Assessment of ultrasound guidance for major vascular access and percutaneous neural blockade

January 2014

MSAC application no 1183

Assessment report

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The Medical Services Advisory Committee (MSAC) is an independent committee which has been established to provide advice to the Minister for Health on the strength of evidence available on new and existing medical technologies and procedures in terms of their safety, effectiveness and cost effectiveness. This advice will help to inform government decisions about which medical services should attract funding under Medicare.

MSAC's advice does not necessarily reflect the views of all individuals who participated in the MSAC evaluation.

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Purpose of application

An application requesting MBS listing of ultrasound imaging for the practice of anaesthesia for patients requiring a central line catheter for vascular access or percutaneous neural blockade was received from Australian Society of Anaesthetists (ASA) by the Department of Health and Ageing in January 2012. The application was further updated in May 2012.

Ultrasound imaging for anaesthesia practice had been claimed through the MBS item 55054. On 01 November 2012, access to MBS item 55054 was removed for anaesthetists, as the use of ultrasound in conjunction with an anaesthetic procedure has never been assessed for safety, effectiveness and cost-effectiveness. The Applicant proposed two new MBS items for ultrasound guidance of percutaneous major vascular access and percutaneous neural blockade for delivery of surgical anaesthesia. Based on this, patient populations indicated for these procedures are detailed in Table 1.

Table 1 Patient populations indicated for ultrasound guidance of percutaneous major vascular access and percutaneous neural blockade

Procedure	Patient population
Percutaneous major vascular access	These patients require major vascular access for anaesthetic delivery. The majority of the patients are likely to undergo major surgeries (for example, cardiac surgery, neurosurgery and trauma) and may have significant comorbidities (particularly cardiovascular). Major vascular access is generally achieved by cannulation and/or catheterisation of a central vein, while some patients would require major arterial access. The internal jugular vein is the most common access point for major elective surgery, while the external jugular, subclavian and femoral veins are also used for access.
Percutaneous neural blockade	This group of patients is likely to receive regional or local anaesthesia by a single-shot needle insertion and/or placing a catheter adjacent to a nerve or nerve plexus. Catheterisation is used when continuous anaesthetic agents need to be supplied to maintain the anaesthetic effect. Nerve blockade may be used in association with various surgical procedures (for example, limb and abdominal surgeries). It may also be used as the primary form of anaesthesia, often in patients with significant comorbidities for whom other techniques, such as general anaesthesia, may pose a higher risk or be contraindicated

The two new items are proposed to be listed in the Therapeutic and Diagnostic Services Subgroup of Group T.10 (Category 3 Therapeutic procedures), instead of Category 5, Diagnostic Imaging Services.

This assessment reports on the safety, effectiveness and cost-effectiveness of ultrasound guidance for the practice of anaesthesia for patients requiring the insertion of central line catheters for major vascular access or the placement of percutaneous neural blockade in order to inform MSAC's decision-making regarding public funding of the intervention.

Proposal for public funding

The proposed MBS item descriptors for the percutaneous major vascular access and percutaneous neural blockade for delivery of surgical anaesthesia are present in Table 2 and Table 3.

Table 2 Proposed MBS item descriptor major vascular access

Category 3 Group T10, Subgroup 19 – Therapeutic Procedures
The use of two-dimensional ultrasound scanning to assist percutaneous major vascular access in anaesthesia [Explanatory note. This item applies to the use of ultrasound guidance during catheterisation (and cannulation) of major blood vessels. The item may be used in addition to the relevant item for vascular catheterisation (and cannulation). Explanatory note. T.1.20. Therapeutic procedures may be provided by a specialist trainee, applies]
Fee: $58.35 (3 RVG units)

Category 3: Therapeutic procedures; Group T.10: Relative Value Guide for Anaesthesia; Subgroup 19: Therapeutic and Diagnostic Services. RVG: Relative Value Guide.

Table 3 Proposed MBS item descriptor for percutaneous neural blockade

Category 3 Group T10, Subgroup 19 – Therapeutic Procedures
The use of two-dimensional ultrasound guidance to assist percutaneous neural blockade in anaesthesia [Explanatory note. This item may be used in addition to the relevant nerve block item. Explanatory note. T.1.20. Therapeutic procedures may be provided by a specialist trainee, applies]
Fee: $58.35 (3 RVG units)

Category 3: Therapeutic procedures; Group T.10: Relative Value Guide for Anaesthesia; Subgroup 19: Therapeutic and Diagnostic Services. RVG: Relative Value Guide.

According to the application the proposed fee for both MBS items includes a professional component ($29.20) and a practice component ($29.15). The allocation of three RVG units is based on a comparison of the nature of the service to other services of similar complexity and skill, already funded by the items of Group T10. The fee is not expected to vary according to patient sub-population. Practitioners other than anaesthetists may use ultrasound guidance for both vascular access and placement of neural blocks; however, access to the proposed items is limited to anaesthetists.

A team from the Australian Safety and Efficacy Register of New Interventional Procedures-Surgical (ASERNIP-S) and the Centre for Health Economics Research and Evaluation (CHERE) was engaged to conduct a systematic review of the literature and an economic evaluation of ultrasound imaging for the practice of anaesthesia for patients requiring the insertion of central line catheters for vascular access or for percutaneous neural blockade.

Current arrangements for public reimbursement

Prior to 01 November 2012, ultrasound guidance for percutaneous major vascular access and percutaneous neural blockade was reimbursed under MBS item 55054. Subsequent to this date, access to this item has been removed for anaesthetists. Nerve block for anaesthesia can be claimed under generic anaesthesia items. Percutaneous nerve blocks placed for management of post-operative pain management are claimed under item numbers 22040, 22045 and 22050. Current MBS items for vascular access are 13815,

13319 and 22020 for central venous access and items 13818 and 22015 for central arterial access. MBS items 22015 and 22020 are relevant in association with anaesthesia.

Background

The intervention has not previously been considered by the Medical Services Advisory Committee (MSAC).

Prerequisites to implementation of any funding advice

Over 200 ultrasound systems are listed on the Australian Register of Therapeutic Goods (ARTG) as of May 2012, of which approximately 60 are listed in the category applicable to this report with 46 of these 60 being deemed fit-for-purpose. The two most widely used ultrasound machine identified in this assessment are manufactured by Fujifilm SonoSite Pty Ltd and GE Healthcare Australia Pty Ltd. These instruments are approved by the Therapeutic Goods Administration (TGA) as detailed in Appendix G. As such, appropriate ultrasound technology reflected in the included studies and necessary to deliver the proposed new MBS items is available for use within Australian clinical practice.

Generally public hospitals and large private hospitals would provide the ultrasound machines for use in the anaesthesia practice. Some ultrasound machines may be dedicated to anaesthesia use. However, hospital-owned equipment may be used for other purposes as well, and may not be readily available for use with anaesthesia.

The specialist training curriculum of the Fellowship of the Australian and New Zealand College of Anaesthetists (FANZCA) includes compulsory training in the use of ultrasound. The Australian and New Zealand College of Anaesthetists (ANZCA) and the Australian Society of Anaesthetists (ASA) hold regular workshops on the use of ultrasound in anaesthesia practice. In addition, various institutions offer continuing education and training courses for anaesthetists to gain and practice relevant skills. All specialized courses and training are coordinated by the Anaesthesia Continuing Education Coordinating Committee (ACECC)(ACECC 2011), as a part of the Australian and New Zealand College of Anaesthetists (ANZCA) (ANZCA 2013).

Practitioner statement

The ASA claim that there will be a higher success rate and fewer adverse events following anaesthetic insertions with ultrasound guidance compared to the landmark technique. This would result in less nursing care and analgesics, patients would spend less time in hospital, and display a more rapid return to normal function.

Due to these purported advantages of ultrasound-guidance, it is suggested by the applicant that the utilisation of ultrasound-guidance for anaesthesia will become common practice for many practitioners. If, as is the case for Fellowship of ANZCA, ultrasound training is a compulsory part of the anaesthetists' expertise, and if machines are readily available in surgical settings, trainees and less experienced practitioners may routinely use the technique with an intention of reducing potential complications.

Clinical need

Not all patients requiring major vascular access or nerve blockade procedures as part of their anaesthesia care will require ultrasound guidance to facilitate placement. Certain experienced practitioners may be confident to provide these procedures in the absence of ultrasound guidance. It may be that lower numbers of ultrasound devices in certain rural and remote areas may limit the use of ultrasound guidance in certain locations.

Reviewing the Australian and New Zealand Registry of Regional Anaesthesia (AURORA) data for nerve blocks performed between January 2006 to May 2008 (Barrington et al 2009) and June 2011 to February 2012 (Barrington and Kluger 2013) reveals that individual hospitals included in the registry are performing 32 to 42 neural blocks per month. For these procedures the preference for guided placement that utilises ultrasound with or without electrical nerve stimulation (ENS) has increased from 63 per cent (2006 – 2008) to 86 per cent (2011 – 2012) (AURORA). In addition, there has been a move away from procedures that utilise ENS assisted placement (with or without ultrasound). The preferred technique is now ultrasound without accompanying ENS.

MBS data show that between 2008 and 2011, the proportion of claims under item 55054 that were associated with anaesthesia increased from 0.95 per cent to 14 per cent of the total claims under this items. This represents a practitioner preference for the use of ultrasound guidance within anaesthesia for either the insertion of major vascular access lines or placement of neural blocks. Prior to 2008, the low number of claims is not reflective of the proportion of procedures recorded with AURORA that utilised ultrasound during the placement of neural blockade.

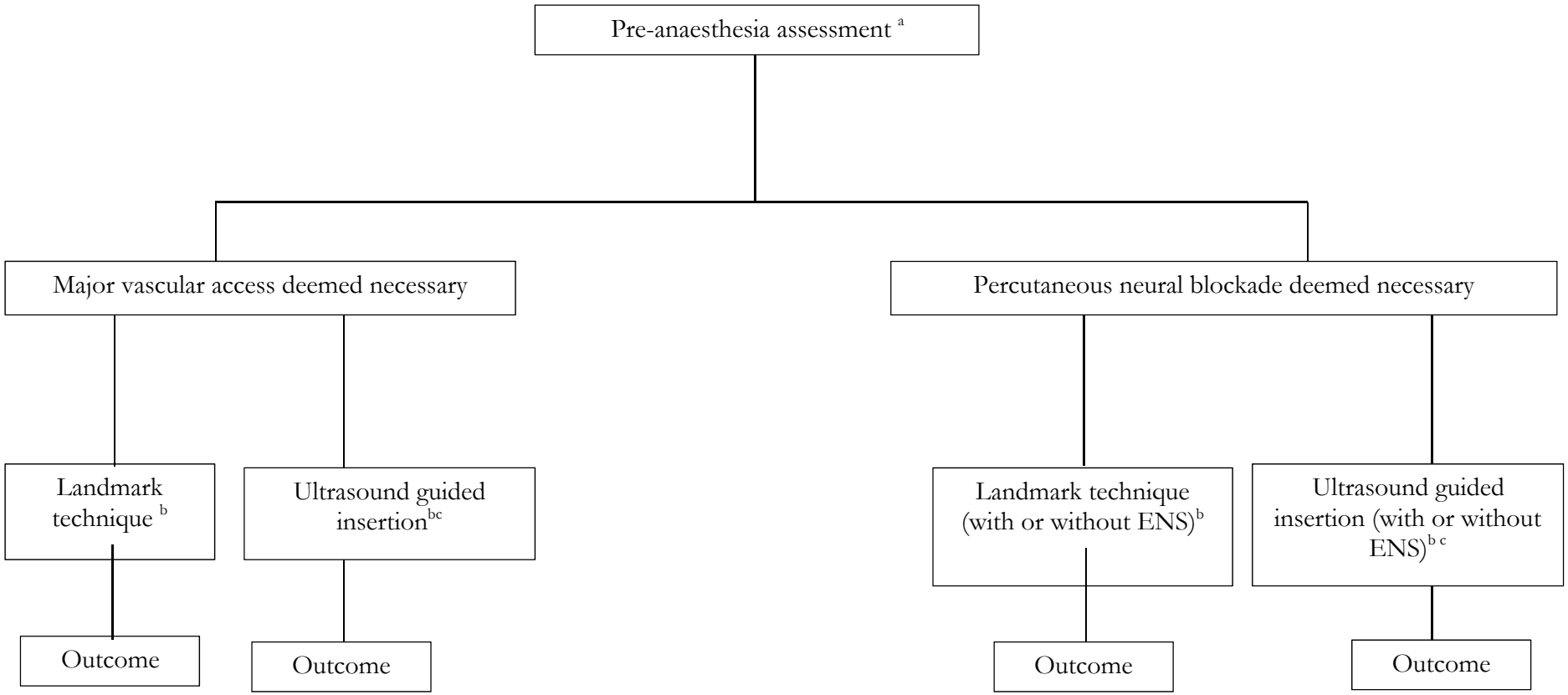
The use of percutaneous neural blocks in both adult and paediatric populations is established in Australian clinical practice (Barrington and Kluger 2013). Nerve blocks are used either as standalone anaesthesia or for postoperative analgesia in combination with systemic anaesthesia and may also be used for chronic pain. The benefits include, but are not limited to, better post-operative pain management and reduced morbidity. Increasing awareness of and improvements in ultrasound technology will impact clinical advice and patient choice. As of 2010, evidence synthesised in systematic reviews on the use of ultrasound in regional anaesthesia indicate that ultrasound is at least equivalent to other placement techniques and depending on the location of the nerve may improve the block performance as well as reduce the risk of complication.

Ultrasound guidance has been used in clinical practice to aid central vascular access for a number of years (la Grange et al 1978). Visualisation of anatomical structures identifies inter-patient variations thereby improving both placement and performance of central lines. For paediatrics central lines are often the preferred access over peripheral sites due to vessel size. In this population, complications are not rare when inserting central lines, which is also in part attributable to variability in vascular anatomy (Costello et al 2013). Similar to adults, the use of ultrasound in the placement of central lines may improve placement and hence reduce risk of complications.

The current clinical algorithm for percutaneous nerve blockade and central vascular access is illustrated in Figure 1. For the proposed new items, the clinical algorithm remains the same (Figure 2), although the costs of the ultrasound component will be

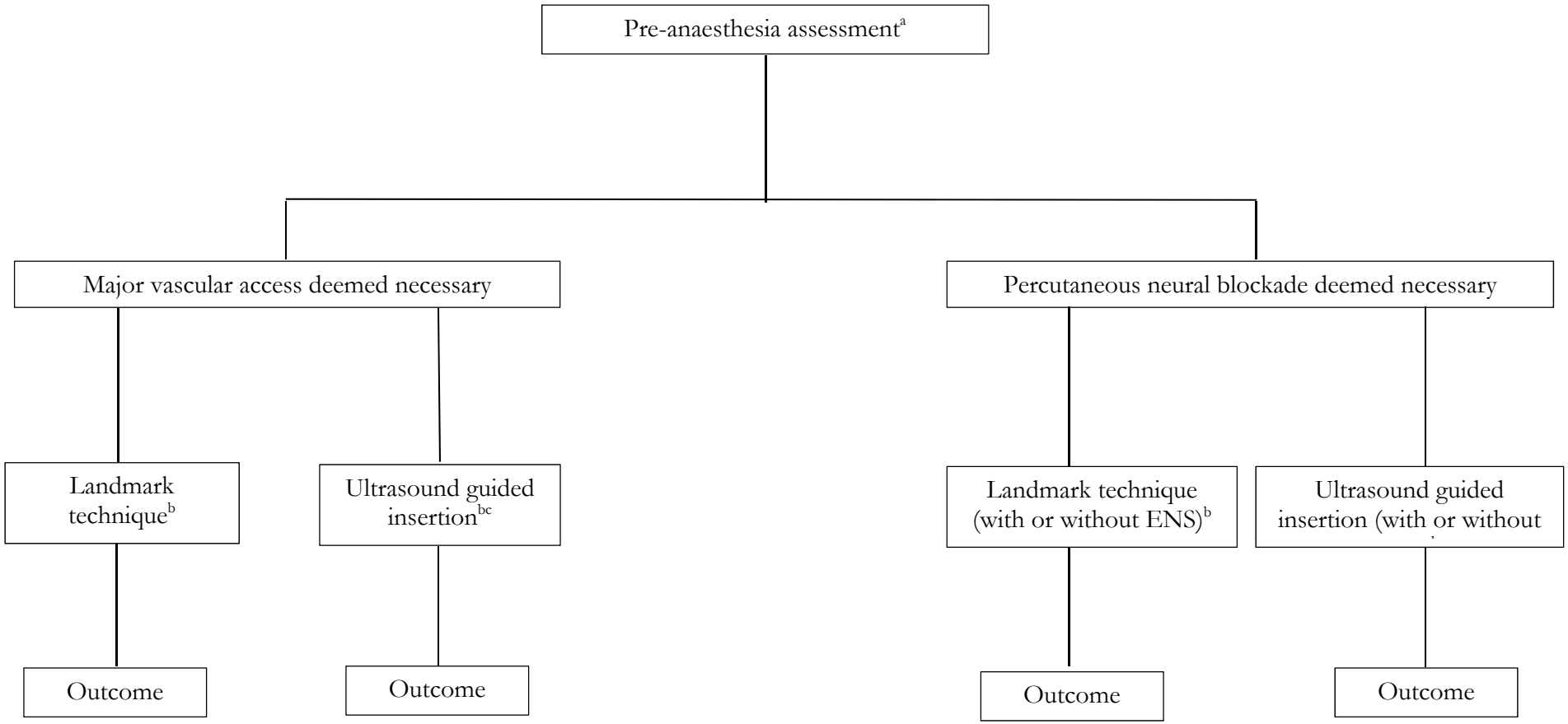
incurred by the MBS. The algorithms are taken from Decision Analytic Protocol (DAP) 1183.

Figure 1 Current clinical management algorithm in major vascular access and neural blockade



a Any circumstance that require anaesthesia for surgery. Patients who require independent pain management or analgesia are not a part of this population.
b Insertion of a cannula, catheter or needle.
c MBS Item 55054 (access has been restricted for the current purposes on 01 November 2012)
Landmark technique: Insertion of a cannula, catheter or needle performed based on anaesthetist's knowledge of human anatomy, experience and judgement; ENS: Electrical nerve stimulation.

Figure 2 Proposed clinical management algorithm in major vascular access and neural blockade



a Any circumstance that require anaesthesia for surgery. Patients who require independent pain management or analgesia are not a part of this population.
b Include insertion of a cannula, catheter or needle.
c Proposed MBS items.
Landmark technique: insertion of a cannula, catheter or needle performed based on anaesthetist's knowledge of human anatomy, experience and judgement; ENS: Electrical nerve stimulation.

Comparator to the proposed intervention

Landmark technique

Landmark technique of inserting a cannula, catheter or needle in major vascular access and percutaneous neural blockade is currently performed based on the anaesthetist's knowledge of human anatomy, experience and judgement, which differ from practitioner to practitioner. It does not require additional resources and there is no associated MBS item.

Electrical nerve stimulation

In patients who receive percutaneous nerve blockade, ENS can be used in combination with the landmark technique to indicate the location of nerves (Abrahams et al 2009; Macintyre et al 2010). Nerve stimulation has been the 'gold standard' modality to guide nerve blocks prior to the introduction of ultrasound (Abrahams et al 2009). Some nerve blocks may be performed with a combination of ultrasound and electrical nerve stimulation guidance.

Whilst ENS indicates the location of nerves the technique has limitations. It does not identify vessels, muscles, fascia and visceral structures. Evidence of nerve location disappears after injecting 1–2 ml of the anaesthetic agent; hence, nerve stimulation cannot be used to localise nerves thereafter (Perlas et al 2006). The threshold of the electrical stimulus required to stimulate a nerve differs between nerves. The electrical stimulus elicits a motor response. If the neural structures are 'sensory only', or a patient has had a muscle relaxant as part of their anaesthesia technique, ENS cannot be applied, as no motor response will be obtained.

ENS devices vary in complexity and cost (see Economic Considerations). There is no MBS item for the use of ENS in providing anaesthesia. Existing MBS items for neural blockade provide the same fee regardless of the technique used to locate the neural structure.

Scientific basis of comparison

Vascular access:

A total of seven systematic reviews were identified that were relevant to this report. These reviews were published between 1996 and 2013. Three of the systematic reviews were rated as being good quality using a modified AMSTAR appraisal tool (Appendix I). The reviews investigated patients undergoing central venous access (six reviews), and peripherally-inserted central catheter (PICC) access (one review) with subpopulation analysis of anatomical location of the access and the age of patients.

In addition, nine RCTs were identified that were not published in the systematic reviews.

Nerve block

A total of ten systematic reviews were identified that had relevance to this report. These reviews were published between 2009 and 2013. All systematic reviews were critically appraised using a modified AMSTAR tool (Appendix I); three were rated as being of good quality. The reviews investigated a range of populations (patients requiring nerve blocks as a component of anaesthesia for surgery, or use of neural blockade for postoperative analgesia as well as non-operative pain management). The reviews also assessed upper and lower extremity nerve blocks as well as truncal blocks.

In addition, 30 RCTs were identified which were not published in the systematic reviews.

Comparative safety

Vascular access:

Systematic reviews:

All of the systematic reviews concluded that ultrasound localisation of central vascular access was equivalent to or an improvement on the anatomical landmark technique for all reported safety and effectiveness outcomes.

Meta-analysis:

Results from 34 randomised controlled trials (RCTs) were pooled to inform the meta-analysis. The following outcomes were statistically significant in favour of ultrasound guidance compared to the landmark technique:

- Inappropriate vascular puncture was reported in 28 RCTs with a total patient population of 4,409. Ultrasound use significantly reduced the risk of vascular puncture (RR 0.32, 95%CI:0.22-0.47, P<0.001).
- Haematoma was reported in 17 RCTs with a total patient population of 3,423. Ultrasound use significantly reduced the risk of vascular puncture (relative risk (RR) 0.34, 95% confidence interval (CI): 0.20-0.58, P<0.001).
- Pneumothorax was reported in seven RCTs with a total patient population of 1,847. Ultrasound use significantly reduced the risk of pneumothorax (RR 0.21, 95% CI: 0.06-0.71, P=0.01).
- Haemothorax was reported in three RCTs with a total patient population of 703. Ultrasound use significantly reduced the risk of haemothorax (RR 0.10, 95% CI: 0.02-0.56, P=0.009).

Ultrasound was equivalent to the landmark method for the following outcomes:

- Aggregate adverse events, reported in two RCTs with a patient population of 119 (RR 0.92, 95% CI: 0.50-1.69, P=0.797).
- Catheter related adverse events, reported in three RCTs with a patient population of 266 (RR 0.64, 95% CI: 0.29-1.43, P=2.82).
- Infection, reported in one RCT with a patient population of 38 (RR 1.36, 95% CI:0.46-4.04, P=0.583).
- Nerve damage, reported in one RCT with a patient population of 201 (RR 0.14, 95% CI:0.01-2.96, P=0.209).

Percutaneous nerve blockade

Systematic reviews:

All of the systematic reviews concluded that ultrasound guided placement of percutaneous nerve blocks was either equivalent to or an improvement on the comparators of landmark or electrical nerve stimulator techniques.

Meta-analysis:

Upper and lower limb nerve blocks formed the majority of the evidence base. Results from 54 RCTs were pooled to inform the meta-analysis. The following outcomes were statistically significant in favour of ultrasound guidance compared to the landmark or electrical nerve stimulator techniques

- Inappropriate vascular puncture was reported in 17 RCTs with a total of 1,071 patients. Ultrasound significantly reduced the risk of inappropriate vascular puncture (RR 0.27, 95% CI: 0.15 - 0.50, P < 0.001)
- Haematoma was reported in seven RCTs with a total of 223 patients. Ultrasound significantly reduced the risk of haematoma (RR 0.27, 95% CI: 0.28 - 0.74, P = 0.01)

- Nerve injury was reported in 11 RCTs representing 1,577 patients. Ultrasound reduced the risk of nerve injury (RR 0.51, 95% CI: 0.37 - 0.72, P < 0.001).

Ultrasound was equivalent to either the landmark or ENS methods for the following outcome:

- Paraesthesia was reported in ten RCTs with a total of 676 patients (RR 0.62, 95% CI: 0.26 – 1.5, P = 0.292).

Overall conclusion with respect to comparative safety

Overall the use of ultrasound reduces the prevalence of most safety outcomes compared to the landmark technique (vascular access) and both landmark and ENS comparators (percutaneous neural blockade).

No incidence of major events (for example seizure, permanent nerve damage or embolisms) were reported for patients in any group. HESP has advised that major adverse events are rare.

Main issues / caveat regarding these conclusions:

Assessing the impact of ultrasound on the reported adverse events is limited by their infrequent occurrence in RCTs primarily designed to assess effectiveness outcomes. This is especially true for serious adverse events requiring clinical intervention. This is further compounded by small sample size associated with most of the included RCTs.

For vascular access the current evidence base mainly addresses central venous access with the limited evidence for arterial access and PICC line placement. There does appear to be congruency of evidence for different access sites; however, caution should be exercised in extrapolating evidence from central venous studies to arterial access and PICC line placement.

For percutaneous neural blockade the evidence base is dominated by upper (brachial) and lower (sciatic) extremity neural blocks. In the three RCTs on truncal blocks no adverse events were reported.

Comparative effectiveness

Vascular access

Systematic reviews:

All of the systematic reviews concluded that ultrasound localisation of central vascular access was equivalent to or an improvement on the anatomical landmark technique for all reported outcomes.

Meta-analysis:

The following outcomes were statistically significant in favour of ultrasound guidance compared to the landmark technique:

- Cannulation time was reported in 17 RCTs with a total patient population of 1,486, ultrasound use significantly reduced the cannulation time (DM -0.78, 95% CI:-1.16 - -0.40, =<0.001).
- The number of attempts required was reported in 17 RCTs with a total patient population of 3,060. Ultrasound use significantly reduced the number of attempts required (DM -1.19, 95% CI: -1.49 - -0.89, P<0.001).
- The number of failed attempts was reported in 32 RCTs with a total patient population of 6,229. Ultrasound use significantly reduced the risk of failure (RR 0.26, 95% CI: 0.19-0.37, P<0.001).
- The risk of failure on first attempt was reported in 12 RCTs with a total patient population of 1,697. Ultrasound use significantly reduced the risk of failure on first attempt (RR 0.52, 95% CI: 0.43-0.63, P<0.001).

Percutaneous nerve blockade

Systematic reviews:

All of the systematic reviews concluded that ultrasound-guided placement of nerve blocks was either equivalent to or an improvement on the comparators of landmark or electrical nerve stimulator techniques.

Meta-analysis

The following outcomes were statistically significant in favour of ultrasound guidance compared to the landmark or ENS-guided technique:

- Time to administer block was reported in 26 RCTs with a total of 2,025 patients. Ultrasound significantly reduced time to administer a nerve block (difference in mean time (min) -1.66, 95% CI: -2.32 to -1.01, P < 0.001).
- Number of needle redirects was reported in 14 RCTs with a total of 834 patients. Ultrasound significantly reduced number of needle redirections necessary to place a nerve block (difference in mean number of attempts, -1.23, 95% CI: -1.83 to -0.64, P < 0.001).
- Failed nerve blocks were reported in 42 RCTs with a total of 4,611 patients. Ultrasound significantly reduced the risk of nerve block failure (RR 0.41, 95% CI: 0.34 - 0.50, P < 0.001).
- Onset time was reported in seven RCTs with a total of 500 patients. Ultrasound significantly reduced the time for onset of an overall assessment of nerve block (difference in mean time (min) -4.41, 95% CI: -8.84 to -0.08, P = 0.046).
- The outcome of time for patient readiness for surgery was reported in two RCTs with a total of 191 patients. Ultrasound significantly reduced the time for patients to be ready for surgery (difference in mean time (min), -12.23, 95% CI: -20.73 to -3.72, P = 0.005).

Ultrasound was equivalent to either the landmark or ENS methods for the following outcomes:

- Number of skin punctures was reported in five RCTs with a total of 158 patients (difference in mean number of punctures, -0.04, 95% CI: -0.25 to -0.18, P =0.735).
- Onset time motor block was reported in three RCTs with a total of 169 patients (difference in mean (min) -2.85, 95% CI -9.65 to -3.95, P = 0.411).
- Onset time sensory block was reported in 11 RCTs with a total of 613 patients (difference in mean (min) -2.87, 95% CI -6.24 to -0.49, P = 0.094).
- Time to first analgesia was reported in three RCTs with a total of 151 patients (difference in mean (hr) 2.82, 95% CI -3.32 to 8.96, P = 0.367).

Overall conclusion with respect to comparative clinical effectiveness

Overall the use of ultrasound to facilitate major vascular access and percutaneous nerve blockade results in improved procedural and clinical performance.

Main issues around the evidence and conclusions for clinical effectiveness

Blinding of the proceduralists to intervention technique is impossible for ultrasound guided vascular access and percutaneous neural blockade. The use of appropriately blinded assessors was not explicitly reported for all of the included studies. Also, blinding of patients to the intervention was rarely reported and patient knowledge may have influenced the security of assessor blinding. The potential impact of this on the reported outcomes could not be assessed.

The other methodological issue related to poor description of patient withdrawal, both with regard to numbers that were withdrawn and reasons why withdrawal occurred. However, given that most studies focused on immediate effects of the procedure a significant number of studies had a 100 per cent patient retention.

For vascular access, in the majority of studies, time to complete cannulation is considered skin-to-skin. Although statistically significant, the mean difference between techniques is less than one minute. The clinical impact of this time efficiency is minimal for most clinical scenarios. There was no evidence regarding the pre-procedure preparation time and only limited evidence on the impact of imaging on the overall procedure time. As such, the impact of these parameters on the overall complexity and time to perform ultrasound guided vascular access cannot be assessed from the available evidence.

Overall, the observed improvements in effectiveness associated with the ultrasound should have a positive impact on patient comfort; however, no or only limited evidence of patient-related impacts was extractable from the evidence base included in this assessment.

For nerve block, a range of anaesthetic agents were used in the included RCTs. Drug use regimes were reported as being those used in clinical practice to affect appropriate levels and duration of anaesthesia. As such the choice of anaesthetic agent was not considered in the assessment of ultrasound effectiveness when compared to landmark and electrical nerve stimulation guidance methods.

The use of ultrasound resulted in a statistically significant reduction in the skin-to-skin time for placement of nerve blocks when compared with ENS. In contrast, ultrasound extended the time for placement when compared with a landmark method. However, the observed differences in procedure time were less than three minutes for the ENS comparator and one minute for landmark techniques. The clinical significance of these

differences is considered low, but this is not assessable from the current evidence base. The procedural metric of needle redirects was defined by the need to retract the needle by a defined distance and then readvance without breaking the skin. Ultrasound reduced the necessity for needle redirects and this reflects the direct visual identification of the anatomy and ability to visually monitor placement in real-time. The impact of this should reduce the potential physical damage associated with repositioning of the needle

Overall: the use of ultrasound for guiding the placement of neural blockade is at least equivalent, if not better than comparator techniques. Furthermore, the improvement in block characteristics should have a positive benefit for patients and patient flow through a surgical unit.

Economic evaluation

Ultrasound cost per procedure

The total cost per ultrasound procedure is summarised in Table 4, and is based on 100 to 1000 procedures per machine per year, an ultrasound machine cost of $25,000 to $45,000, and is with and without the proposed MBS fee. The capital cost per ultrasound procedure is sensitive to the cost of the ultrasound machine and the total number of procedures performed. Under the base case assumptions (assuming an ultrasound machine cost of $40,000 and 500 procedures per machine per year), the capital cost per ultrasound procedure is $22. Including costs for consumables ($16), the total cost per procedure is $38. With the most conservative assumptions (that is $45,000 machine cost and 100 procedures per year) the figure rises to $139; under the most optimistic assumptions (that is $25,000 machine cost and 1,000 procedures per year) the figure falls to $23.

Table 4 Ultrasound cost per procedure by procedures per year and machine cost

Procedures per machine per year	Machine cost: $25,000 - proposed MBS fee	Machine cost: $25,000 + proposed MBS fee[a]	Machine cost: $40,000 - proposed MBS fee	Machine cost: $40,000 + proposed MBS fee[a]	Machine cost: $45,000 - proposed MBS fee	Machine cost: $45,000 + proposed MBS fee[a]
100	$89	$197	$126	$235	$139	$247
500	$31	$139	$38	$147	$41	$149
1000	$23	$132	$27	$136	$28	$137

a Proposed MBS fee is $58.35, therefore the 75% MBS benefit is $43.76. The assumed patient co-payment is $65;

The Applicant has proposed a MBS fee of $58.35 for ultrasound guidance for both vascular access and neural blockade (DAP, page 12). This is based on three Relative Value Guide (RVG) units to align it with the fees and units allocated to the existing RVG ultrasound items. The Applicant states this fee includes a professional component ($29.20) and a practice component ($29.15) and that the allocation of three RVG units is based on a comparison of the nature of the service to other services of similar complexity and skill, already funded by the items of Group T10. According to the DAP (page 8), the pre-service component of ultrasound includes an explanation to the patient about the use of ultrasound, its benefits, the procedure and preparation and checking of the device. According to the Applicant, pre-service takes approximately 10–15 minutes. The scan itself takes another 5–10 minutes. Following feedback from the Department of Health, and noting that the procedures for which ultrasound guidance is proposed already have existing MBS items, the MSAC may wish to consider if an additional fee is appropriate for the ultrasound procedure and the level of reimbursement. Therefore the

results of the economic analysis are presented with and without the inclusion of the proposed fee. Based on anaesthetist-related claims for MBS item 55054 for the financial year 2012/2013, the assumed patient co-payment is $65. The total cost per ultrasound procedure for the base case scenario, including the MBS benefit and assumed patient co-payment is $147 ($38+$43.76+$65).

Nerve stimulation cost per procedure

Assuming a machine cost of $1,000 and 500 procedures per year, the cost per nerve stimulation procedure is $0.42. For 1000 and 100 procedures per year, the cost per procedure is $0.21 and $2.10, respectively. For nerve stimulation there are no additional costs for consumables and there is no relevant MBS item.

