997[41]	US: Aloka 650 CL. Real-time US guidance (7.5 MHz linear array probe)	Not reported	No	FV (both sides)	Emergency department	Medic: two emergency medicine residents in postgraduate years 3 and 4; 15–20 procedures Landmark; 6–10 procedures US
Johnson *et al.*, 1996[24] (abstract)	US: 5 MHz US transducer	Not reported	No	IJV (side not reported)	ICU	Unclear: not reported
Lefrant *et al.*, 1998[32]	Doppler US: Vermon. Pulsed and continuous Doppler US guidance (described as real-time)	Not reported	–	SV (both sides)	ICU	Anaesthetist: one staff anaesthetist, untrained in Doppler guidance before the study
Mallory *et al.*, 1990[28]	US: US guidance (Hewlett-Packard 7702A real-time 2-D US unit with a 5 MHz resolution) (image)	Not reported	No	IJV (side not reported)	ICU	Medic: senior ICU staff and critical care fellows; number not reported; mean 6 years' experience
Nadig *et al.*, 1998[31]	US: Picker CS9100, Convex 3.5 MHz US	Not reported	No	IJV (both sides)	Not reported	Unclear: physicians; clinical experience 1–7 years
Slama *et al.*, 1997[38]	US: Sonos 100 (Hewlett-Packard). 2-D US scanner, 7.5 MHz transducer	Not reported	No	Right IJV	ICU	Unclear: junior house staff (interns or residents) under the direct supervision of a senior physician after at least three demonstrations by an experienced operator and three attempts of right IJV using landmark
Soyer *et al.*, 1993[40]	US: Portable SDR (Phillips) US unit with 7.5 MHz probe. (image)	18-G needle catheter	No	Right IJV	Not reported	Radiologist: two radiologists with the same experience
Sulek *et al.* 2000[39]	US: Hewlett-Packard. A 2-D, 5 MHz surface US transducer	Either 7-Fr triple-lumen or 9-Fr introducer sheath	No	IJV (both sides)	Operating room of a university affiliated hospital	Anaesthetist: anaesthetist; all operators experienced in IJV cannulation (at least 60 IJV catheter placements) with known expertise in the use of US-guided IJV technique
Teichgräber *et al.* 1997[11]	US: Toshiba SSA 270A. US 5 MHz linear transducer	Not reported	Unknown	IJV (side not reported)	Clinic	Unclear: physicians; number and experience not reported
Troianos *et al.* 1991[36]	US: Site Rite, (Dymax) 7.5 MHz and Sonos 500 (Hewlett-Packard) 5.0 MHz transducers)	18-gauge x 6.35-cm-long radiopaque catheter	Unknown	Right IJV	Not reported	Unclear: not reported

continued

***TABLE 11* contd** *Therapy details*

Study	ULD type	Catheter size	Needle guide	Insertion point	Study setting	Operator
Verghese *et al.* 1999[37]	US: Site Rite. Real-time US 9 MHz transducer	18-gauge	Yes	IJV (side not reported)	Theatre	Anaesthetist: number not reported; board-eligible anesthesia fellows who completed residency training in anesthesia
Verghese *et al.* 2000[5]	Doppler US and US: Smart Needle Doppler probe, 14 MHz transducer OR Site Rite 7.5 MHz transducer	18-G	Yes (for US)	IJV (side not reported)	Theatre	Anaesthetist: number not reported; paediatric anaesthesia fellows
Vucevic *et al.* 1994[34]	Doppler US: Smart Needle	Not reported	–	Right IJV	Not reported	Anaesthetist: two consultant anaesthetists; ten procedures
Woody *et al.* 2001[25] (abstract)	US: 7.5 MHz probe	Not reported	Unknown	Not reported	High-volume urban emergency department	Medic: emergency medicine resident; 1 hour's training

TABLE 12 *Study site, and inclusion/exclusion criteria*

Study	Study site	Inclusion criteria	Exclusion criteria
Alderson *et al.*, 1993[10]	Canadian urban children's hospital	Children < 2 years, scheduled for cardiac surgery	Prior cardiac surgery
Bold *et al.* 1998[26]	USA tertiary care, outpatient oncology centre	Patients stratified for three known risk factors: prior surgery in the SV region, prior radiotherapy at the attempted catheterisation site and an abnormal weight-height ratio. All patients had at least one factor that may be associated with increased risk for failure or complication (body mass index, prior surgery in region or SV, or prior radiology at catheterisation site)	None listed
Branger *et al.*, 1995[6] (IJV)	French teaching hospital	Patients needing hemodialysis, aphresis or parenteral nutrition requiring CVC	Known risk factors such as thoracic abnormality, respiratory distress, major obesity, or restlessness
Branger *et al.*, 1995[6] (SV)	French teaching hospital	Patients needing hemodialysis, aphresis or parenteral nutrition requiring CVC	Known risk factors such as thoracic abnormality, respiratory distress, major obesity, or restlessness
Gilbert *et al.*, 1995[27]	USA tertiary care, teaching hospital	High-risk patients with pre-existing obesity or coagulopathy requiring IJV cannulation	None described
Gratz *et al.* 1994[33]	USA tertiary care, teaching hospital	CT/vascular surgery patients	None recorded
Gualtieri *et al.*, 1995[35]	US urban, teaching hospital	Clinical indications requiring CVA: assessment of CVP; administration of nutrition/drugs/fluid; and as a conduit for pulandmarkonary artery catheterisation	Patient required CVA after cardiopulandmarkonary arrest and other emergency situations; informed consent unavailable
Hilty *et al.*, 1997[41]	USA urban, teaching hospital emergency department, during CPR	Patients presenting in cardiopulandmarkonary arrest to the emergency department	None recorded
Johnson *et al.*, 1996[24] (abstract)	Not reported	Critically ill	None reported
Lefrant *et al.* 1998[32]	French teaching hospital	Low-risk patients, requiring catheterisation of the SV when both the single operator and the US probe were available	Patients < 18 years old; significant coagulopathy; previous SV cannulation attempts; prior surgery in the area; emergency CVA required
Mallory *et al.*, 1990[28]	USA tertiary care, teaching hospital	Conscious patients requiring urgent or urgent-elective IJV cannulation; informed consent	Not recorded

continued

***TABLE 12* contd** *Study site, and inclusion/exclusion criteria*

Study	Study site	Inclusion criteria	Exclusion criteria
Nadig *et al.*, 1998[31]	German teaching hospital	None recorded	None recorded
Slama *et al.* 1997[38]	French university hospital	Admission to ICU, requiring insertion of CVC	None recorded
Soyer *et al.*, 1993[40]	French hospital (type not reported)	Thrombocytopenia, severe coagulopathy, or marked ascites	Patients indicated for standard percutaneous transhepatic liver biopsy
Sulek *et al.*, 2000[39]	USA university affiliated hospital; operating room	Adult patients without previous IJV catheter placement	Patients were excluded from randomisation if there was a history of radical neck dissection, carotid endarterectomy, carotid artery stenosis, contra-indications to the Trendelenburg position or refusal to participate
Teichgräber *et al.*, 1997[11]	German university teaching hospital	Patients undergoing routine catheterisation of the IJV	Not reported
Troianos *et al.*, 1991[36]	USA tertiary care, teaching hospital	Cardiothoracic surgery patients	None recorded
Verghese *et al.*, 1999[37]	USA university teaching hospital	Infants scheduled for cardiovascular surgery, younger than 12 months, weighing less than 10 kg	None recorded
Verghese *et al.*, 2000[5]	USA university teaching hospital	Infants scheduled to undergo internal jugular cannulation during cardiac surgery	None recorded
Vucevic *et al.*, 1994[34]	British hospital	Cardiac surgery and ICU patients	None recorded
Woody *et al.*, 2001[25] (abstract)	USA urban hospital	Not reported	None reported

TABLE 13 *Patient characteristics*

Study	Age	Sex	Diagnoses	Coagulopathy	Height-weight ratio	Other factors	Baseline comparability
Alderson *et al.*, 1993[10]	Landmark 281 (218) days; US 258 (170) days. Each group contained three neonates and 17 infants	Not reported	Not reported	Not reported	Weight only		Yes
Bold *et al.*, 1998[26]	US 50; landmark 30	Doppler US 44:75; landmark 53:68	Recorded not reported	Not reported	Reported		Not recorded
Branger *et al.*, 1995[6] (IJV)	Not recorded	Not recorded	Not recorded	Not recorded	Not recorded		Unknown
Branger *et al.*, 1995[6] (SV)	Not recorded	Not recorded	Not recorded	Not recorded	Not recorded		Unknown
Gilbert *et al.*, 1995[27]	Obesity landmark 58.4 ± 13.3; obesity Doppler US-guided 62.7 ± 13.4; coagulopathy landmark 57.9 ± 14.2; coagulopathy Doppler US-guided 55.8 ± 15.7	M:F obesity landmark 15:8; obesity Doppler US-guided 5:10; coagulopathy landmark 17:18; coagulopathy Doppler US-guided 9:17	Not recorded	Recorded. High-risk coagulopathic patients were recruited	Recorded. High-risk obese patients were recruited	Tragus-to-notch distance	Yes
Gratz *et al.*, 1994[33]	Yes	Yes. M:F 27:14	Not recorded	Not recorded	Recorded		Yes
Gualtieri *et al.*, 1995[35]	Not recorded	Not recorded	Not recorded	Not recorded	Not recorded		No
Hilty *et al.*, 1997[41]	65 ± 15 years	Recorded. M:F 13:7	Not recorded	Not recorded	Recorded	No femoral scars from previous surgery/injection drugs. 8/20 patients had no palpable pulse with CPR	Yes

continued

***TABLE 13* contd** *Patient characteristics*

Study	Age	Sex	Diagnoses	Coagulopathy	Height-weight ratio	Other factors	Baseline comparability
Johnson *et al.*, 1996[24] (abstract)	Yes	Not reported	Not reported	Recorded not reported	Recorded	APACHE III score; neck anatomy	Yes
Lefrant *et al.*, 1998[32]	Doppler US-guided 67 median; landmark 68 median	M:F Doppler US-guided 84/59 median; landmark 68 median	Recorded	Recorded not reported	Recorded	Ventilated patients	Yes
Mallory *et al.*, 1990[28]	Not recorded	Not recorded	Not recorded	Not recorded	Not recorded		No
Nadig *et al.*, 1998[31]	US 1.7	Not recorded	Not recorded	Not recorded	Not recorded	IJV cross section (cm^3)	Yes (for age only)
Slama *et al.*, 1997[38]	Landmark 66 ± 16; US 65 ± 17	Landmark 69% M; US 66%	Not recorded	Not recorded	Height and weight recorded only	APACHE II score; simplified acute physiologic score; neck width at the thyroid cartilage; distance between sternum and thyroid cartilage (neck length); maximal diameter of IJV; presence of thrombus or abnormal position of the jugular vein noted	Yes
Soyer *et al.*, 1993[40]	Mean 49 years	M:F 27:20	Reported	Recorded not reported	Not reported	None recorded	Yes
Sulek *et al.*, 2000[39]	Right IJV landmark: 58 ± 7; right IJV US: 61 ± 5; left IJV landmark: 60 ± 6; left IJV US: 57 ± 8	Right IJV landmark: 25:5; right IJV US: 23:7; left IJV landmark: 26:4; left IJV US: 25:5	Not reported	Not reported	Recorded	Demographic data analysed using analysis of variance	No
Teichgräber *et al.*, 1997[71]	Not reported	Not reported	Not reported	Not reported	Not reported		Unknown

continued

***TABLE 13* contd** *Patient characteristics*

Study	Age	Sex	Diagnoses	Coagulopathy	Height-weight ratio	Other factors	Baseline comparability
Troianos *et al.*, 1991[36]	Recorded not reported	Recorded not reported	Recorded not reported	Not reported	Recorded not reported		Yes
Verghese *et al.*, 1999[37]	Landmark 5.9 ± 4.4 months (median 6.0); US 6.4 ± 3.8 months (median 6.0)	Not recorded	Not recorded	Not recorded	Weight only		Yes
Verghese *et al.*, 2000[5]	1 day to 12 months	Not recorded	Not recorded	Not recorded	Weight only		Yes
Vucevic *et al.*, 1994[34]	Not recorded	Not recorded	Not recorded	Not recorded	Recorded	Previous cannulations; previous unsuccessful attempts	Yes
Woody *et al.*, 2001[25] (abstract)	Not reported	Not reported	Not reported	Not reported	Not reported		Unknown