Vascular access economic analysis

The benefits of using ultrasound compared with the landmark technique for vascular access include fewer failed cannulations and a reduction in the incidence of complications. The results of the cost-effectiveness analysis are presented as the incremental cost per failed cannulation avoided. The cost of the ultrasound procedure and the cost implications of treating pneumothorax and haemothorax events are considered. Given the majority of evidence is for venous access, specifically for internal jugular vein (IJV) and subclavian vein (SCV) access, this is the focus for the vascular access economic analysis.

Table 5 summarises the failed cannulation attempts avoided, and pneumothorax and haemothorax events avoided, with the use of ultrasound guidance compared with the landmark technique. The incidence of pneumothorax and haemothorax is higher for SCV cannulations and therefore the results are presented separately for IJV and SCV cannulations. With the use of ultrasound, the risk of a failed cannulation attempt was avoided in 9% of IJV cannulations and 14% of SCV cannulations. For IJV cannulations, ultrasound resulted in 0.98 fewer pneumothorax events and 1.03 fewer haemothorax events for every 100 cannulations, and the cost saving is estimated to be $15 ($8 + $7). For SCV cannulations, ultrasound resulted in 3.45 fewer pneumothorax events and 4.03 fewer haemothorax events for every 100 cannulations, and the cost saving is estimated to be $63 ($35 + $28).

Table 5 Risk of failed cannulation attempts, and incidence and cost of pneumothorax and haemothorax events

	Risk ratio (95% CI) (A)	Landmark (B)	Ultrasound (C=B x A)	Risk difference (D=C-B)	Cost per event (E)	Total cost (D x E)
Failed cannulation attempts						
IJV	0.22 (0.13, 0.35)	11%	2%	9%	NA	NA
SCV	0.11 (0.03, 0.45)	16%	2%	14%	NA	NA
Pneumothorax						
IJV	0.19 (0.03, 0.89)	1.25%	0.26%	0.98%	$782	$8
SCV	0.41 (0.03, 5.64)	4.37%	0.92%	3.45%	$1,027	$35
Haemothorax						
IJV	0.10 (0.02, 0.56)[a]	1.15%	0.12%	1.03%	$704	$7
SCV	0.10 (0.02, 0.56)[a]	4.48%	0.45%	4.03%	$704	$28

IJV, internal jugular vein; NA, not applicable, SCV, subclavian vein
a Risk ratio is for all cannulation sites combined as insufficient data for analysis by subgroups according to site.

The incremental cost per failed cannulation avoided is summarised in Table 6 for IJV and SCV access.

For SCV cannulations, the savings due to fewer pneumothorax and haemothorax events ($63) with ultrasound is greater than the ultrasound capital and consumable costs ($38). Ultrasound also results in fewer failed cannulation attempts and hence is the dominant procedure. If the proposed MBS benefit and associated assumed patient co-payment are included, the cost of the ultrasound procedure ($147) is greater than the savings due to fewer complications ($63), and the incremental cost per failed cannulation avoided is $600.

The incidence of complications with IJV cannulations is lower than for SCV cannulations and the savings due to the avoidance of complications with ultrasound is less ($15 versus $63). Without the proposed MBS benefit, the incremental cost per failed cannulation avoided is $256. Including the proposed MBS benefit increases the incremental cost per failed cannulation avoided to $1,467.

Sensitivity analyses demonstrate the results are sensitive to the assumed number of procedures performed per ultrasound machine per year. For IJV access, the incremental cost per failed cannulation avoided varies from $133 (for 1,000 procedures per year and no MBS benefit) to $1,233 (for 100 procedures per year and no MBS benefit). For SCV access, ultrasound is dominant for 1,000 procedures per year (and no MBS benefit) and the incremental cost per cannulation avoided is $450 for 100 procedures per year (and no MBS benefit). For SCV cannulations, the results are also sensitive to the cost of treating pneumothorax events. If the cost of treating each event is reduced from $1,027 to $230, ultrasound is no longer dominant and the incremental cost per failed cannulation avoided is $15.

Table 6 Incremental cost per failed cannulation avoided with the use of ultrasound vs landmark technique for vascular access

	IJV access without MBS benefit	IJV access with MBS benefit[a]	SCV access without MBS benefit	SCV access with MBS benefit[a]
Base case analysis Cost of ultrasound procedure (A)	$38	$147	$38	$147
Cost savings from complications avoided with ultrasound vs landmark				
Pneumothorax (B)	$8	$8	$35	$35
Haemothorax (C)	$7	$7	$28	$28
Total cost (A – B – C)	$23	$132	-$25	$84
Reduction in failed cannulation attempts with ultrasound vs landmark	0.09	0.09	0.14	0.14
Incremental cost per failed cannulation avoided	$256	$1,467	Dominant	$600

a Proposed MBS fee is $58.35, therefore the 75% MBS benefit is $43.76. The assumed patient co-payment is $65.

The resource and clinical implications of avoiding a failed cannulation attempt are difficult to quantify, but potentially include avoidance of delays starting surgery, and reducing the risk of complications. Calvert (2004) estimated the cost of a failed cannulation due to a 10-minute delay to surgery to be GBP73 (2002 prices). From the data shown in Table 6, the use of ultrasound for IJV cannulations would be cost neutral if each failed cannulation attempt cost $256 (where there is no additional MBS fee for ultrasound guidance).

The economic analysis considers the cost of treating pneumothorax and haemothorax events but not the clinical implications for the patient. Further, other complications such as nerve damage, infections and catheter-related venous thrombosis may be avoided with the use of ultrasound (Lamperti et al 2012); however, there are insufficient data to quantify the impact of ultrasound on these events. The clinical implications of these events are generally short-term, but in rare cases can be serious and even fatal (Cook and MacDougall-Davis 2012).

Nerve block cost analysis

The benefits of using ultrasound compared with nerve stimulation or the landmark technique for peripheral nerve blocks are varied and include reduced need for supplemental anaesthesia, improved postoperative analgesia, a lower dose of local anaesthetic and a reduction in the incidence of complications. Because the benefits cannot easily be incorporated into a single effectiveness measure a cost analysis is presented for nerve blockade. The costs of the ultrasound and nerve stimulation procedures and the local anaesthetic, and the cost implications of improved postoperative pain control and treating local anaesthetic systemic toxicity (LAST) events, are considered.

Based on data from the AURORA registry, analgesia is the aim for close to 100% of nerve blocks. In 40% of blocks the aim is anaesthesia, primarily together with analgesia. Data from the AURORA registry also suggest ultrasound has replaced nerve stimulation in Australian clinical practice. Therefore, the main focus of the economic analysis for nerve blockade is a comparison of ultrasound and nerve stimulation.

A summary of the potential cost offsets with ultrasound guidance compared with nerve stimulation for nerve blockade is presented in Table 7.

A number of RCTs have demonstrated the dose of local anaesthetic can be reduced when using ultrasound guidance compared with nerve stimulation or the landmark technique. A reduction of 48 milligrams of ropivacaine is assumed based on data from the AURORA registry, and the associated cost saving is $4. This saving may not be realised as the ampules are single use and hence a reduction in dose may lead to increased wastage rather than a reduction in the number of ampules used. However, as anaesthetists gain confidence with using lower doses of local anaesthetic when using ultrasound, the dose may be further reduced as reductions of greater than 50% were observed in some of the RCTs.

A statistically significant reduction in block failure was demonstrated with ultrasound compared with nerve stimulation or the landmark technique. For procedures in which the nerve block is being used to provide anaesthesia, a reduction in the rate of block failures may reduce the need for supplemental nerve blocks or general anaesthesia. A reduced need for supplemental anaesthesia has not been consistently demonstrated in the RCTs, and therefore the cost implications associated with this have not been calculated; any reduction in supplemental anaesthesia would decrease the incremental cost for ultrasound. For procedures in which the nerve block is being used to provide postoperative analgesia, a reduction in the rate of block failures may lead to improved postoperative pain management. Improved postoperative pain control and reduced use of opioids has been demonstrated in some RCTs. However based on a systematic review, Choi and Brull (2011) concluded that there is insufficient evidence to define the effect of ultrasound guidance on acute pain control. An economic analysis conducted

alongside a RCT demonstrated ultrasound resulted in a reduction of postoperative morphine and bupivacaine, and postoperative nursing care compared with nerve stimulation (Ehlers 2012). Applying Australian costs to the resource use results in a saving of $20 ($3 + $5 + $12).

Vascular puncture and hence injection of local anaesthetic into the vascular system may in rare cases result in LAST. The incidence of LAST is too low to be assessed in RCTs, however data have been collected as part of the AURORA registry (Barrington and Kluger 2013). Ultrasound guidance significantly reduced the incidence of LAST compared with no ultrasound guidance (0.59 vs 2.1 per 1000 blocks, p=0.004). Approximately 40% of the LAST events were classified as major and included clinical symptoms such as seizures and cardiac arrest. The cost of treating a seizure is estimated to be $3,311, and the savings associated with the reduced incidence of major LAST events is approximately $2. This is potentially an underestimate of the savings as only the costs associated with treating major LAST events have been considered.

Table 7 Potential cost offsets associated with using ultrasound for peripheral nerve blocks

Resource	Units	$/unit	Cost	% of cost
Reduced dose of local anaesthetic, mg	48	$0.09	$4	15%
Reduced dose of postoperative morphine, mL	14.8	$0.21	$3	12%
Reduced dose of postoperative local anaesthetic, mL	15	$0.30	$5	19%
Reduced nursing time postoperative, minutes	19	$0.63	$12	46%
Reduced incidence of major LAST, events per 1000 blocks	0.65	$3.31	$2	8%
Total cost savings with ultrasound			$26	100%

LAST, local anaesthetic systemic toxicity

A summary of the overall cost implications of using ultrasound compared with nerve stimulation for nerve blockade is presented in Table 8.

Without inclusion of the proposed MBS benefit, the additional cost per procedure with ultrasound compared with nerve stimulation is $12. With the inclusion of the proposed MBS benefit and patient co-payment, the additional cost per procedure with ultrasound compared with nerve stimulation is $121 ($12 plus the proposed MBS benefit of $43.76 and assumed patient co-payment of $65). Sensitivity analyses demonstrate the results are sensitive to the assumed number of procedures performed per ultrasound machine per year. Without the proposed MBS benefit, the incremental cost per ultrasound procedure varies from $1 (for 1,000 procedures per year) to $100 (for 100 procedures per year). The results are also sensitive to the cost offset for improved postoperative pain management. Excluding this cost increases the incremental cost per ultrasound procedure from $12 to $32.

Table 8 Incremental cost with the use of ultrasound vs nerve stimulation for nerve blockade

	Without MBS benefit	With MBS benefit[a]
Base case analysis		
Cost of ultrasound procedure (A)	$38	$147
Cost of nerve stimulation procedure (B)	$0.42	$0.42
Incremental cost of procedure (A - B = C)	$38	$147
Potential cost offsets (D)	$26	$26
Incremental cost per procedure with ultrasound (C - D)	$12	$121

a Proposed MBS fee is $58.35, therefore the 75% MBS benefit is $43.76. The assumed patient co-payment is $65.

Overall conclusion with respect to comparative cost-effectiveness

Vascular access

- For SCV cannulations, the savings due to fewer pneumothorax and haemothorax events ($63) with ultrasound is greater than the ultrasound capital and consumable costs ($38). Ultrasound also results in fewer failed cannulation attempts and hence is the dominant procedure. If the proposed MBS benefit and patient co-payment are included, the cost of the ultrasound procedure ($147) is greater than the savings due to fewer complications ($63), and the incremental cost per failed cannulation avoided is $600.
- For IJV cannulations the savings due to the avoidance of complications with ultrasound is $15. Without the proposed MBS benefit, the incremental cost per failed cannulation avoided is $256. Including the proposed MBS benefit and patient co-payment increases the incremental cost per failed cannulation avoided to $1,467.

Nerve blockade

Without inclusion of the proposed MBS benefit, the additional cost per procedure with ultrasound compared with nerve stimulation is $12. With the inclusion of the proposed MBS benefit and associated patient co-payment, the additional cost per procedure with ultrasound compared with nerve stimulation is $121.

The potential cost offsets associated with using ultrasound are highly uncertain and may not be realised in practice. For vascular access the resource use costs associated with avoiding pneumothorax and haemothorax events are based on a single study conducted in the United Kingdom. For nerve blockade the costs associated with improved postoperative pain control, a reduced dose of local anaesthetic and avoidance of major LAST events have been estimated. The reduced resource use associated with improved pain management is from a single trial conducted in Denmark in which patients received a continuous sciatic nerve block. The applicability of the results from this study to Australian clinical practice is unknown. There is evidence that the dose of local anaesthetic can be reduced with ultrasound guidance, however the optimal dose is currently unknown and will vary by nerve location. LAST events are rare, and hence the impact of ultrasound guidance on these events can only be assessed in large registries, such as AURORA.

Financial/budgetary impacts

MBS services for vascular access procedures (MBS items 22015 and 22020) and nerve block procedures for postoperative analgesia (MBS items 22040, 22045 and 22050) for the financial years 2008/2009 – 2012/2013 are summarised in Table 9. MBS services for nerve block procedures for anaesthesia have been estimated assuming 40% of all nerve block procedures are for anaesthesia.

Table 9 MBS services for vascular access procedures (MBS items 22015 and 22020) and nerve block procedures for postoperative analgesia (MBS items 22040, 22045 and 22050), and estimated number of services for nerve block procedures for anaesthesia

Financial year	Item 22015 (vascular access)	Item 22020 (vascular access)	Item 22040 (analgesia)	Item 22045 (analgesia)	Item 22050 (analgesia)	Nerve blocks for anaesthesia	Total	Growth
2008/2009	5062	19866	20638	6327	14379	27563	93835	
2009/2010	4937	20528	22338	6619	15992	29966	100380	7.0%
2010/2011	4946	20892	22878	6904	16417	30799	102836	2.4%
2011/2012	4964	21787	23789	6651	17286	31817	106294	3.4%
2012/2013	5303	22294	24668	6645	18110	32949	109969	3.5%

Source: MBS statistical reports (http://www.medicareaustralia.gov.au/statistics/mbs_item.shtml)

Prior to 1 November 2012, ultrasound guidance was claimed by anaesthetists using MBS item 55054. The number of anaesthetist-related claims for item 55054 for the 2008/2009 – 2011/2012 financial years are presented in Table 10. In 2008/2009 ultrasound was used in 9% of vascular access and nerve block procedures, and this increased to 30% in 2011/2012, and to 34% in the period July to October 2012. In 2011/2012 and 2012/2013 approximately 10% of anaesthetist-related claims for item 55054 were for vascular access, 55% were for nerve blocks for postoperative pain management, and 35% were not for either of these services and hence were likely for nerve blocks for anaesthesia.

Table 10 Anaesthetist-related MBS services for ultrasound guidance (MBS item 55054) and use as a percentage of vascular access and nerve block procedures

Year	Total services for vascular access and nerve blocks (A)	Anaesthesia related claims for Item 55054[a] (B)	Use of ultrasound (B/A)
2008/2009	93835	8744	9%
2009/2010	100380	19094	19%
2010/2011	102836	27290	27%
2011/2012	106294	32041	30%
July-Oct 2012	38319	13205	34%

Source: MBS statistical reports (http://www.medicareaustralia.gov.au/statistics/mbs_item.shtml)
a Data provided by Department of Health. An anaesthetist-related claim was defined as a claim by a Provider with one of the following registered specialties current on date of service or derived specialty for the quarter of service being one of these specialties: Anaesthetics-specialist (051), Anaesthetics-intensive care (060), Resuscitation (075), Anaesthetics-non-specialist (216) and Anaesthetics-trainee (400).

Based on a 3.4% annual growth in the number of services for nerve block and vascular access procedures, use of ultrasound in 60% of procedures and the proposed MBS benefit of $43.76, the cost to the MBS in 2014/2015 and 2015/2016 is $3.1m and $3.2m, respectively (Table 11). Assuming the proportion of procedures in which ultrasound guidance is used increases to 90%, the cost to the MBS in 2014/2015 and 2015/2016 is $4.6m and $4.8m, respectively.

Table 11 Estimated MBS services and benefits for ultrasound guidance

Year	Estimate total services for nerve block and vascular access[a]	60% use of ultrasound: Services	60% use of ultrasound: MBS benefit	90% use of ultrasound: Services	90% use of ultrasound: MBS benefit
2013/2014	113708	68225	$2,985,507	102337	$4,478,260
2014/2015	117574	70544	$3,087,014	105816	$4,630,521
2015/2016	121571	72943	$3,191,972	109414	$4,787,959

a Assuming a 3.4% annual increase in the number of services

Assuming a patient co-payment of $65 per procedure, the total patient co-payment in 2015/2016 with the use of ultrasound guidance in 60% and 90% of procedures would be $4.7m and $7.1m, respectively.

The capital and consumable costs for each ultrasound guided procedure is estimated to be $38 (equipment = $22, consumables = $16). Based on 72,943 services (use in 60% of procedures) in 2015/2016, the capital and consumable cost is approximately $2.8m. Based on 109,414 services (use in 90% of procedures) in 2015/2016, the capital and consumable cost is approximately $4.2m. The potential reductions in health care costs due to reduced postoperative care, reduced use of local anaesthetic and pain medications, and a reduced incidence of complications have not been quantified for the financial forecasts as the cost savings are uncertain and may not be realisable.

Other relevant factors

The use of ultrasound imaging in these services has been shown to reduce serious complications, improve patient safety and increase the overall success rates of the relevant interventions, such that it is now recommended as an essential component of these procedures.

Introduction

The Medical Services Advisory Committee (MSAC) has reviewed the use of real time ultrasound guidance (USG), which is a technology for the visualisation of anatomical features to facilitate vascular access and placement of percutaneous neural blockade. MSAC evaluates new and existing health technologies and procedures for which funding is sought under the Medicare Benefits Scheme in terms of their safety, effectiveness and cost-effectiveness, while taking into account other issues such as access and equity. MSAC adopts an evidence-based approach to its assessments, based on reviews of the scientific literature and other information sources, including clinical expertise.

MSAC's Terms of Reference and membership are in Appendix A. MSAC is a multidisciplinary expert body, comprising members drawn from such disciplines as diagnostic imaging, pathology, surgery, internal medicine and general practice, clinical epidemiology, health economics, consumer health and health administration.

This report summarises the assessment of current evidence for ultrasound guidance for major vascular access and percutaneous neural blockade.

Background

Ultrasound guidance for major vascular access and percutaneous neural blockade

Up to 1 November 2012 MBS item 55054 (ultrasonic cross-sectional echography, in conjunction with a surgical procedure using interventional techniques, not being a service associated with a service to which any other item in this Group applies; Category 5, diagnostic imaging services) had been claimed by anaesthetists when using ultrasound guidance in association with the provision of anaesthetic services. To a lesser extent MBS item 55056 was also being used for a minority of anaesthesia claims. This item is associated with ultrasound machines which are over ten years old.

This assessment investigates the proposal for two new MBS items for the use of ultrasound guidance to assist with vascular access in anaesthesia and for percutaneous neural blockade in anaesthesia.

The procedure

Ultrasound or sonography is a common imaging technology used for a variety of clinical purposes including diagnosis, therapy, and the detection of anatomical features, diagnosis and therapy. A range of ultrasound machines from multiple manufacturers are readily available in Australian clinical practice. Many of these machines are small and portable, and are, available at the point-of-care which facilitates their use for a range of therapeutic services.

Ultrasonography is a safe, non-invasive imaging procedure that does not produce ionizing radiation (Marhofer et al 2005). Sound frequencies used in medical sonography range from 1MHz to 20MHz and are poorly transmitted by air and bone, but are effectively transmitted by fluid and soft tissues. Higher frequencies provide a more detailed image, but are not able to penetrate into deep tissues. As a result, sonography of the neck or peripheral anatomy (including veins, and also in the case of children) is often high frequency, whereas lower frequencies are used to image deeper anatomical features such as lumbar neuroaxial structures in adults (Chan 2011). These characteristics coupled with real-time processing means ultrasound imaging may be utilised for the identification of a patient's anatomy including the vasculature and nerves, and also help account for inter-patient anatomical variations. For the purposes of vascular penetration and percutaneous nerve location, a small, portable two-dimensional real-time device with or without colour Doppler and high frequency transducer (6-13MHz) would be considered adequate (Ihnatsenka and Boezaart 2010). Lower frequency transducers (2 – 5MHz) may be required for identification of deeper structures (Baldi et al 2007; Chan 2011).

The focus of this assessment is the use of ultrasound guidance to facilitate accurate needle penetration and placement for vascular access (veins and arteries) and nerve block. A range of techniques are available. Most commonly, real-time ultrasound is used to provide ongoing images of the patient's anatomy. Although ultrasound can be used prior to the procedure to establish the anatomy and to mark the area for needle penetration, this is not reflective of current clinical practice and is not the focus of this assessment. The ultrasound probe may be linear or concave. Although a concave probe often provides a larger image which may be beneficial for diagnostic purposes, a linear

probe provides a more accurate depth (Ihnatsenka and Boezaart 2010). Certain ultrasound probes are available with needle guides which may improve the accuracy of needle penetration. Other variables in terms of the use of the ultrasound include the scanning of anatomical plane (for example axial/transverse), the ultrasound view (commonly short axis for anatomical structures), the angle of incidence (a perpendicular view will provide improved definition and better needle visualisation), and whether the needle is presented in-plane or out-of-plane to the transducer (Ihnatsenka and Boezaart 2010).

Ultrasound guidance is used in combination with the proceduralist's anatomical knowledge to improve the accuracy of needle placement. In the provision of nerve blocks ultrasound may also be used in combination with electronic nerve stimulation (ENS). During ENS, a peripheral nerve or plexus is electrically stimulated to bring about a nerve response which is then used to identify the distance from the electrode needle to the nerve.

As such, ultrasound can be used to guide cannulation, catheterisation and needle insertion to improve procedural performance and minimise the risk of complications. Ultrasound use in anaesthesia practice dates back to 1978, when la Grange and colleagues described its use for supraclavicular block (la Grange et al 1978). In summary, detailed real-time ultrasound images facilitate the interpretation of the neuro-vasculature structures and the relative positioning of the needle to intended target. Images provide details of any tissue movement, including responses to pressure arising from the insertion of the probe, or from the presence of the probe itself. Although not essential for this technique, echo-dense needles are available for use with ultrasound-guidance. Larger needles are generally more readily visible on ultrasound (Griffin and Nicholls 2010).

The decision on the need for vascular access and regional anaesthesia and analgesia, together with the technique of delivery is made at the compulsory pre-anaesthesia assessment (ANZCA 2010). According to the ASA, time taken to deliver both the pre-service (10–15 minutes) and procedure (5–10 minutes) is approximately 15–35 minutes and is delivered once with no post-procedure component. Most patients would only require these procedures only once or on a small number of occasions during their lifetime.

Intended purpose

Ultrasound guidance is proposed to assist needle placement accuracy in association with anaesthesia services, namely for vascular access and for percutaneous nerve blockade. These interventions are essential for patient management both during anaesthesia and for post-operative care. The requirement for regional anaesthesia and major vascular access is dependent on a number of variables including the choice of anaesthetic, patient factors, and the need for clinical monitoring, and will be determined on a per-patient basis. Vascular access and percutaneous nerve blockade are necessary clinical interventions for a significant number of surgeries. The need for such interventions is assessed during the compulsory pre-anaesthesia assessment. This assessment (MBS items 17610, 17615, 17620 and 17625) allows the anaesthetist to plan anaesthesia and to consider risks for insertion- and anaesthesia-related complications based on patient presentation, history and co-morbidities, and the type of surgery. The assessment provides an opportunity for the anaesthetist to decide whether ultrasound guidance is required in order to avoid potential complications from an insertion (ANZCA 2010).

The utility of ultrasound in this context is proposed to improve procedural performance and reduce the risk of adverse events. In some countries ultrasound-guidance is considered to be the gold standard in delivery of local and regional anaesthesia (Hopkins 2007), although other commentators have raised concerns regarding the use of ultrasound-guidance, including issues associated with potential cytotoxic effects of the energy emitted by the device (Cory 2009).

The proposed new services include both pre-service and service components. The pre-service includes an explanation to the patient about the use of ultrasound, its benefits, the procedure, and information about the preparation and checking of the device. These can be considered distinct from the pre-anaesthesia assessment covered by MBS items 17610, 17615, 17620 and 17625.

To use ultrasound, anaesthetists need training and experience specific to ultrasonography. The specialist training curriculum of the Fellowship of the Australian and New Zealand College of Anaesthetists (FANZCA) includes compulsory training in the use of ultrasound. The Australian and New Zealand College of Anaesthetists (ANZCA) and the ASA also hold regular workshops on the use of ultrasound in anaesthesia practice. As such formal training sessions in the use of ultrasound are regularly made available for the purposes of initial training and the maintenance of skills.

General practitioners recognised by ANZCA do provide some anaesthesia services, although training in the use of ultrasound appears not to be an integral part of their training in anaesthesia. It is also acknowledged that other practitioners such as critical care practitioners, emergency medicine physicians, radiologists, oncologists, paediatricians and cardiologists also perform procedures such as major vascular access, and may also use ultrasound. These specialties are within the scope of this assessment.

Vascular access

Although the cannulation of peripheral vessels is sufficient for the majority of cases, major vascular access is required for specific indications such as monitoring of cardiovascular physiology, the administration of certain therapeutic agents and the administration of large volumes of fluid. Vascular access may be needed in the intensive care unit, in critical care, for emergency care or for peri- and post-surgical care for elective procedures.

For long-term vascular access catheters may be stabilised through the use of tunnelling (either percutaneous or open). However, the role of tunnelled catheters for central vascular cannulation is independent of the use of ultrasound for placing these lines and is not investigated in this assessment. Additionally, although ultrasound guidance can also be used to improve outcomes for the placement of haemodialysis catheters and other similar services, the use of this technology outside anaesthetic-related services is beyond the scope of this assessment. Finally, although ultrasound can be used to assist in accessing peripheral veins, especially where access has been difficult with landmark methods, this use of ultrasound is not within the scope of this assessment.

Central vein catheters

Central venous catheters are inserted for a number of reasons including haemodynamic monitoring, intravenous delivery of blood products and medication (including antibiotics and chemotherapy), total parenteral nutrition and management of fluids (NICE 2002). Central venous catheters may be used when peripheral veins are not readily accessible

(Shrestha and Gautam 2011). The most common sites for puncture include the internal (also external) jugular vein, the subclavian vein, and the femoral vein. The decision for choice of vein is made on a per-patient basis and depends on the reason for central venous catheters insertion.

The potential adverse events of central venous catheters include arterial puncture, arteriovenous fistula, pneumothorax, haemothorax, thromboembolism, air embolism, nerve injury, and failed attempts at catheter placement which can impact patient comfort and add to the time of the intervention (NICE 2002).

PICC

Peripherally-inserted central catheters (PICC) are an alternative to standard central venous catheters where long-term venous access is required for ongoing patient therapy. The PICC is placed in peripheral veins, often of the upper limb (NICE 2002), and the catheter tip is positioned in a central vein (commonly the superior vena cava or close to the junction of the superior vena cava and the right atrium). The advantages of PICC include the ability to place a line at the bedside under local anaesthesia, and a longer indwelling time, a lower risk of accidental arterial puncture and of pneumothorax (Schweickert et al 2009). Complications may also occur during PICC insertion, and may also be related to the ongoing presence of the catheter in a vein. Thrombosis that puts the patient at risk of pulmonary emboli, catheter infection, obstruction or migration is one example (Li et al 2013b; Stokowski et al 2009).

PICC may be inserted by anaesthetists, nurses or radiologists.

Central artery catheters

Intra-arterial access is used to provide continuous monitoring of systemic arterial pressure and to provide access to arterial blood sampling (Schwemmer et al 2006). Arterial cannulation is also the first step of any endovascular procedure (Spiliopoulos et al 2011). Commonly the radial artery and also the femoral artery are used as the target vessel.

Percutaneous nerve blockade

There are two types of nerve blockade based on level of neural inhibition - peripheral and central. Peripheral local anaesthesia is achieved via nerve blocks to single nerves or nerve plexuses. Epidural, spinal and paravertebral (collectively known as neuraxial) anaesthesia are considered regional or central blocks because they directly inhibit the central nervous system. Anaesthetic agents are administered by single shot needle insertion or catheterisation adjacent to nerves or nerve plexuses. The aim of administration is to deliver the local anaesthetic as close as possible to the nerve structure, providing a 'doughnut' of anaesthetic agent around the target nerve (Griffin and Nicholls 2010).

The choice of anaesthesia depends on a variety of clinical and non-clinical considerations including the type of anaesthesia indicated (general, regional, local anaesthesia or combinations of these), the complexity of surgery, the level of expected post-surgical pain, site of the surgery, the patient's medical status and the resources available. Minor surgical procedures may be provided with a regional anaesthetic nerve block, thus avoiding the use of general anaesthesia. There is some evidence to show that there is a non-significant trend to reduced length of stay when patients receive local nerve

blockade (either with or without general anaesthesia) compared to general anaesthesia and no local nerve blockade (Corey et al 2013).

Peripheral or regional nerve blocks can provide effective post-surgical analgesia, avoiding or reducing need for systemic analgesics such as opioids. This is more common for major surgeries associated with significant post-surgical pain, for example major limb surgeries or abdominal procedures.

The anaesthetic agent may be provided as a bolus or via an indwelling catheter. The choice of method of delivery will depend on the type and duration of anaesthesia or analgesia required. The most common types of anaesthetic agents used are lignocaine, bupivacaine/levobupivicaine, and ropivacaine. The local anaesthetics prilocaine and procaine are also available but used much less frequently, while dental blocks often involve the use of articaine.

Common nerve blocks are shown in Table 12. Major peripheral nerve or plexus blocks include those proximal to the elbow or knee. In these locations nerves are complex bundles and typically collocate with other important anatomy such as major arteries. Minor blocks would typically involve single distal peripheral nerves. There are a large number of nerve plexuses. The choice of nerve for provision of the block would be associated with the location of the surgery.

Table 12 Common nerve blocks

Region	Nerve blocks
Upper limb	axillary block, infraclavicular block, interscalene block, mid humeral block, peripheral nerve block - median nerve, musculocutaneous nerve blocks, radial nerve block, ulnar nerve block, supraclavicular block, brachial plexus block
Lower limb	ankle block, femoral nerve block, lateral femoral cutaneous nerve block, obturator nerve block, saphenous nerve block, sciatic nerve blocks - gluteal region, popliteal region, proximal thigh region, subgluteal region
Thorax and abdomen	ilioinguinal/iliohypogastric nerve block, neuraxial block, psoas compartment block, thoracic paravertebral block, transversus abdominis plane (TAP) block

Taken from (Sawyer et al 2000).

Regional, as opposed to peripheral, nerve blockades include procedures that block the transmission of nerve signals at or near the spinal cord. Neuraxial anaesthesia is a collective term relating to local anaesthetics placed around the nerves of the central nervous system and includes epidural injections (where the anaesthetic agent is placed in the epidural space), caudal epidural analgesia (involving the puncture of the sacrococcygeal membrane), and the intrathecal injection (also called a sub-arachnoid or spinal block where the agent is placed directly into the sub-arachnoid space). A paravertebral block involves the injection of a local anaesthetic agent in a space local to where the spinal nerves emerge from the intravertebral foramina.

Procedural complications related to nerve blockade may arise from the incorrect placement of a needle, cannula or catheter, and these may result in inadvertent injection of an anaesthetic agent or other injuries. Accidental delivery of a regional anaesthetic agent into the vasculature can result in drug toxicity leading to seizure, cardiovascular collapse, or depression of the central nerve systems (Cameron et al 2007; Grewal et al 2006).

Other adverse events include nerve injuries from the use of excessive pressure, direct contact or undue stretching. Symptoms of direct nerve injuries are significant and include anaesthesia, paraesthesia (tingling, burning, prickling, or numbness of the skin), hypaesthesia (decreased sensation), hyperaesthesia and pain. According to the Royal College of Anaesthetists, nerve injury as a result of peripheral nerve blocks is uncommon (<3%) and the majority (92-97%) of affected patients recover within four to six weeks, while 99 per cent of affected patients recover within a year. Permanent nerve damage is estimated to have occurred in between 1 in 5,000 and 1 in 30,000 nerve blocks (Brull et al 2007; Fischer 2007; Greensmith and Murray 2006). The classification of potential nerve injuries is shown in Table 13.

Table 13 Classification of potential nerve injuries (Seddon and Sunderland classifications)

Seddon class	Sunderland class	Function	Pathological basis	Prognosis
Neurapraxia	Type 1	Focal conduction block	Local myelin injury, primarily larger fibres. Axonal continuity, no Wallerian degeneration.	Recovery in weeks to months.
Axonotmesis	Type 2	Loss of nerve conduction at injury site and distally.	Disruption of axonal continuity with Wallerian degeneration.	Axonal regeneration required for recovery. Good prognosis since original end organs reached.
	Type 3	Loss of nerve conduction at injury site and distally.	Loss of axonal continuity and endoneural tubes. Perineurium and epineurium preserved.	Disruption of endoneurial tubes, haemorrhage and oedema produce scarring. Axonal misdirection, poor prognosis. Surgery may be required.
	Type 4	Loss of nerve conduction at injury site and distally.	Loss of axonal continuity. Endoneural tubes and perineurium. Epineurium remains intact.	Total disorganisation of guiding elements. Intraneural scarring and axional misdirection. Poor prognosis. Surgery necessary.
Neurotmesis	Type 5	Loss of nerve conduction at injury site and distally.	Severance of entire nerve.	Surgical modification of nerve ends required. Prognosis guarded and dependent upon nature of injury and local factors.

Taken from Sunderland (1951).

Clinical need and burden of disease

According to the Australian Institute of Health Welfare (AIHW), a total of 2,665,986 patients received anaesthesia over the 2010-2011 period in Australia. The majority of these patients (86%) received general anaesthesia, 11 per cent received nerve blocks and less than 1 per cent received epidural or spinal anaesthesia (AIHW 2012).

In terms of the use of ultrasound for anaesthesia services, MBS data show that 26,363 claims under item 55054 where made in association with an anaesthetic procedure in the financial year 2010–11. This number represents approximately 1% of all anaesthesia procedures and 14% of the services claimed under item 55054 during this period (Table 15).

Data derived from the Australian and New Zealand Registry of Regional Anaesthesia (AURORA) indicate that reporting hospitals performed an average of 388 and 499 neural blockades per hospital for 2005-08 and 2011-12 respectively (Barrington et al 2009);

(AURORA). Although limited, this evidence indicates a continuing and growing utilisation of regional anaesthesia within Australia. The proportion of regional nerve blocks that had a component of ultrasound guidance either standalone or in combination with electrical nerve stimulations increased from 63 per cent during 2006 – 2008 to 87 per cent during 2011 – 2012 (AURORA). Furthermore, nearly 60 per cent of procedures in financial year 2011 – 2012 were conducted using ultrasound only as the guidance technique.

MBS utilisation data is also available for the anaesthetic services that may be associated with ultrasound guidance. These data are shown in Appendix P. In summary, there were 90,202 claims for services relevant to central arterial access and anaesthesia in 2012–2013 (item 22025). In the same time period, 37,371 services were claimed for items relevant to central venous access (items 13815, 22020) and 49,423 services were provided associated with percutaneous neural blockade associated with post-surgical pain (items 22040, 22045, 22050).

Central vascular access is commonly required for fluid, drug (including anaesthetics), haemodynamic monitoring and the provision of blood products for patients during major surgery. This vascular access may also be needed in critical care patients, such as patients undergoing chemotherapy. According to the AIHW in 2009–2010 there were 1,891 procedures for central vein catheterisation in a neonate (ICD procedure code 13319-00), 3,845 procedures for central vein catheterisation (13815-00), and 57,172 procedures for percutaneous central vein catheterisation (13815-01) (AIHW 2013). In addition, during the same period there were 11,103 catheterisations of central arteries (code 34524-00) (excluding catheterisations of the umbilical and intra-abdominal artery).

Percutaneous local anaesthetic nerve blockade is becoming more widely available as an anaesthetic for minor surgery, and as an analgesic for major surgery. Nerve block provides alternative options compared to other types of anaesthesia or analgesia. Due to its local action, nerve blocks offer reduced adverse events and decrease unwanted drug reactions associated with systemic agents. They provide an option for people who may be contraindicated to general anaesthesia. For peripheral nerve blocks, AIHW data shows that there were 14,661 procedures for ICD block number 63, administration of anaesthetic agent around other peripheral nerve, in 2009–2010.

In 2009-2010 there were 15,662 procedures for epidural, spinal or caudal injection or infusion (ICD block chapter I, block numbers 33-37, 39 injection infusion of epidural, spine, caudal) (AIHW 2013). Specifically with regard to the use of local anaesthesia, there were 444 epidural injections of local anaesthetic (18216−27), 1,156 epidural infusions of local anaesthetic (18216−00), and 11 caudal infusion of local anaesthetic (18216−09).

According to expert clinical input, ultrasound technology is becoming more commonly used to improve interventional performance and clinical outcomes for the above vascular access and percutaneous nerve blockade procedures. Fellowship of the Australian and New Zealand College of Anaesthetists (FANZCA) includes compulsory training in the use of ultrasound.

Existing procedures

Landmark-guided

In the absence of ultrasound, major vascular access and identification of nerve for nerve blockade would be achieved using an alternative guidance technique. Typically, these would involve landmark techniques that are based on the anaesthetist's knowledge of human anatomy, as well as the anaesthetist's experience and judgement, which differs from practitioner to practitioner. In the landmark insertion method, surface anatomical landmarks are used, and the expected anatomical relationship of the vein, artery or peripheral nerve or nerve plexus, to guide skin or vessel puncture and also the passage of the needle through the vessel. Accurately localising neuro-vasculature can be difficult when inter-individual anatomical variations are present. For some patients, landmark guidance may be more difficult, for example for thin or obese patients, children and adolescents, for patients with oedema, or in the case of obstetrics where hormonal activity softens ligaments which are used to guide needle penetration. In addition, access to neuro-vascular structures becomes difficult when patients are hypovolemic, hypoxic or hypotensive. Patient posture can also affect the relative location of neurovascular and surrounding organs.

Anatomical landmark guidance does not require additional resources and there is no associated MBS item.

Electrical nerve stimulation-guided

Non-ultrasound guidance techniques are available for the placement of percutaneous nerve blocks. These are based on anatomical landmarks with or without electrical nerve stimulation. Nerve stimulation has traditionally been a common modality to guide nerve blocks prior to the introduction of ultrasound (Abrahams et al 2009). Some nerve blocks may be performed with a combination of ultrasound and electrical nerve stimulation guidance.

While ENS indicates the location of nerves, the technique has limitations. It does not identify vessels, muscles, fascia and visceral structures. Evidence of nerve location disappears after injecting 1–2 mL of the anaesthetic agent; hence, nerve stimulation cannot be used to localise nerves thereafter (Perlas et al 2006). The threshold of the electrical stimulus required to stimulate a nerve differs between nerves. The electrical stimulus elicits a motor response. If the neural structures are 'sensory only', or a patient has had a muscle relaxant as part of their anaesthesia technique, ENS cannot be applied as no motor response will be obtained.

There is no MBS item for the use of ENS in providing anaesthesia. Existing MBS items for neural blockade provide the same fee regardless of the technique used to locate the neural structure.

The use of non-ultrasound techniques for neural block placement has declined from 37 per cent during 2006–2008 to 13 per cent during 2011–2012 (AURORA). These data indicate that guidance techniques that do not involve ultrasound are now the exception.

Marketing status of the technology

A large number of ultrasound systems are listed in the Australian Register of Therapeutic Goods (ARTG), and represent a variety of applications including diagnostic, therapeutic and point-of-care machines (Appendix G). The ultrasound devices used in the studies included in this assessment are available for Australian clinical practice. The two most widely used ultrasound machine as identified in the international peer-reviewed literature are manufactured by Brad Australia Pty Ltd (ARTG: 141585 Fujifilm SonoSite Pty Ltd (ATRG: 118714, 193635 and 215880) and GE Healthcare Australia Pty Ltd (ATRG: 92889, 93418, 123899, 123902, 125536, 126295, 198951 and 166229). These instruments and other that are fit for purpose are registered with the ARTG and approved by Therapeutic Goods Administration (TGA).

Transducers appropriate for ultrasound guided vascular access and nerve blockade are available within Australia (e.g. ARTG: 143642, 118863, and 124215).

Many manufacturers offer a procedure pack associated with specific devices. This pack includes sterile gel, a cover for the transducer, and may also come with a needle guide (e.g. ATRG: 198806).

In summary, appropriate ultrasound technologies and ancillary equipment necessary to deliver the proposed new MBS items are available for use within Australia.

Current reimbursement arrangements

Ultrasound guidance to facilitate vascular access and nerve blockade procedures in association with anaesthesia is commonly used in Australia in both public and private practice. A number of services were claimed through MBS item 55054 (Table 14) until 1 November 2012. The number of claims made for the item from 2000–2011 follows in Table 15. There has been a gradual increase in the number of services and number of anaesthesia-related claims over the past 10 years.

MBS item 55026 has also been used in a smaller percentage of anaesthesia-related claims. This item is used for ultrasound devices which are over 10 years old.

Table 14 Previous MBS item used in ultrasound guidance in the practice of anaesthesia

Category 5 Group I1,Subgroup 1 - Diagnostic Imaging services
MBS Item 55054   Ultrasonic cross-sectional echography, in conjunction with a surgical procedure using interventional techniques, not being a service associated with a service to which any other item in this group applies. (See para DIQ of Explanatory Notes to this category)   Fee: $109.10 Benefit: 75% = $81.85 85% = $92.75   Explanatory note DIQ: To provide an incentive to bulk-bill, for out-of-hospital services that are bulk-billed, the Schedule Fee is reduced by 5% and rebates provided at 100% of this revised fee (except for item 61369).   <Previous - Item 55049 Next - Item 55059>

Item Start Date: 01-Jul-1993; Description Start Date: 01-Nov-1993; Schedule Fee Start Date: 01-Nov-2004.
Category 5: Diagnostic Imaging Services; Group I1: Ultrasound; Subgroup 1: General.

Table 15 Number of services claimed for MBS item 55054

Financial year	Number of services	Anaesthesia related claims*	Proportion of the total (%)
2000/2001	45,922	NR	NR
2001/2002	53,254	NR	NR
2002/2003	62,188	NR	NR
2003/2004	70,784	NR	NR
2004/2005	81,828	5	<0.001
2005/2006	96,431	108	0.1
2006/2007	107,688	274	0.2
2007/2008	120,093	1121	0.9
2008/2009	142,780	7222	5.1
2009/2010	163,585	17,291	10.6
2010/2011	187,417	26,363	14.1
2011/2012	206.701	32,041	15.5
2012/2013	208,881	13,205	6.3

*data provided by the Applicant; NR: not reported
Source: Australian Government Department of Health, https://www.medicareaustralia.gov.au/statistics/mbs_item.shtml, accessed 16 December 2013

Currently there is no MBS item for ultrasound guidance for vascular access and nerve blockade procedures. There is also no MBS item for electrical nerve stimulation for nerve blockade procedures. However, there are a number of MBS items for the procedures for which ultrasound guidance is proposed to benefit (see also Appendix P).

There are four MBS items for vascular access for veins and arteries (22020, 22015, 13815 13818 and 13819). Medicare benefits for PICC can also be claimed under these items (Medicare note T1.6).

Catheters for central vascular lines may be non-tunnelled or tunnelled, where the catheters are passed under the skin to increase stability. MBS items 34527 and 24528 are available dependent upon whether the technique is open or percutaneous. However, this procedure would be undertaken independently of the initial puncture and would not be impacted by the use of ultrasound.

There are a number of MBS items for nerve blockade. Where the nerve blockade is used for general anaesthesia the block attracts benefits under the Group T10 anaesthesia item. For post-operative analgesia, there are three items (22040, 22045 and 22050) which vary according to the location of the block (femoral and/or sciatic nerves for hip, knee, foot or ankle surgery, and brachial plexus in conjunction with shoulder surgery). There are 44 other items for nerve block in Group T7, 18233 to 18298. An item in Group T7 is administered by a medical practitioner in the course of a surgical procedure undertaken by that practitioner. When a block is carried out in cases not associated with an operation, such as for intractable pain or during labour, the service falls under Group T7.

For epidural or intrathecal regional blocks for post-operative pain management, there are two items (22031, 22036). There are a number of items for the intrathecal or epidural infusion of a therapeutic substance (18216, 18219, 18226, 18227), and also an item for the intrathecal or epidural insertion of a spinal catheter for the management of chronic intractable pain (39125).

Approach to assessment

Objective

The objective of this assessment is to describe the evidence in relation to safety, effectiveness and economic considerations for the use of ultrasound imaging for the practice of anaesthesia for patients requiring a central line catheter for major vascular access or placement of percutaneous neural blockade. This information will be used to inform the decision-making regarding funding of this service through the MBS.

Expert advice

Doctors Nixon and Barrington of the Health Expert Standing Panel (HESP) provided expert guidance to the evaluators to ensure that the assessment was clinically relevant. Input was also provided by the Surgical Services section of the Department of Health. The assessment was directed by Decision Analytic Protocol 1183 which was finalised through the Protocol Advisory Sub-Committee (PASC) in January 2013.

Clinical decision pathway

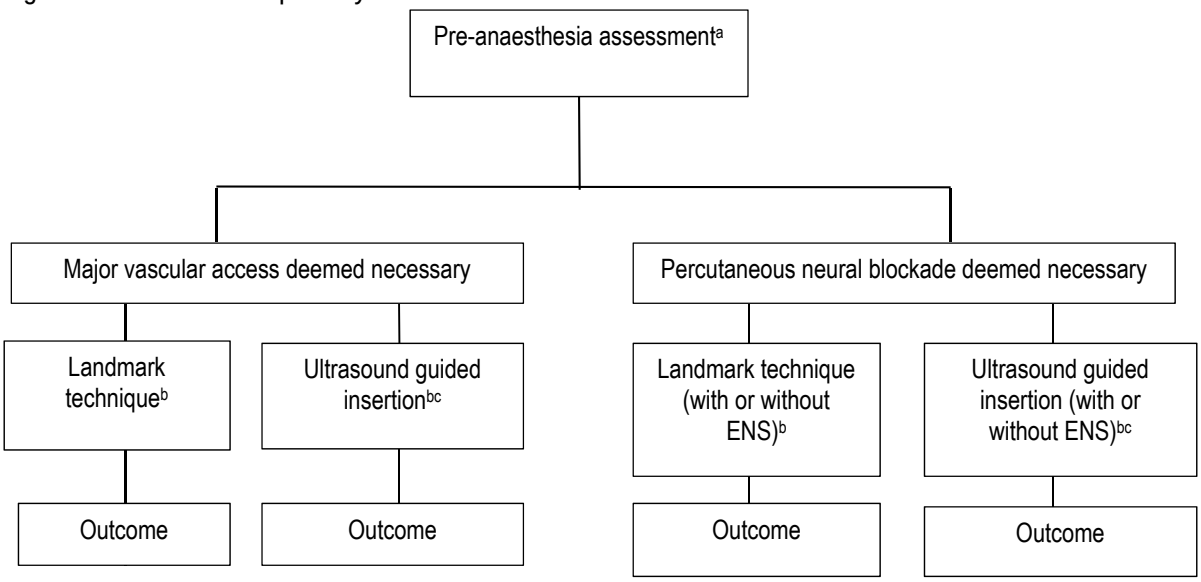
PICO (population, intervention, comparator, outcomes) criteria are used to develop well-defined clinical questions for each assessment. This involves focusing the question on the following four elements (Sunderland 1951):

- The target population for the intervention;
- The intervention being considered;
- The comparator or current intervention, that is, that mostly likely to be replaced or supplemented by the new intervention;
- The clinical outcomes most relevant to assessing safety and effectiveness.

Clinical questions can be defined in part through the development of flow charts. Flowcharts help define the place of the intervention within the clinical management of a condition, including whether the intervention will be used incrementally, or will replace a current intervention. This assists with identifying the correct comparator for the intervention against which safety, effectiveness and cost-effectiveness can be measured.

The flow chart provided below in Figure 3 is a clinical pathway developed in conjunction with, and agreed upon by, the PASC specifically for this assessment of real-time ultrasound for major vascular access and percutaneous neural blockade.

Figure 3 Clinical decision pathway



a Any circumstance that require anaesthesia for surgery. Patients who require independent pain management or analgesia are not a part of this population.
b Insertion of a cannula, catheter or needle.
c MBS Item 55054 (access has been restricted for the current purposes on 01 November 2012) .
Landmark technique: Insertion of a cannula, catheter or needle performed based on anaesthetist's knowledge of human anatomy, experience and judgement; ENS: Electrical nerve stimulation.

Comparators

As described previously, there is more than one alternative option for needle guidance for anaesthetic techniques. For this assessment, the comparator is considered to be either one or a combination of the following:

Landmark technique

Landmark techniques for inserting a cannula, catheter or needle in major vascular access and percutaneous neural blockade are based on knowledge of anatomy and practitioner experience.

Electrical nerve stimulation

In patients who receive percutaneous nerve blockade, ENS can be used in combination with the landmark technique to indicate the location of nerves (Abrahams et al 2009; Macintyre et al 2010).

Research questions

Safety

1. What is the safety of ultrasound guidance for percutaneous major vascular access compared with landmark guidance techniques?

2. What is the safety of ultrasound guidance for percutaneous neural blockade compared with landmark or electric nerve stimulator (ENS) guidance techniques?

Effectiveness

1. What is the effectiveness of ultrasound guidance for percutaneous major vascular access when compared with landmark guidance techniques?

2. What is the effectiveness of ultrasound guidance for percutaneous neural blockade when compared with landmark or ENS guidance techniques?

Cost effectiveness

1. What is the cost-effectiveness of ultrasound guidance for percutaneous major vascular access when compared with landmark guidance techniques?

2. What is the cost-effectiveness of ultrasound guidance percutaneous neural blockade when compared with landmark or electric nerve ENS guidance techniques?

Review of literature

Literature sources and search strategies

Medical literature searches were conducted in five bibliographic databases: PubMed, EMBASE, Current Content, The Cochrane Library and the Centre for Reviews and Dissemination (CRD) of the University of York databases. In addition, the websites of clinical practice guidelines and current clinical trials were searched. A complete list of these websites is provided in Appendix C. A comprehensive search strategy using a range of relevant search terms (for key words, phrases, Medical Subject Headings (MeSH) and EmTree terms) was used. The search strategies are shown in Appendix C. The use of a sensitive strategy identified a wide range of studies and indications and reduced the possibility that relevant studies may be missed. Potentially relevant studies were identified from the inception of the databases to October 2013. The bibliographies of all included studies were hand-searched for any relevant references that may have been missed by the literature searches (pearling). Separate searches were conducted for nerve block and vascular access.

Although not considered a primary focus of the assessment, a search was also conducted for neuraxial anaesthesia. This indication was noted to be of interest by PASC although no separate PICO were defined. The methodology and results of these focused searches are provided separately in Appendix O.

Selection criteria

The inclusion and exclusion criteria for study selection used in this assessment are listed in Table 16. Where needed, expert clinical input from HESP was obtained to confirm the choice of included studies.

Table 16 Selection criteria for inclusion of studies

Selection criteria	Conditions
Study design	Systematic reviews (SRs) and clinical studies (including randomised controlled trials (RCTs) and pseudo randomised controlled trials) were included. Non-systematic reviews, non-randomised comparative studies, and case series , case reports, articles identified as preliminary reports where results are published in later versions, articles in abstract form, letters, editorials, and animal, in-vitro and laboratory studies were excluded.
Population	The population is defined as patients who receive ultrasound guidance for delivery of anaesthetic services. There are two sub-populations To assist with percutaneous major vascular access These patients require major vascular access for anaesthetic services. To assist with percutaneous neural blockade This group of patients is likely to receive regional or local anaesthesia by a single-shot needle insertion and/or placing a catheter adjacent to a nerve or nerve plexus. Catheterisation is used when continuous anaesthetic agents need to be supplied to maintain the anaesthetic effect.
Intervention	Ultrasound guidance. Ultrasound may be used either with or without ENS for placement of neural blockade. Anaesthetics agent can be delivered either as a single shot or via catheter for continuous infusion. The intervention may be provided by a range of specialists including, anaesthetists, critical care practitioners, and emergency medicine physicians.
Comparator	Landmark-guided technique: based on the anaesthetist's knowledge of human anatomy, experience and judgement. For neural blockade, anaesthetic agent can be delivered either as a single shot or via catheter for continuous infusion. Electrical nerve stimulation (ENS)-guided technique: In patients who receive percutaneous nerve blockade, ENS can be used in combination with the landmark technique to indicate the location of nerves
Outcomes	Safety: • Complications or adverse events following an insertion (for example haematoma, pneumothorax, nerve injuries) • Complication or adverse events following the entire procedure • Anaesthetic toxicity • Any other adverse events or complications that occur following the use of ultrasound guidance in cannula (catheter) or needle insertion procedures should be considered Effectiveness: • Success rate - viable insertion at first attempt • Failed insertion attempts • Time to perform the insertion (for example time to initiate/perform a block) • Time to onset of anaesthesia • Volume or amount of anaesthesia required • Any patient-related outcome (for example quality of life)
Language	Non-English language articles were not included unless they appeared to provide a higher level of evidence than included English language articles.

Search results

For each search strategy the process of study selection for this report went through four phases:

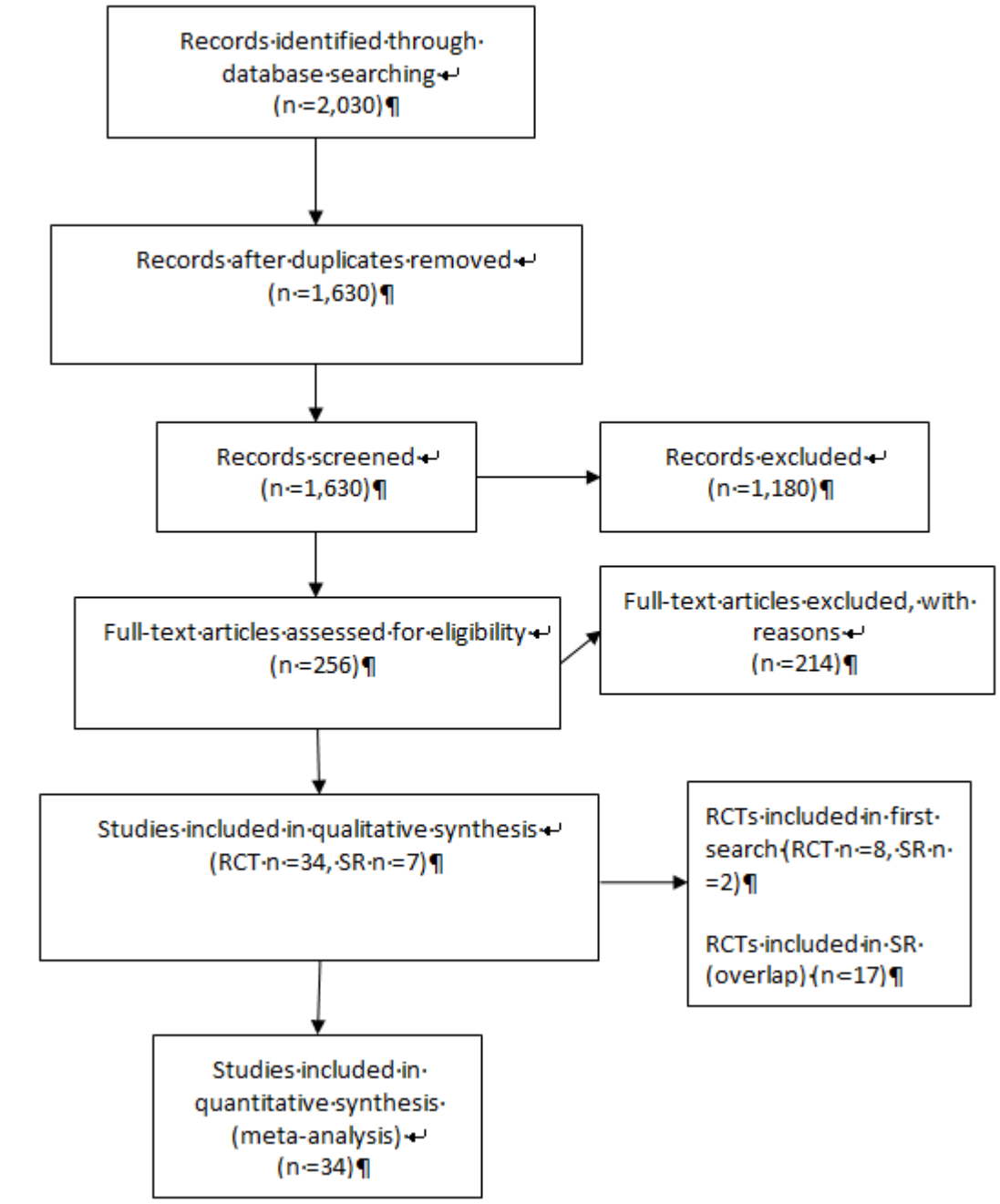
1. All reference citations retrieved from all literature sources were collated into an EndNote X4 database.
2. Duplicate references were removed.
3. Studies were excluded, on the basis of the citation information (title and abstract), if it was obvious that they did not meet the pre-specified inclusion criteria. All other studies were retrieved for full-text assessment.
4. Studies were included to address the research questions if they met the pre-specified criteria applied by the evaluator on the full-text articles. Those articles meeting the inclusion criteria formed the evidence base.

Any doubt concerning inclusion at phase four was resolved by consensus between two evaluators. The results of the process of study selection are provided in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart in Figure 4 and Figure 5. Separate strategies were conducted for percutaneous nerve blockade and central vascular access.

For major vascular access, a number of studes were excluded as they involved access for haemodialysis (n=166) and for peripheral vein access (n=28), which were outside the scope of this assessment (Figure 4).

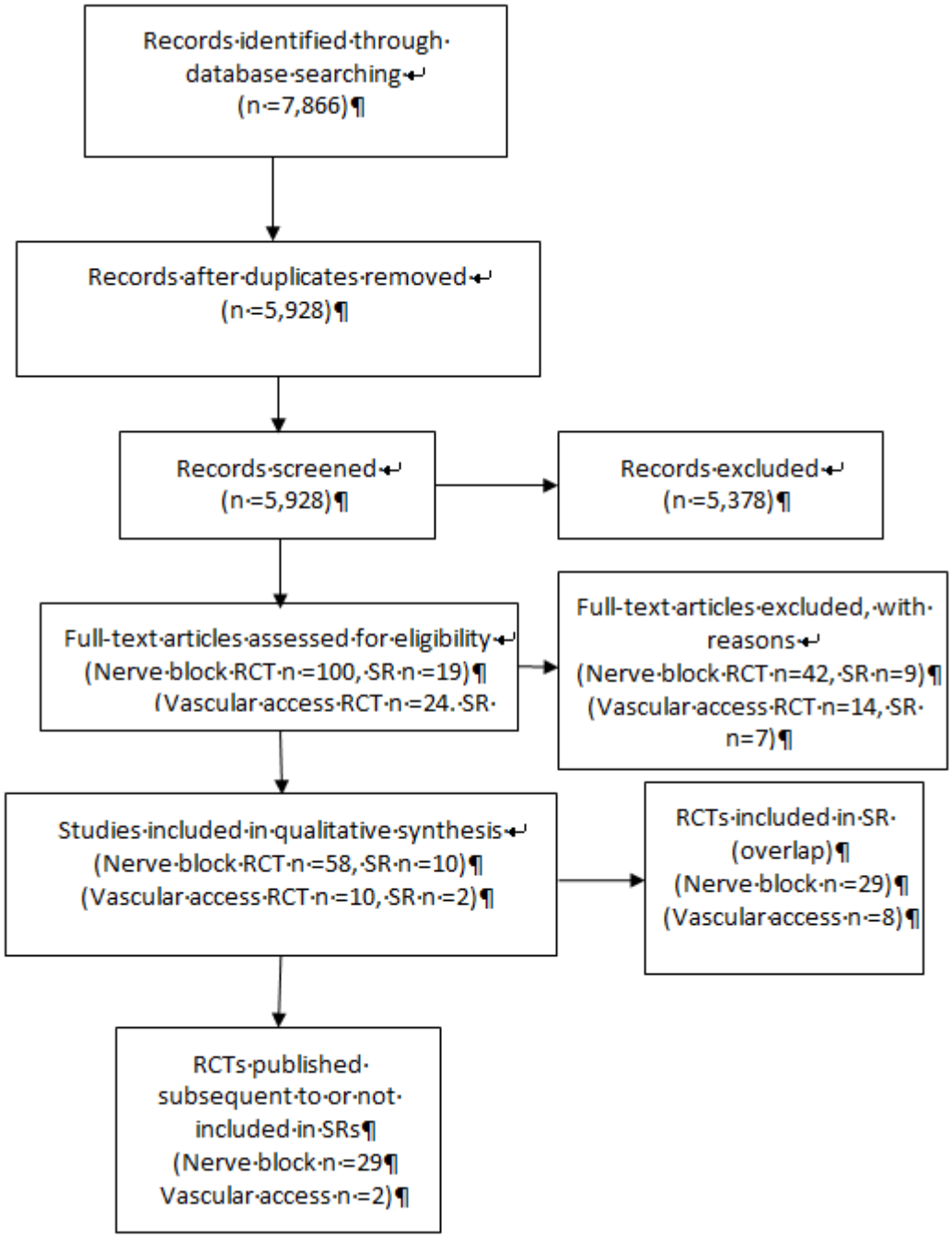
Lists of all included studies, and of studies excluded following full text review, with reason, are provided in Appendix D and E respectively. A number of relevant systematic reviews were identified for all indications. Further detail regarding each systematic review and information in terms of data overlap and duplication is provided in the results section.

Figure 4 Summary of the process used to identify and select studies for major vascular access



Adapted fromPRISMA (2014)

Figure 5 Summary of the process used to identify and select studies for vascular access and percutaneous nerve blockade



Adapted from PRISMA (2014)

Data extraction and analysis

Data were extracted by one evaluator and checked by a second using standardised data extraction tables developed a priori. Data were only reported if stated in the text, tables, graphs or figures of the article, or if they could be accurately extrapolated from the data presented. Descriptive statistics were extracted or calculated for all safety and effectiveness outcomes in the individual studies, including numerator and denominator information.

Included studies

All studies that were retrieved for full-text review and found to meet the eligibility criteria for inclusion are listed in Appendix D, stratified by indication and level of evidence.

Studies that were retrieved for full-text review but were found to be ineligible according to the inclusion criteria are provided in Appendix E**Error! Reference source not found.** with reasons for exclusion.

Appraisal of the evidence

Appraisal of the evidence was conducted at three stages:

1. Appraisal of the applicability and quality of individual studies included in the review;
2. Appraisal of the precision, size and clinical importance of the primary outcomes used to determine the safety and effectiveness of the intervention;
3. Integration of this evidence for conclusions about the net clinical benefit of the intervention in the context of Australian clinical practice.

Validity assessment of individual studies

The evidence presented in the selected studies was assessed and classified using the dimensions of evidence defined by the National Health and Medical Research Council (NHMRC 2009).

These dimensions (Table 17) consider important aspects of the evidence supporting a particular intervention and include three main domains: strength of the evidence, size of the effect and relevance of the evidence. The first domain is derived directly from the literature identified as informing a particular intervention. The last two require expert clinical input as part of their determination.

Table 17 Evidence dimensions

Type of evidence	Definition
Strength of the evidence	
Level	The study design used, as an indicator of the degree to which bias has been eliminated by design.*
Quality	The methods used by investigators to minimise bias within a study design.
Statistical precision	The *p*-value or, alternatively, the precision of the estimate of the effect. It reflects the degree of certainty about the existence of a true effect.
Size of effect	The distance of the study estimate from the "null" value and the inclusion of only clinically important effects in the confidence interval.
Relevance of evidence	The usefulness of the evidence in clinical practice, particularly the appropriateness of the outcome measures used.

* See Table 18

Strength of the evidence

The three sub-domains (level, quality and statistical precision) are collectively a measure of the strength of the evidence.

Level

The 'level of evidence' reflects the effectiveness of a study design to answer a particular research question. Effectiveness is based on the probability that the design of the study has reduced or eliminated the impact of bias on the results.

The NHMRC evidence hierarchy provides a ranking of various study designs (levels of evidence) by the type of research question being addressed (Table 18).

Table 18 Designations of levels of evidence according to type of research question

Level	Intervention [a]
I [b]	A systematic review of level II studies
II	A randomised controlled trial
III-1	A pseudo randomised controlled trial (i.e. alternate allocation or some other method)
III-2	A comparative study with concurrent controls: ▪ Non-randomised, experimental trial [c] ▪ Cohort study ▪ Case-control study ▪ Interrupted time series with a control group
III-3	A comparative study without concurrent controls: ▪ Historical control study ▪ Two or more single arm study [d] ▪ Interrupted time series without a parallel control group
IV	Case series with either post-test or pre-test/post-test outcomes

a Definitions of these study designs are provided on pages 7-8 How to use the evidence: assessment and application of scientific evidence (NHMRC 2000b).

b A systematic review will only be assigned a level of evidence as high as the studies it contains, excepting where those studies are of level II evidence. Systematic reviews of level II evidence provide more data than the individual studies and any meta-analyses will increase the precision of the overall results, reducing the likelihood that the results are affected by chance. Systematic reviews of lower level evidence present results of likely poor internal validity and thus are rated on the likelihood that the results have been affected by bias, rather than whether the systematic review itself is of good quality. Systematic review quality should be assessed separately. A systematic review should consist of at least two studies. In systematic reviews that include different study designs, the overall level of evidence should relate to each individual outcome/result, as different studies (and study designs) might contribute to each different outcome.

c This also includes controlled before-and-after (pre-test/post-test) studies, as well as adjusted indirect comparisons (ie utilise A vs B and B vs C, to determine A vs C with statistical adjustment for B).

d Comparing single arm studies ie case series from two studies. This would also include unadjusted indirect comparisons (ie utilise A vs B and B vs C, to determine A vs C but where there is no statistical adjustment for B).

Note A: Assessment of comparative harms/safety should occur according to the hierarchy presented for each of the research questions, with the proviso that this assessment occurs within the context of the topic being assessed. Some harms are rare and cannot feasibly be captured within randomised controlled trials; physical harms and psychological harms may need to be addressed by different study designs; harms from diagnostic testing include the likelihood of false positive and false negative results; harms from screening include the likelihood of false alarm and false reassurance results.

Note B: When a level of evidence is attributed in the text of a document, it should also be framed according to its corresponding research question eg level II intervention evidence; level IV diagnostic evidence; level III-2 prognostic evidence.

Source: NHMRC (2009).

Quality

Systematic reviews were critically appraised for methodological quality using the AMSTAR appraisal tool (Appendix I). The median score of 6 was chosen to differentiate good quality systematic reviews (≥6) from poor quality reviews (>6) (CADTH 2006). Included RCTs were examined with respect to the adequacy of allocation concealment and blinding (if possible), handling of losses to follow-up, and any other aspect of the study design or execution that may have introduced bias use an assessment tools adapted from critical appraisal tools developed by Downs and Black and van Tulder and Assendelft (Appendix I, Table 75). Each RCT was judged on internal validity (measures of bias and confounding) and external validity (gereralisability) (Downs and Black 1998).

Two evaluators critically appraised each of the included studies, and any disagreement was resolved with discussion.

Statistical precision

Statistical precision was determined using statistical principles. Small confidence intervals and *p*-values give an indication as to the probability that the reported effect is real and not attributable to chance (NATA 2014). Studies need to be appropriately designed and powered in terms of the study population to ensure that any real difference between groups will be detected in the statistical analysis.

Size of effect

For intervention studies of ultrasound guidance for major vascular access and percutaneous neural blockade it was important to assess whether statistically significant differences between the intervention and comparator arms were clinically relevant. The size of the effect was determined, as well as whether the 95% confidence interval (CI) included only clinically important effects.

Relevance of evidence

The outcomes being measured in this report were assessed as to whether they were appropriate and clinically relevant. Inadequately validated (predictive) surrogate measures of a clinically relevant outcome were avoided (NATA 2014). The relevant outcomes were informed by the PASC-approved protocol for 1183.

Meta-analysis

Where possible, outcome data from RCTs were combined using meta-analysis. Individual studies were judged according to their research questions and other aspects of their design (including the PICO) to determine which could be grouped in this manner. The final decision of which studies to include in each meta-analysis was made by two researchers (DT and JD). Detailed rationale for each meta-analysis is provided in the Results section.