APACHE, Acute Physiology and Chronic Health Evaluation; F, female; M, male

TABLE 14 *Quality assessment*

Study	Patient characteristics	Insertion method standardised	Randomisation method	Post-randomisation exclusions	Intention-to-treat analysis
Alderson *et al.*, 1993[10]	1	Yes	Not reported	No	Yes
Bold *et al.*, 1998[26]	4	Yes	Computer-generated block randomisation process	No	Yes
Branger *et al.*, 1995[6] (IJV)	0	Yes	Random tables	Yes	No
Branger *et al.*, 1995[6] (SV)	0	Yes	Random tables	Yes	No
Gilbert *et al.*, 1995[27]	4	Yes	Not reported	No	Yes
Gratz *et al.*, 1994[33]	4	Yes	Not reported	1/41	No
Gualtieri *et al.*, 1995[35]	0	Yes	Random number	1/53	No
Hilty *et al.*, 1997[41]	3	Yes	Computer-generated randomisation chart	No	Yes
Johnson *et al.*, 1996[24] (abstract)	3	Unclear	Not reported	No	Unclear
Lefrant *et al.* 1998[32]	5	Yes	Random number	No	Yes
Mallory *et al.*, 1990[28]	0	Yes	Not reported	No	Yes
Nadig *et al.*, 1998[31]	1	Yes	By lot	No	Yes
Slama *et al.*, 1997[38]	2	Yes	Not reported	No	Yes
Soyer *et al.*, 1993[40]	4	Yes	Not reported	No	Yes
Sulek *et al.*, 2000[39]	3	Yes	Computer-generated randomisation table	No	Yes
Teichgräber *et al.*, 1997[11]	0	Yes	Not reported	No	Yes
Troianos *et al.*, 1991[36]	4	Yes	Not reported	No	Yes
Verghese *et al.*, 1999[37]	1	Yes	Computer-generated randomisation table	No	Yes
Verghese *et al.*, 2000[5]	1	Yes	Computer-generated randomisation table	No	Yes
Vucevic *et al.*, 1994[34]	1	Yes	Not reported	No	Yes
Woody *et al.*, 2001[25] (abstract)	0	Unclear	Not reported	No	Yes

TABLE 15 *Findings*

Study	Intervention	Failures	Attempts to success	Complications	Seconds to success	No. US successes post-landmark failure	No. successes on first attempt
Alderson *et al.*, 1993[10]	Landmark	4/20	2.0 (1.0)	Eight inability to pass Seldinger wire into superior vena cava; two carotid artery puncture	56.4 (range 48.9)	–	Not recorded
	US	0/20	1.35 (0.7)	Three inability to pass Seldinger wire into superior vena cava; one carotid artery puncture	23.0 (range 27.4)		Not recorded
	Doppler US	–	–	–	–		–
Bold *et al.*, 1998[26]	Landmark	23/121	Not recorded	1/121 (0.8%) (hemothorax (sic.))	Not recorded (landmark 27/34)	18/21	Not recorded
	US	–	–	–	–		–
	Doppler US	36/119	Not recorded	2/119 (1.7%) (one haematoma, one catheter malposition)	Not recorded		Not recorded
Branger *et al.*, 1995[6] (IJV)	Landmark	5/15	2.4 ± 0.6	Unclear	187 ± 73	3/5	Not reported
	US	–	–	–	–		–
	Doppler US	1/14	2.3 ± 0.4	Unclear	401 ± 380		Not reported
Branger *et al.*, 1995[6] (SV)	Landmark	4/50	1.9 ± 0.7	Unclear	153 ± 56	2/4	Not reported
	US	–	–	–	–		–
	Doppler US	3/48	1.5 ± 0.3	Unclear	362 ± 105		Not reported
Gilbert *et al.*, 1995[27]	Landmark	17/44	1.7	13/49 (eight carotid artery puncture; five hematoma formation)	188.5 ± 193	12/17 (landmark 12/21)	13/44
	US	–	–	–	–		–
	Doppler US	5/32	1.4	3/49 (one carotid artery puncture; two haematoma formation)	283.5 ± 228		18/32
Gratz *et al.*, 1994[33]	Landmark	5/20	2.8 ± 2.9	0/20	226.0 ± 332	–	11/20
	US	–	–	–	–		–
	Doppler US	0/20	1.4 ± 0.9	0/20	283.5 ± 228		17/20
Gualtieri *et al.*, 1995[35]	Landmark	15/27	2.5 (No SD or range given)	11/27: three arterial puncture; five haematoma; three malposition	Not recorded	12/15	Not recorded
	US	2/25	1.4	1/25: one arterial puncture	Not recorded		Not recorded
	Doppler US	–	–	–	Not recorded		Not recorded

continued

***TABLE 15* contd** *Findings*

Study	Intervention	Failures	Attempts to success	Complications	Seconds to success	No. US successes post-landmark failure	No. successes on first attempt
Hilty *et al.*, 1997[41]	Landmark	7/20	5 ± 5	None reported	124.2 ± 69	–	Not recorded
	US	2/20	2.3 ± 3 (p = 0.0057)	None reported	121.0 ± 60 (p = 0.0001)		Not recorded
	Doppler US	–	–	–	–		–
Johnson *et al.*, 1996[24] (abstract)	Landmark	2/37 (5%)	3.2 ± 2.1	14/37 (carotid puncture and haematoma)	210 ± 255	–	16%
	US	1/33 (3%)	1.6 ± 1.2	5/33	77 ± 108		67%
	Doppler US	–	–	–	–		–
Lefrant *et al.*, 1998[32]	Landmark	13/143	Median 1	24/143 (16.8%): 11 arterial puncture; three pneumothorax; 11 wrong position of the catheter tip	27 (range 15–240)	–	94/143 (65.7%)
	US	–	–	–	–		–
	Doppler US	19/143	Median 1	8/143 (5.6%): five arterial puncture; two pneumothorax; one wrong position of the catheter tip. p = not significant	300 (range 94–900)		92/143 (64.3%)
Mallory *et al.*, 1990[28]	Landmark	6/17	3.1	Not recorded	Not recorded	6/6 (landmark 0/0)	7/17
	US	0/12	1.8	Not recorded	Not recorded		7/12
	Doppler US	–	–	Not recorded	Not recorded		–
Nadig *et al.*, 1998[31]	Landmark	13/37	Not recorded	0/37	288 ± 132	10/13	30 (83%)
	US	0/36	Not recorded	0/36	204 ± 54		13 (35%)
	Doppler US	–	–	–	–		–
Slama *et al.*, 1997[38]	Landmark	10/42	Not recorded	5/42: 5 carotid artery punctures (12%)	235 ± 408	–	11/42 (26%)
	US	0/37	Not recorded	5/37: 5 carotid artery punctures (14%)	95 ± 174 (p < 0.06)		16/37 (43%)
	Doppler US	–	–	–	–		–
Soyer *et al.*, 1993[40]	Landmark	5/23 (22%)	4 ± 1.53	1/23 (4%) (carotid artery puncture)	Mean 240 ± 120	5/5	Not recorded
	US	0/24 (0%) (p < 0.05)	1.54 ± 0.66 (p < 0.001)	0/24 (0%)	Mean 480 ± 120		Not recorded
	Doppler US	–	–	–	–		–

continued

TABLE 15 contd *Findings*

Study	Intervention	Failures	Attempts to success	Complications	Seconds to success	No. US successes post-landmark failure	No. successes on first attempt
Sulek *et al.*, 2000[39]	Landmark	Right IJV 1/30; left IJV 4/30	Right IJV 2.1 ± 0.9; left IJV 3.5 ± 1.3	Right IJV 4/30 patients (four arterial puncture, four haematoma, one failed guide-wire); left IJV 8/30 (six arterial puncture, six haematoma; four failed guide-wire)	Right IJV 137 ± 139; left IJV 247 ± 176	–	Not recorded
	US	Right IJV 1/30; left IJV 2/30	Right IJV 1.5 ± 2.0; left IJV 2.3 ± 0.7	Right IJV 2/30 patients (one arterial puncture, two haematoma, one failed guide-wire); left IJV 4/30 (two arterial puncture, four haematoma; two failed guide-wire)	Right IJV 58 ± 71; left IJV 138 ± 139		Not recorded
	Doppler US	–	–	–	–		–
Teichgräber *et al.*, 1997[11]	Landmark	26/50 (52%)	Not recorded	14/50 (neck haematoma 10%; plexus irritation 6%; carotid artery puncture 12%)	Mean 51.4 (range 3–820)	–	Not recorded
	US	2/50 (4%)	Not recorded	3/50 (neck haematoma 2%; plexus irritation 4%; carotid artery puncture 0%)	Mean 15.2 (range 8–76)		Not recorded
	Doppler US	–	–	–	–		–
Troianos *et al.*, 1991[36]	Landmark	3/83	2.8 ± 3.0	7/83 (seven carotid artery punctures)	117 ± 136	–	45/83
	US	0/77	1.4 ± 0.7	1/77 (one carotid artery puncture)	61 ± 46		56/77
	Doppler US	–	–	–	–		–
Verghese *et al.*, 1999[37]	Landmark	12/52 (23.1%)	3.3 ± 2.8	13/52 (25%): all carotid punctures	840 ± 906	–	Not recorded
	US	0/43 (0%)	1.3 ± 0.6	0/43	252 ± 168		Not recorded
	Doppler US	–	–	–	–		Not recorded
Verghese *et al.*, 2000[5]	Landmark	3/16 (18.7%)	Median: 2	Three (19%) carotid artery pucture	396 ± 318	–	–
	US	1/16 (6%)	Median: 1 ($p < 0.05$ landmark and Smart Needle vs. imaging method)	One (6%) carotid artery puncture	270 ± 222		–
	Doppler US	3/13 (23%)	Median: 2	Two (15%) carotid artery puncture	534 ± 366		–

continued

***TABLE 15* contd** *Findings*

Study	Intervention	Failures	Attempts to success	Complications	Seconds to success	No. US successes post-landmark failure	No. successes on first attempt
Vucevic *et al.*, 1994[34]	Landmark	1/20	20.5	1/20	Easy group: 59.2 ± 38.7; difficult group: 322.6 ± 173.9	–	Not recorded
	US	–	–	–	–		–
	Doppler US	2/20	17.0	1/20	Easy group: 91.8 ± 38.7; difficult group: 167.6 ± 90.4		Not recorded
Woody *et al.*, 2001[25] (abstract)	Landmark	Not reported	3.111	Not reported	457.407 (no SD or range)	–	Not reported
	US	Not reported	1.394 ($p < 0.0002$)	Not reported	60.938 (no SD or range)		Not reported
	Doppler US	–	–	–	–		–

SD, standard deviation

Appendix 3

Meta-analyses

Meta-analyses were performed in the Cochrane Collaboration's Review Manager 4.1 software (http://www.cochrane.de/cochrane/revman.htm).