Comprehensive Meta-Analysis V2.2.064 (Biostat, Englewood, NJ) was used to perform appropriate meta-analyses to generate point estimates of effect size and test for statistical heterogeneity of the included studies. Overall effect sizes are represented in a forest plot format with sub-group analysis detailed in a tabulated format. The heterogeneity of outcomes across the studies was estimated by the I^2 statistic (a scale of 0-100% where <25% is considered low heterogeneity, 25-75% considered moderate heterogeneity and ≥75% is considered high heterogeneity) (Higgins 2011). A conservative approach was taken in data combination, for example a random effects model was chosen for each continuous or dichotomous analysis. Results for dichotomous events are expressed as a risk ratio and for continuous data as mean and standard deviation. If required, means and standard deviations were estimated according the method of Hozo et al (Hozo et al 2005). A P value of <0.05 was considered statistically significant. All statistical tests were two sided. Data not amenable to statistical aggregation have been presented in a table and narrative format.

Assessment of the body of evidence

Appraisal of the body of evidence was conducted along the lines suggested by the NHMRC in their guidance on clinical practice guideline development (NHMRC 2009). Five components are considered essential by the NHMRC when judging the body of evidence:

1. The evidence base – which includes the number of studies sorted by their methodological quality and relevance to patients;
2. The consistency of the study results – whether the better quality studies had results of a similar magnitude and in the same direction, i.e. homogenous or heterogeneous findings;
3. The potential clinical impact - appraisal of the precision, size and clinical importance or relevance of the primary outcomes used to determine the safety and effectiveness of the test;
4. The generalisability of the evidence to the target population;
5. The applicability of the evidence - integration of this evidence for conclusions about the net clinical benefit of the intervention in the context of Australian clinical practice.

A matrix for assessing the body of evidence for each indication, according to the components above, was used for this assessment (see Table 19).

Table 19 Body of evidence assessment matrix

Component	A Excellent	B Good	C Satisfactory	D Poor
Evidence base [a]	One or more level I studies with a low risk of bias or several level II studies with a low risk of bias	One or two level II studies with low risk of bias or a systematic review/several level III studies with low risk of bias	One or two level III studies with a low risk of bias, or level I or II studies with a moderate risk of bias	Level IV studies, or level I to III studies/systematic reviews with high risk of bias
Consistency [b]	All studies consistent	Most studies consistent and inconsistency may be explained	Some inconsistency reflecting genuine uncertainty around clinical question	Evidence is inconsistent
Clinical impact	Very large	Substantial	moderate	Slight or restricted
Generalisability	Population/s studied in body of evidence are the same as the target population	Population/s studied in the body of evidence are similar to the target population	Population/s studied in body of evidence different to target population for guideline but it is clinically sensible to apply this evidence to target population [c]	Population/s studied in body of evidence different to target population and hard to judge whether it is sensible to generalise to target population
Applicability	Directly applicable to Australian healthcare context	Applicable to Australian healthcare context with few caveats	Probably applicable to Australian healthcare context with some caveats	Not applicable to Australian healthcare context

a Level of evidence determined from the NHMRC evidence hierarchy (Table 18).
b If there is only one study, rank this component as 'not applicable'.
c For example, results in adults that are clinically sensible to apply to children OR psychosocial outcomes for one cancer that may be applicable to patients with another cancer.
Source: NHMRC (2009).

Results of assessment

Ongoing clinical trials

Websites of clinical trials agencies were searched to identify relevant ongoing or unpublished clinical trials related to the use of ultrasound guidance for major vascular access and percutaneous neural blockade. These websites included the Australian Clinical Trials Registry (www.anzctr.org.au), ClinicalTrials.gov (www.clinicaltrials.gov) and Current Controlled Trials ISRCTN (www.controlled-trials.com) (Appendix F).

As of December 2013 a total of 36 and 75 trials investigating the use of ultrasound guidance for major vascular access or percutaneous neural blockade were identified, respectively (Table 68 and Table 69). Four of the 111 identified trials were specific to a paediatric population. The remaining trials were either without age limits or restricted to patients older than16 or 18 years of age. The majority of included registered clinical trials have been, or are being, conducted within the USA, Europe or Australia and New Zealand. The reported recruitment varies with median patient numbers of 100 (range; 20 – 6,314) and 78 (range; 19 – 1,002) for vascular access and nerve block clinical trials respectively.

Title analysis of the ongoing clinical trials reveals a move away from the evaluation of effectiveness of ultrasound compared with existing guidance techniques such as anatomical landmarks or ENS to trials targeting the refinement of the ultrasound technique. Examples of refinements include: ultrasound imaging techniques to visualise needles or catheters, evaluation of new echo-dense needles, use of needle guides, comparing difference in the site of access and re-evaluating effective dose of anaesthetic agents. However, there are ongoing clinical trials that are still evaluating ultrasound against traditional guidance methods, especially for complex interventions or new applications.

- The number of current clinical trials indicates that interest in developing both the technique of ultrasound guidance and its application is strong, which likely reflects ultrasound guidance becoming preferred clinical practice for major vascular access and placement of neural blocks.
- Overall, no current clinical trials were identified that add significantly to the current evidence base regarding the clinical utility of ultrasound guidance compared to alternative techniques for needle localisation for anaesthetic services.

Systematic reviews: Vascular access

Descriptive characteristics of included systematic reviews

Seven systematic reviews were identified that addressed the research questions of this assessment with respect to the safety and effectiveness of ultrasound to guide vascular access. The descriptive characteristics of these studies are shown in Table 20. This table shows the total number of included studies in each systematic review and also shows the number of included studies that were identified in the independent search undertaken for this assessment. The included studies in each systematic review generally aligned closely with the RCTs identified for inclusion in this assessment. Our searches identified >95% of the RCTs included in the systematic reviews (seeTable 78 and Table 79 Appendix J); however, only one of the four included studies in Krstenic et al. (2008) was identified. Our search was targeted to find RCT and systematic review evidence, and the three unidentified studies which did not meet these criteria were not identified by our search strategy.

In each review the comparator was the landmark technique. Each systematic review varied slightly in terms of its research questions, which were mainly related to the population focus. Some reviews had a broad focus, and others concentrated on specific populations. Also, studies varied in terms of inclusion or exclusion of Doppler ultrasound guidance, and in terms of whether ultrasound was used prior to needle insertion to guide the landmark technique, or was used during the needle-insertion in a real-time manner. For the purposes of this assessment studies using Doppler ultrasound and those using ultrasound solely for pre-location are excluded as this does not align with current clinical practice.

The meta-analysis by Wu et al. (2013) investigated the use of 2D ultrasound in adult and paediatric patients undergoing central venous access via the femoral, internal jugular and subclavian veins. Calvert et al. (2003) investigated the use of 2D and Doppler ultrasound for central venous and PICC access in adults and children via the femoral, internal jugular and subclavian veins. The meta-analysis by Keenan (2002) investigated the use of Doppler needle probe and external probe ultrasound techniques in patients requiring central venous access of the femoral, internal jugular and subclavian veins. Randolph et al. (1996) investigated the use of real-time ultrasound and Doppler ultrasound in adult and paediatric patients for internal jugular and subclavian venous access. The systematic review by Mehta et al. (2013) investigated the use of ultrasound guided central venous access in adult patients admitted to the emergency department. Sigaut et al. (2009) investigated the use of ultrasound to guide internal jugular vein access in paediatric patients. The systematic review by Krstenic et al (2008) investigated the ultrasound-guided placement of PICCs in adults by nurses.

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Table 20 Systematic reviews for major vascular access: study characteristics

Review	Question of the review	Inclusion/exclusion criteria	Number of included studies	Number of studies identified in our searches	Intervention Comparator	Heterogeneity
(Wu et al 2013) Broad review of patients undergoing CVC including separate outcomes reported for adults, children, and IJV, SCV and FV access sites	The effect of real-time ultrasound on the clinical outcomes of patients receiving central venous catheterisation	RCTs with participants who underwent central venous cannulation (no matter what the indication was) where the intervention was US and the comparator LM, reporting cannulation failure and clinical adverse events. Studies were excluded if patient allocation was not randomised or the method used was inappropriate, the intervention was auditory Doppler guidance or not clarified, the control was not LM, the puncture site was not central or full text was not available.	25 publications containing 26 RCTs (4,185 procedures)	24	US Landmark	Heterogeneity judged as low for hematoma, haemothorax and pneumothorax outcomes and moderate for cannulation failure and arterial puncture outcomes. Meta-analysis undertaken
(Calvert et al 2003b) Broad review of patients undergoing CVC including separate outcomes reported for adults, children, and IJV, SCV and FV access sites	To investigate the clinical and cost effectiveness of US for central venous access	RCTs of the clinical effectiveness of US or Doppler US for central venous lines were included. Comparator of landmark or surgical cut-down method. Only studies where at least one of: number of failed placements, complications, risk of failure on first attempt, number of attempts for successful cannulation, time or rate of success after failure by another technique were reported Studies were excluded if they were non-English language or quasi-random design,	18 RCTs of which 12 are relevant to this review	17	US Landmark	Failure rate, number of attempts and time outcomes reported for IJV cannulation in adults all had significant heterogeneity. Meta-analysis undertaken
(Keenan 2002) Broad review of patients undergoing CVC including outcomes reported for IJV, SCV and FV access sites	To update the relative effectiveness and safety of the use of US to place CVCs compared with the landmark method and to suggest a potential research agenda on the use of these catheters	Any RCT or quasi-randomised controlled trial. Any patient who required placement of a CVC using US as the intervention reporting at least one of: time to cannulation, success on first attempt, number of attempts, success rate.	18 studies (17 RCTs, 1 quasi-random)	17	US or Doppler US Landmark	Noted as significant (P<.00001 for failure rate, success on first attempt, and time to insertion, and P<.0002 for arterial puncture rate) Meta-analysis undertaken

Review	Question of the review	Inclusion/exclusion criteria	Number of included studies	Number of studies identified in our searches	Intervention Comparator	Heterogeneity
(Randolph et al 1996) Broad review of patients undergoing CVC including outcomes reported for IJV and SCV access sites	To estimate the effect of US guidance on central venous catheter placement	RCTs including adult or paediatric patients. US or Doppler US for placement of central venous catheters reporting any of: time of placement, number of attempts, rate of successful placement, complication rate or rate of success after failure with another method.	8 See note above	8	US or Doppler US Landmark	Non-significant heterogeneity except for time to catheter placement Meta-analysis undertaken
(Mehta et al 2013) Review of CVC specific to procedures performed on adults in the emergency department	To assess the success and complication rate between US and landmark CVC placement by ED physicians	ED patients over 18 years requiring CVC placement for any reason deemed necessary by the ED physician. Intervention US, comparator landmark. Reporting success rates. Studies were excluded if patients received CVC for cardiopulmonary resuscitation	1	1	US Landmark	N/A
(Sigaut et al 2009b) Review of CVC specific to procedures performed in children where access was via the internal jugular vein	To determine the advantages of using US prelocation and/or guidance, in comparison with the classical landmark method during IJV access in children and infants	Only English language published articles were included	5 of which 3 are relevant to this review (the other two studies consider US prelocation rather than guidance)	4/5 (3/3 relevant studies)	US Landmark	Acceptable according to the following criteria: I^2>40% and P<0.1 with the exception of number of punctures and incidence of haematoma, haemothorax and pneumothorax.
(Krstenic et al 2008) Review of PICC placement by nurses in adult patients	In adult patients undergoing a PICC procedure does nurse use of 2-D US compared with the landmark method reduce first time PICC insertion failure	Studies were included if they assessed adult patients undergoing a PICC procedure by a nurse using 2D ultrasound insertion compared with the landmark method and reported the number of successful and failed insertion attempts	4 (no RCTs, 1 controlled trial)	1 controlled trial)	US Landmark	Chi squared test for heterogeneity not significant Meta-analysis undertaken

Abbreviations: CI, confidence interval. CVC, central venous catheter. IJV, internal jugular vein. SCV, subclavian vein. FV, femoral vein. NR, not reported

Critical appraisal of Systematic reviews

The quality of the systematic reviews was assessed using the AMSTAR instrument (Appendix I).

Table 21 summarises the critical appraisal of the included systematic reviews of ultrasound guidance for major vascular access. Three systematic reviews were judged as being good quality with four reviews being judged as poor quality. All reviews provided *a priori* study design. Information pertaining to the scientific quality of the included studies was well reported and was used appropriately to formulate conclusions. In all studies where a meta-analysis was conducted the methods used to combine the findings were appropriate. Only three of the systematic reviews explicitly stated duplicate study selection and extraction was conducted. Comprehensive literature searches were poorly conducted or reported in four of the reviews with either only one database being searched (two studies) or failure to report the date limits for the searches (two studies). Excluded studies were listed in two systematic reviews; however, failure to report this detail may be due to the nature of publishing a systematic review in a peer reviewed journal where space is limited. Baseline characteristics of patients were poorly reported in all but two of the reviews, as was the likelihood of publication bias. No review adequately reported conflict of interest. In some instances it was not possible to determine from a systematic review whether or not a certain element had been completed or not. These were recorded as 'cannot answer', and were given a score of zero.

Table 21 Methodological quality appraisal of systematic reviews on ultrasound guidance for vascular access using the AMSTAR tool (Shea et al 2007)

Question	Review characteristics	(Wu et al 2013)	(Calvert et al 2003b)	(Keenan 2002)	(Randolph et al 1996)	(Mehta et al 2013)	(Sigaut et al 2009b)	(Krstenic et al 2008)
1	Was an *a priori* design provided?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2	Was there duplicate study selection and data extraction?	Yes	Cannot answer	Cannot answer	Cannot answer	Cannot answer	Yes	Yes
3	Was a comprehensive literature search performed?	Yes	Yes	No	No	Yes	No	No
4	Was the status of publication (i.e. grey literature) used as an inclusion criterion?	Yes	Yes	No	No	Cannot answer	Cannot answer	Yes
5	Was a list of studies (included and excluded) provided?	No	Yes	No	Yes	No	No	No
6	Were the characteristics of the included studies provided?	No	Yes	No	No	Yes	No	No
7	Was the scientific quality of the included studies assessed and documented?	Yes	Yes	Yes	Yes	Yes	No	Yes
8	Was the scientific quality of the included studies used appropriately in formulating conclusions?	Yes	Yes	Yes	Yes	Yes	No	Yes
9	Were the methods used to combine the findings of studies appropriate?	Yes	Yes	Yes	Yes	NA	Yes	Yes
10	Was the likelihood of publication bias assessed?	Yes	No	No	No	No	Yes	No
11	Was the conflict of interest stated?	No	No	No	No	No	No	No
Totals	Yes	8	8	4	5	5	4	6

Question	Review characteristics	(Wu et al 2013)	(Calvert et al 2003b)	(Keenan 2002)	(Randolph et al 1996)	(Mehta et al 2013)	(Sigaut et al 2009b)	(Krstenic et al 2008)
	No	3	2	6	5	3	6	5
	Cannot answer	-	1	1	1	2	1	-
	Not applicable	-	-	-	-	1	-	-

NA: not applicable

Is it safe?

Five of the seven systematic reviews reported on safety outcomes (Table 80, Appendix K). Meta-analyses by Wu et al. (2013) and Keenan (2002) found ultrasound guided central venous catheterisation was associated with significantly lower risk of arterial puncture than the landmark method ($P<0.001$). Subgroup analyses by Wu et al. (2013) found that there was a significant decrease in puncture risk when access was via the internal jugular vein and subclavian veins. There was no significant difference for the femoral vein. In children, neither Wu et al (2013) nor Sigaut et al. (2009) found significant difference in risk of arterial puncture between the ultrasound and landmark methods.

Wu et al. (2013) found a significantly lower risk of haematoma associated with ultrasound guidance than landmark. This was true for the internal jugular and subclavian veins when considered separately. There was no significant difference between ultrasound and landmark techniques for the femoral vein. In children, Wu et al. (2013) found no significant difference in haematoma formation between ultrasound and landmark guidance; however, Sigaut et al. (2009) found ultrasound use had significantly lower odds ratio of haematoma than the landmark method.

In the adult population, the risk of pneumothorax and haemothorax were significantly lower with ultrasound use than the landmark method ($P<0.05$ and $P<0.01$ respectively) (Wu et al 2013). A subpopulation analysis found significantly lower risk of pneumothorax in patients where access was via the internal jugular vein. For access via the subclavian vein the difference was not significant and access via the femoral vein was not reported. For haemothorax, a subpopulation analysis found significantly lower risk in patients where access was via the subclavian vein. For access via the internal jugular vein the difference was not significant. Access via the femoral vein was not reported.

Placement complications were reported by Calvert et al. (2003) and were significantly lower in patients receiving ultrasound guided vascular access via the internal jugular and subclavian veins (data for femoral vein access was not reported). In children, ultrasound guided access via the internal jugular vein had a significantly lower rate of complication compared to landmark (subclavian and femoral veins were not reported). The rate of overall complication was reported by Wu et al. (2013) and Keenan (2002) both of whom found a significantly lower risk of complication with ultrasound use.

Is it effective?

All seven of the systematic reviews reported on effectiveness outcomes. The most commonly reported outcomes were the failure rate of catheterisation, the number of attempts and the time required for the procedure. For the four studies that reported on central venous access placement in adults, ultrasound significantly reduced the failure rate of catheterisation in all studies (Table 81, Appendix K). In the two studies that also included a subgroup group analysis on the location of the access, the reduction in failed attempts associated with ultrasound was statistically significant in all sites except the femoral vein in Calvert et al. (2003) (P=0.09). In children both Wu et al. (2013) and Sigaut et al. (2009) reported no significant difference in failure rates for ultrasound compared to landmark, although in all cases outcomes favoured ultrasound-guidance.

For the two studies that reported on the effect of ultrasound on the number of attempts required to successfully place the central venous catheter in adults, ultrasound was associated with a statistically significant reduction in each study (Calvert et al 2003a; Keenan 2002). In a subpopulation analysis on location of access by Calvert et al. (2003) there was a statistically significant reduction in the number of attempts at each site. In children, Sigaut et al. (2009) found ultrasound was associated with significantly fewer attempts required to achieve successful catheterisation than the landmark method.

Three studies reported on the time required for successful catheterisation, Calvert et al. (2003), Randolph et al. (1996) and Sigaut et al. (2009). None reported a significant difference between the ultrasound and landmark groups for either adult or paediatric populations.

Mehta et al. (2013) reported one RCT that found a significantly higher relative success rate associated with the use of ultrasound guided central venous access in the emergency department.

For the one study reporting on the placement of PICCs by nurses in adult patients, ultrasound was associated with a significantly lower risk of failure than the landmark technique.

Summary

From the seven included systematic reviews shown above, four were identified as being of relevance in terms of the patient populations and the questions of the review, and of appropriate quality.

Wu et al. (2013) is a good quality systematic review that reports central venous outcomes including outcomes for a broad range of relevant subpopulations (adults, children, internal jugular vein access, subclavian vein access and femoral vein access) and form the basis of our analysis. In addition to this, two supplementary reviews have been identified; Sigaut et al. (2009) reports outcomes specific to paediatric cardiac patients and Mehta et al. (2013) reports outcomes specific to adults being treated in an emergency department setting.

Krstenic et al. (2008) is a good quality systematic review that reports outcomes of PICC placement in adult patients by nurses. This is the only systematic review identified that reports outcomes for PICC placement. No systematic reviews were identified that report outcomes for central arterial access.

Key findings

- Seven systematic reviews were identified for appraisal.
- Four systematic reviews were of appropriate quality and reported on specific research questions that were of direct relevance to this assessment. One of these was a recent study of good quality which was a broad review of central venous access.
- No systematic review was identified which investigated central arterial access.
- For safety, ultrasound guidance is associated with a statistically significant reduction in the risk of arterial puncture, haematoma, pneumothorax and haemothorax.
- For effectiveness, ultrasound guidance is associated with a statistically significant reduction in the failure rate of procedures and the number of attempts to successfully place a central line
- The identified systematic reviews are applicable to this review with respect to their scope and research question.
- Our independent literature searches identified the majority of studies which were included in the systematic reviews. Studies not identified in our strategy were non-randomised comparative studies.
- Overall the evidence provided by the systematic reviews was consistent, both in terms of the included studies and the overall results and conclusions.
- RCT evidence published after the search date of the most up-to-date, good quality and appropriate systematic review (Wu et al 2013) or which provided evidence that was not included in the identified systematic reviews shall be used to supplement the systematic review evidence.

Randomised controlled trials: Vascular access

Descriptive characteristics of included studies

From our independent literature searches, included RCTs were selected for appraisal that were published after the search date of the most up-to-date, good quality and appropriate systematic review (Wu et al 2013), or which provided evidence that was not included in the identified systematic reviews (that is, ultrasound-guided central arterial access).

Tabulated details of the RCTs are shown in Appendix M.

Study information

A total of nine RCTs investigated ultrasound-guided vascular access via an artery (n=2), central vein (n=5) or a peripherally inserted central catheter (PICC) (n=2), all of which compared ultrasound guided vascular access with landmark guided access were included (Table 84, Appendix M). Eight of the studies were randomised and two studies were pseudo-randomised trials (Iwashima et al 2008; Miller et al 2002).

The number of patients treated in each of the included studies ranged from 33 to 240 (mean 108 patients). There was variation in both the access site and the underlying clinical need for vascular access. There were two studies reporting arterial access; in these studies access was obtained either via the femoral artery for a purpose which was not reported (Dudeck et al 2004) or via the axillary artery for haemodynamic monitoring and blood gas sampling (Killu et al 2011). In the five studies where access was via a central vein; two reported on the internal jugular vein, one detailed access via the femoral and two studies evaluated a combination of femoral, internal jugular and/or subclavian veins. Reasons for venous access were elective surgery (one study), heart disease (one study) and various clinical needs (two studies). One study did not report reasons for the required vascular access. In the two studies where access was via a PICC line, one failed to report the location of puncture while the other reported placement via the basilica vein. The clinical need for PICC line placement was required intravenous (IV) therapy lasting longer than 7 days or administering chemotherapy with or without total parental nutrition.

Of the nine included studies, three used proceduralists with experience in vascular access using the landmark technique. In one study only inexperienced residents conducted the procedures and one study used a combination of experienced and inexperienced operators. Operator experience was unclear in the five remaining studies. Operators included anaesthesiologists (one study), radiologists (one study), nurses (one study), PICC specialists (one study), residents (one study) and a combination of operators (two studies).

Patient population

Study characteristics differed between studies (Table 85, Appendix M). Most studies were concerned with catheter insertion in adult patients (seven studies) while two studies reported on catheter insertion in paediatric populations. In the studies that involved adults, patients were scheduled for interventional radiology, haemodynamic monitoring (or blood gas sampling), elective, emergency or cardiovascular surgery, admitted to ICU or ED or were patients undergoing chemotherapy. Paediatric patients were scheduled for cardiac surgery or IV therapy lasting longer than seven days.

Inclusion criteria were consistent across most studies, where all patients of the relevant indication, and in some cases patients of a certain age, were considered for inclusion Exclusion criteria varied between studies, and included (but are not limited to) age, pregnancy and failure to obtain consent criteria. In addition, previous intervention at the proposed site of access, patients contraindicated for the intervention or abnormal anticoagulation parameters were cited as exclusion criteria. One study did not report any exclusion criteria. Of the four studies that reported how many patients were excluded, this ranged from four to 257. Five studies did not report this information.

Instrumentation

The ultrasound devices used as the intervention in the included studies are detailed in Table 86 (Appendix K). In total, equipment supplied by seven manufacturers was used by the authors of the included studies. Manufacturers included; Toshiba (Tokyo, Japan), SonoSite (Bothell, WA, USA), Dymax (Dymax Corp. Pittsburgh, PA, USA), Bard (Murray Hill, New Jersey, USA), Bard-Dymax II (Access Systems Inc. Salt Lake City, UT), Ecoscan (manufacturer not reported) and GE Healthcare (Fairfield, CT, USA). The frequency of ultrasound used was most commonly was7.5 MHz.

One study (Hayashi and Amano 2002) investigated two interventions, comparing ultrasound with a 3.75 MHz or a 7.5 MHz scanning probe to landmark guided access. For the remaining eight studies the comparison was a single ultrasound technique /instrument with a landmark method. Needle guides were not used. The most commonly used landmark was palpation of either the femoral, axillary or carotid arteries. One study used respiratory jugular venodilation, one study used visualisation and palpation of the peripheral venous system and one study did not report the anatomic landmark used. Finally, two studies (Airapetian et al 2013; Ray et al 2013) compared ultrasound guidance to two comparators; an anatomic landmark (4 cm below the angle of the mandible or the sternocleidomastoid muscle) and ultrasound marking (UM) where ultrasound was used to locate the internal jugular or femoral vein; however, the needle puncture was performed without ultrasound guidance.

The most widely used needle in the intervention groups was an 18 G (four studies). However, 20 G and 21 G needle and a 1.9-3.0F catheter were each used in one study. The type of needle used was not reported in two studies. Sonographically dense needles were not reported to have been used. For the comparator group the type of needle used was poorly reported with four studies not reporting this information. For the five studies that did report this information the type of needle used was a 14 G or 19 G needle or a 1.9-3.0 F catheter.

Ultrasound dense needles were not reported in any study and needle guides were not used.

Critical appraisal of randomised controlled trials: Vascular access:

Nine RCTs were identified that addressed the research questions of the current assessment with respect to safety and effectiveness of ultrasound guidance for vascular access. A checklist adapted from Van Tulder et al (1997) and Downs and Black (1998) was used by two independent assessors to determine the methodological quality of the included RCTs (Table 75). The internal validity was rated as moderate in three RCTs and poor in six. The external validity was rated as good in five RCTs and moderate in four.

Two of the RCTs reported to have undertaken power calculations and recruited the sample size necessary to detects statistically meaningful differences between treatment groups(Airapetian et al 2013; Li et al 2013b).

Three of the RCTs reported appropriate randomisation techniques (computer generated), and four RCTs failed to report the method of randomisation. Two studies were identified as pseudo RCTs, having used alternate allocation to designate patients to treatments. Only two RCTs reported concealment of treatment allocation. None of the RCTs reported that the patient was blinded to the intervention and only one reported that the outcome assessor was blinded. Given the nature of the intervention it would be impossible for the provider to be blinded and thus all studies were marked as not applicable for this study characteristic.

Eight of the RCTs clearly described their inclusion criteria and seven clearly described their exclusion criteria. One RCT reported inclusion criteria but no exclusion criteria. In seven of the RCTs the patient groups in each arm were similar at baseline. In one RCT the patients at baseline differed significantly in age and gender and although not analysed statistically, there were differences in the percentage of patients described as difficult (had severe peripheral vascular disease, coagulopathy, obesity, abnormal anatomy or history of intravenous drug abuse) between the treatments. One RCT did not report baseline characteristics for both treatments.

All RCTs employed a short term follow-up (outcome assessment ≤ 3 months after randomisation). None reported any long-term follow-up outcomes (> 3 months after randomisation). However, one study did report the patient's degree of comfort after PICC placement at 3 months. While no study reported on losses to follow-up it appeared from the reporting of patient numbers in the analyses or from flow diagrams that there were no losses in five of the RCTs (Airapetian et al 2013; Dudeck et al 2004; Miller et al 2002). In two of the RCTs the losses to follow-up were unclear as they did not report patient numbers with their analyses (Hayashi and Amano 2002; Killu et al 2011), although one of these RCTs did report that four out of fifteen landmark procedures were aborted (Killu et al 2011). One RCT reported 14 and18 losses in the ultrasound and landmark treatments respectively (63 % follow-up overall), owing to not being able to successfully access the femoral vein (Iwashima et al 2008). The remaining RCT described losses to follow-up in a CONSORT diagram of recruited patient numbers although there is a lack of consistency between the patient numbers reported and the total numbers analysed (Li et al 2013b).

Is it safe?

Adverse events are reported numerically and textually for most of the included RCTs (Table 87, Appendix M). The textual reporting is a reflection of the rarity of these events. To overcome this limitation, and capture adverse event data, the data extractions included the textual description of recorded adverse events. Negative statements were only converted to numerical data if text explicitly stated the absence of the adverse event.

All nine included studies reported on safety outcomes, most studies reported unwanted arterial or venous puncture, some studies also reported the incidence of procedural complications, haematoma, pneumothorax and nerve injury. Subpopulations or secondary outcomes which were considered by a small number of studies are reported in text only.

Arterial access

Two studies investigated the safety of ultrasound placement of arterial central lines compared to the landmark technique (Dudeck et al 2004; Killu et al 2011). Both studies reported no significant difference in the number of venous punctures and the incidence of haematoma between the ultrasound and landmark groups. There were no procedural complications in either the landmark or ultrasound groups in both studies, and no incidences of nerve injury were observed for either technique. In Dudeck et al. (2004) no patients suffered from pneumothorax. This outcome was not reported in Killu et al. (2011). Dudeck et al. (2004) reported on two subpopulations of patients; those with a leg circumference greater than 60 cm and those with a weak arterial pulse. In line with the overall population, patients in both subpopulations reported no significant difference in the incidence of adverse events of any kind between the ultrasound and landmark groups.

Venous access

Five studies investigated the safety of ultrasound compared to the landmark technique, four in adult patients and one in paediatric patients. Considering adult patients, Airapetian et al (2013) found ultrasound guidance significantly reduced the incidence of arterial puncture compared to the landmark technique. In contrast, Hayashi et al. (2002) and Ray et al.; (2013) reported a non-significant trend for fewer arterial punctures using ultrasound guidance as compared to the landmark method. Airapetian et al. (2013) also found ultrasound guidance significantly reduced the number of mechanical complications and the incidence of haematoma; however, there was no significant difference in events of catheter colonisations between the ultrasound and landmark groups. This study reported no incidences of pneumothorax or nerve injury in either group. Ray et al. (2013) reported one haematoma in the landmark group compared to none in the ultrasound group; however, the statistical significance of this is not reported. Miller et al. (2002) reported no significant differences in overall complication rate between the ultrasound and landmark groups.

In children, Iwashima et al. (2008) reported significantly fewer femoral artery punctures using ultrasound compared with the landmark method.

Two studies investigated the ultrasound-guided placement of PICC compared with a landmark technique, Li et al (2013) in adult patients and de Carvalho Onofre et al. (2012) in paediatric patients. de Carvalho Onofre et al. (2012) did not report any safety outcomes. In adults, Li et al. (2013) reported no significant difference in the total number

of complications between the ultrasound and landmark groups. The use of ultrasound guidance was associated with a significantly lower rate of mechanical phlebitis compared with landmark guidance. There was no incidence of infection or venous thrombosis in patients who received ultrasound guidance, compared to incidences of 6.3 and 8.3 per cent respectively for infection and venous thrombosis in patients who received landmark guidance (P= not significant). There was no significant difference in the rates of contact dermatitis between the two groups.

Is it effective?

The choice of outcome measures varied between trials. Most studies reported needle redirects and/or skin puncture, the success rate of the placement and the time taken for needle placement as outcomes (Table 88, Appendix M). We have discussed any subpopulations or secondary outcomes which were considered by a small number of studies in the text only.

Two studies investigated the effectiveness of ultrasound placement of arterial central lines compared to the landmark technique (Dudeck et al 2004; Killu et al 2011). Both studies found no significant difference in the number of needle redirects or skin punctures and the time for the procedure. Dudeck et al. (2004) investigated a subpopulation of patients with a leg circumference of greater than 60 cm and patients with a weak arterial pulse. In each of these subpopulations the ultrasound group had significantly fewer needle redirects and skin punctures ($P < 0.05$) than the landmark group. The ultrasound group had a significantly shorter procedure time than the landmark group for both subpopulations ($P < 0.04$).

Five studies investigated the effectiveness of ultrasound placement of central venous lines compared to the landmark technique, four in adult patients and Iwashima et al. (2008) in paediatric patients. Considering adult patients, Airapetian et al. (2013) and Miller et al. (2002) both found ultrasound guidance significantly reduced the number of skin punctures per patient compared to the landmark technique (and compared to ultrasound marking technique in Airapetian et al. (2013)). Airapetian et al. 2013 also found that ultrasound guidance had a significantly higher success rate than the landmark method. In contrast, Hayashi et al. (2002) and Ray et al. (2013) found that while ultrasound had higher success rates than the landmark method; the difference was not significant. Hayashi et al. (2002) also compared the access rate (the percentage of procedures that were successful at first puncture) of the ultrasound and landmark methods and found ultrasound was significantly more successful. In addition, Hayashi et al. (2002) found no significant difference when comparing an ultrasound operating at 3.75 MHz and an ultrasound operating at 7.5 MHz for all outcome measures. The time taken for needle placement was reported in two studies; both Airapetian et al. (2002) and Miller et al. (2002) found ultrasound guidance resulted in significantly faster needle placement than both the landmark and ultrasound mark techniques. Ray et al. (2013) found ultrasound guidance resulted in significantly faster vascular access and catheter placement than the landmark method however there was no statistically significant difference between the ultrasound guidance an ultrasound mark groups.

In children, Iwashima et al. (2008) found that while ultrasound had higher success rates than the landmark method, the difference was not statistically significant. Similarly, the percentage of patients whose procedure was complete in less than five minutes was similar in both cohorts.

Two studies investigated the effectiveness of ultrasound placement of PICCs compared to the landmark technique, Li et al. (2013) in adult patients and de Carvalho Onofre et al. (2012) in paediatric patients. In adults, Li et al. (2013) reported a success rate of 100 per cent for PICCs inserted in the ultrasound group compared to a 96 per cent success rate in the landmark group; however, the statistical significance was not reported. This study also reported the degree of patient comfort and found patients in the ultrasound group were significantly more comfortable than those in the landmark group at one week, one month, two months and three months post insertion. Unplanned catheter removal was significantly lower in the ultrasound group although measures of needle tip malposition during and after needle placement were not significantly different between the two groups. In children, de Carvalho Onofre et al (2012) found significantly improved success rates and access rates for the ultrasound-guided group compared to the landmark-guided group. The ultrasound guided PICC placement was significantly faster than the landmark guided PICC placement.