Data were combined to estimate the relative risk and associated 95% CIs across studies using the random effects model for the following outcomes:

- the number of failed catheter placements
- the number of catheter placement complications
- the risk of failure on first catheter placement attempt.

Data were combined to estimate the weighted mean difference and associated 95% CIs across studies using the random effects model for the following outcomes:

- the number of attempts to successful catheterisation
- the number of seconds to successful catheterisation.

Outcomes reported in abstracts have been excluded from the meta-analyses. Outcomes for Doppler US have been reported separately from those for US. Outcomes for infants have been reported separately from those for adults.

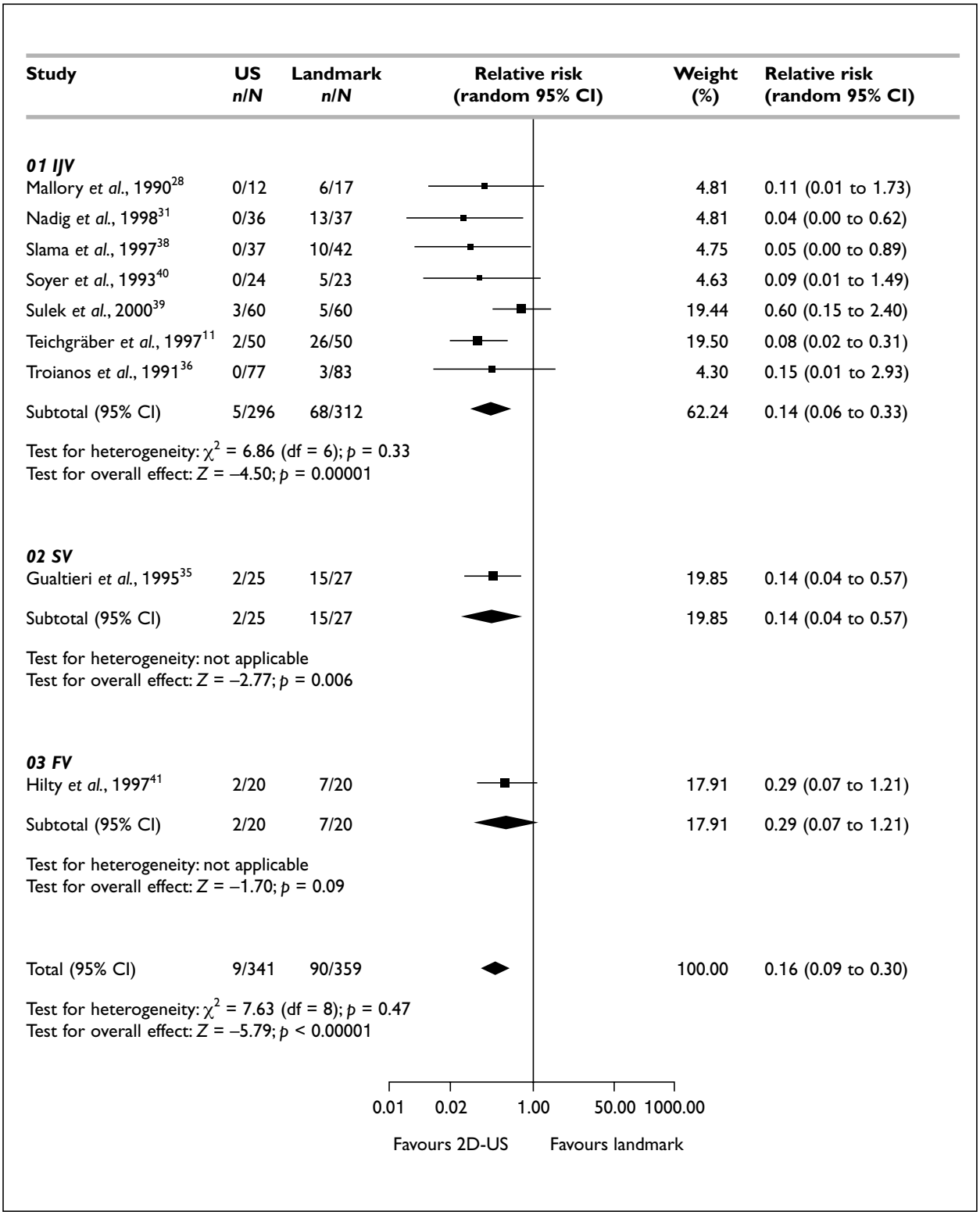

FIGURE 4 *Effect of US guidance on number of failed catheter placements: adults*

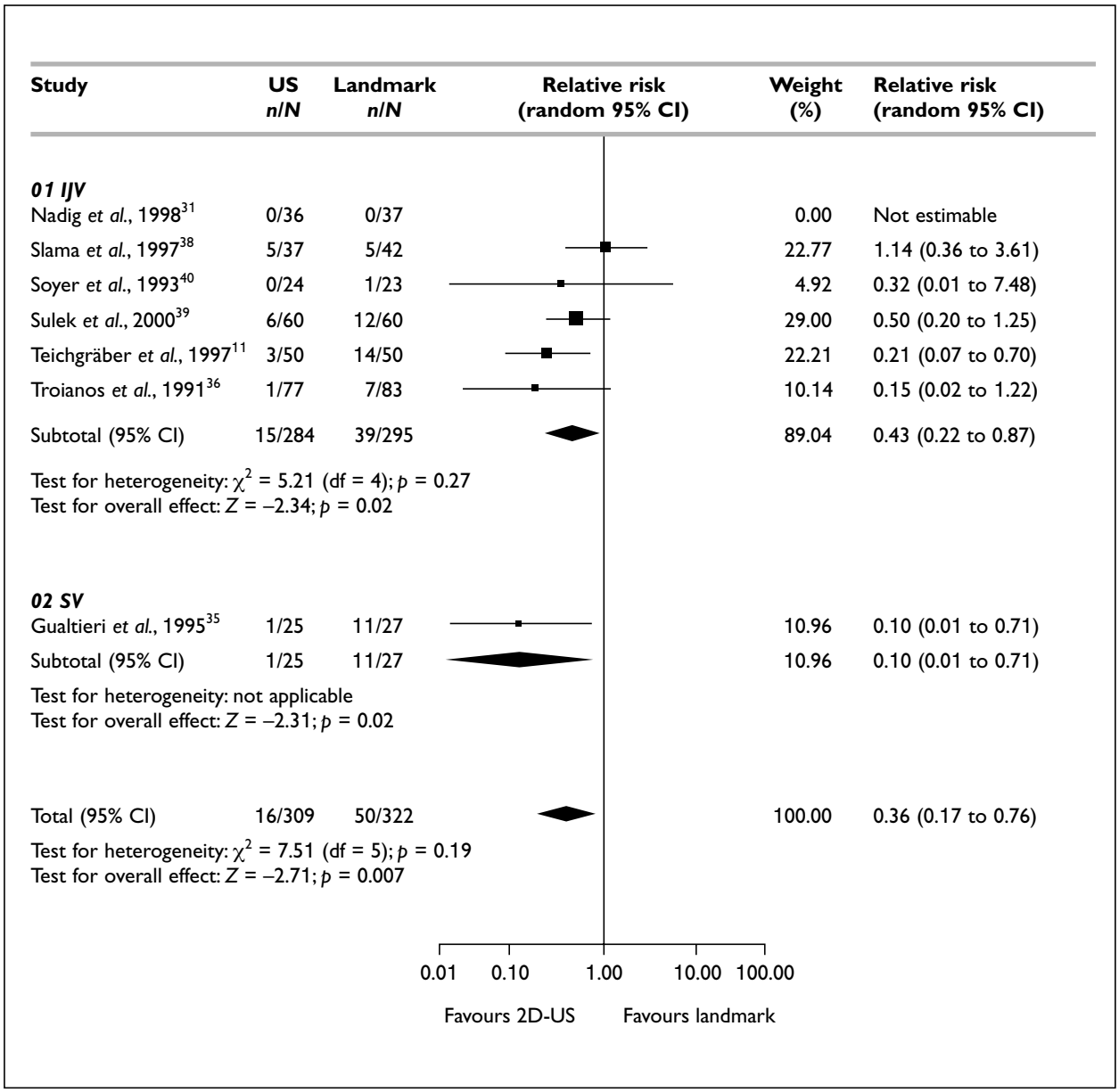

FIGURE 5 *Effect of US guidance on the number of catheter placement complications: adults*

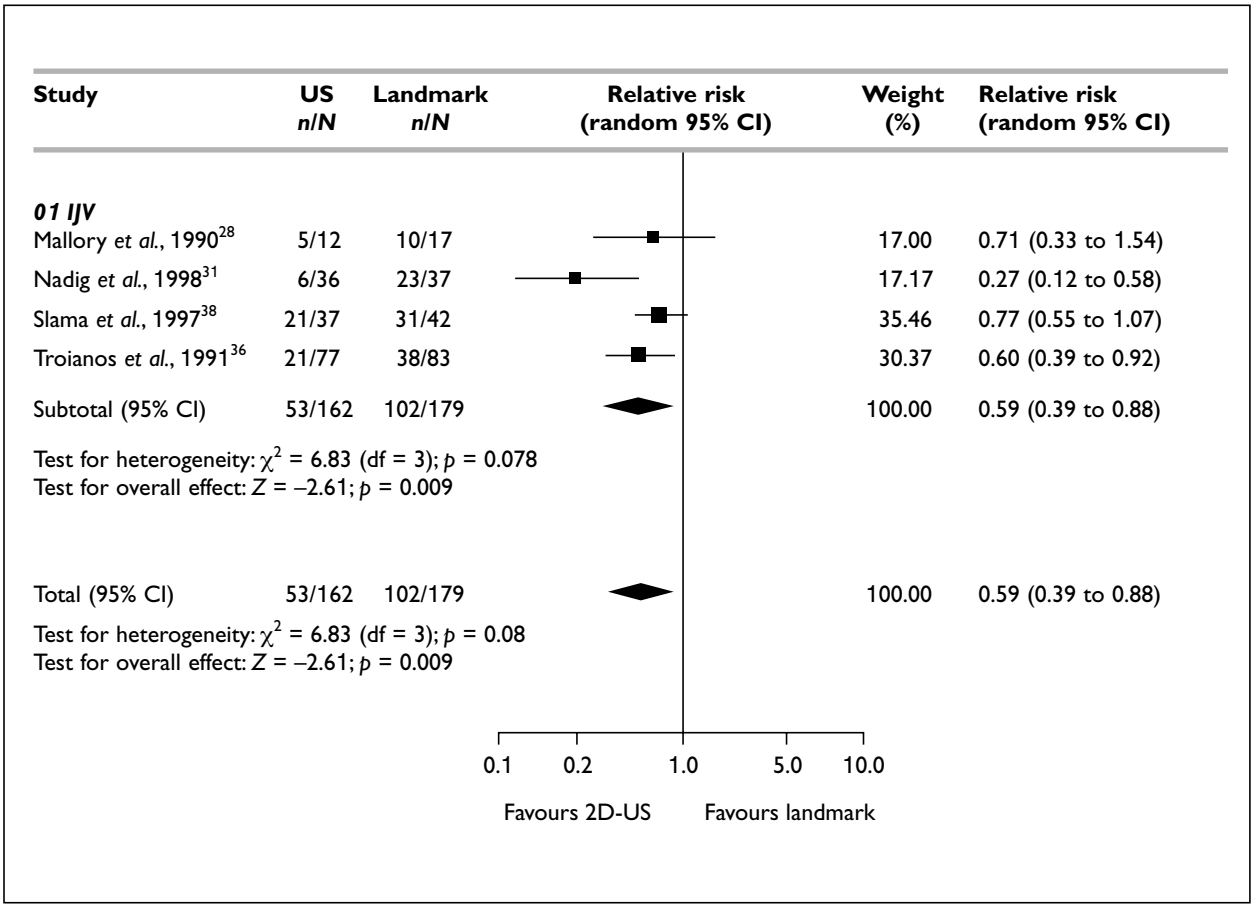

FIGURE 6 *Effect of US guidance on the risk of failure on first catheter placement attempt: adults*

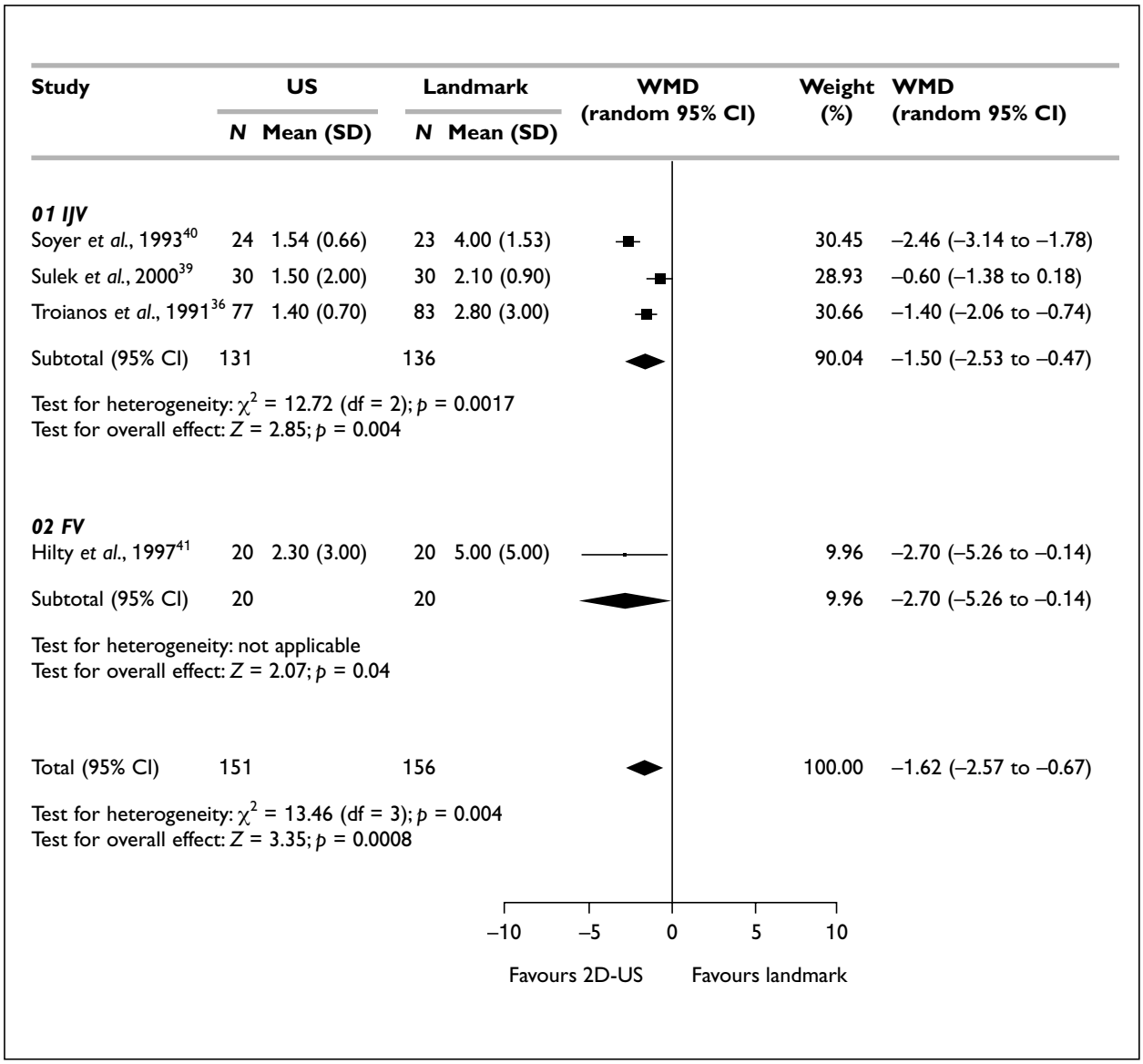

FIGURE 7 *Effect of US guidance on the number of attempts to successful catheterisation: adults*

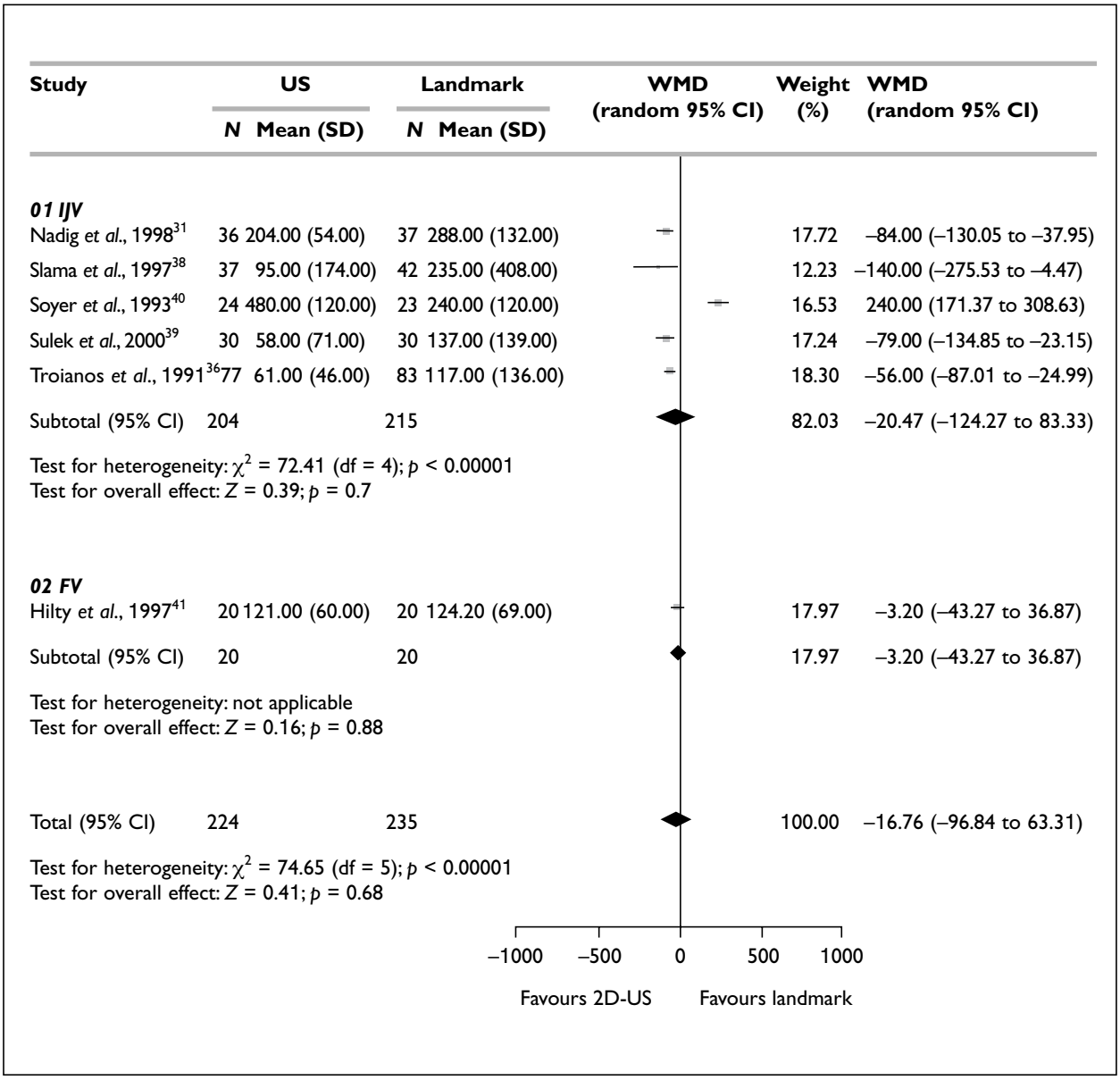

FIGURE 8 *Effect of US guidance on the number of seconds to successful catheterisation: adults*