Killu et al. (2011) investigated how operator experience influenced the effectiveness of ultrasound guided central venous access by comparing the time taken for needle placements performed by Fellows and residents. In the ultrasound group, fellows took an average of 6.02 ± 3.20 minutes and residents took an average of 8.58 ± 5.79 minutes. The difference between these times was not significant. In the landmark group fellows took an average of 5.60 ± 4.31 minutes which was not significantly different from the ultrasound group. Residents in the landmark group took an average of 14.82 ± 12.14 minutes to perform the procedure, which was significantly slower than Fellows in the landmark group and both Fellows and residents in the ultrasound group.

Miller et al. (2002) also examined operator experience in a sub population of patients with severe peripheral vascular disease in whom central venous access was predicted to be difficult. Inexperienced operators required an average of 1.48 ± 0.87 attempts in the ultrasound group and 3.29 ± 2.79 attempts in the landmark group. Procedure times were 1.93 ± 3.77 minutes and 8.58 ± 12.84 minutes in the ultrasound and landmark groups respectively. Experienced operators required an average of 1.36 ± 0.67 attempts in the ultrasound group and 2.67 ± 2.08 attempts in the landmark group. Procedure times were 0.93 ± 1.37 minutes and 3.0 ± 2.0 minutes in the ultrasound and landmark groups respectively. No P-values were reported for these outcome measures.

Meta-analysis: Vascular access

The total evidence base included in the meta-analysis for vascular access comprised of 34 RCTs. These studies were identified in the independent search of electronic databases and pearling the reference lists of retrieved systematic reviews (Table 20). Twenty five of the identified RCTs have previously been included in published systematic reviews. The remaining nine RCTs that have not been previously described were subjected to quality appraisal data extraction for information relevant to safety and effectiveness (Table 87 and Table 88, Appendix M). These RCTs are described in detail in the previous section. Extracted data were then pooled with relevant data from RCTs reported by the included systematic reviews, which was extracted independently by two reviewers. Where data extraction from the systematic reviews was not possible, data was extracted from the primary studies. Data from studies not represented in the identified systematic reviews (for example, central arterial catheter access) were also extracted.

Safety:

Safety (adverse) events reported to be associated with major vascular access protocols, irrespective of guidance method, are inappropriate vascular puncture, haematoma, catheter misplacement or malfunction, nerve damage or paraesthesia, infection, pneumothorax and haemothorax.

Inappropriate vascular puncture

Twenty eight of the 34 report event data for inappropriate vascular puncture (IVP) and represents a total patient population of 4,409. The prevalence of IVP for this population was 2.3 per cent and 9.2 per cent for vascular access guided by either the ultrasound or landmark guidance methods, respectively. The analysis showed that ultrasound guidance of vascular access significantly reduced the risk of vascular puncture compare with the landmark technique (RR 0.32, 95% CI: 0.22-0.47, $P < 0.001$, Figure 6, Table 22). The risk of IVP was significantly lowered with ultrasound use for access via the IJV (RR 0.28, 95% CI: 0.17-0.48, $P < 0.001$, Table 22), the subclavian vein (RR 0.17, 95% CI: 0.04-0.76, $P = 0.021$, Table 22) and for studies where the access site was mixed (RR 0.24, 95% CI: 0.06-0.93, $P = 0.038$, Table 22). There was no statistically significant difference in risk of IVP between ultrasound and landmark techniques for arterial and femoral vein access (Table 22). The risk of IVP was significantly lowered by ultrasound use for both adult (RR 0.28, 95% CI: 0.17-0.46, $P < 0.001$, Table 22) and paediatric populations (RR 0.43, 95% CI: 0.19-0.96, $P = 0.041$, Table 22).

Figure 6 Individual study and the pooled (random effects model) risk ratios for inappropriate vascular puncture during ultrasound or landmark guided placement of central lines

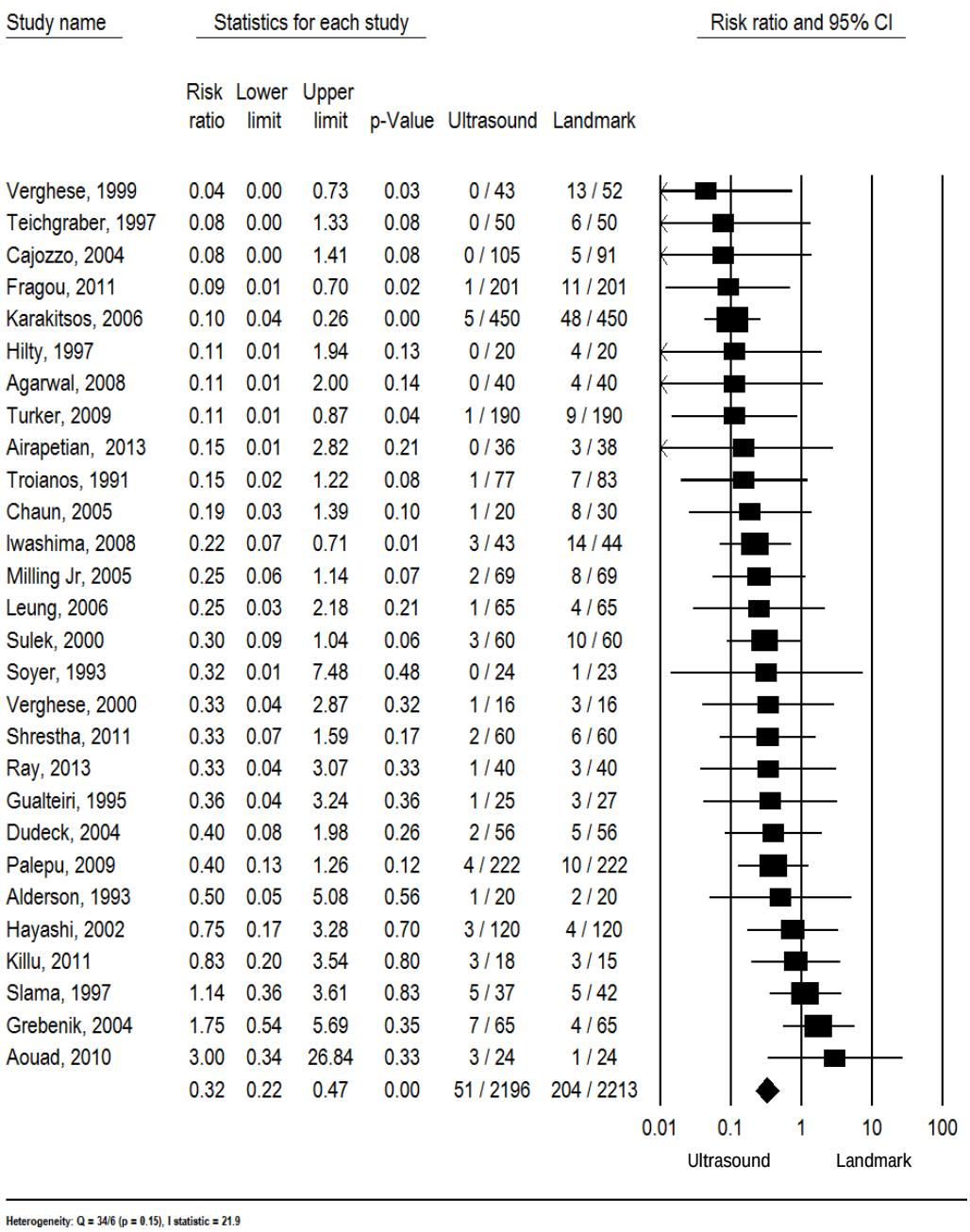


Table 22 Summary of meta-analysis statistics for overall pooled analysis and subgroups based on access site or patient age for the risk ratios associated with inappropriate vascular puncture during ultrasound or landmark guided placement of central lines.

Grouping	No of studies	Point estimate	CI_{lower} (95%)	CI_{upper} (95%)	P value
Overall	28	0.32	0.22	0.47	P < 0.001
Arterial	2	0.54	0.12	2.45	P = 0.421
FV	3	0.32	0.08	1.23	P = 0.098
IJV	18	0.28	0.17	0.48	P < 0.001

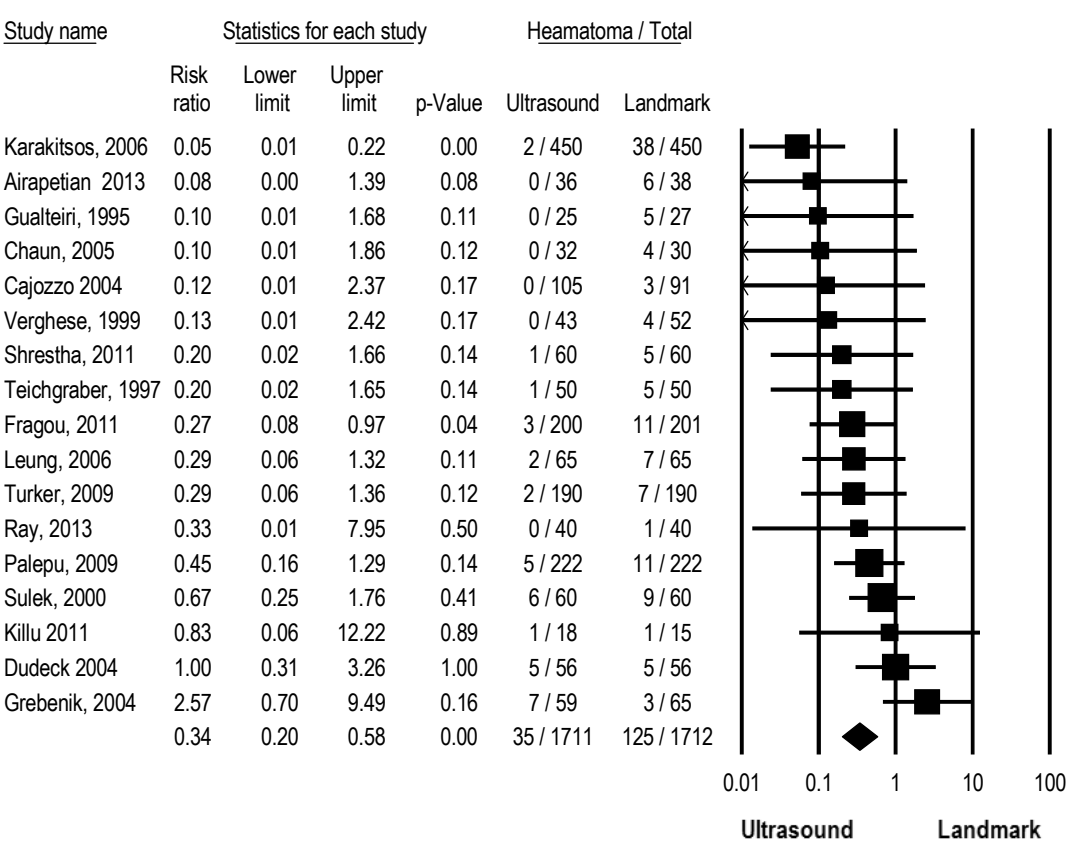
Grouping	No of studies	Point estimate	CI_{lower} (95%)	CI_{upper} (95%)	P value
SCV	2	0.17	0.04	0.76	P = 0.021
Mixed sites	3	0.24	0.06	0.93	P = 0.038
Adults	16	0.28	0.17	0.46	P< 0.001
Children	7	0.43	0.19	0.96	P = 0.041

Data are reported as the pooled risk ratio using a random effect model. CI, confidence interval; FV, femoral vein; IJV, internal jugular vein; SCV, subclavian vein

Haematoma

Seventeen of the 34 RCTs report event data for haematoma and represents a total patient population of 3,423. The prevalence of haematoma for this population was 2.05 per cent and 7.30 per cent for vascular access guided by either the ultrasound or landmark guidance methods, respectively. The analysis showed that ultrasound guidance of vascular access significantly reduced the risk of haematoma compare with the landmark technique (RR 0.34, 95% CI: 0.20-0.58, P < 0.001, Figure 7, Table 23). The risk of haematoma was significantly lowered with ultrasound use for access via the IJV (RR 0.36, 95% CI: 0.22-0.65, P < 0.001, Table 23), the subclavian vein (RR 0.25, 95% CI 0.09-0.76, P = 0.014, Table 23) and for studies where the access site was mixed (RR 0.10, 95% CI: 0.01-0.90, P = 0.040, Table 23). The risk of haematoma was significantly lowered by ultrasound use for adults (RR 0.36, 95% CI: 0.21-0.60, P < 0.001, Table 23). All other sub-group analysis returned non-significant differences between guidance methods. In addition, one RCT reported no incidences of haematoma in either the intervention or control groups.

Figure 7 Individual study and the pooled (random effects model) risk ratios for haematoma formation during ultrasound or landmark guided placement of central lines



Heterogeneity: Q = 25.1(p = 0.069), I statistic = 36.2

Table 23 Summary of meta-analysis statistics for overall pooled analysis and subgroups based on access site or patient age for risk ratios associated with haematoma formation during ultrasound or landmark guided placement of central lines.

Grouping	No of studies	Point estimate	CI_{lower} (95%)	CI_{upper} (95%)	P value
Overall	17	0.34	0.20	0.58	P < 0.001
Axillary artery	1	0.83	0.45	15.49	P = 0.903
Femoral artery	1	1.00	0019	5.26	1.000
IJV	12	0.36	0.20	0.65	P = 0.001
SCV	3	0.25	0.09	0.76	P = 0.014
Mixed	2	0.10	0.01	0.90	P = 0.040
Adults	13	0.36	0.21	0.60	P < 0.001
Children	3	0.86	.24	3.08	P = 0.823

Data are reported as the risk ratio pooled using a random effect model. CI, confidence interval; FV, femoral vein; IJV, internal jugular vein; SCV, subclavian vein

Pneumothorax

Seven of the 34 RCTs report event data for pneumothorax and represents a total patient population of 1,847. The prevalence of pneumothorax for this population was 0.11 per cent and 3.02 per cent for vascular access guided by either the ultrasound or landmark guidance methods, respectively. The analysis showed that ultrasound guidance of vascular access significantly reduced the risk of pneumothorax compared to the landmark technique (RR 0.21, 95% CI: 0.06-0.71, P = 0.01, Figure 8, Table 24). All sub-group analysis returned non-significant differences between guidance methods; however, all demonstrated a trend towards the ultrasound intervention. Five studies reported no incidence of pneumothorax in either the intervention or control groups.

Figure 8 Individual study and the pooled (random effects model) risk ratios for pneumothorax formation during ultrasound or landmark guided placement of central lines

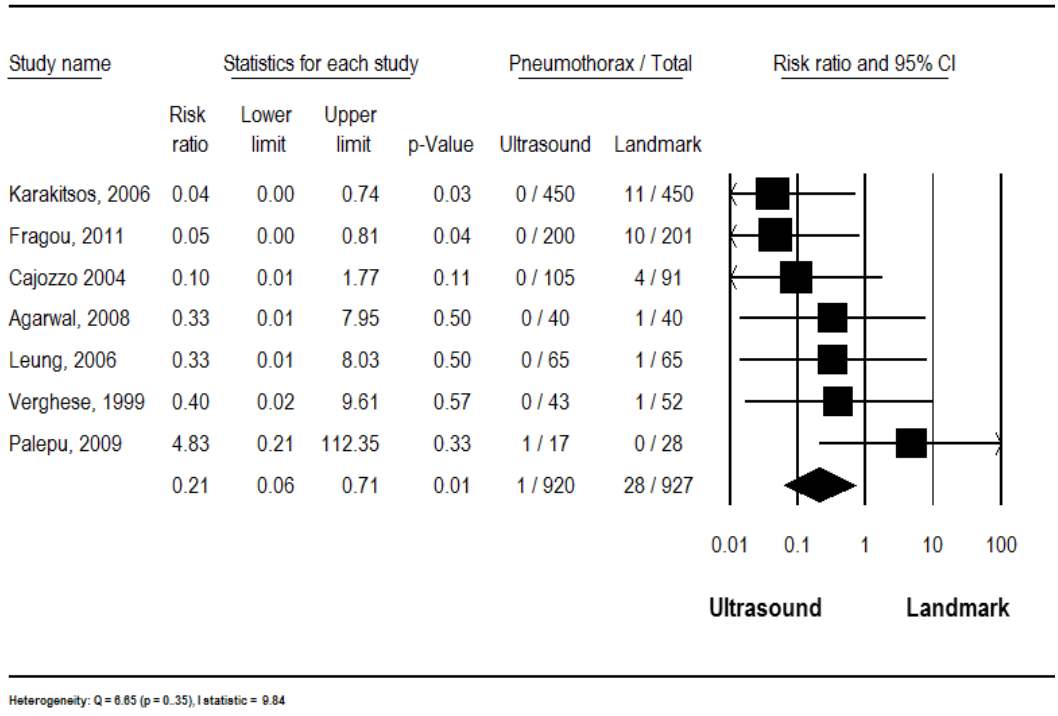


Table 24 Summary of meta-analysis statistics for overall pooled analysis and subgroups based on access site or patient age for risk ratios associated with pneumothorax formation during ultrasound or landmark guided placement of central lines

Grouping	No of studies	Point estimate	CI_{lower} (95%)	CI_{upper} (95%)	P value
Overall	7	0.21	0.06	0..71	P = 0.01
IJV	4	0.19	0.03	0.89	P = 0.093
SCV	2	0.41	0.03	5.64	P = 0.506
Mixed	1	0.09	0.01	3.70	P = 0.209
Adults	4	0.22	0.03	1.44	P = 0.114
Children	1	0.40	0.01	20.88	P = 0.651

Data are reported as the risk ratio pooled using a random effect model. CI, confidence interval; FV, femoral vein; IJV, internal jugular vein; SCV, subclavian vein

Other adverse events

Nine of the 34 RCTs report event data for other adverse events (aggregate adverse event data, catheter related adverse events, haemothorax, infection and nerve damage).

The incidence of adverse events reported as aggregate data for this population (2 studies, total population 220) was 36.6 per cent and 34.4 per cent with a RR of 0.92 (95% CI: 0.50-1.69, P = 0.79, Figure 9, Table 25) for vascular access guided by either the ultrasound or landmark guidance methods, respectively.

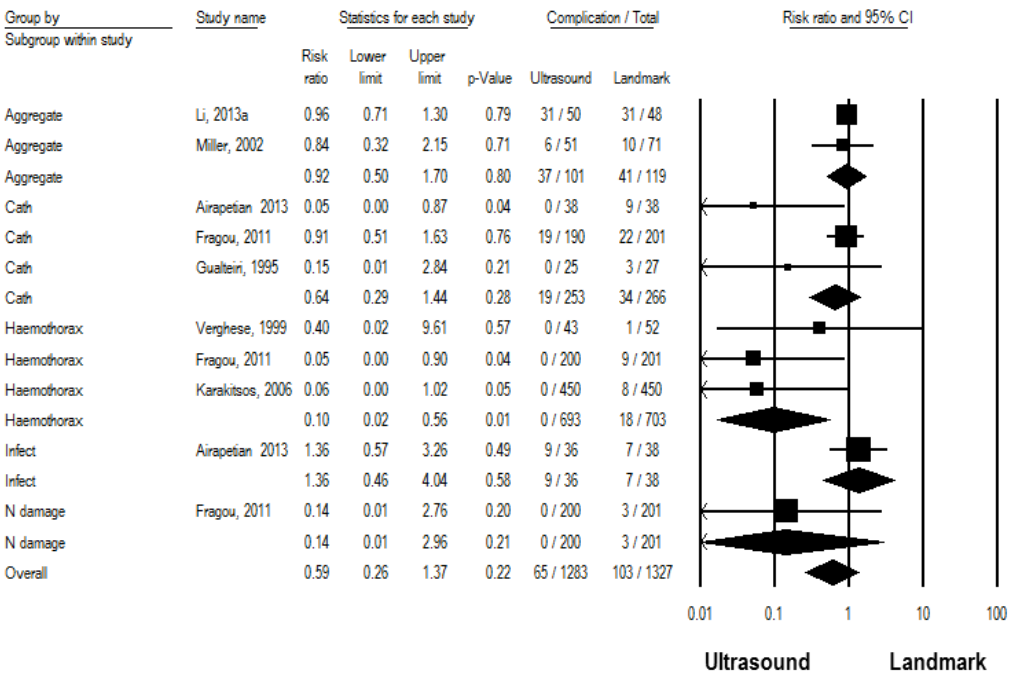
Three of six studies that reported on catheter related events recorded the occurrence of adverse events and these three studies represent a patient population of 519. In this population, adverse events occurred in 7.51 per cent and 12.78 per cent when vascular access was performed using either the ultrasound or landmark guidance methods, respectively. Statistically, both procedures were equivalent for the clinical scenarios reported in these included studies (RR 0.64, 95% CI: 0.29-1.43, P = 0.282, Figure 9, Table 25).

In studies that reported on haemothorax events the use of ultrasound to guide vascular access significantly reduced the risk of this adverse event occurring (RR 0.10, 95% CI: 0.02-0.56, P = 0.009, Figure 9, Table 25). . Furthermore, three of the six studies (total population 1396 patients) reported the occurrence of haemothorax events, the prevalence of this adverse event was zero per cent for the ultrasound technique compared with 2.56 per cent for vascular access using a traditional landmark technique.

Vascular access is a potential route of infection. However, this potential adverse event was only reported in three studies and only one of these recorded the occurrence of events in either the ultrasound or landmark groups. In this small-scale study of 74 patients, the incidence of infection was 25 per cent and 18 per cent for vascular access guided by either the ultrasound or landmark guidance methods, respectively. This apparent difference in the occurrence of infection was not statistically significant (RR 1.356, 95% CI: 0.46-4.04, P = 0.583, Figure 9, Table 25).

The final adverse event reported in the included studies was that of nerve damage. Four of the five studies stated there was no occurrence of nerve damage in either ultrasound or landmark groups. In the remaining study that included 401 patients, the prevalence of nerve damage was zero per cent and 1.49 per cent for vascular access guided by either the ultrasound or landmark guidance methods, respectively. The relative risk of not suffering nerve damage was in favour of ultrasound; however, this was not statistically significant (RR 0.144, 95% CI: 0.01-2.96, P = 0.209, Figure 9, Table 25).

Figure 9 Individual study and the pooled (random effects model) risk ratios for occurrence of aggregate, catheter events, haemothorax, infections, and nerve damage during ultrasound or landmark guided placement of central lines.



Heterogeneity: Q = 15.4 (p = 0.08), I statistic = 41.71

Table 25 Summary of meta-analysis statistics for pooled risk ratios for aggregate, catheter events, haemothorax, infections, and nerve damage formation during ultrasound or landmark guided placement of central lines.

Grouping	No of studies	Point estimate	CI_{lower} (95%)	CI_{upper} (95%)	P value
Aggregate adverse events	2	0.92	0.50	1.69	P = 0.797
Catheter related adverse events	3	0.64	0.29	1.43	P = 0.282
Haemothorax	3	0.10	0.02	0.56	P = 0.009
Infection	1	1.36	0.46	4.04	P = 0.583
Nerve damage	1	0.14	0.01	2.96	P = 0.209

Data are reported as the risk ratio pooled using a random effect model. CI, confidence interval; FV, femoral vein; IJV, internal jugular vein; SCV, subclavian vein

Effectiveness:

Effectiveness outcomes reported to be associated with major vascular access protocols, irrespective of guidance method, are the mean time to cannulate the vessel, the mean number of attempts required to cannulate the vessel, the number of failed cannulations and the access rate (number of success on the first attempt).

Cannulation time

Seventeen of the 34 RCTs report data for cannulation time; this represents a total patient population of 2,964. The use of ultrasound was associated with a faster mean cannulation time (difference in means -0.78 min, 95% CI: -1.16 to -0.40, P < 0.001, Figure 10 Table 26). The time required for ultrasound cannulation compared to landmark guided cannulation was significantly shorter when access was via the IJV (difference in means -0.84 min, 95% CI: -1.36 to -0.33, P = 0.001, Table 26) and when the access site was mixed (difference in means -4.98 min, 95% CI: -7.14 to -2.82, P < 0.001, Table 26). The time required for cannulation was not significantly different between the two groups for access via the axillary artery, the femoral artery, the femoral vein or the subclavian vein (Table 26). Ultrasound use was associated with statistically shorter cannulation times in both adult (difference in means -0.81 min, 95% CI: -1.39 to -0.22, P = 0.007) and paediatric populations (difference in means -1.56 min, 95% CI: -2.96 to -0.17, P = 0.028), Table 26.

Figure 10 Individual study and the pooled (random effects model) differences in mean time for cannulation time for the placement of central lines when performed under ultrasound or landmark guidance

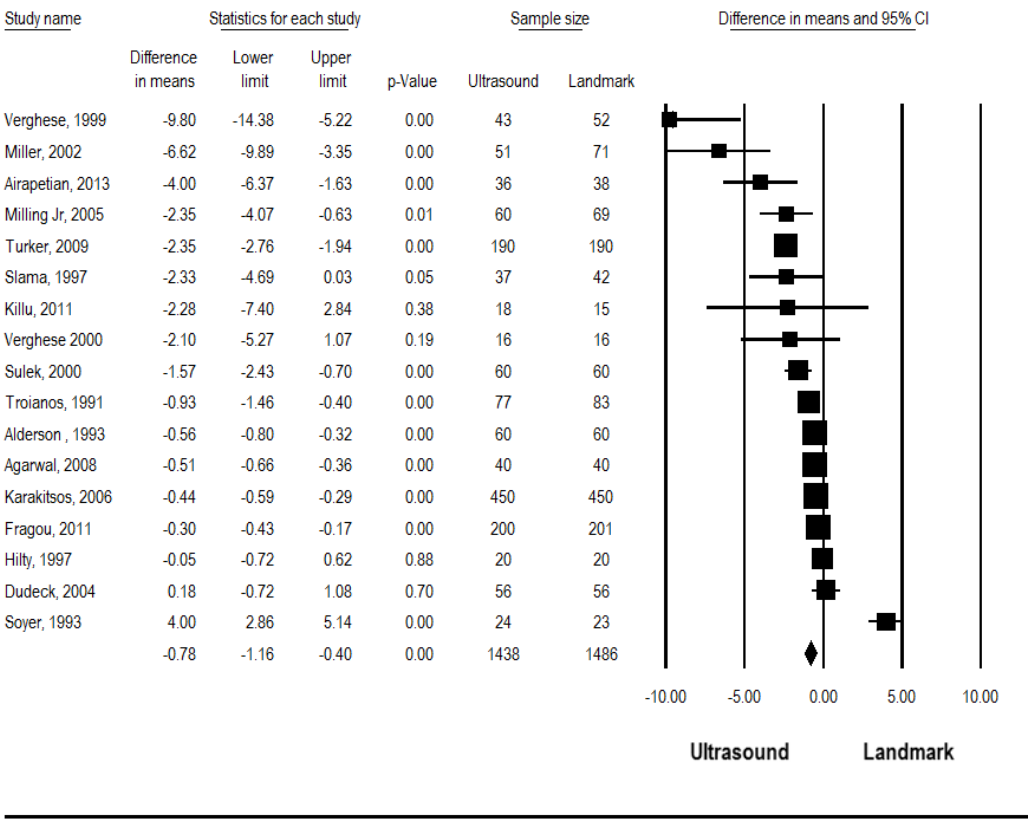


Table 26 Summary of meta-statistics for the pooled and subgroups based on access site or patient age differences in mean time for catheter placements during ultrasound or landmark guided placement of central lines.

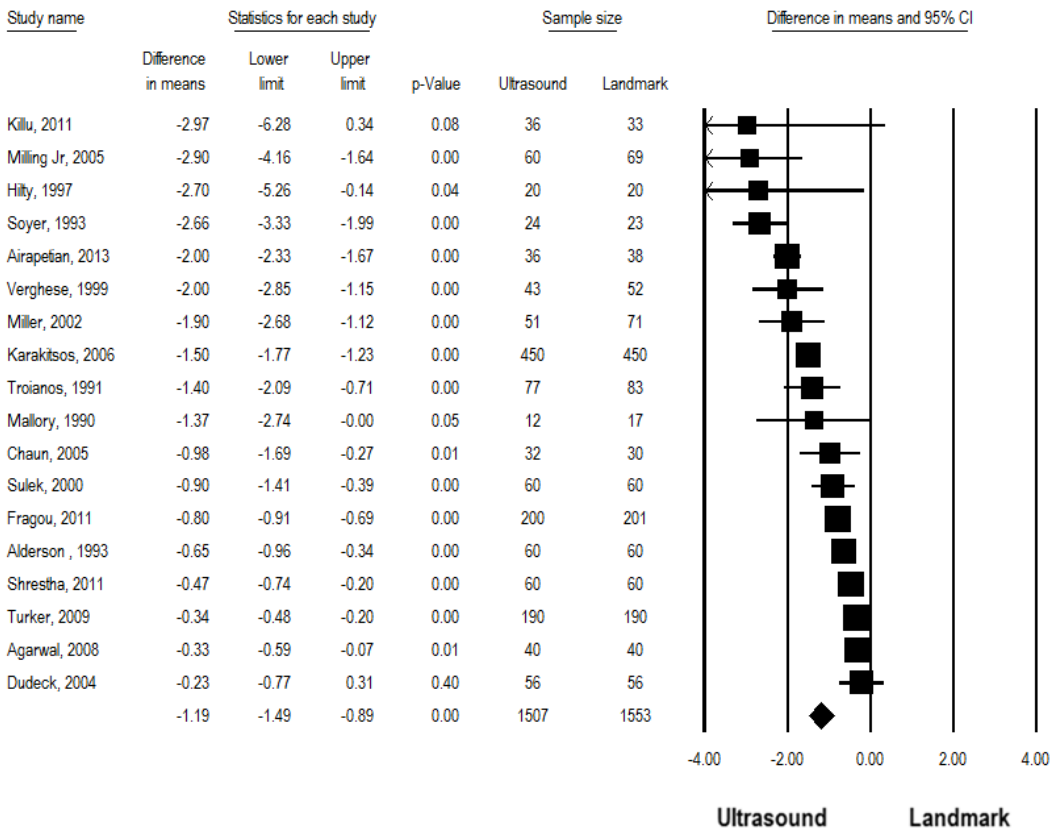
Grouping	No of studies	Point estimate	CI_{lower} (95%)	CI_{upper} (95%)	P value
Overall	17	-0.78	-1.16	-0.40	P < 0.001
Axillary artery	1	-2.28	-7.57	3.01	P = 0.399
Femoral artery	1	0.18	-1.45	1.81	P = 0.829
FV	1	-0.05	-1.56	1.47	P = 0.948
IJV	11	-0.84	-1.36	-0.33	P = 0.001
SCV	1	-0.30	-1.66	1.06	P = 0.667
Mixed	2	-4.98	-7.14	-2.82	P < 0.001
Adults	12	-0.81	-1.39	-0.22	P = 0.007
Children	3	-1.56	-2.96	-0.17	P = 0.028

Data are reported as the risk ratio pooled using a random effect model. CI, confidence interval; FV, femoral vein; IJV, internal jugular vein; SCV, subclavian vein

Number of attempts

Seventeen of the 34 RCTs reported data for the mean number of attempts required to successfully cannulate the vessel and represent a total patient population of 3,060 patients. The use of ultrasound was associated with reduction in the mean number of attempts required to affect cannulation (difference in means -1.163, 95% CI: -1.49 to -0.89, P < 0.001, Figure 11 Table 27). The number of attempts required for ultrasound cannulation compared to landmark guided cannulation was significantly reduced when access was via the IJV (difference in means -1.15, 95% CI: -1.53 to -0.78, P < 0.001, Table 27) and when the studies reported on multiple access sites (difference in means -1.96, 95% CI: -2.86 to -1.06, P < 0.001, Table 27). The number of attempts required for cannulation was not significantly different between the two methods for access via the axillary artery, the femoral artery, the femoral vein and the subclavian vein (Table 27). However, ultrasound use to assist vascular access was associated with statistically shorted cannulation times in both adult (difference in means -1.244, 95% CI: -1.614 to -0.88, P < 0.001) and paediatric populations (difference in means -1.13, 95% CI: 1.89-0.38, P = 0.003, Table 27).

Figure 11 Individual study and the pooled (random effects model) mean difference for the number of attempts to affect placement of central lines by ultrasound or landmark guided techniques.