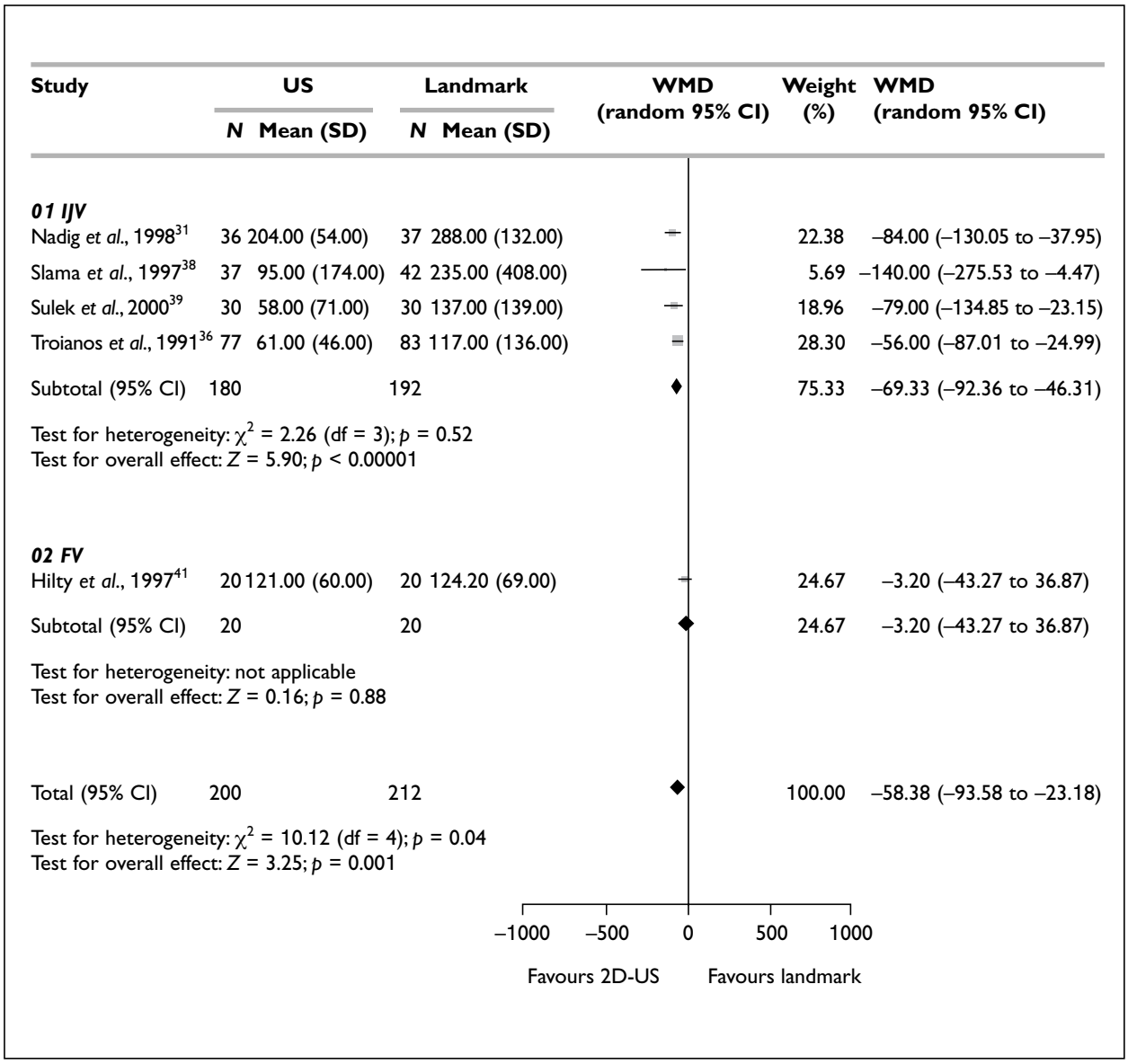

FIGURE 9 *Effect of US guidance on the number of seconds to successful catheterisation: adults (excluding outcomes from Soyer* et al.*)*

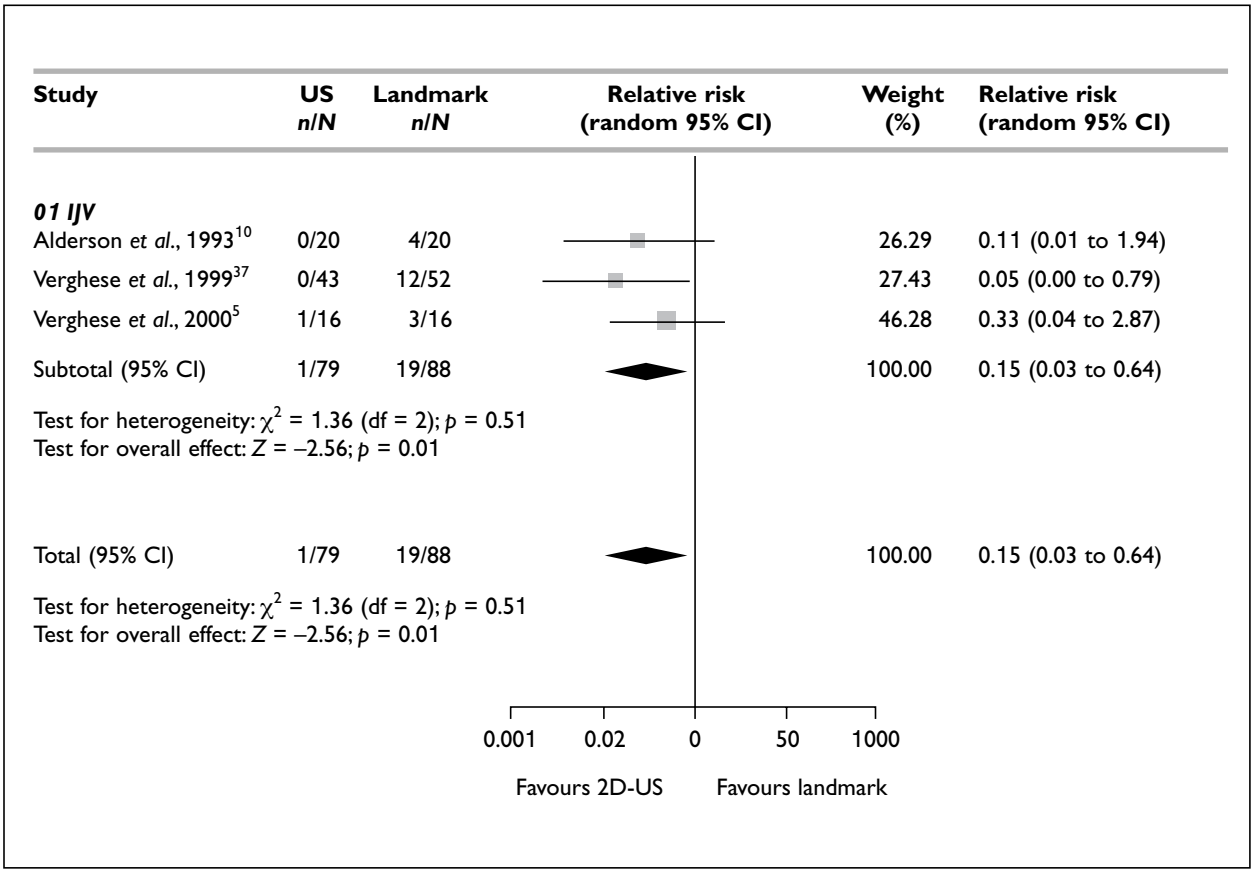

FIGURE 10 *Effect of US guidance on number of failed catheter placements: infants*

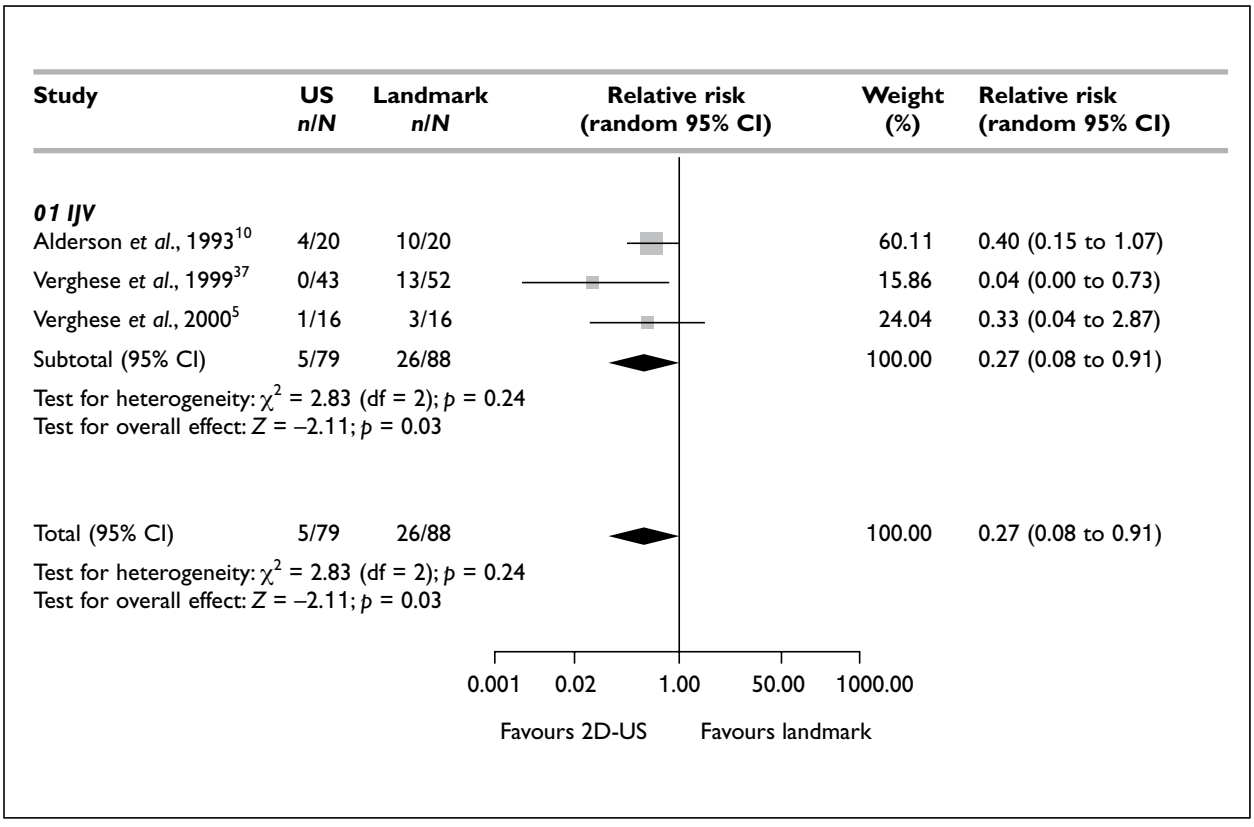

FIGURE 11 *Effect of US guidance on the number of catheter placement complications: infants*

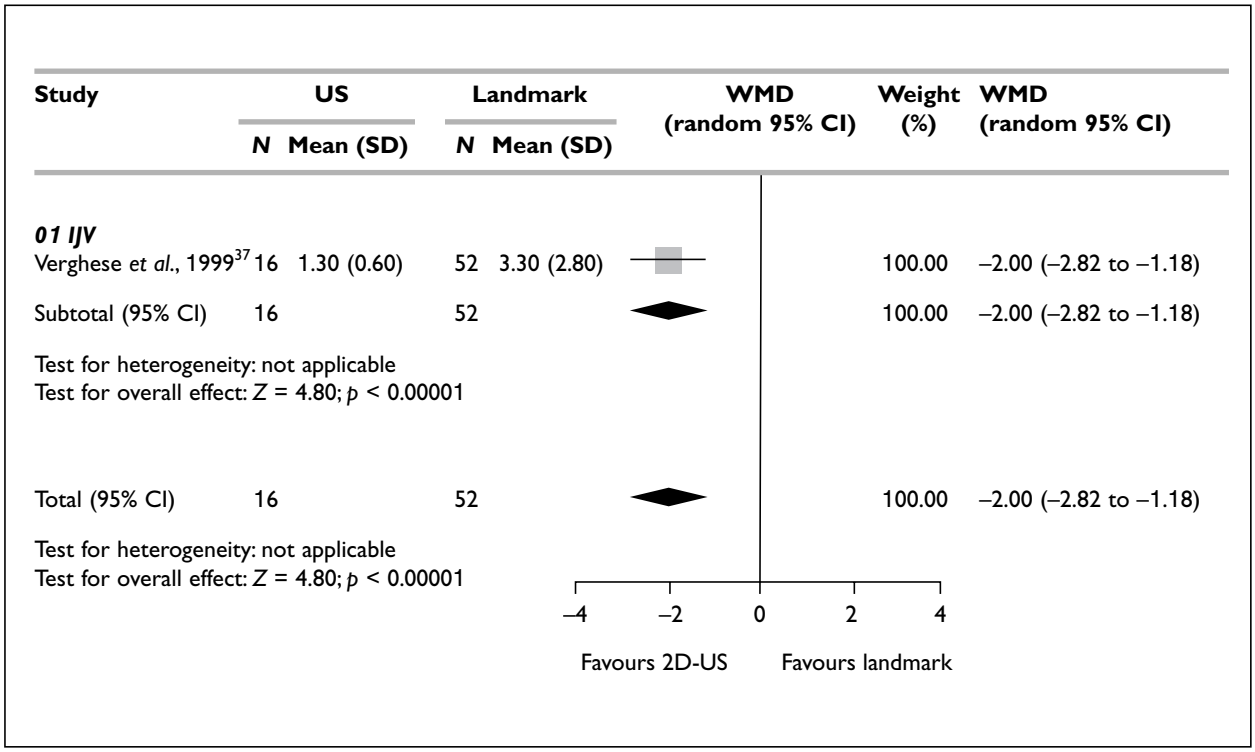

FIGURE 12 *Effect of US guidance on the number of attempts to successful catheterisation: infants*

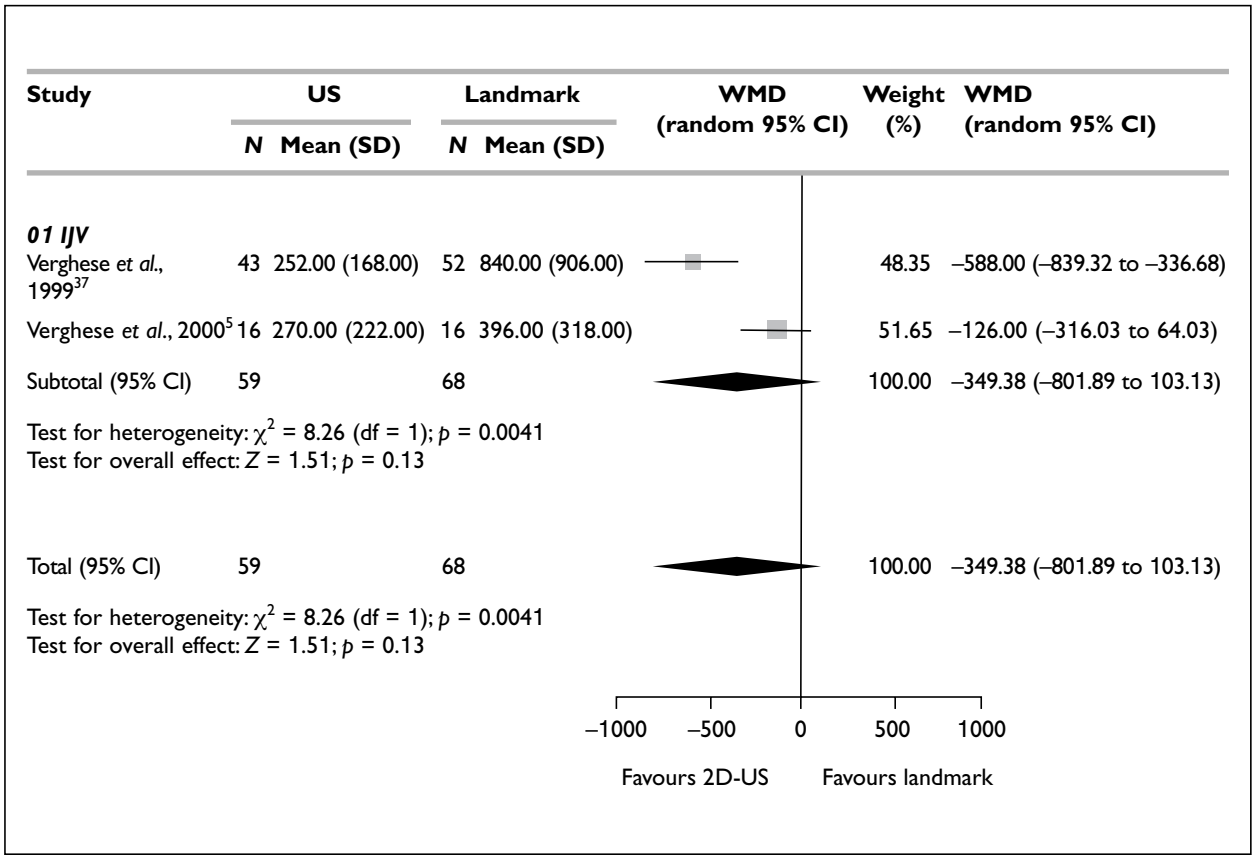

FIGURE 13 *Effect of US guidance on the number of seconds to successful catheterisation: infants*

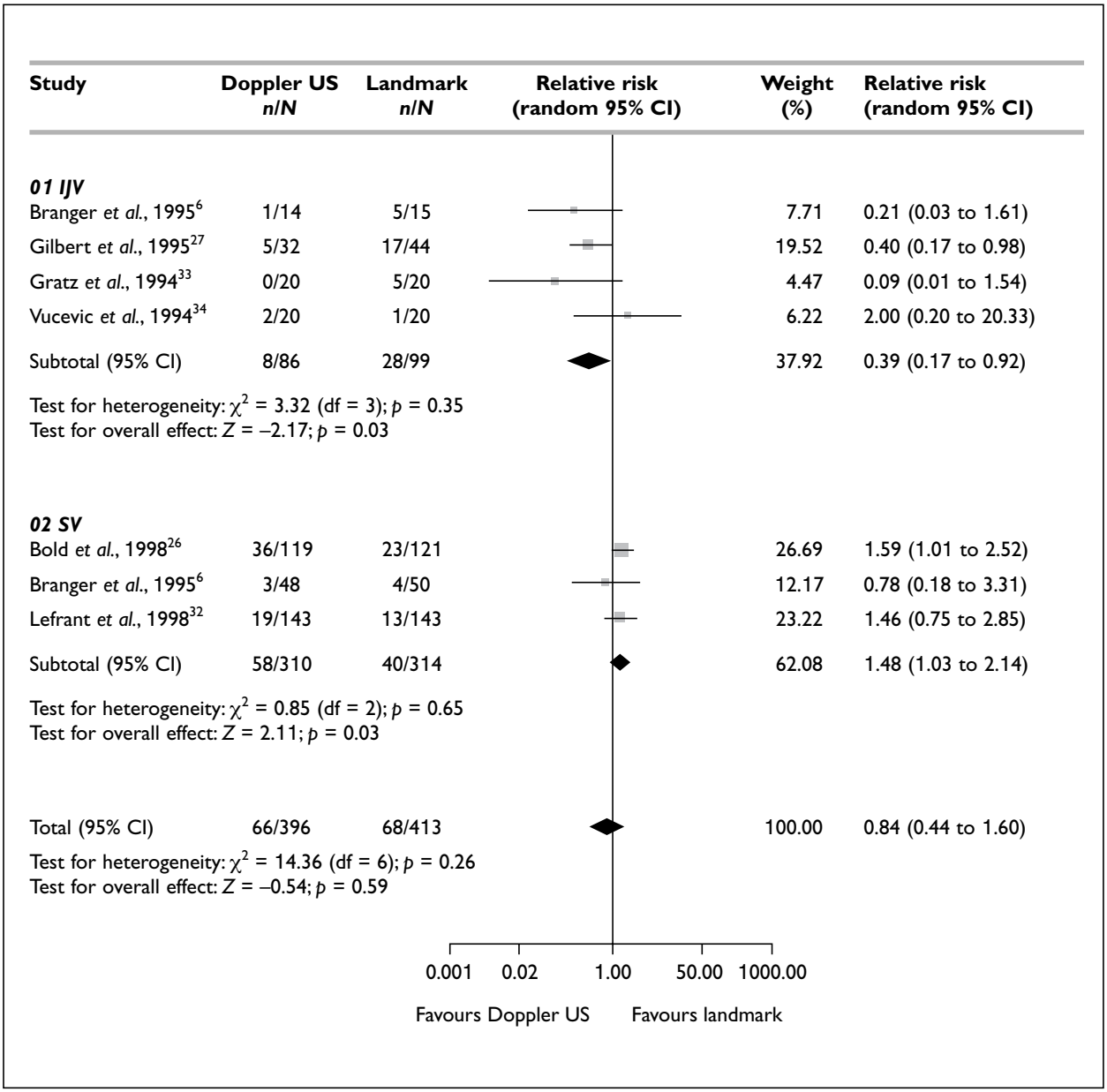

FIGURE 14 *Effect of Doppler US guidance on number of failed catheter placements: adults*

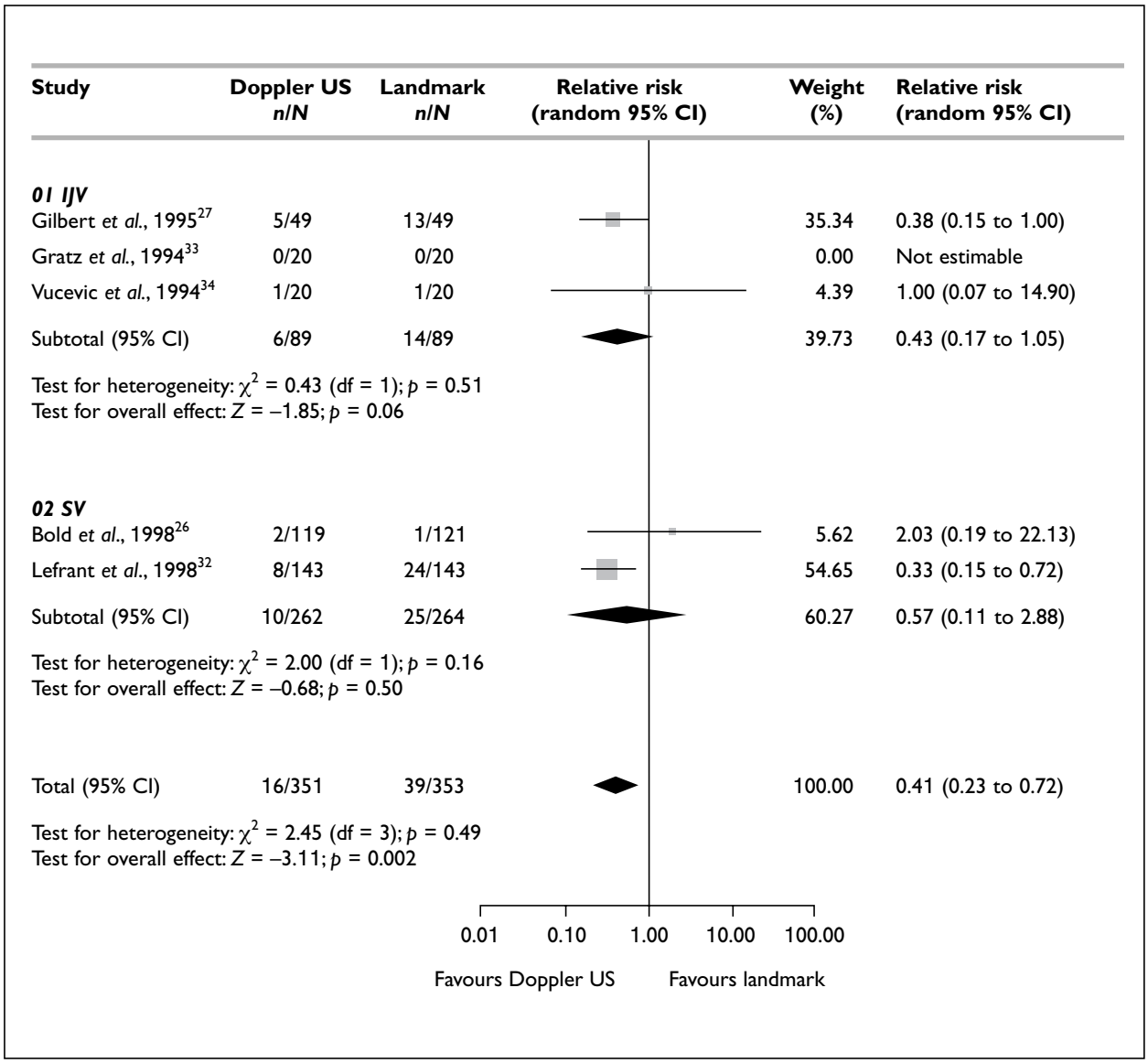

FIGURE 15 *Effect of Doppler US guidance on the number of catheter placement complications: adults*