Heterogeneity: Q = 205.0 (p < 0.001), I statistic = 91.7

Table 27 Summary of meta-statistics for the pooled and subgroup analysis based on access site or patient age: mean differences in the number of attempts to gain vascular access during ultrasound or landmark guided placement of central lines

Grouping	No of studies	Point estimate	CIlower (95%)	Clupper (95%)	P value
Overall	18	-1.19	-1.49	-0.89	P < 0.001
Axillary artery	1	-2.09	-6.47	0.52	P = 0.100
Femoral artery	1	-0.23	-1.49	1.03	P = 0.719
FV	1	-2.70	-5.50	0.10	P = 0.058
IJV	12	-1.15	-1.53	-0.78	P < 0.001
SCV	1	-0.80	-1.94	0.34	P = 0.168
Mixed	2	-1.96	-2.85	-1.06	P < 0.001
Adults	14	-1.24	-1.61	-0.88	P < 0.001
Children	3	-1.13	-1.89	-0.38	P = 0.003

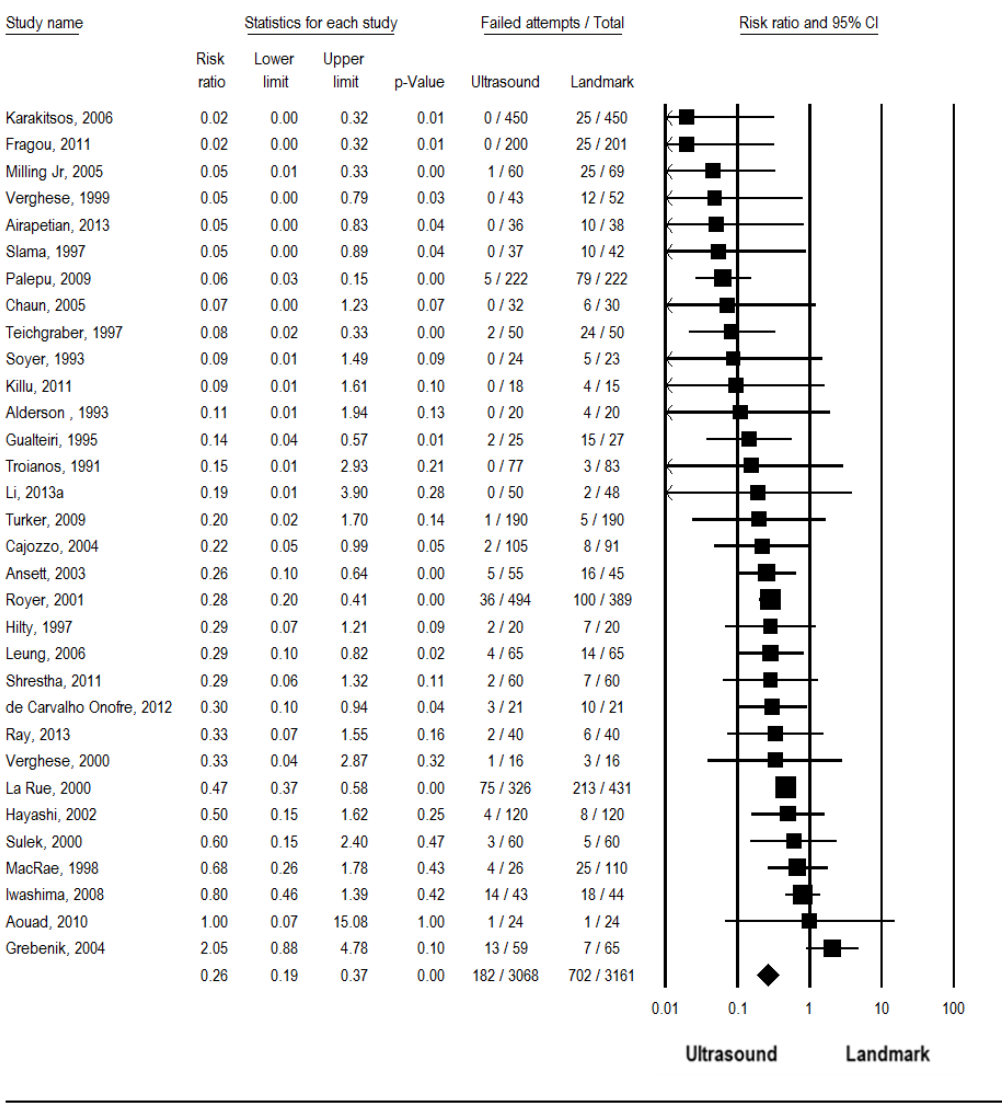
Data are reported as the risk ratio pooled using a random effect model. CI, confidence interval; FV, femoral vein; IJV, internal jugular vein; SCV, subclavian vein

Failed cannulation attempts

Thirty two of the 34 RCTs reported event data for failed cannulation attempts and represents a total patient population of 6,229. The prevalence of failed attempts for this population was 5.93 per cent and 22.21 per cent for vascular access guided by either the ultrasound or landmark guidance methods, respectively. The risk of failed cannulation under ultrasound guidance was significantly lower as compared with the landmark technique (RR 0.26, 95% CI: 0.19-0.37, P < 0.001,

Figure 12, Table 28). Sub-group analysis for access site revealed that the risk of failed cannulation was significantly lowered in ultrasound groups when access was via the IJV (RR 0.22, 95% CI: 0.13-0.35, P < 0.001, Table 28), the subclavian vein (RR 0.11, 95% CI 0.03-0.45, P < 0.002, Table 28), for studies where the access site was mixed (RR 0.14, 95% CI: 0.03-0.73, P = 0.019 Table 28) and for PICC access (RR 0.36, 95% CI: 0.20-0.67, P = 0.001, Table 28). For the included studies, patient age was a significant factor. In adults, ultrasound significantly lowered the risk of a failed cannulation (RR 0.24 95% CI: 0.17-0.35, P < 0.001, Table 28); however, this benefit was not observed for studies that evaluated the impact of ultrasound guidance of vascular access in a paediatric population (RR 0.56, 95% CI: 0.29-1.09, P = 0.09, Table 28).

Figure 12 Individual study and the pooled (random effects model) risk ratios for failed cannulation attempts during ultrasound or landmark guided placement of central lines



Heterogeneity: Q = 78.4 (p < 0.001), I statistic = 60.5

Table 28 Summary of meta-statistics for the pooled and subgroups based on access site or patient age: risk ratios for failed cannulation attempts during ultrasound or landmark guided placement of central lines

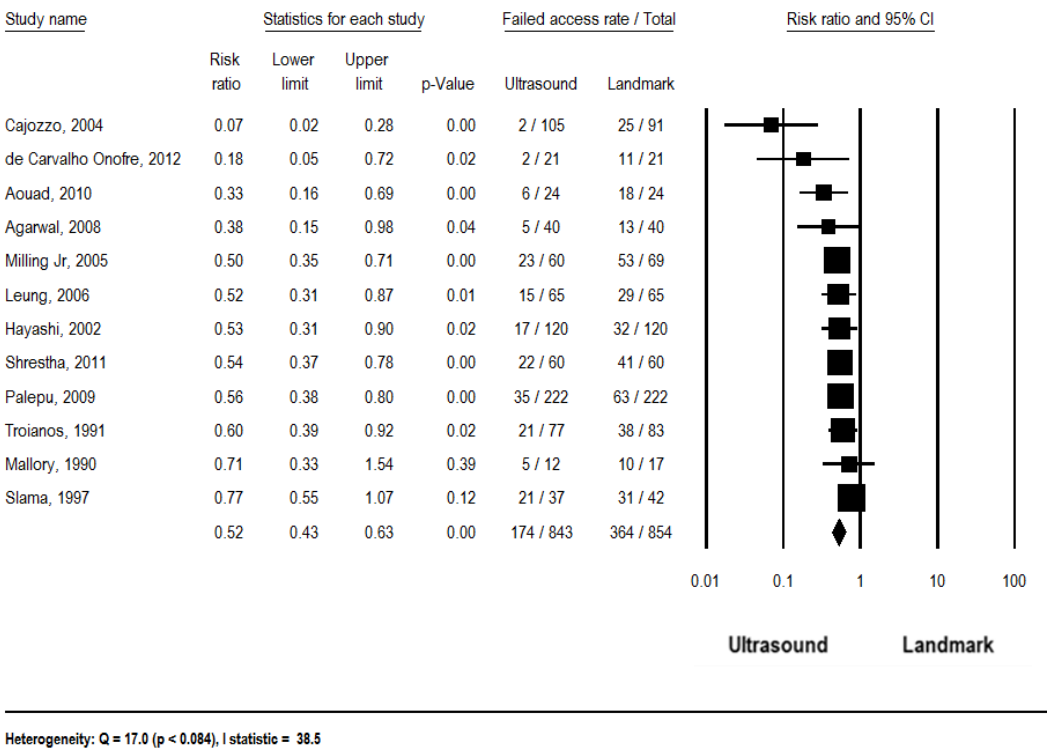
Grouping	No of studies	Point estimate	CI_{lower} (95%)	CI_{upper} (95%)	P value
Overall	32	0.26	0.19	0.37	P < 0.001
Axillary artery	1	0.09	0.04	2.04	P = 0.132
FV	3	0.61	0.22	1.66	P = 0.331
IJV	18	0.22	0.13	0.35	P < 0.001
SCV	3	0.11	0.03	0.45	P = 0.002
Mixed	2	0.14	0.03	0.73	P = 0.019
PICC	6	0.36	0.20	0.67	P = 0.001
Adults	21	0.24	0.16	0.35	P < 0.001
Children	8	0.56	0.29	1.09	P = 0.09

Data are reported as the risk ratio pooled using a random effect model. CI, confidence interval; FV, femoral vein; IJV, internal jugular vein; SCV, subclavian vein

Failure on the first attempt

Twelve of the 34 RCTs reported event data for failure on the first attempt and represents a total patient population of 1,697. The prevalence of failed first attempts for this population was 20.64 per cent and 42.62 per cent for vascular access guided by either the ultrasound or landmark guidance methods, respectively. Meta-analysis showed that ultrasound guidance of vascular access significantly reduced the risk of failure on the first attempt compared with the landmark technique (RR 0.52, 95% CI: 0.43-0.63, P < 0.001, Figure 13, Table 29). The risk of failure on the first attempt was significantly lowered with ultrasound use for access via the IJV (RR 0.58, 95% CI: 0.50-0.67, P < 0.001, Table 29), the femoral vein (RR 0.33, 95% CI 0.16-0.69, P = 0.003, Table 29), for studies where the access site was mixed (RR 0.07, 95% CI: 0.02-0.29, P<0.001 Table 29) and for PICC access (RR 0.18, 95% CI: 0.05-0.72, P = 0.015, Table 29). There was no statistically significant difference in risk of failure at first attempt between ultrasound and landmark techniques for subclavian vein access (Table 29). The risk of failure at first attempt was significantly lowered by ultrasound use for both adults (RR 0.57, 95% CI: 0.46-0.70, P < 0.001) and children (RR 0.29, 95% CI: 0.14-0.58, P < 0.001 Table 29).

Figure 13 Individual study and the pooled (random effects model) risk ratios for failure on first attempt during ultrasound or landmark guided placement of central lines



Heterogeneity: Q = 17.0 (p < 0.084), I statistic = 38.5

Table 29 Summary of meta-statistics for the pooled and subgroups based on access site or patient age: risk ratios for failure on first attempt attempts during ultrasound or landmark guided placement of central lines

Grouping	No of studies	Point estimate	CI_{lower} (95%)	CI_{upper} (95%)	P value
Overall	12	0.52	0.43	0.63	P < 0.001
FV	1	0.33	0.16	0.69	P = 0.003
IJV	9	0.58	0.50	0.67	P < 0.001
SCV	1	0.62	0.19	2.01	P = 0.424
Mixed	1	0.07	0.02	0.29	P < 0.001
PICC	1	0.18	0.05	0.72	P = 0.015
Adults	7	0.57	0.46	0.70	P < 0.001
Children	2	0.29	0.14	0.58	P < 0.001

Data are reported as the risk ratio pooled using a random effect model. CI, confidence interval; FV, femoral vein; IJV, internal jugular vein; SCV, subclavian vein

Summary of central vascular access

A total of seven systematic reviews were identified that were relevant to this report. These reviews were published between 1996 and 2013. Three of the systematic reviews were rated as being good quality using a modified AMSTAR appraisal tool. The reviews investigated a range of populations (patients undergoing central venous access and PICC access with subpopulation analysis of anatomical location of the access and the age of patients).

All the systematic reviews concluded that ultrasound localisation of central vascular access was equivalent to or an improvement on the anatomical landmark technique.

In total, results 34 RCTs were pooled to inform the meta-analysis of which 9 represent studies not included in other systematic reviews. Central venous access was highly represented in the evidence base.

Safety

The following outcomes were statistically significant in favour of ultrasound guidance compared to the landmark technique:

- Inappropriate vascular puncture was reported in 28 RCTs with a total patient population of 4,409. Ultrasound use significantly reduced the risk of vascular puncture (RR 0.32, 95% CI:0.22-0.47, P < 0.001)
- Haematoma was reported in 17 RCTs with a total patient population of 3,423. Ultrasound use significantly reduced the risk of vascular puncture (RR 0.34, 95% CI: 0.20-0.58, P < 0.001)
- Pneumothorax was reported in seven RCTs with a total patient population of 1,847. Ultrasound use significantly reduced the risk of pneumothorax (RR 0.21, 95% CI: 0.06-0.71, P = 0.01)
- Haemothorax was reported in three RCTs with a total patient population of 703. Ultrasound use significantly reduced the risk of haemothorax (RR 0.10, 95% CI: 0.02-0.56, P = 0.009)

Ultrasound was equivalent to the landmark method for the following outcomes:

- Aggregate adverse events, reported in two RCTs with a patient population of 119 (RR 0.92, 95% CI: 0.50-1.69, P = 0.797)
- Catheter related adverse events, reported in three RCTs with a patient population of 266 (RR 0.64, 95% CI: 0.29-1.43, P = 2.82)
- Infection, reported in one RCT with a patient population of 38 (RR 1.36, 95% CI:0.46-4.04, P = 0.583)
- Nerve damage, reported in one RCT with a patient population of 201 (RR 0.14, 95% CI: 0.01-2.96, P = 0.209).

Effectiveness

The following outcomes were statistically significant in favour of ultrasound guidance compared to the landmark technique:

- Cannulation time was reported in 17 RCTs with a total patient population of 1,486, ultrasound use significantly reduced the cannulation time (DM -0.78, 95% CI:-1.16 - -0.40, P < 0.001)
- The number of attempts required was reported in 17 RCTs with a total patient population of 3,060. Ultrasound use significantly reduced the number of attempts required (DM -1.19, 95% CI: -1.49 - -0.89, P < 0.001)
- The number of failed attempts was reported in 32 RCTs with a total patient population of 6,229. Ultrasound use significantly reduced the risk of failure (RR 0.26, 95% CI: 0.19-0.37, P < 0.001).
- The risk of failure on first attempt was reported in 12 RCTs with a total patient population of 1,697. Ultrasound use significantly reduced the risk of failure on first attempt (RR 0.52, 95% CI: 0.43-0.63, P < 0.001)

Overall central arterial access was not highly represented in the literature (2 studies). Studies reporting the use of ultrasound for PICC lines are also less common (6 studies).

Systematic reviews: percutaneous neural blockade

Descriptive characteristics of included studies

Ten systematic reviews were identified that addressed the research questions of the current assessment with respect to the safety and effectiveness of ultrasound to guide percutaneous neural blockade (Table 30). The comparators were nerve stimulation, the trans-arterial technique or other landmark method.

A review by Yuan et al investigated the use of ultrasound guided brachial plexus block compared to electrical nerve stimulation for regional anaesthesia in adults (Yuan et al 2012). Walker at al (2011) investigated ultrasound guidance of peripheral nerve blocks for regional anaesthesia compared with any other method of guidance (electrical nerve stimulation, the trans-arterial technique or a landmark method). Gelfand et al (2011) compared ultrasound guided nerve block to electrical nerve stimulation or landmark for the analgesic efficacy of regional anaesthesia. Choi and Brull (2011) investigated the use of ultrasound guided nerve block for acute pain management compared with electrical nerve stimulation or the landmark method. A review by McCartney et al compared ultrasound guided brachial plexus block compared with electrical nerve stimulation, the trans-arterial technique or other landmark methods (McCartney et al 2010). Neal (2010) compared ultrasound guided nerve block for regional anaesthesia compared with electrical nerve stimulation. Liu et al (2009a) compared ultrasound guidance for peripheral nerve blocks compared with electrical nerve stimulation, the trans-arterial technique or other landmark methods. Abrahams et al (2009) investigated the use of ultrasound guided nerve block for peripheral nerve blocks compared to electrical nerve stimulation. Rubin et al. (2009) investigated the use of ultrasound to guide peripheral and neuraxial nerve blocks in children. Three of the included RCTs are relevant to this section of the report. A recent systematic review by Bhatia and Brull (2013) investigated the use of ultrasound compared to electrical nerve stimulation or landmark to guide nerve block for chronic pain management, and as a result of this focus only one of the included studies had a relevant population and study design for this report.

Table 30 Systematic reviews for percutaneous nerve block: study characteristics

Review	Question of the review	Inclusion/exclusion criteria	Number of included studies	Number of studies identified in our searches	Heterogeneity	Intervention Comparator
Bhatia and Brull 2013	Performance efficacy and safety of ultrasound guidance compared with traditional techniques for interventional chronic pain procedures	RCTs, case series and retrospective reviews, English language, human subjects. US compared to traditional techniques (loss of resistance, mechanical elicitation of paraesthesia, peripheral nerve stimulation, landmark, fluoroscopy, CT, MRI) or resultant sensory changes or anatomical dissection (cadaver studies)	46 studies of which 1 RCT containing 50 patients is relevant to this review	1	N/A	Ultrasound (US) Landmark (LM
Yuan et al 2012	Does ultrasound use decreases the risk of vascular puncture, hemi-diaphragmatic paresis and Horner syndrome and increases the success rate of nerve block	RCTs in all languages that compared US to nerve stimulation for brachial plexus block. Adults >18 years, any sample size	14 studies (1,030 patients)	13	No evidence of heterogeneity	Ultrasound Electrical Nerve Stimulation (ENS)
Walker et al 2011	Does ultrasound improve success rates and effectiveness of regional anaesthetic blocks? Does ultrasound reduce complications associated with regional anaesthetic blocks?	RCTs comparing US with at least one other method of nerve localisation (landmark, paraesthesia or nerve stimulation). Adult patients undergoing surgery where block is primary anaesthetic or provides post-operative analgesia Children <16 years, epidural, spinal anaesthetic injections and chronic pain treatments were excluded	18 studies (1,344 patients)	18	Such that meta-analysis was inappropriate	10 studies compared US to ENS, 4 studies compared US+ENS to ENS, 2 trials compared US to LM, 1 trial compared US to a trans-arterial technique, 1 trial compared US to US + ENS

Review	Question of the review	Inclusion/exclusion criteria	Number of included studies	Number of studies identified in our searches	Heterogeneity	Intervention Comparator
Gelfand et al 2011	Does US improve the analgesic efficacy of peripheral nerve blocks for surgical procedures	RCT, nerve blocks conducted for surgical procedure, comparison of US alone to method without ultrasound. Patients of any age. Trials where ultrasound was used in conjunction with another method and those where the purpose of the nerve block was not for a surgical procedure were excluded.	16 studies (1,264 patients)	17	I^2=38% for success rate US vs. all non-US methods	US compared to ENS (14 studies) trans-arterial technique (1 study) and LM (1 study).
Choi and Brull 2011	The effect of ultrasound guidance compared with traditional nerve localisation techniques for interventional management of acute pain	RCTs, US compared to other nerve localisation techniques (nerve stimulation, manual elicitation of paraesthesia and landmark) Studies were excluded if they did not specifically compare US to another technique or did not report at least one of: pain severity, opioid consumption, sensory block duration and time to first analgesia request	23 studies (1,674 patients)	23	Such that meta-analysis was inappropriate	US compared to ENS (15 studies) US + ENS compared to ENS (2 studies), US compared to LM (6 studies)
Liu et al 2010	The benefits of ultrasound guided peripheral nerve block compared to other localisation techniques	RCTs comparing US guidance to an alternative technique of localisation during peripheral nerve blocks were included.	16 studies for upper extremity, 8 studies for lower extremity (2,031 patients)	24	NR	US compared to ENS (20 studies), US compared to trans-arterial method (2 studies), US compared to LM (2 studies)

Review	Question of the review	Inclusion/exclusion criteria	Number of included studies	Number of studies identified in our searches	Heterogeneity	Intervention Comparator
McCartney et al 2010	The benefits of US for brachial plexus block	RCTs that compared the use of US with any pre-existing technique for upper extremity block or any study that compared two different US based techniques. RCTs where different anaesthesia volumes were assessed or studies where different blocks with a different localisation technique was used for each block were excluded. Letters to the editor, abstracts, non-peer reviewed studies, case reports and case series without comparison were excluded.	25 studies of which 19 RCTs are relevant to this review (the 6 excluded studies compared two US techniques) (1,687 patients)	22	NR	US compared to ENS 18 studies, US compared to LM (1 study)
Neal 2010	What effect does ultrasound guided regional anaesthesia have on patient safety compared to other nerve localisation techniques	RCTs and case series , English language	22 RCTs (1,863 patients)	21	NR	US compared to ENS (18 studies) US compared to trans-arterial technique (2 studies) US compared to LM (1 study) US compared to fascial click (1 study)
Abrahams et al 2009	How does US guidance influence the success of peripheral nerve blocks compared to nerve stimulator guidance	Prospective data collection, randomisation, comparison of US and nerve stimulation for peripheral nerve block in humans. Studies judged low quality were excluded	13 studies (946 patients)	10	Assessed – did not prevent meta-analysis	

Review	Question of the review	Inclusion/exclusion criteria	Number of included studies	Number of studies identified in our searches	Heterogeneity	Intervention Comparator
Rubin et al 2009	What is the safety and efficacy of US guided paediatric peripheral nerve and neuraxial blocks	All English language reviews and RCTs, comparing US guided neuraxial or peripheral nerve blocks in children were included.	12 studies of which 3 are relevant	3	NR	US compared to ENS

Critical appraisal of the systematic reviews

The quality of the systematic reviews was assessed using the AMSTAR instrument (Appendix I).

The quality of the identified systematic reviews is shown in Table 31. The median score of 6 was chosen to differentiate good quality systematic reviews (≥6) from poor quality reviews (<6) (CADTH 2006). Based on these criteria three systematic reviews are classified as being good quality with the remaining seven reviews being adjudged poor quality. All reviews provided *a priori* study design. Information pertaining to the scientific quality of the included studies was generally well reported; however, the use of the scientific quality of the included RCTs to formulate conclusions was only performed by five out of the ten reviews. Approximately half of the studies performed and adequately reported a comprehensive search strategy and study selection. Data extraction was performed in duplicate in only one third of the studies. Two studies provided a list of excluded studies and only one review provided adequate baseline characteristics for the included studies. No studies adequately reported conflict of interest. For the three reviews which undertook a meta-analysis, all used an appropriate methodology.

Table 31 Methodological quality appraisal of systematic reviews on ultrasound guidance for percutaneous neural blockade using the AMSTAR tool

	Review characteristics	Bhatia and Brull 2013	Yuan et al 2012	Walker et al 2011	Gelfand et al 2011	Choi and Brull 2011	McCartney et al 2010	Neal 2010	Liu et al 2010	Abrahams et al 2009	Rubin et al 2009
1	Was an 'a priori' design provided?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2	Was there duplicate study selection and data extraction?	Cannot answer	Yes	Yes	No	Yes	Cannot answer	Cannot answer	Cannot answer	Cannot answer	Cannot answer
3	Was a comprehensive literature search performed?	No	No	Yes	No	Yes	Yes	Yes	No	Yes	Yes
4	Was the status of publication (i.e. grey literature) used as an inclusion criterion?	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
5	Was a list of studies (included and excluded) provided?	No	No	Yes	No	No	No	No	No	Yes	No
6	Were the characteristics of the included studies provided?	No	No	No	Yes	No	No	No	No	No	No
7	Was the scientific quality of the included studies assessed and documented?	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
8	Was the scientific quality of the included studies used appropriately in formulating conclusions?	Yes	Yes	Yes	Yes	No	No	No	No	Yes	No
9	Were the methods used to combine the findings of studies appropriate?	NA	Yes	NA	Yes	NA	NA	NA	NA	Yes	NA
10	Was the likelihood of publication bias assessed?	No	Yes	Yes	No	No	No	No	No	Yes	No
11	Was the conflict of interest stated?	No	No	No	No	No	No	No	No	No	No
	Yes	4	7	8	4	5	4	4	3	8	4
	No	5	4	2	7	5	5	5	6	2	5
	Cannot answer	1	0	0	0	0	1	1	1	1	1
	Not applicable	1	0	1	0	1	1	1	1	0	1

Is it safe?

Table 82 (Appendix L) provides a summary of the safety metrics reported on for the included systematic reviews. Seven of the ten systematic reviews reported on safety outcomes. All seven systematic reviews (including two meta-analyses) found ultrasound use lowers the incidence of vascular puncture compared to the comparator.

Incidence of paraesthesia was reported by three reviews. Abrahams et al (2009) found no significant difference between ultrasound and the comparator, Neal (2010) found ultrasound use lowered the incidence of paraesthesia in two studies; however, there was no significant difference found in 20 studies. Walker et al. (2011) found one study favoured ultrasound use and one study favoured the comparator. Two reviews reported incidence of nerve injury; Bhatia and Brull (2013) reported no incidences in the ultrasound group compared to three incidences in the comparator. Neal (2010) found ultrasound use lowered the incidence of nerve injury compared with the comparator, five studies did not find a significant difference between the groups and one study favoured the use of the comparator. Incidence of neurological symptoms was reported by two reviews, Yuan et al. (2012) reported no significant difference between the ultrasound and comparator groups after meta-analysis; Abrahams et al. (2009) similarly reported no significant difference between the two groups.

Walker et al. (2011) and Abrahams et al. (2009) both reported that there were no incidences of major complications (including pneumothorax, anaesthesia toxicity or permanent neurological damage) in any patients in the included studies. Bhatia and Brull (2013) reported no incidence of pneumothorax in any patients. Two studies included the overall incidence of complications, in Walker at al. (2011) one trial found ultrasound use lowered the incidence of complications; however, in Choi and Brull (2011) 20 studies found no significant difference in the incidence of complications between the ultrasound and comparator groups.

A number of other safety outcomes were also reported. Yuan et al. (2012) reported ultrasound use significantly lowered the risk of complete hemi-diaphragmatic paralysis; the risk of partial paralysis was not significantly difference between the ultrasound and comparator groups. Walker at al. (2011) reported ultrasound use lowered the incidence of haematoma formation in eight trials. Choi and Brull (2011) reported lower incidence of headache with ultrasound use in three studies.

Is it effective?

Table 83 provides a summary of the effectiveness outcomes of the included systematic reviews. Nine of the ten systematic reviews reported on effectiveness outcomes. For the five reviews that report on time to perform the nerve block, one meta-analysis found ultrasound use significantly reduced the time required compared with the comparator (Abrahams et al 2009); however, the meta-analysis by Yuan et al. (2012) did not find any significant difference between ultrasound and the comparator. Walker at al. (2011) reported five studies where ultrasound was favoured and five studies where there was no significant difference. McCartney et al. (2010) reported four studies where ultrasound was favoured, four studies where there was no significant difference and three studies where the comparator was favoured. Lui et al. (2010) reported five studies where ultrasound was favoured, five studies where the time difference was not significant and one study where the comparator was favoured.

Block onset time was reported in five reviews. A meta-analysis by Abrahams et al. (2009) found ultrasound significantly decreased the time needed for the block to be effective. However, a meta-analysis by Yuan et al. (2012) found no significant difference in time for both sensory and motor block when neural blocks are placed with an ultrasound guided protocol as compared with the comparator technique. McCartney et al. (2010) reported six studies where ultrasound was favoured for sensory block, one study where the comparator was favoured for sensory block and one study where ultrasound was favoured for motor block. Liu et al. (2010) reported 13 studies that favoured ultrasound use, five studies where there was no significant difference and no studies where the comparator was favoured. Rubin et al (2009) reported one RCT that favoured ultrasound use.

Block duration was reported by five reviews; no studies favoured the comparator. A meta-analysis by Abrahams et al. (2009) found ultrasound guided nerve blocks had a significantly longer duration than the comparator. Choi and Brull (2011) reported three studies where ultrasound was favoured and five studies where there was no significant difference. McCartney et al. (2010) reported two studies where ultrasound was favoured. Liu et al. (2010) reported one study where ultrasound was favoured and eight studies where there was no significance difference between ultrasound and the comparator. Rubin et al (2009) reported two RCTs where ultrasound was favoured.

Three reviews reported on the requirement for co-administered drugs. Abrahams et al. (2009) found ultrasound guidance resulted in a significantly reduced risk of requiring a rescue block compared to the comparator. Choi and Brull (2011) reported three studies where ultrasound was favoured for opioid consumption and four studies where the difference was no significant. Liu et al. (2010) reported three studies where ultrasound was favoured for rescue anaesthesia and 14 where the difference was not significant. One study reported ultrasound was favoured for supplement analgesia use and 12 studies reported no significant difference.

Two reviews reported the number of skin punctures and / or needle passes required for successful block, in all cases (7 studies total) ultrasound was favoured.

Four reviews reported pain or discomfort levels, Bhatia and Brull (2013) reported one study where ultrasound guidance for nerve block resulted in lower pain scores than the comparator. Walker et al. (2011) reported one study where ultrasound was favoured and five studies where the difference was not significant. Choi and Brull (2011) reported eight

studies where ultrasound was favoured for pain at rest and eight studies where there was no significant difference. One study was reported where ultrasound was favoured for pain at movement and three studies where there was no significant difference. Choi and Bull (2011) additionally reported patient's satisfaction level and length of hospital stay, for satisfaction; ultrasound was favoured in two studies and three studies did not find a significant difference between ultrasound and the comparator. Neither of the two included studies in Choi and Brull (2011) which reported length of hospital reported a significance difference between US and the comparator.

Two reviews, Abrahams et al. (2009) and Lui et al. (2010), reported block completeness. Abrahams et al. (2009) found ultrasound guidance resulted in significantly higher block completeness at 30 minutes post administration than the comparator. Lui et al. (2010) reported six studies where ultrasound use increased block completeness and six studies where there was no significant difference between ultrasound and the comparator.

Summary

From the ten included systematic reviews shown above, three were identified as being of appropriate quality and of relevance in terms of the patient populations and the questions of the review.

Walker et al. (2011) is a recent and good quality systematic review that reports nerve block outcomes across a broad range of patient populations and forms the basis of our analysis. In addition to this, two supplementary reviews have been identified; Bhatia and Brull (2013) reports outcomes specific to chronic pain management and Choi and Brull (2011) reports outcomes specific to acute pain management.

Key findings

Ten systematic reviews were identified for appraisal. Three systematic reviews were of appropriate quality and reported on specific research questions that were of direct relevance to this assessment. One of these (Walker et al 2011) was a recent study of good quality which was a broad review of percutaneous nerve block.

For safety, ultrasound guidance is associated with a reduction in the risk of vascular puncture. Ultrasound appears to be equivalent to comparator techniques with regards to the prevalence of paraesthesia, nerve injury, neurological symptoms and overall complications. Prevalence of major complications is rare for both groups.

For effectiveness, ultrasound guidance is associated with a reduction in the block onset time, the number of needle passes required for successful block administration, pain or discomfort levels, the failure rate of procedures and the number of attempts to successfully place a nerve block. Ultrasound is associated with an increase in the duration of the nerve block. Ultrasound appears to be equivalent to comparator techniques with regards to the time required to place the block and the use of co-administered drugs.

The identified systematic reviews are applicable to this review with respect to their scope and research question.

Our searches identified greater than 95 per cent of the studies which were included in the systematic reviews.

Key findings
Overall the evidence provided by the systematic reviews was consistent, both in terms of the included studies and the overall results and conclusions. RCT evidence published after the search date of the most up-to-date, good quality and appropriate systematic review (Walker et al 2011) or which provided evidence that was not included in the identified systematic reviews was used to supplement the systematic review evidence.

Randomised controlled trials: percutaneous neural blockade

Tabulated descriptive and outcome data for the included RCTs are shown in Appendix N.

Descriptive characteristics of included studies

Study information

A total of 29 studies (Table 89, Appendix N) which used ultrasound-guided nerve blocks for perioperative anaesthesia/analgesia (n=24 studies) or for non-surgical pain management (n=2) were identified as being published after the search date of the most recent systematic review (Walker et al 2011). A small number of studies investigated the efficacy of ultrasound-guided nerve blocks in healthy volunteers (n=3). All of these studies were randomised, with the exception of two which utilised pseudo-randomisation, and all compared ultrasound-guided nerve block delivery with electrical nerve stimulation-guidance (n=18), landmark-guidance (n=10), or both (n=1).

The number of patients treated in each of the included studies ranged from 20 to 273 (mean 75 patients). The majority of included studies treating an adult population (n=25) compared with a paediatric population (n=4).

The majority of included studies performed their blocks in the upper limb region (n=15), including blocks to the axially fossa (n=1), brachial plexus (n=10), cervical spine (n=1), median and ulnar (n=1) and supracapsular nerves (n=2). Eleven studies performed lower limb blocks to the peroneal nerve (n=1), sciatic nerve (n=6), sural nerve (n=1), saphenous nerve (n=1) and femoral nerve (n=2) and three studies performed trunk blocks.

Of the 29 studies performing ultrasound-guided nerve blocks, 23 reported proceduralist details. A single anaesthetist carried out the nerve block in 13 of the included studies. Ten studies employed two or more anaesthetists and nine studies performed procedures by an experienced anaesthetist or a trainee under the guidance of an experienced anaesthetist or physician. Most of these studies specified that proceduralists were skilled in regional anaesthesia (n=16) and some in ultrasound-guided regional anaesthesia specifically (n=8). For all studies the administration mode for anaesthetic agent at placement was bolus although this may have been converted to continuous infusion if a catheter had been placed.

In the studies where ultrasound-guided nerve blocks were associated with a surgical procedure (n=24 studies), 11 reported the use of regional anaesthesia as the sole

anaesthetic modality. Ten used regional nerve blocks in conjunction with general anaesthesia and six used regional nerve blocks with a sedation protocol.

Patient population

Study characteristics detailing populations as well as inclusion and exclusion criteria are provided in Table 90 (Appendix N). Of the included studies, 25 evaluated the effectiveness of ultrasound guidance for the placement of neural blockades in adult patients18 years of age or older. In 16 of these studies the patients were aged between 40 – 60 years. Seven studies covered patients aged between 18 to 39 years and only two studies report on a population older than 65 years, with one study reporting on patients 80 years or older. All three volunteer-based studies were conducted in adults aged between 18 to 58 years, as such they include individuals that are of similar age to participants in patient-based RCTs. For paediatric populations, the included patients were aged up to 48 months. Within any given study, subject age was similar in the intervention and comparator groups.

No bias towards either sex was reported for studies that included a mix population. However, in two studies the number of patients reported in the male and female groups did not correspond to the total number of patients reported for intervention and comparator study arms (Ponde and Diwan 2009).

For 18 of the included studies the physical status of patients was classed by the ASA grade scheme. Of these, 12 included patient ranging from Grade I (normal healthy) to Grade III (severe systemic disease) with the remaining six studies evaluating patients classified as being ASA I – II. However, the distribution of ASA grade across intervention groups was not reported and effectiveness outcomes were not stratified by ASA status, as such the impact of ASA status within a given study cannot be assessed.

Inclusion criteria for patient-based investigations were consistent across studies. These included the primary indication for which the neural blockade is given, surgery where the preferred anaesthesia is a regional neural blockade, post-operative management following moderate to severely painful surgery, chronic pain management or acute pain management within an emergency department setting. Other study-specific inclusion criteria included to capacity to provided informed consent, ability to interact with staff and comprehension of pain score tools. Exclusion criteria were generally more extensively reported and included serious co-morbidities (for example cardiac or respiratory problems), allergies to anaesthetic agents, neuropathy and prior recent use of opiates. Eleven of the studies that reported on patient-based studies the number of patients excluded with reasons ranged from zero to 169. The remaining studies did not report the number of excluded patients.