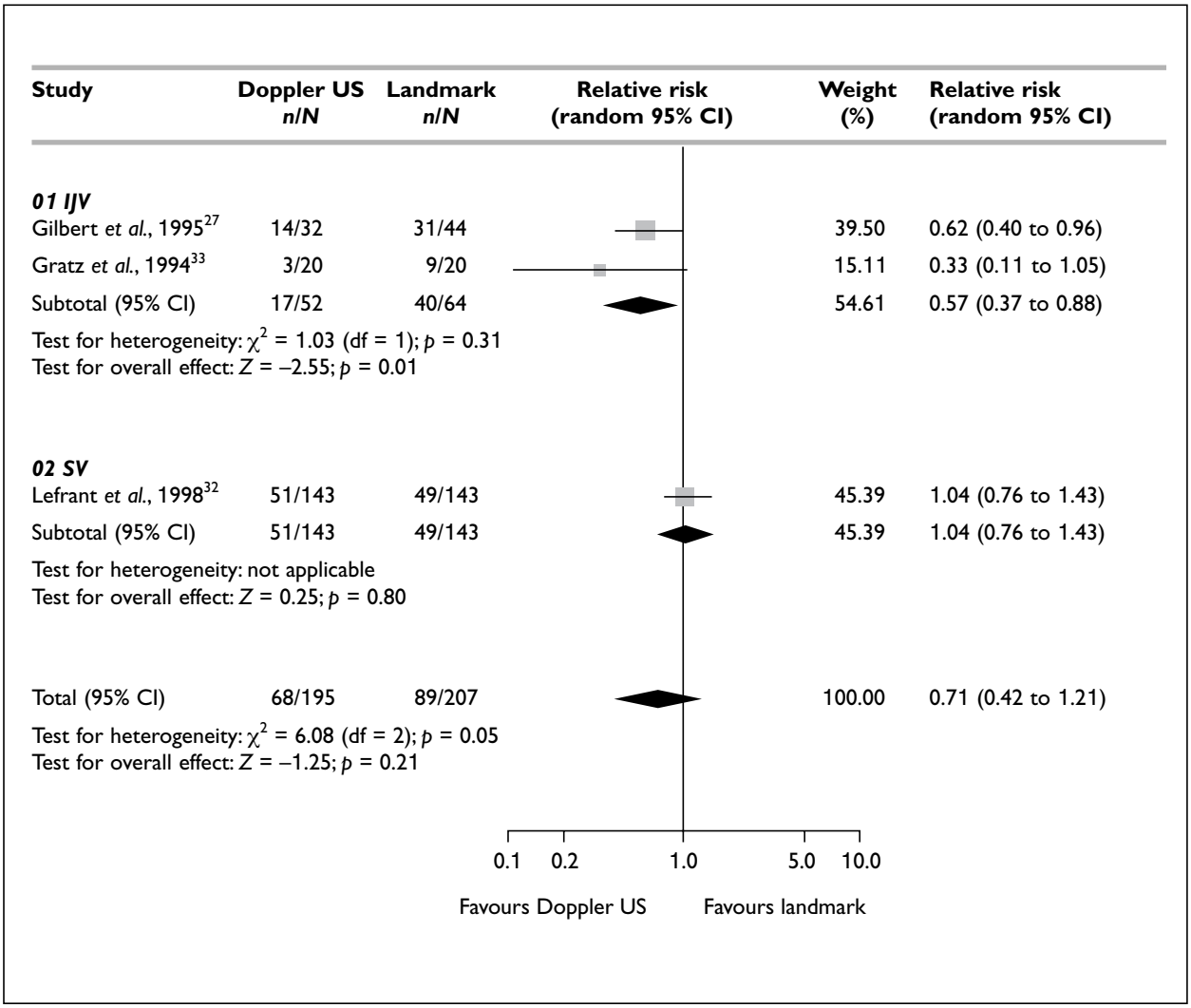

FIGURE 16 *Effect of Doppler US guidance on the risk of failure on first catheter placement attempt: adults*

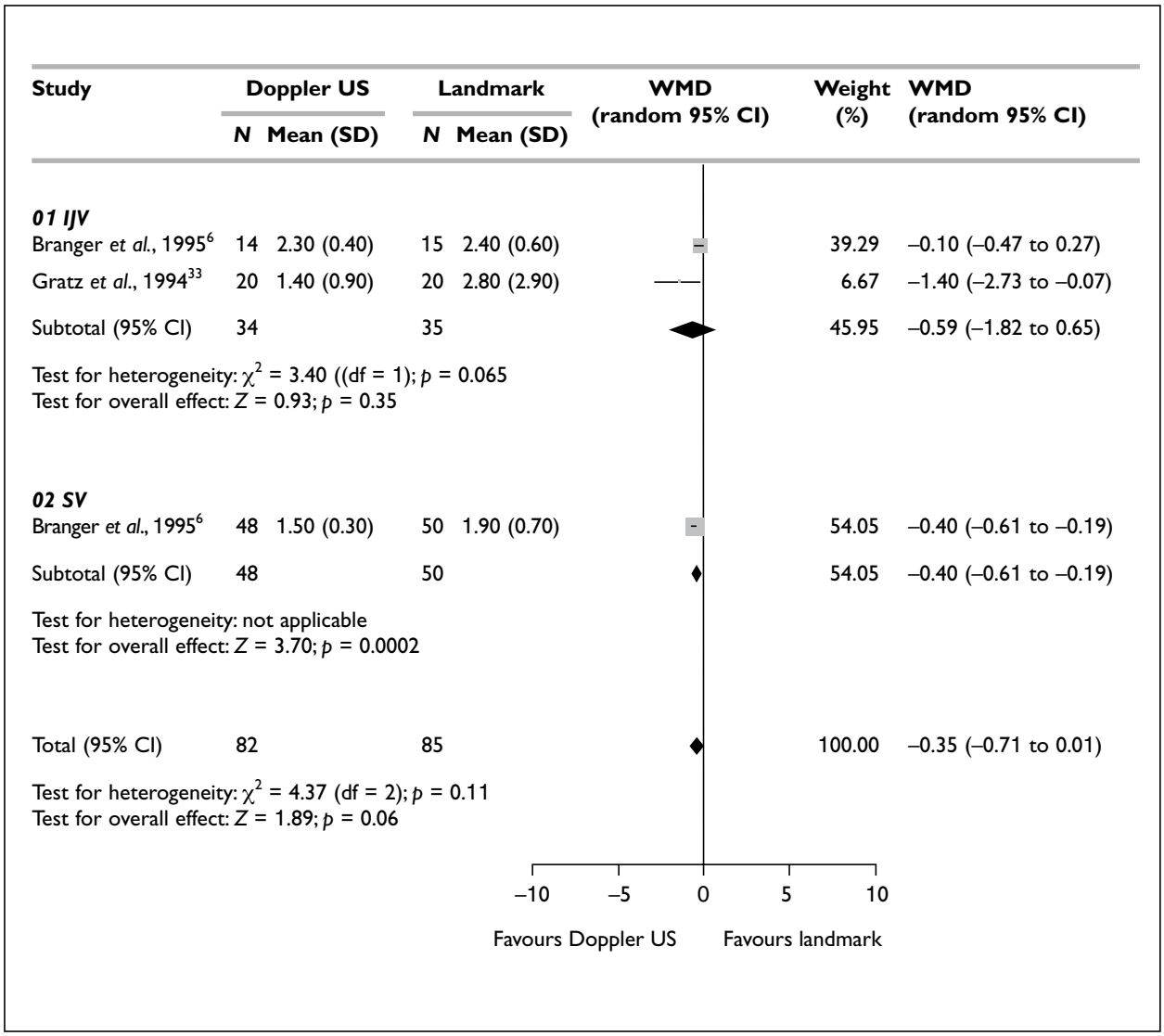

FIGURE 17 *Effect of Doppler US guidance on the number of attempts to successful catheterisation: adults*

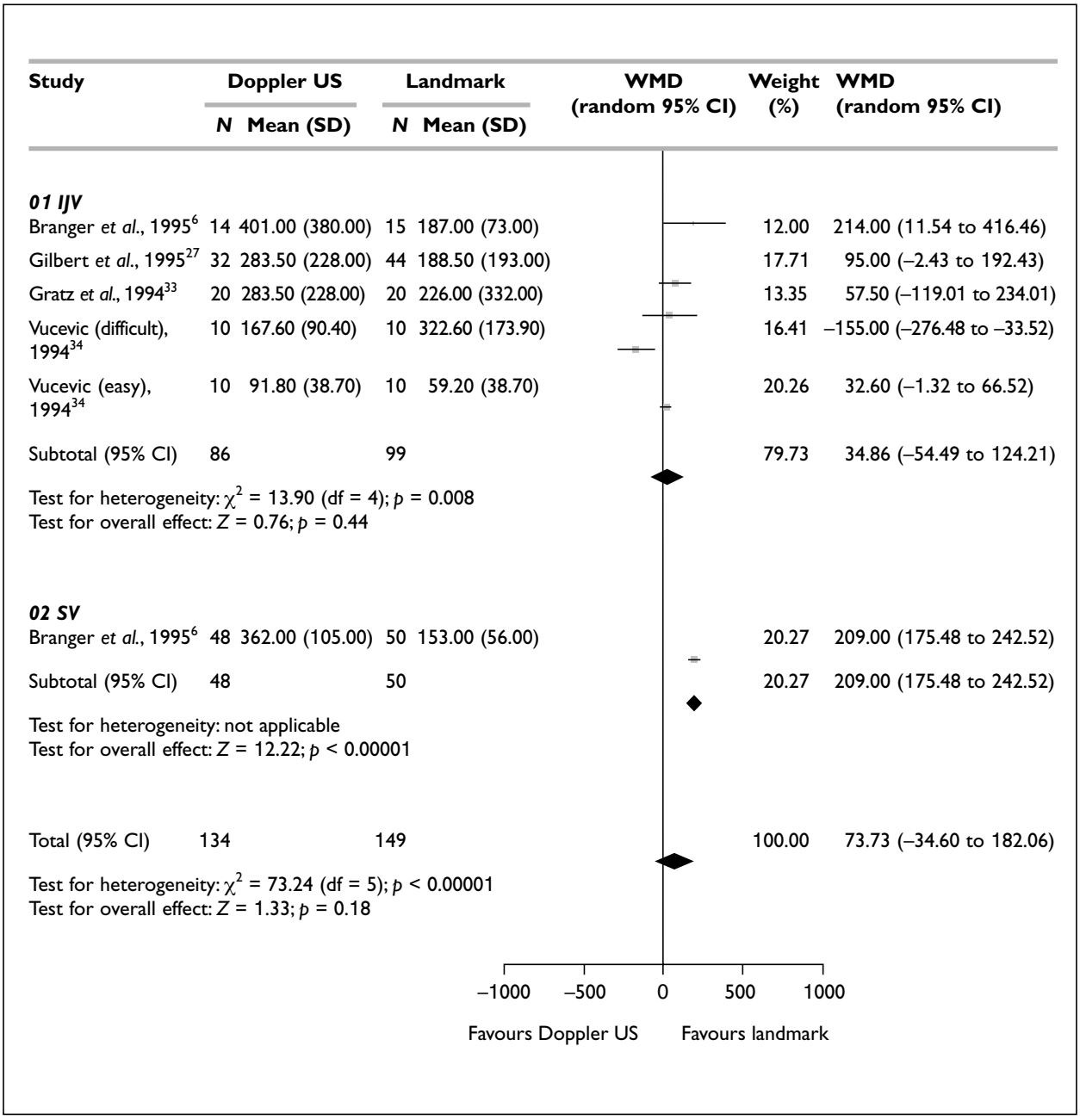

FIGURE 18 *Effect of Doppler US guidance on the number of seconds to successful catheterisation: adults*