Overall, the included studies are representative of the patient populations that are likely to receive the procedure of neural blockade in the Australian clinical context. As such, the studies provide an appropriate evidence-base to determine the effectiveness of intervention that may be translated to use within Australia.

Instrumentation

Instrumentation and setting used for both the ultrasound and electrical nerve stimulator techniques are detailed in Table 91 (Appendix N). Among the 29 extracted studies, 17 listed various models of devices manufactured by SonoSite. Where ultrasound frequencies for imaging were reported for SonoSite, settings ranged from 6MHz to 13MHz. A further nine studies reported on the use of ultrasound machines manufactured by GE Healthcare. Other manufacturers included Phillips, Accuvix, Advanced Technology Laboratory and Aloka. The imaging frequencies are similar to the SonoSite device; however, reported frequency for GE Healthcare instruments were of narrow band width. Two studies reported the use of single band ultrasound at either 10MHz or 12MHz setting. However, all studies that reported frequency settings were within the overall range of 2 – 13MHz. The needle used for placement of block or catheter was consistent between intervention and comparator groups in 17 of the included studies. For the remaining 12 studies, 11 did not reported the needle type for the comparator group and one study (Ko et al 2013) reported a that different needle was used in the intervention compared with the comparator group. The most widely used needle was a 22 G; however, the length of the needle varies from study to study. The range of the needle length used in the include studies ranged from 38mm (1.5 inch) to 100 mm (4 inch). Ultrasound dense needles were not reported in any study, and needle guides were not used.

Anatomical orientation for imaging was reported in six of the 29 included studies. Furthermore, 16 of the included studies imaged the needle in-plane with the ultrasound probe whereas six studies reported on an out-of-plane technique. Only one study compared the impact of needle presentation by image orientation for the safety and effectiveness for the placement of a neural blockade using ultrasound (Bloc et al 2010).

For electrical nerve stimulators, most of the included studies use equipment manufactured by Braun Medical, Germany. The stimulus current was ranged from 0.3 mA to 1.5 mA, with stimulating frequency between 1 to 2Hz.

Critical appraisal of RCTs

Twenty nine RCTs were identified that addressed the research questions of the current assessment with respect to safety and effectiveness of ultrasound for percutaneous neural blockade. A checklist adapted from Van Tulder et al (1997) and Downs and Black (1998) was used by two independent assessors to determine the methodological quality of the included RCTs (Table 76, Appendix I). The internal validity was rated as good in six RCTs, moderate in 20 and poor in three. The external validity was rated as good in 29 RCTs.

Only three of the RCTs did not report conducting power calculations on appropriate outcomes to recruit the sample size necessary to detect statistically meaningful differences between treatment groups (Gorthi et al 2010; Salem et al 2012; Zencirci 2011).

Twenty one of the RCTs reported appropriate randomisation techniques, three did not report what their method of randomisation was (Gurkan et al 2008; Reid et al 2009; Zencirci 2011) and in five RCTs the method of randomisation was unclear from the description provided. Four of the five in which it was unclear reported only that sealed envelopes were used. Twenty one of the RCTs reported concealment of treatment allocation. Eight RCTs reported that the patient was blinded to the intervention and 23 reported that the outcome assessor was blinded (Antonakakis et al 2010; Aveline et al 2011; Bendtsen et al 2011; Brull et al 2009; Danelli et al 2012; Danelli et al 2009; Faraoni et al 2010; Fredrickson and Danesh-Clough 2009; Gurkan et al 2008; Kent et al 2013; Ko et al 2013; Liu et al 2009b; Maalouf et al 2012; Min et al 2011; O'Sullivan et al 2011; Ponde et al 2013; Ponde and Diwan 2009; Ponrouch et al 2010; Redborg et al 2009; Sala-Blanch et al 2012; Trabelsi et al 2013; Tran et al 2010). Given the nature of the intervention it would be impossible for the provider to be blinded and thus this dimension of the checklist was recorded as not applicable for all studies.

Inclusion and or exclusion criteria were described in all but two RCTs. In one no criteria were reported and in the second the application of criteria to patient selection was unclear.

All RCTs employed a short term follow-up (outcome assessment ≤ 3 months after randomisation). One study reported long term follow-up outcomes (> 3 months after randomisation), this study by Aveline et al reported pain at 6 months using a visual analogue scale and the Douleur Neuropathique 4 neuropathic pain scale. In 19 studies losses to follow-up were reported and documented, in a further four studies the reporting of losses to follow-up were unclear and in a final six no reporting of losses to follow-up was provided.

Is it safe?

Adverse events are reported both numerically and textually within most of the included RCTs. The textual reporting is a reflection of the rarity of these events. To overcome this limitation, and capture adverse event data, the data extractions included the textual description of recorded adverse events. Statements were only converted to numerical data if text explicitly stated the absence of the adverse event.

Lower limb neural blockade

Adverse events occurred rarely in the 11 included RCTs for lower limb percutaneous neural blockade (Table 92, Appendix N). Of these ten reported data on adverse events. Overall ultrasound is equivalent to comparator guidance techniques.

Trunk neural blockade

No insertion related adverse events or procedural complications were reported in the three studies that provide evidence on neural blockade of the trunk (Table 93, Appendix N). The only extractable adverse event data related to a single patient who experienced a femoral extension of regional anaesthesia requiring the patient to be admitted to the surgical ward delaying discharge by one day.

Upper limb neural blockade

Adverse events are rarely reported in the 15 included studies (Table 94, Appendix N). Five studies report vascular punctures events for comparator guidance techniques, two of which favour ultrasound. However, the statistical significance is unknown. Reported procedural complications include transient paraesthesia, skin infiltration, accidental aspiration of blood and regional anaesthetic toxicity. Again, no evidence suggests that there is a significant difference between the ultrasound guided neural blockade and comparator techniques. Haematoma was rarely reported and the use of ultrasound was without effect on the incidence of this adverse event. One study reported a positive impact of ultrasound on the occurrence of paraesthesia that reached statistical significant ($P < 0.001$). The study by Stub et al reported on post-procedure pain and in this study the use of ultrasound significantly ($P < 0.05$) reduced the incidence of this adverse event. None of the studies report on pneumothorax, therefore this adverse event was omitted from the tabulation

The study by Renes et al. (2009) was design to determine the impact of guidance technique on adverse event of hemi-diaphragmatic paralysis following inter-scalene brachial plexus nerve block. The incidence of hemi-diaphragmatic paresis reduced from 93% to 13% ($P < 0.001$). However, due to the limited sample size (15 participants per study group) the repeatability of this outcome is unknown.

Is it effective?

Lower limb neural blockade

Among the 11 included studies, seven of them reported the needle redirection count (Table 95, Appendix N). Needle redirects are defined as the need to withdraw the needle by a defined distance with a subsequent advancement to reposition the needle. This procedure is also termed needle passes. For three of the seven studies ultrasound was reported to be equivalent to comparator with respect to needle redirects. The remaining four studies reported a reduction in the need for needle redirection and this reduction was reported to be statistically significant in two studies.

Block failure is variously described as exceeding a predetermined time for identification of the nerve and injection of anaesthetic agent through to surgical anaesthesia not being achieved. The impact of ultrasound on such block failures was reported in five of the 11 studies. Of these five studies, three reported statistically significant ($P < 0.05 – P < 0.001$) reductions in the number of block failures for the ultrasound guidance group . The remaining two studies reported either equivalence between techniques or a trend in favour of ultrasound. .

Time for needle or catheter placement was recorded as a primary effectiveness outcome for six of the 11 studies. Of these, four studies compared ultrasound with electrical nerve stimulation while a landmark technique was the comparator for the remaining two studies. Time to needle or catheter placement was shorter for ultrasound guidance as compared with electrical nerve stimulator technique. This effect reached statistical significance for three studies (Kent et al 2013). In contrast, for the studies that compared ultrasound to a landmark comparator the time taken to place a needle or catheter using ultrasound guidance was longer and this difference was statistically significant ($P < 0.05$). Overall, ultrasound does appear to reduce the time needed for placement of needle or catheter when compared with electrical nerve stimulation.

Nerve block characteristics were reported in six of the 11 included studies. Block characteristics are defined as the time at which either sensory or motor function is lost or the proportion of patients that experience a regional anaesthesia at a given time post injection. Four studies reported the proportion of patients with sensory or motor block at defined times post placement. For these four studies the use of ultrasound during the placement of the neural blockade significantly ($P < 0.05 – P < 0.001$) increased the proportion of patients with either a sensory or motor block.

The final two block characteristic reported were the duration of the regional anaesthesia and the volume of anaesthetic agent need to induce or maintain the anaesthetic effect. Two studies reported on the duration of regional anaesthesia. Ponde et al. (2009) reported a statistically significant ($P < 0.001$) extension of block duration. With respective to volume of anaesthetic used, the study by Danelli et al was designed to determine the $MEAV_{50}$ of mepivacaine to effectively block the sciatic nerve. The authors of this study reported a reduction in volume from 19mL down to 12mL of 0.5% mepivacaine to induce a surgical anaesthesia in 50 per cent of patients. The study by Maalouf et al. (2012) reported that the cumulative post-operative use of 0.2% ropivacaine was reduced from 200mL to 50mL in the ultrasound group.

Trunk neural blockade

Three studies are included for nerve blocks located to the truck region (Table 96, Appendix N). None of the studies reported the number of needle redirections or skin punctures. Only one study reported on block failure. No failures were reported for penile nerve blocks performed under ultrasound guidance as compared with 20 per cent with the landmark technique. One of the studies reported on the time taken for needle placement. The use of ultrasound resulted it a median placement of 115s as compared with 40s for the landmark group, this difference was statistically significant ($P < 0.001$). Furthermore, this result is similar to those reported in studies on lower limb nerve block that compared ultrasound guidance with a landmark technique.

Upper limb neural blockade

The needle redirects, skin puncture or depth of needle insertion are reported in four of the 15 included studies (Table 97, Appendix N). Three of the four studies that reported needle redirects compared an ultrasound guidance technique with electrical nerve stimulation. Two of these studies reported a statistically significant ($P < 0.05$) decrease in needle redirections. In contrast, the study by Salem et al reported that ultrasound increased the need for redirection compared with the electrical nerve stimulator groups. However, the redirects were precipitated not by the visual placement of the needle but whether or not an electrical stimulation evoked a muscle contraction once the needle had be placed under ultrasound guidance. The remaining study reported that the number of redirects was equivalent when ultrasound was compared with a landmark technique.

Block failure was reported for seven of the 11 included studies. Six reported a trend for a decrease in block failure when ultrasound is used to guide the placement of the neural blockade. For one of these, the improvement with respective to block failure was statistically significant ($P < 0.01$). The remaining study that reported characteristics that can be classified as being a failed block reported equivalence between guidance techniques.

Time to needle or catheter placement was reported for 11 of the 15 studies. Eight of these compared ultrasound with electrical nerve stimulation with three of these studies reporting a statistically significant ($P < 0.05$ to $P < 0.001$) reduction in time to placement. Three studies reported equivalence between these two guidance techniques and one study demonstrated ultrasound guidance extended the placement time ($P < 0.05$). A further three studies evaluated ultrasound against a landmark technique. One reported a significant increase in time to placement. However, two studies reported equivalence for time to placement for these two guidance techniques.

The block characteristics were reported in nine of the 15 included studies. Regarding block characteristics, three of the nine studies reported equivalence between ultrasound and the comparator guidance technique. Trabelsi et al reported that the onset time was significantly ($P < 0.01$) reduced for neural blockades placed under ultrasound guidance. In addition, three studies reported on readiness for surgery, two reported the time to surgery and one reported the proportion of patients ready at 20min post-neural block placement. Two of these studies reported statistically significant ($P < 0.05$ – $P < 0.001$) improvement for the ultrasound guided neural blockades, while the other reported equivalence between the two guidance techniques.

The final effectiveness measure is volume anaesthetic that can effectively induce a regional anaesthesia. Ponrouch and co-workers assess the $MEAV_{50}$ of mepivacaine for

neural blockade of the median and ulnar nerves. For the median nerve the use of ultrasound to guide placement reduced the $MEAV_{50}$ by 50 per cent when compared with blocks placed using electric nerve stimulation. However, these authors report equivalent $MEAV_{50}$ for both the ultrasound and electric nerve stimulator techniques for the ulnar nerve.

Overall, the evidence indicates that neural blockade performed using ultrasound guidance is at least equivalent to, and for some characteristic significantly better than, the performance of neural block placed using either the electric nerve stimulator or landmark guidance techniques. However, the included studies are bias to the blockade of the sciatic nerve (lower limb) and the brachial plexus (upper limb). In addition, only three studies that assessed nerve blocks associated with the truncal blocks met the review inclusion criteria. As such, caution should be exercised in generalising the effectiveness data extracted from the included studies.

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Meta-analysis: Nerve block

The total evidence base included in the meta-analysis for nerve block comprised of 58 RCTs, these were identified in our search of electronic databases and pearling the reference lists of retrieved systematic reviews (Table 80). Twenty nine of the identified RCTs have previously been included in published systematic reviews. The remaining 29 RCTs that have not been described previously were subjected to data extraction for information relevant to safety and effectiveness (Table 92 to Table 97, Appendix L). Extracted data were the then pooled with the primary data reported by the recent, relevant and high quality systematic reviews (Choi and Brull 2011; Walker et al 2011). Comparator guidance techniques are landmark (LM) including trans-arterial (TA), electrical nerve stimulation (ENS) or ultrasound with electrical nerve stimulation (US + ENS). In cases of high statistical heterogeneity as indicated by the Q and I^2 statistics, data were further integrated using sub-groupings selected *a priori* and based on comparator method, the anatomical location of nerve block, or through data coded based on the description of block failure or block characteristics.

Safety:

Safety (adverse) events reported to be associated with nerve block protocols, irrespective of guidance method, are the inappropriate vascular puncture, haematoma, paraesthesia and nerve injury.

Vascular puncture

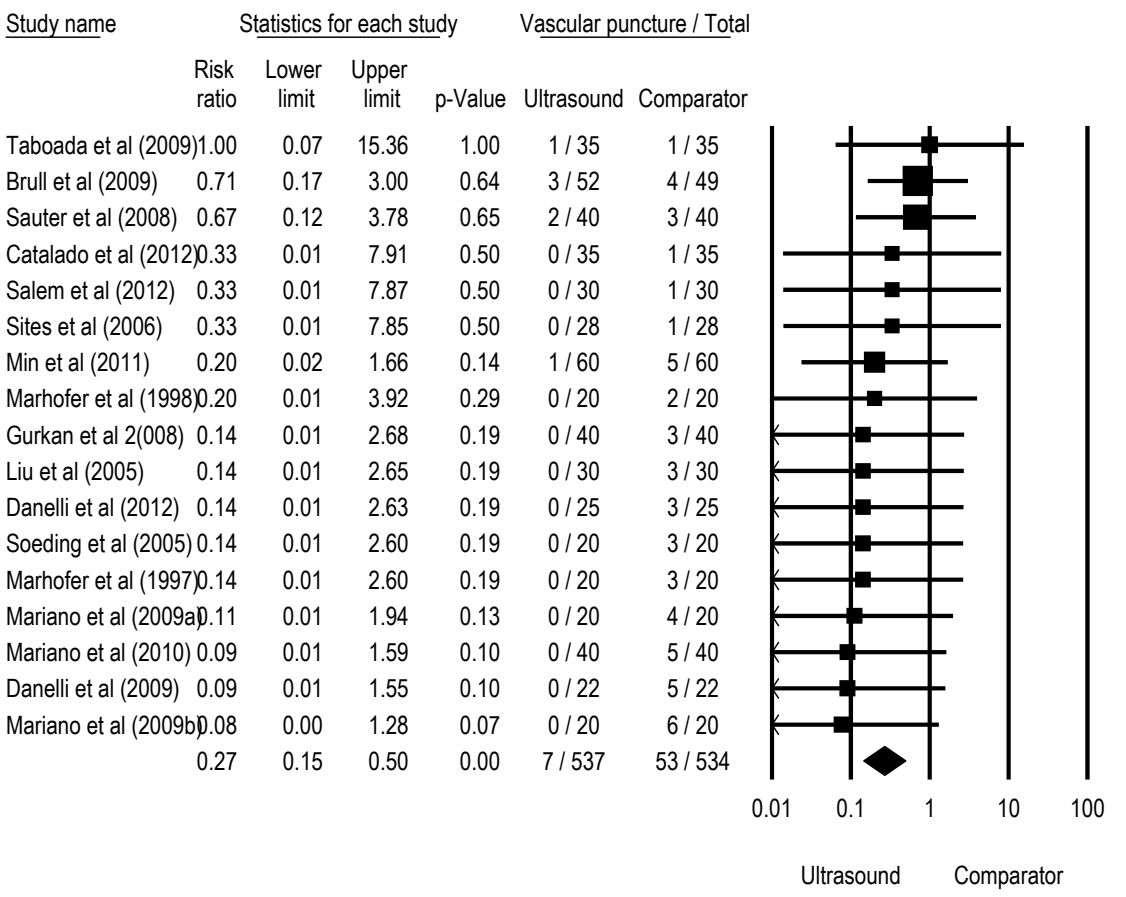
Twenty seven of the 58 RCTs reported event data for inappropriate vascular puncture (IVP) of these 17 had data that could be combined in a meta-analysis and represents a total patient population of 1,071. The prevalence of IVP for this population was 1.30 per cent and 9.92 per cent for nerve block guided by either the ultrasound or other (electrical nerve simulator, landmark) guidance methods, respectively. The analysis showed that ultrasound guidance of nerve block significantly reduced the risk of vascular puncture compare to all comparators (RR 0.27, 95% CI: 0.15 - 0.50, $P < 0.001$, Figure 14, Table 32). The risk of IVP was significantly lowered for ultrasound use when compared with nerve stimulation (RR 0.28, 95% CI: 0.14 - 0.56, $P < 0.001$, Table 32). There was no risk reduction for ultrasound use compared to landmark and trans-arterial methods or for the use of ultrasound with electrical nerve stimulator compared to nerve stimulator alone. Ultrasound use significantly lowered the risk of IVP for both upper and lower nerve blocks (Table 32).

Table 32 Summary of meta-analysis statistics for overall pooled analysis and subgroups based on comparator and block location for inappropriate vascular puncture during ultrasound or comparator guided placement of percutaneous neural blockades

Grouping	No of studies	Point estimate	CI_{lower} (95%)	CI_{upper} (95%)	P value
Overall	17	0.27	0.15	0.50	P < 0.001
US vs. LM	1	0.143	0.01	2.60	P = 0.189
US vs. ENS	12	0.28	0.14	0.56	P < 0.001
US vs. TA	1	0.33	0.01	7.85	P = 0.495
US+ENS vs. ENS	3	0.26	0.06	1.19	P = 0.081
Upper extremity	10	0.36	0.17	0.78	P = 0.009
Lower extremity	7	0.152	0.05	0.43	P < 0.001

Data are reported as the pooled risk ratio using a random effect model

Figure 14 Individual study and the pooled (random effects model) risk ratios for inappropriate vascular puncture during ultrasound or comparator guided placement of percutaneous neural blockades



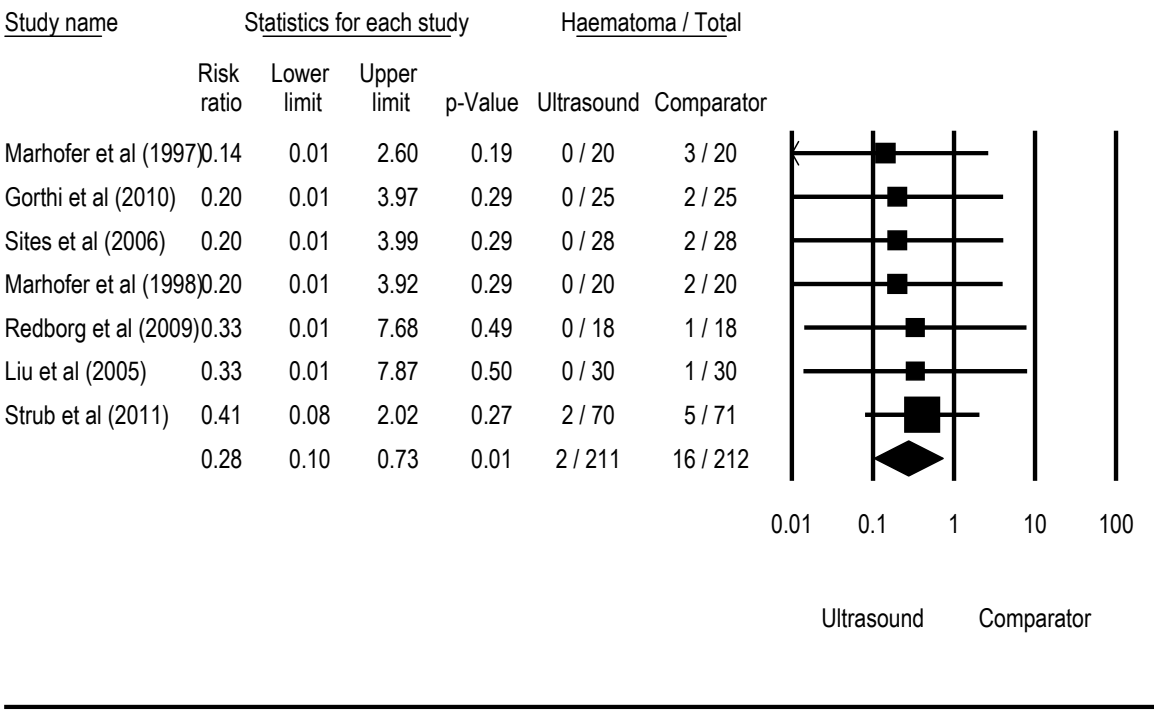
Heterogeneity: Q = 6.97(p =0.974)), I statistic = 0

Haematoma

Fifteen of the 58 RCTs reported event data for haematoma; of these seven had data that could be combined in a meta-analysis and represent a total patient population of 423.

The incidence of haematoma for this population was 0.95 per cent and 7.5 per cent for nerve block guided by either the ultrasound or other (electrical nerve simulator, landmark) guidance methods, respectively. The analysis showed that ultrasound guidance of nerve block did significantly reduced the risk of haematoma compare to all comparators (RR 0.28, 95% CI: 0.10 – 0.74, P = 0.01, Figure 15, Table 33). However, when analysed by comparator sub-groups, no statistical significant risk reduction was obverse for ultrasound use when compared to electrical nerve stimulation, landmark and trans-arterial methods or for the use of ultrasound with electrical nerve stimulator compared to electrical nerve stimulator alone. Furthermore, ultrasound use did not significantly lower the risk of haematoma for either upper or lower nerve blocks (Table 33).

Figure 15 Individual study and the pooled (random effects model) risk ratios for haematoma formation during ultrasound or a comparator guided placement of percutaneous neural blockades



Heterogeneity: Q = 0.58 (p =0.997), I statistic = 0

Table 33 Summary of meta-analysis statistics for overall pooled analysis and subgroups based on comparator and block location for haematoma formation during ultrasound or comparator guided placement of percutaneous neural blockades

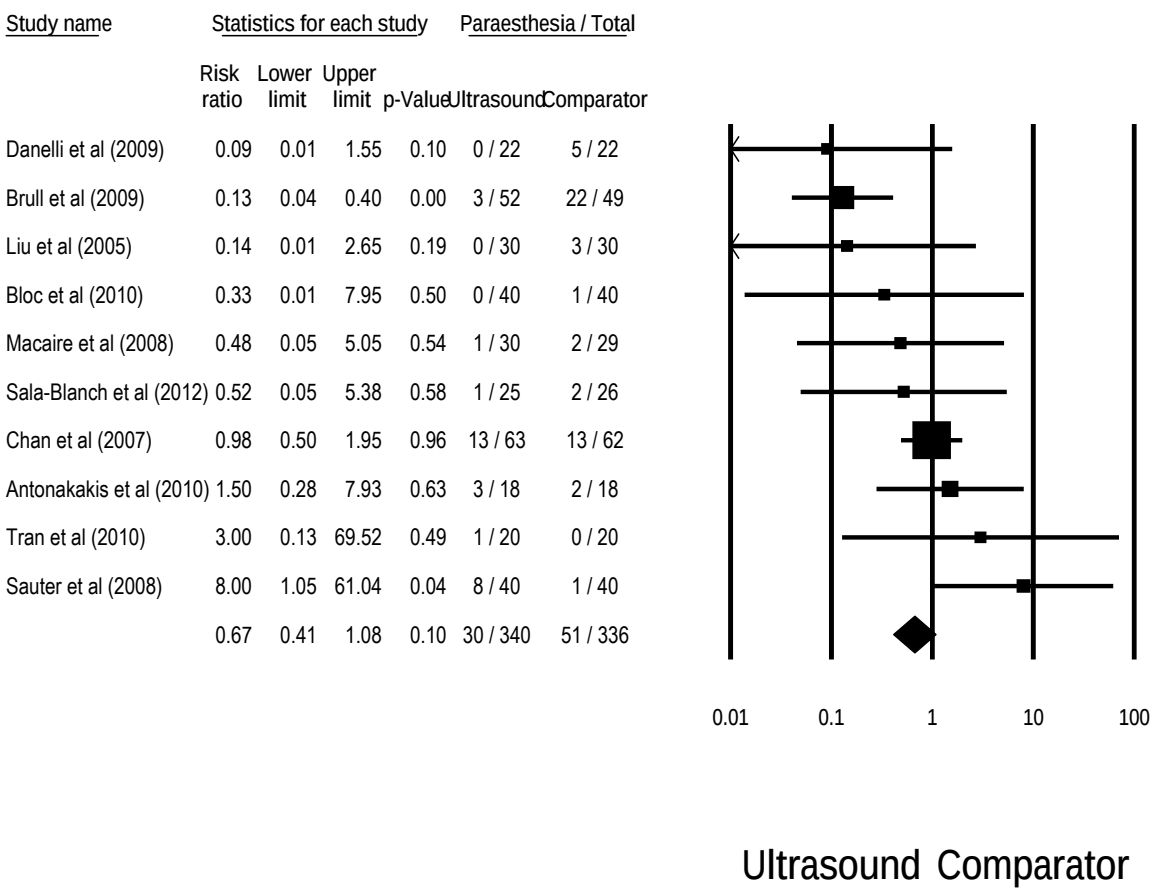
Grouping	No of studies	Point estimate	CI_{lower} (95%)	CI_{upper} (95%)	P value
Overall	7	0.28	0.10	0.74	P = 0.01
US vs. LM	3	0.34	0.10	1.25	P = 0.105
US vs. ENS	3	0.21	0.04	1.17	P = 0.075
US vs. TA	1	0.20	0.01	3.99	P = 0.29
Upper extremity	4	0.32	0.10	1.03	P = 0.057
Lower extremity	8	0.21	0.04	1.17	P = 0.075

Data are reported as the pooled risk ratio using a random effect model

Paraesthesia

Fifteen of the 58 RCTs reported event data for paraesthesia of these ten had data that could be combined in a meta-analysis and represent a total patient population of 676. The prevalence of paraesthesia for this population was 8.82 per cent and 15.18 per cent for nerve block guided by either the ultrasound or comparator guidance methods, respectively. The analysis showed that ultrasound guidance of nerve block did not significantly reduced the risk of paraesthesia compare to comparators (RR 0.620, 95% CI: 0.255-1.508, P=0.292, Figure 16, Table 34). There was no significant risk reduction associated with ultrasound use when compared to either electrical nerve stimulation or landmark methods.

Figure 16 Individual study and the pooled (random effects model) risk ratios for the occurrence of paraesthesia during ultrasound or comparator guided placement of percutaneous neural blockades



Heterogeneity: Q = 20.0 (p = 0.0.18), I statistic = 55.1

Table 34 Summary of meta-analysis statistics for overall pooled analysis and subgroups based on comparator and block location for the occurrence of paraesthesia during ultrasound or comparator guided placement of percutaneous neural blockades.

Grouping	No of studies	Point estimate	CI_{lower} (95%)	CI_{upper} (95%)	P value
Overall	10	0.620	0.255	1.508	P = 0.292
US vs. LM	2	1.880	0.226	15.632	P = 0.559
US vs. ENS	8	0.484	0.179	1.317	P = 0.155

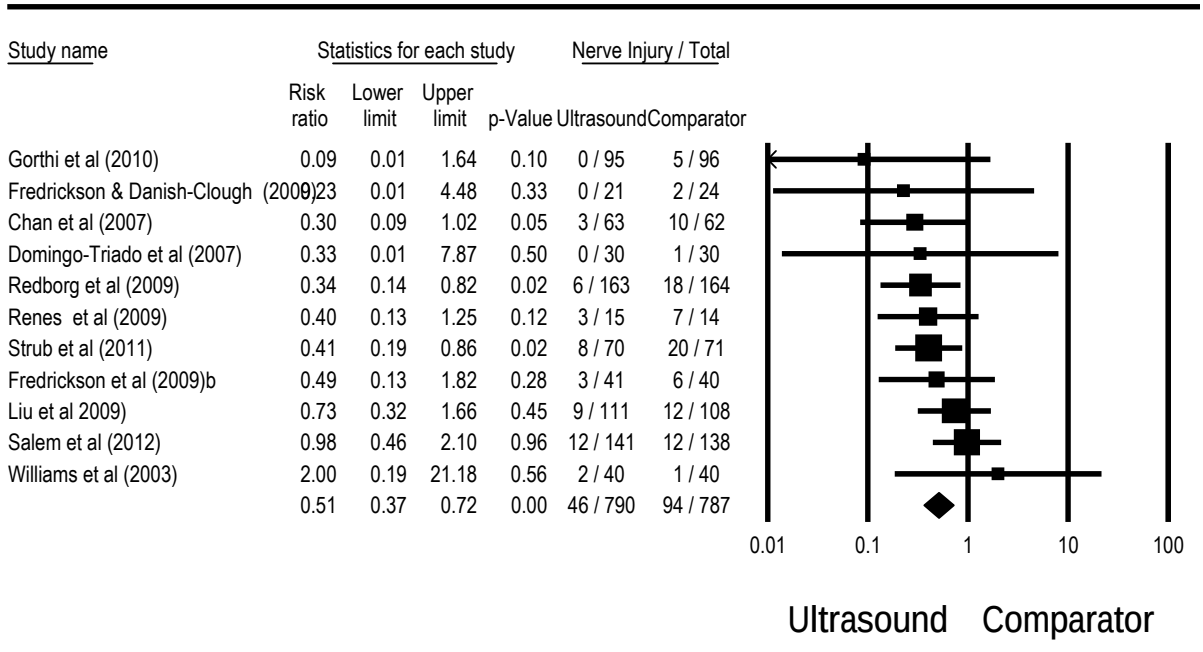
Data are reported as the pooled risk ratio using a random effect model

Nerve injury

Seventeen of the 58 RCTs report event data for nerve injury of these 11 reported report data that was combinable by meta-analysis and represents a total patient population of 1,577. The incidence of nerve injury for this population was 5.82 per cent and 11.94 per cent for nerve block guided by either the ultrasound or comparator guidance methods,

respectively. The analysis showed that ultrasound guidance of nerve block significantly reduced the risk of nerve injury compared to all comparators (RR 0.51, 95% CI: 0.37 - 0.72 P<0.001, Figure 17, Table 35). Ultrasound use was associated with a significantly lower risk of nerve injury than electrical nerve stimulation (RR 0.44, 95% CI: 0.24 - 0.81 P<0.001, Table 35) and landmark (RR 0.30, 95% CI: 0.16 - 0.57 P<0.001, Table 35) methods. There was no significant risk reduction for the use of ultrasound with electrical nerve stimulator compared to electrical nerve stimulator alone. Ultrasound use was associated with a significantly lower risk of nerve injury for upper nerve blocks (RR 0.48, 95% CI: 0.32 - 0.70 P<0.001, Table 35); however, there was no significant difference for lower nerve blocks (Table 35).

Figure 17 Individual study and the pooled (random effects model) risk ratios for nerve injury during ultrasound or comparator guided placement of percutaneous neural blockades



Heterogeneity: Q = 8.63 (p = 0.567), I statistic = 0

Table 35 Summary of meta-analysis statistics for overall pooled analysis and subgroups based on comparator and block location for nerve injury during ultrasound or comparator guided placement of percutaneous neural blockades.

Grouping	No of studies	Point estimate	CI_{lower} (95%)	CI_{upper} (95%)	P value
Overall	11	0.51	0.37	0.72	P < 0.001
US vs. LM	3	0.30	0.16	0.57	P < 0.001
US vs. ENS	5	0.44	0.24	0.81	P = 0.008
US+ENS vs. ENS	3	0.99	0.46	2.13	P = 0.975
Upper extremity	9	0.48	0.32	0.70	P < 0.001
Lower extremity	2	0.26	0.03	2.41	P = 0.235

Data are reported as the pooled risk ratio using a random effect model

Effectiveness:

Effectiveness outcomes reported to be associated with nerve block protocols, irrespective of guidance method, are the mean time to administer the block , the mean number of needle redirects, the number of skin puncture, the number of failed blocks, the block onset time and the time until analgesia is required.

Time to administer the block

Twenty six of the 58 RCTs report data on time to administer the block (placement time) and represents a total patient population of 2,025. Across all the studies the use of ultrasound was associated with a faster mean placement time (difference in means -1.66 min, 95% CI: -2.32 to -1.01, P < 0.001, Figure 18, Table 36). The time required for ultrasound guided block placement as compared with a landmark guided placement was significant longer (difference in means 0.92 min, 95% CI: 0.16 – 1.72, P = 0.02, Table 36). In contrast, the time required for ultrasound assisted nerve block placement was shorter when compared with the electrical nerve stimulator guided technique (difference in means -2.14 min, 95% CI: -2.68 to -1.60, P<0.001, Table 36). Similarly, the time required to administer the block was significantly shorter when compared with the trans-arterial or when ultrasound was used in conjunction with electrical nerve stimulation and compared to electrical nerve stimulation (Table 36). The impact of ultrasound on nerve block placement was statistical significant whether the target nerve was located in either the upper or lower extremities. In these comparisons ultrasound significantly reduced placement time when compared with the electrical nerve stimulation method (Table 36).