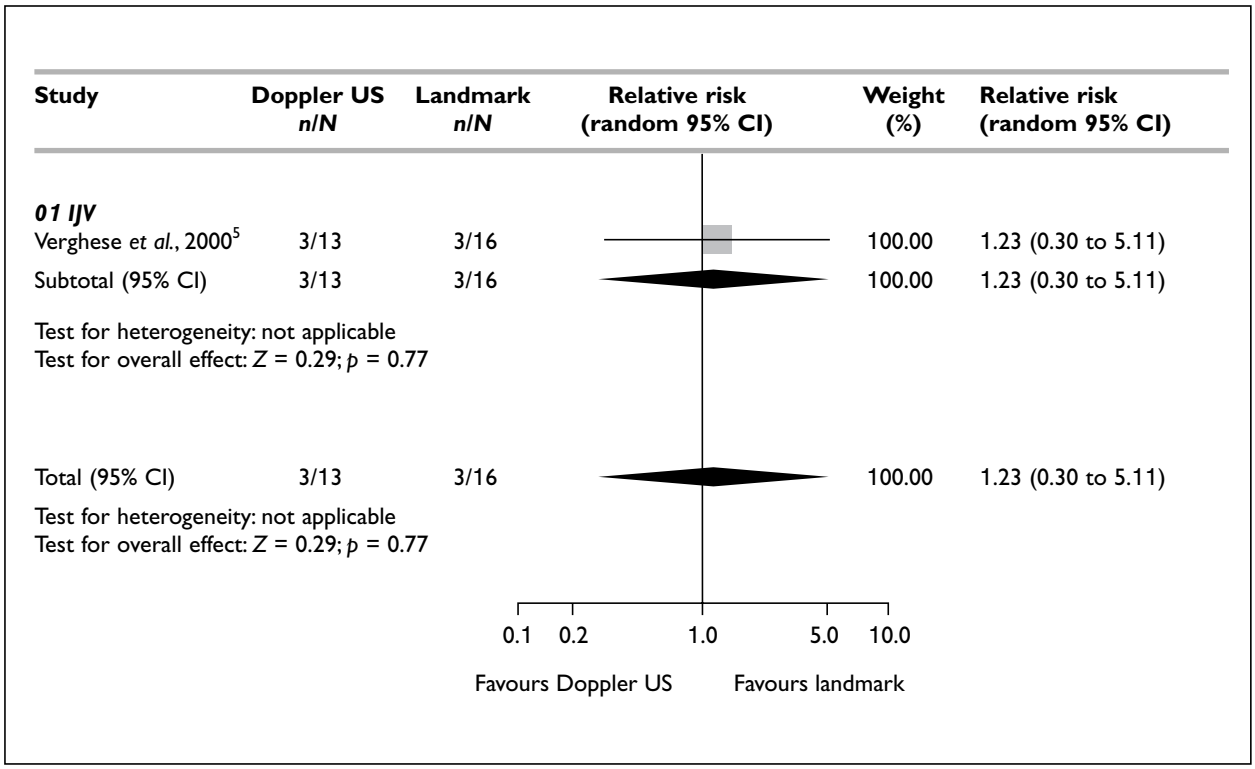

FIGURE 19 *Effect of Doppler US guidance on number of failed catheter placements: infants*

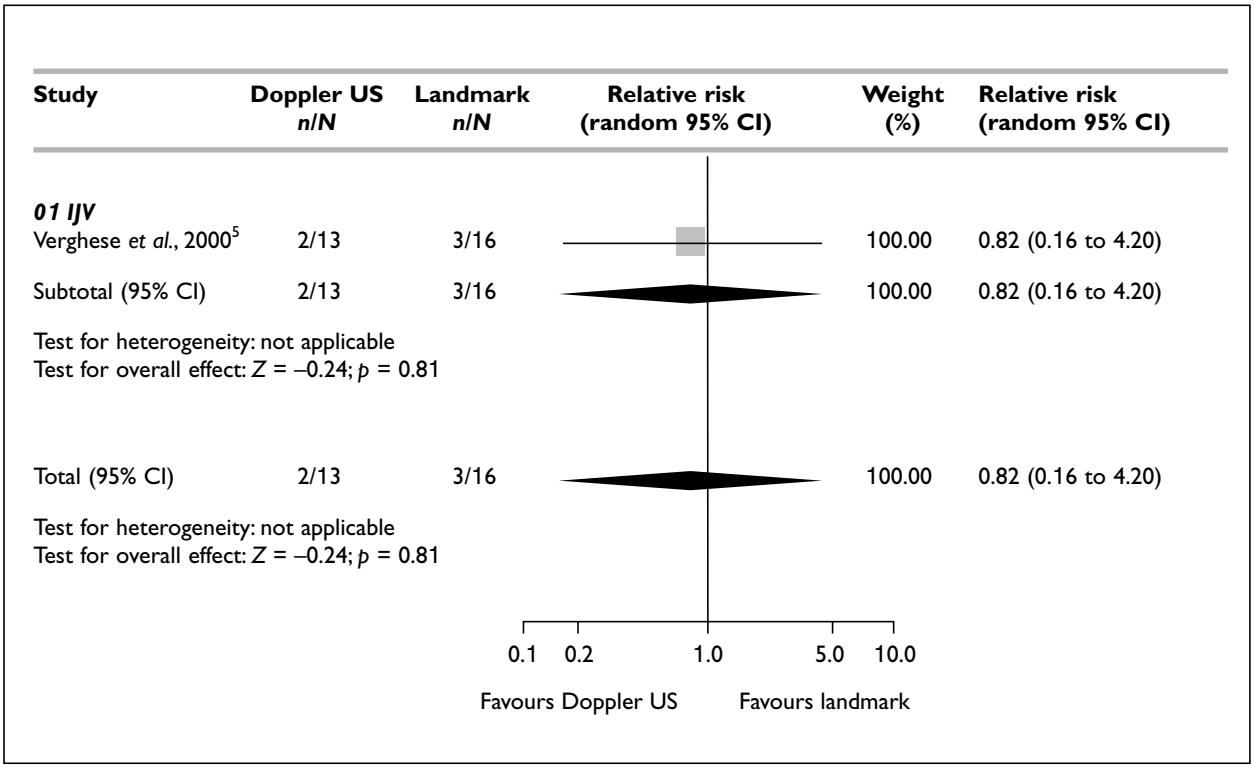

FIGURE 20 *Effect of Doppler US guidance on the number of catheter placement complications: infants*

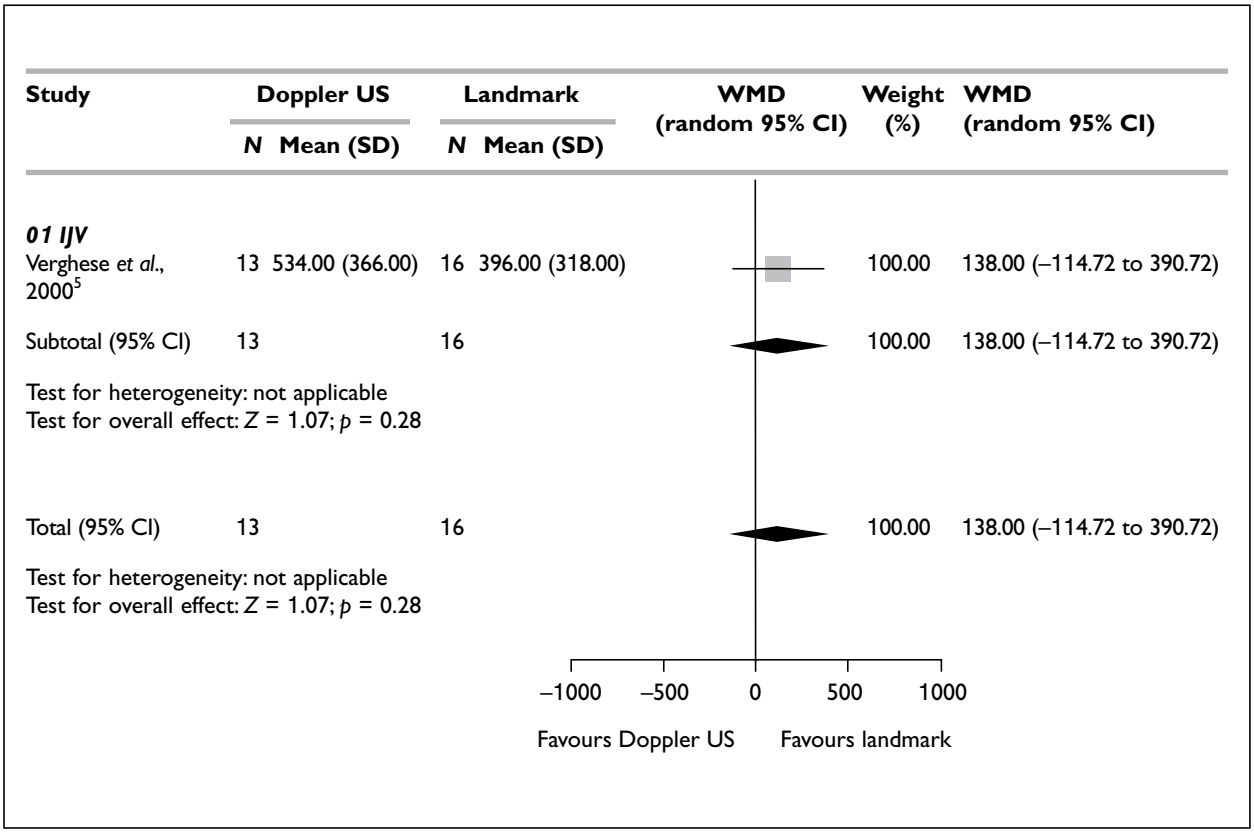

FIGURE 21 *Effect of Doppler US guidance on the number of seconds to successful catheterisation: infants*

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We look forward to hearing from you.

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