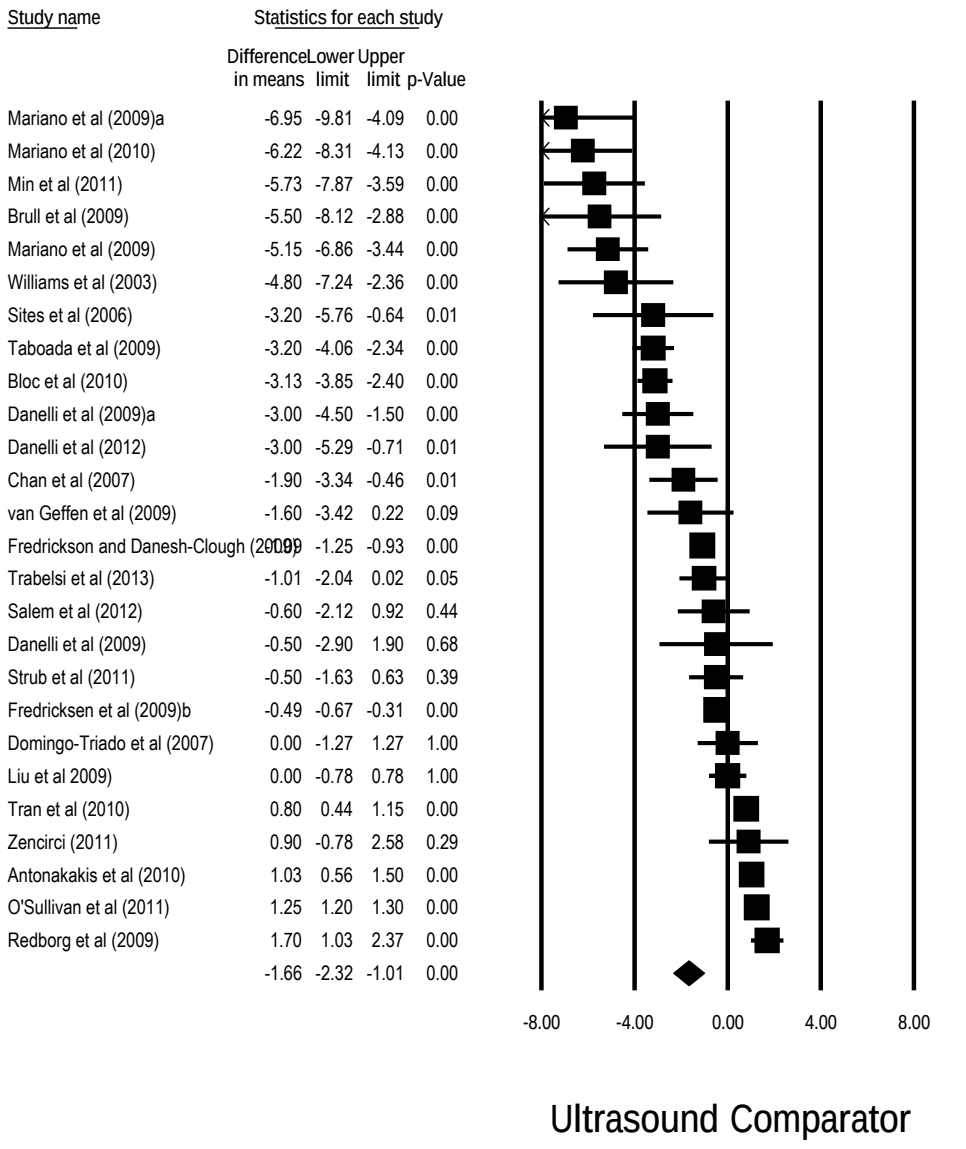
Table 36 Summary of meta-analysis statistics for overall pooled analysis and subgroups based on comparator and block location for the difference in mean placement time for ultrasound or comparator guided placement of percutaneous neural blockades

Grouping	No of studies	Point estimate	CI_{lower} (95%)	CI_{upper} (95%)	P value
Overall	26	-1.663	-2.32	-1.01	P < 0.001
US vs. LM	5	0.92	0.16	1.72	P = 0.02
US vs. ENS	16	-2.139	-2.68	-1.60	P < 0.001
US vs. TA	1	-3.20	-6.25	-0.15	P = 0.04
US+ENS vs. ENS	4	-2.14	-3.35	-0.93	P = 0.001
Upper extremity [1]	14	-2.32	-3.30	-1.33	P < 0.001
Lower extremity[1]	9	-2.93	-4.19	-1.68	P < 0.001

Data are reported as the pooled risk ratio using a random effect model

1: Upper and Lower extremity blocks: Ultrasound vs. ENS comparator only.

Figure 18 Individual study and the pooled (random effects model) difference in mean: placement time for ultrasound or comparator guided placement of percutaneous neural blockades



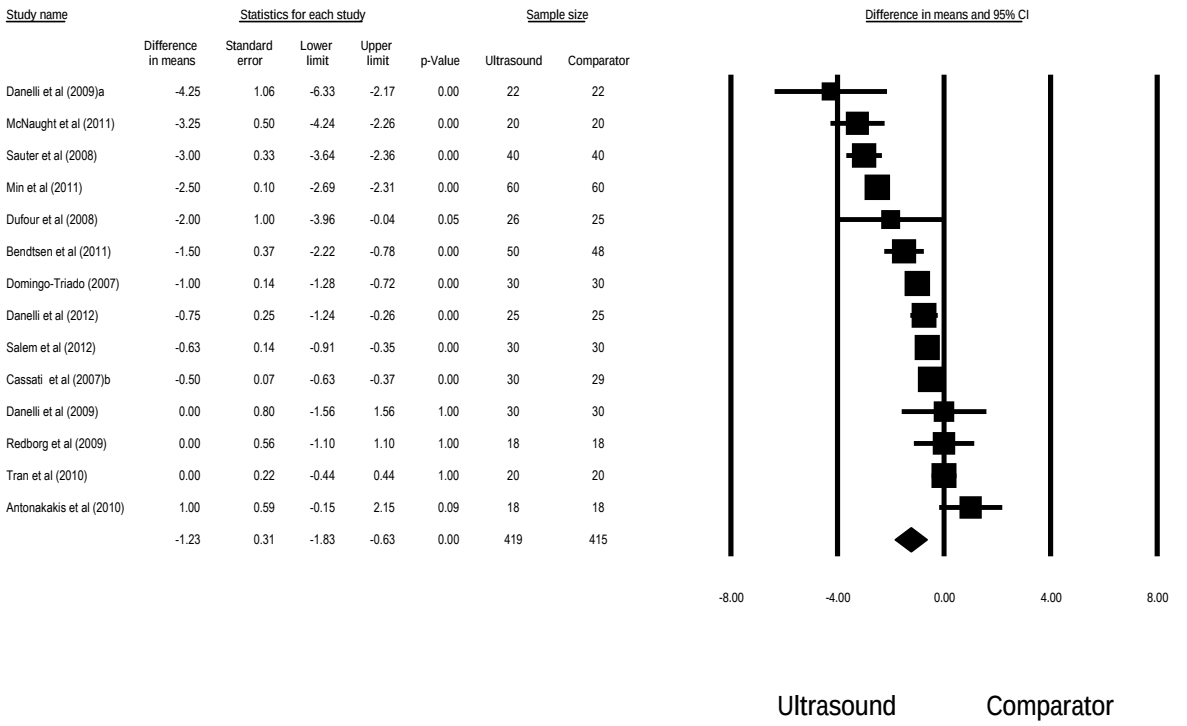
Heterogeneity: Q = 1495 (p < 0.001), I statistic = 98.32

Needle redirects

Fourteen of the 58 RCT's report data for needle redirects and this represents a total patient population of 834 patients. Across all the studies the use of ultrasound was associated with a statistically significant reduction in the number of needle redirects required for successful block placement (difference in means -1.23, 95% CI: -1.83 to -0.64 P <0.001,Figure 19 Table 37). The number of needle redirects required for ultrasound placement compared to electrical nerve stimulator guided placement was significantly fewer (difference in means -1.50, 95% CI: -1.50 to -2.32, P<0.001, Table 37). In contrast, when the comparisons of ultrasound with landmark or ultrasound plus electrical nerve stimulation with electrical nerve stimulation are made no statistically

significant difference in mean number of needle redirects to affect a nerve block placement was observed (Table 37).

Figure 19 Individual study and the pooled (random effects model) difference in mean: needle redirections for ultrasound or comparator guided placement of percutaneous



Heterogeneity: Q = 20.87 (p < 0.001), I statistic = 80.83

Table 37 Summary of meta-analysis statistics for overall pooled analysis and subgroups based on comparator and block location for the difference in mean for number of needle redirection for ultrasound or comparator guided placement of percutaneous neural blockades

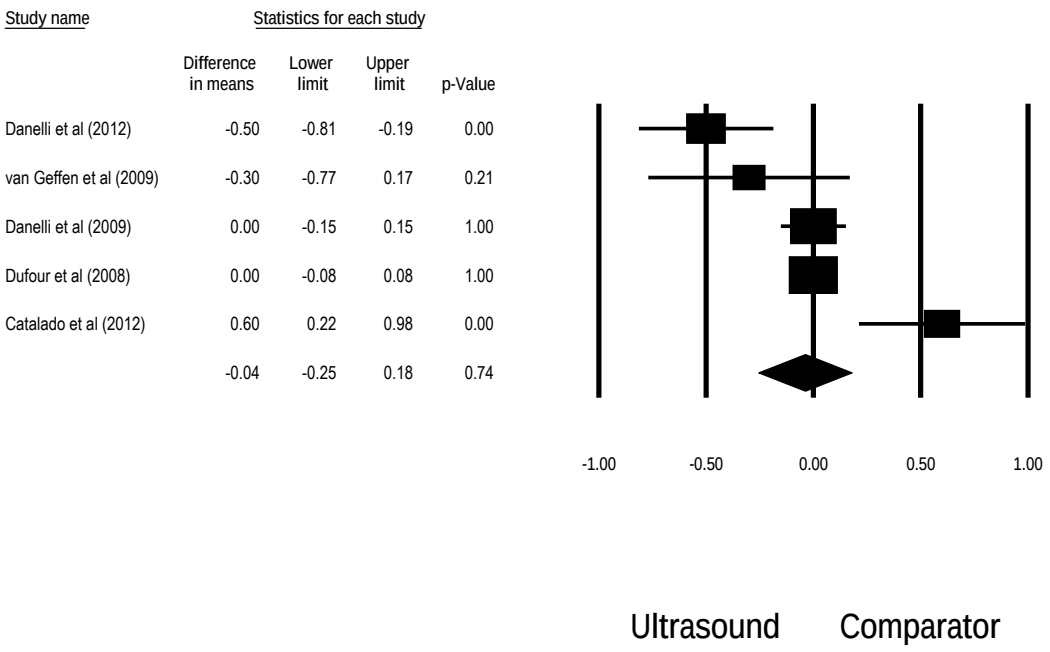
Grouping	No of studies	Point estimate	Cllower (95%)	Clupper (95%)	P value
Overall	14	-1.23	-1.83	-0.64	P < 0.001
US vs. LM	3	0.31	-1.06	1.67	P = 0.659
US vs. ENS	8	-1.50	-2.32	-0.68	P < 0.001
US+ENS vs. ENS	4	-0.91	-1.91	-0.10	P = 0.08

Data are reported as the pooled risk ratio using a random effect model

Skin punctures

Five of the 58 RCTs report data for skin punctures and represents a total patient population of 158 patients. Across all the studies the use of ultrasound was not associated with a statistically significant reduction in the number of skin punctures required for successful block placement (difference in means -0.04, 95% CI: -0.25 to 0.18, P=0.735, Figure 20, Table 38).

Figure 20 Individual study and the pooled (random effects model) difference in mean: number of skin punctures during ultrasound or comparator guided placement of percutaneous



Heterogeneity: Q = 20.8 (p < 0.001), I statistic = 80.8

Table 38 Summary of meta-analysis statistics for overall pooled analysis for the difference in mean for number of skin punctures during ultrasound or comparator guided placement of percutaneous neural blockades

Grouping	No of studies	Point estimate	CI_{lower} (95%)	CI_{upper} (95%)	P value
Overall	5	-0.04	-0.25	0.18	P = 0.735

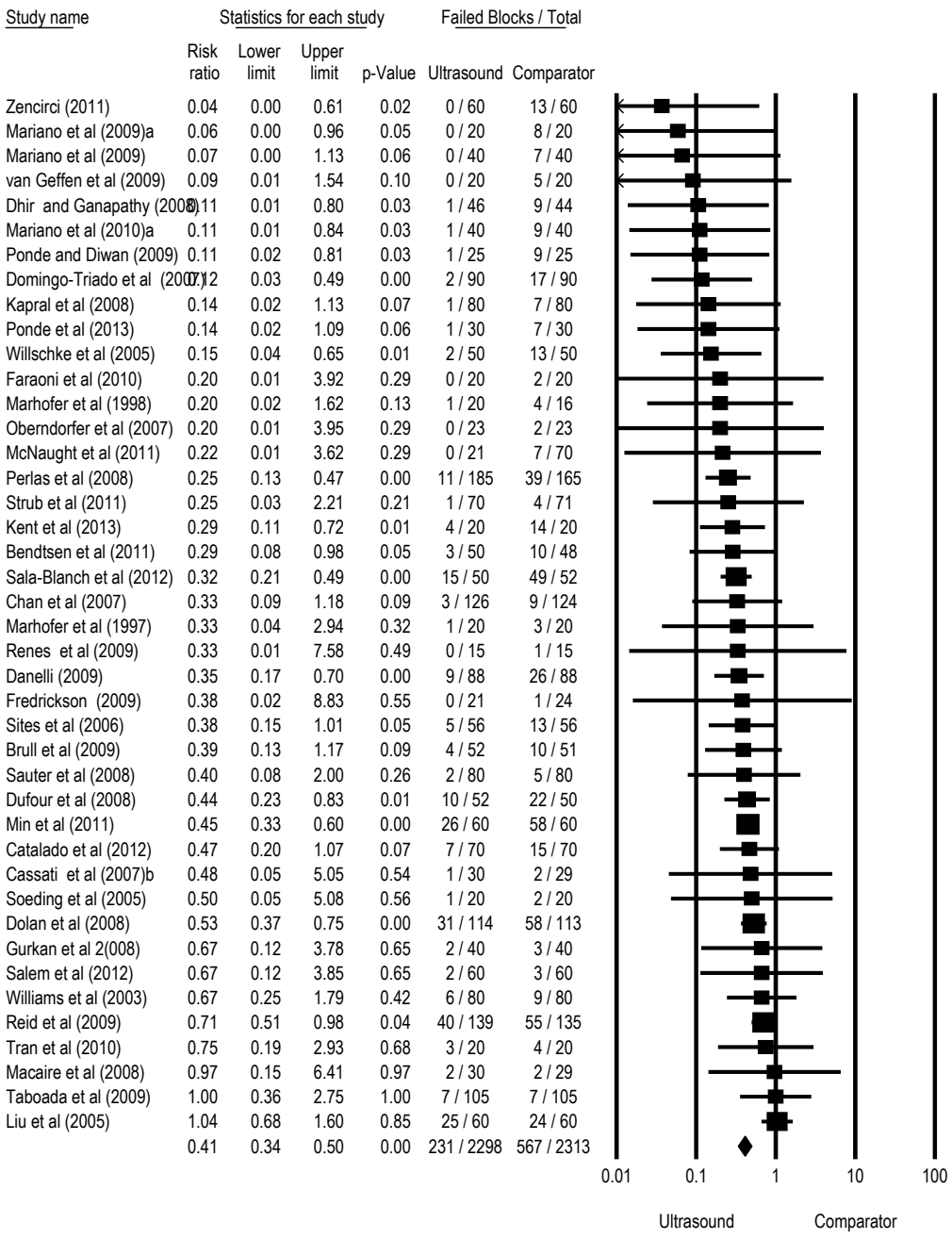
Data are reported as the pooled risk ratio using a random effect model

Failed nerve blocks

Forty two of the 58 RCTs report data for failed nerve blocks and represents a total patient population of 4,611 patients. Across all the studies the use of ultrasound was associated with a statistically significant reduction in the risk of nerve block failure (RR 0.41, 95% CI: 0.34 -0.50, P < 0.001, Figure 21 Table 39). Sub group analysis by comparator, anatomical location of the block, characteristics of block failure (sensory

(SB), motor (MB), procedural (PB)) and need for addition anaesthesia or analgesia are detailed in Table 39.

Figure 21 Individual study and the pooled (random effects model) risk ratio: the occurrence of block failure (aggregate of sensory, motor and procedural failure as well as the need for addition anaesthesia or analgesia) for ultrasound or comparator guided placement of percutaneous



Heterogeneity: Q = 58.4 (p = .0.38), I statistic = 29.8

The use of ultrasound reduced the risk of nerve block failure when compared to all comparators across the included RCTs, with the exception of the single study comparing ultrasound guidance with a trans-arterial technique; the risk reductions were statistically

significant (Table 39). In addition, the reducing effect of ultrasound on the risk of block failure was observed for the three anatomical regions evaluated in the included RCTs and these differences were statistically significantly different. The impact of ultrasound on nerve block failure was assessed according to different classification of block failure. For both sensory and motor block failure the risk ratio was 0.43 (0.29 – 0.65) and 0.47 (0.27 – 0.81), respectively. These reductions in risk are statistically significant. The risk ratio for nerve block failures classified has being procedural in nature was 0.22 (0.07 – 0.68, P = 0.008) when ultrasound was compared with comparator guidance techniques. Furthermore, the use of ultrasound to guide the placement of neural blocks returned an apparent risk ratio in favour of ultrasound for additional anaesthesia or analgesia when compared with the comparator techniques; however, this risk reduction was not significantly different.

Table 39 Summary of meta-analysis statistics for overall pooled analysis for the risk ratio for the occurrence of block failure (aggregate of sensory, motor and procedural failure as well as the need for addition anaesthesia or analgesia) when performing ultrasound or comparator guided placement of percutaneous neural blockades

Grouping	No of studies	Point estimate	CI_{lower} (95%)	CI_{upper} (95%)	P value
Overall	42	0.41	0.34	0.50	P < 0.001
US vs. LM	7	0.53	0.36	0.80	P = 0.002
US vs. ENS	29	0.37	0.28	0.47	P < 0.001
US vs. TA	1	0.39	0.13	1.19	P = 0.096
US+ENS vs. ENS	5	0.43	0.26	0.72	P = 0.001
Upper extremity	21	0.53	0.38	0.73	P < 0.001
Lower extremity	19	0.38	0.31	0.49	P < 0.001
Trunk	2	0.16	0.04	0. 63	P = 0.009
Failed sensory block	22	0.43	0.29	0.65	P < 0.001
Failed motor block	8	0.47	0.27	0.81	P = 0.007
Procedural failure	17	0.22	0.07	0.68	P = 0.008
Requiring additional anaesthesia or analgesia	13	0.61	0.24	1.51	P = 0.282

Data are reported as the pooled risk ratio using a random effect model

Block characteristics

Of the 58 RCTs that reported block characteristics three (169 patients) provided information regarding onset of motor block, 11(613 patients) evaluated the onset of sensory block, seven (500 patients) listed an overall onset time, two reported (191 patients) time ready for surgery and three (151 patients) provided information regarding the time to first analgesia (Table 40). Meta-analysis of block onset times, the use of ultrasound reduces the point estimate for the onset by 2.85 to 4.41 min. The reduction in on onset time was not statistically significant for both the motor (-2.85 min, 95% CI -9.65 to 3.95, P = 0.411) and sensory (-2.87 min, 95% CI -6.24 to 0.49, P = 0.094) onset times. There was, however, a statistically significant reduction in onset time for studies

that reported an overall onset time (-4.41 min, 95% CI: -8.84 to -0.08, P=0.046, Table 40). Two studies reported on the time patients were ready for surgery. Using ultrasound to guide block placement resulted in patients being ready for surgery sooner when compared to patient receiving nerve blocks guided by one of the comparator techniques. The mean difference in the point estimate for this characteristic was -12.23 min (-20.72 to -3.72, P = 0.005, Table 40). Combining the three RCTs that report data on the time until first analgesia administered returned a non-significant extension in the point estimate for this parameter (difference in means (hours) 2.82, 95% CI: -3.32 to 8.96, P=0.367, Table 40).

Table 40 Summary of meta-analysis statistics for the difference in mean: timing characteristic for ultrasound or comparator guided placement of percutaneous neural blockades

Grouping	No of studies	Point estimate	CI_{lower} (95%)	CI_{upper} (95%)	P value
Motor Block onset (min)	3	-2.85	-9.65	3.95	P = 0.411
Sensory Block onset (min)	11	-2.87	-6.24	0.49	P = 0.094
Block onset (type not defined) min	7	-4.41	-8.84	-0.08	P = 0.046
Ready for Surgery	2	-12.23	-20.73	-3.72	P = 0.005
Time to analgesia (hr.)	3	2.82	-3.32	8.96	P = 0.367

Data are reported as the pooled risk ratio using a random effect model

Summary of percutaneous neural blockade

A total of ten systematic reviews were identified that had relevance to this report. These reviews were published between 2009 and 2013. All systematic reviews were critically appraised and three were rated as being of good quality. The reviews investigated a range of populations (patients requiring nerve blocks as a component of anaesthesia for surgery, or use of neural blockade for post-operative analgesia as well as non-operative pain management). In terms of location the reviews also assessed upper and lower extremity nerve blocks as well as truncal blocks. All systematic reviews concluded that ultrasound guided placement of nerve blocks was either equivalent to or an improvement on the comparators of landmark or electrical nerve stimulator techniques. ,

Upper and lower limb nerve blocks formed the majority of the evidence base. In total, results from 58 RCTs were pooled to inform the meta-analysis of which 29 represent studies not included in other systematic reviews.

Safety:

The following outcomes were statistically significant in favour of ultrasound guidance compared to the landmark or electrical nerve stimulator techniques

- Inappropriate vascular puncture was reported in 17 RCTs with a total of 1,071 patients. Ultrasound significantly reduced the risk of inappropriate vascular puncture (RR 0.27, 95% CI: 0.15 - 0.50, P < 0.001)
- Haematoma was reported in seven RCTs with a total of 423 patients. Ultrasound significantly reduced the risk of haematoma (RR 0.27, 95% CI: 0.28 - 0.74, P = 0.01)
- Nerve injury: Eleven RCTs representing 1,577 patients. Ultrasound reduced the risk of nerve injury (RR 0.51, 95% CI: 0.37 - 0.72, P < 0.001).

Ultrasound guidance was equivalent to either the landmark or electrical nerve stimulation methods for the following outcome:

- Paraesthesia was reported in 10 RCTs with a total of 676 patients (RR 0.62, 95% CI: 0.26 – 1.5, P = 0.292).

Effectiveness

The following outcomes were statistically significant in favour of ultrasound guidance compared to the landmark or electrical nerve stimulator techniques:

- Time to administer block was reported in 26 RCTs with a total of 2,025 patients. Ultrasound significantly reduced time to administer a nerve block (difference in mean time (min) -1.66, 95% CI: -2.32 to -1.01, P < 0.001)
- Number of needle redirects was reported in 14 RCTs with a total of 834 patients. Ultrasound significantly reduced number of needle redirections necessary to place a nerve block (difference in mean number of attempts, -1.23, 95% CI: -1.83 to -0.64, P < 0.001)

- Failed nerve blocks were reported in 42 RCTs with a total of 4,611 patients. Ultrasound significantly reduced the risk of nerve block failure (RR 0.41, 95% CI: 0.34 - 0.50, P < 0.001)
- Onset time was reported in seven RCTs with a total of 500 patients. Ultrasound significantly reduced the time for onset of an overall assessment of nerve block (difference in mean time (min) -4.41, 95% CI: -8.84 to -0.08, P = 0.046)
- Patients ready for surgery was reported in two RCTs with a total of 191 patients. Ultrasound significantly reduced the time for patients to ready for surgery (difference in mean time (min) -12.23, 95% CI: -20.73 to - 3.72, P = 0.005).

Ultrasound guidance was equivalent to either the landmark or electrical nerve stimulation methods for the following outcomes:

- Number of skin punctures was reported in five RCTs with a total of 158 patients (difference in mean number of punctures, -0.04, 95% CI: -0.25 to -0.18, P =0.735)
- Onset time for motor block was reported in three RCTs with a total of 169 patients (difference in mean (min) -2.85, 95% CI -9.65 to -3.95, P = 0.411)
- Onset time for sensory block was reported in 11 RCTs with a total of 613 patients. (difference in mean (min) -2.87, 95% CI -6.24 to -0.49, P = 0.094)
- Time to first analgesia was reported in three RCTs with a total of 151 patients (difference in mean (hr.) 2.82, 95% CI -3.32 to 8.96, P = 0.367).

Other relevant considerations

In their original submission of this proposal to the Department, the Australian Society of Anaesthetists stated that ultrasound imaging is used to improve patient outcomes during anaesthesia for a wide range of surgical procedures, in particular for vascular access and local anaesthetic nerve blockade. The ability to view the target vessel or nerve in real time, as opposed to blind injection based on knowledge of anatomy improves the safety of such procedures, by decreasing the probability of inadvertent damage either to the target vessel or nerve or other nearby anatomical structures such as arteries or lung. Ultrasound also provides benefits to the patient by increasing the success rate of such procedures, in comparison to blind techniques.

The use of ultrasound imaging in these services has been shown to reduce serious complications, improve patient safety and increase the overall success rates of the relevant interventions, such that it is now recommended as an essential component of these procedures.

What are the economic considerations?

Economic evaluation of new healthcare technologies is important when determining whether the new initiative offers additional benefits and at what cost. Economic evaluations are able to determine whether the new initiative is dominated by (or dominates) the existing technology, such that the costs are higher (lower) and the effectiveness is less (greater). Economic evaluation is particularly important where the new initiative offers health benefits at additional costs. Within a constrained healthcare budget, determining the additional cost that would be paid for a given health gain is important when ascertaining whether such incremental costs represent value for money.

The usual process for an economic evaluation is first to determine the incremental effectiveness, which is the additional benefits associated with the new technology relative to current practice. The second step is to determine the incremental costs, which is the difference in costs between the new initiative and current practice. Finally the incremental cost-effectiveness ratio (ICER) can be calculated using the following ratio:

$$ICER = \frac{Cost_{New} - Cost_{Comparator}}{Effectiveness_{New} - Effectiveness_{Comparator}}$$

Objective

The economic research questions as stated in 'Approach to assessment' section of this report (and on page 25 of the DAP) are:

1. What is the cost-effectiveness of ultrasound-guided percutaneous major vascular access compared to landmark technique?
2. What is the cost-effectiveness of ultrasound-guided percutaneous nerve blockade compared to landmark technique with or without assistance of ENS?

Search strategies

Any study investigating the use of ultrasound for nerve blocks or major vascular access was systematically identified (see 'Approach to assessment').

Peer-reviewed literature was searched in PubMed, EMBASE, Current Content, The Cochrane Library and CRD databases. Additionally web-based search engines, such as 'Google' and 'Google scholar' were also searched to identify relevant economic studies.

The bibliographies of all included publications were hand-searched for any relevant references that may have been missed by the database search. A comprehensive description of the search strategy was provided earlier (see 'Review of literature').

Background – evidence of cost-effectiveness

Five published economic or cost analyses were identified; two assessing ultrasound for vascular access (Calvert et al 2004; Kinsella and Young 2009) and three assessing ultrasound for nerve blocks (Ehlers et al 2012; Liu and John 2010; Sandhu et al 2004).

Vascular access economic analyses

The two economic analyses for vascular access compared ultrasound and the landmark technique for needle insertion. The design and results for these analyses are summarised in Table 41.

Calvert et al. (2004) undertook a cost-effectiveness analysis from the UK NHS perspective for patients requiring central venous access. Specifically, the base case analysis assumed that central venous lines are inserted using the internal jugular vein in a theatre environment. The costs of the ultrasound machine, and the cost for training to use the machine, were apportioned over the total procedures performed over the machine's lifetime. A total of 780 procedures per year and a lifetime of 3 years for the ultrasound machine were assumed. In addition the cost of consumables (gel and disposable covers) were considered. The cost of GPB6.65 per procedure for ultrasound was offset by a reduction in the number of failed insertions with each failed insertion assumed to delay surgery by 10 minutes (GBP5.11 based on a 7% reduction in first time failed insertions), and a reduction in the cost of treating arterial punctures (GBP3.60 based on a 9% reduction in incidence). Thus there was an overall cost saving per procedure with ultrasound of GBP 2.

Kinsella and Young (2009) undertook a cost analysis based on United States federal reimbursement costs. Based on the reimbursed costs, the additional cost for ultrasound guided central line placement was US$34.86. This was not offset by the cost of treating additional pneumothorax events with the landmark technique (US$1.09 based on a 0.75% reduction in the incidence). As noted by Kinsella, ultrasound guided placement is associated with a reduction in other events, including arterial punctures, cardiopulmonary resuscitation and intubation, that have not been considered in the analysis, and considering them would reduce the incremental cost.

Table 41 Published cost and economic analyses comparing ultrasound and landmark for vascular access

Publication and study design	Cost of US machine per procedure	Additional US costs	Cost savings	Conclusion
Calvert 2004 Cost effectiveness analysis UK NHS perspective Central venous cannulation	• Cost of machine: GBP11,000 (including maintenance) • Amortisation: 3 years • Procedures: 780 per year • Cost per procedure: GBP4.98	• US gel and disposable cover: GBP 0.67 per procedure • Training: GBP1.00 per procedure	• Reduction in first time failed insertions and hence 10 minute delay of surgery: GPB5.11 (7% reduction, 10 min delay = GBP73) • Reduction in arterial punctures: GBP3.60 (9% reduction, cost per puncture = GPB40)	Saving of GBP2 per procedure with US 9% reduction in complications (arterial punctures) with US
Kinsella and Young 2009 Cost analysis United States federal reimbursement Central venous access	• Additional cost of US$34.86 per procedure for US vs landmark technique based on reimbursed costs	Not stated	• Reduction in pneumothorax: US$1.09 (0.75% reduction, cost US$134.49 per event)	The additional cost of US is not offset by the cost for treating pneumothorax

GBP: Great Britain pounds; NHS: National Health Service; UK: United Kingdom; US: ultrasound; US$: United States dollars
Source: Calvert 2004; Kinsella and Young 2009

Nerve block economic analyses

The three nerve block economic analyses compared ultrasound and nerve stimulation. The design and results for these analyses are summarised in Table 42. Sandhu et al. (2004) and Liu et al. (2010) undertook cost analyses using data from American hospitals. Ehlers et al. (2012) undertook a cost-effectiveness analysis alongside a randomised controlled trial conducted at a Danish hospital and information on effects and costs were collected prospectively. In Sandhu et al. (2004) patients received an infraclavicular brachial plexus block for regional anaesthesia. In Ehlers et al. (2012) patients undergoing major foot and ankle surgery received a continuous sciatic nerve block for postoperative analgesia. The type of block was not specified in Liu et al. (2010); different scenarios were presented including blocks for anaesthesia and postoperative analgesia. Sandhu et al. (2004) and Ehlers et al. (2012) concluded ultrasound guided nerve block was less expensive than a block using nerve stimulation, although as discussed below the extent and source of the cost savings varied. For some of the scenarios presented in Liu et al. (2010) ultrasound guided nerve block was less expensive than nerve stimulation.

The costs of the ultrasound and nerve stimulator machines were apportioned over the total procedures performed over the machines' lifetime. The three analyses assumed 1000 procedures per year and a life time of 5 years for both the ultrasound and nerve stimulators. Sandhu et al. (2004) and Ehlers et al. (2012) also considered the cost of consumables (gel, sterile cover and disinfectant towels for Ehlers et al. (2012) and gel for Sandhu et al. (2004)). In the three analyses, the cost of the ultrasound machine per procedure was substantially higher than the cost of the nerve stimulator.

In Sandhu et al. (2004), the estimated additional cost of US$4.80 per procedure for the ultrasound machine and consumables was offset by the use of a less expensive non-insulated needle (saving of US$6.00 for single shot and US$17.70 for catheter insertion) and reduced time for the procedure and time to block onset (21 minute reduction with a cost saving of US$168). Thus there was an overall cost saving per procedure with ultrasound of US$169 for single shot injections and US$180 for catheter insertions.

In Ehlers et al (2012), the additional cost of GBP6.10 per procedure for the ultrasound machine and consumables were offset by the reduced time for catheter insertion (0.5 minute reduction for each of a nurse and physician, GBP0.70), reduced time for postoperative nursing care (18.7 minute reduction, GBP9.80) and reduced need for medications for postoperative break through pain (GBP2.70).

In Liu et al (2010), the additional cost per procedure for the ultrasound machine was US$7.42. Cost offsets included time for the procedure (5 minutes, cost US$11.65) and time to block onset (5 minutes, cost US$11.65), and a reduction in the number of procedures in which general anaesthesia was required as rescue for failed blocks (US$35.22 based on an 8% reduction in use of general anaesthesia).

Table 42 Published cost and economic analyses comparing ultrasound and nerve stimulation for nerve blocks

Publication and study design	Cost of US machine per procedure	Additional US costs	Cost of NS per procedure	Cost savings with US	Conclusion
Sandhu 2004 Cost analysis United States hospital perspective Infraclavicular brachial plexus nerve block for anaesthesia	• Cost of machine: US$17,000 • Procedures: 5000 • Cost per procedure: US$3.40	Gel: US$1.40	Not considered	• Use of non-insulated needle: US$6.00 for single shot and US$17.70 for catheter insertion • Reduced time for procedure: 5 mins, US$40.00 • Reduced time to block onset: 16 mins, US$128.00	A cost saving of $169 for single shot injections and $182 for catheter insertions with US
Liu and John 2010 Cost analysis United States hospital perspective Type of nerve block not specified Anaesthesia or analgesia	• Cost of machine: US$37,800 • Amortisation: 5 years • Procedures per year: 1000 • Cost per procedure: US$7.56	Not considered	• Cost of machine: US$720 • Amortisation: 5 years • Procedures per year: 1000 • Cost per procedure: US$0.14	• Reduced time for procedure: 5 mins, US$11.65 • Reduced ready-for-surgery time: 5 mins, US$11.65 • Reduced need for GA: US$35.22 (8% reduction, cost of GA = $422)	Different scenarios modelled
Ehlers 2012 Cost-effectiveness analysis, prospective collection of effects and costs Danish hospital perspective Continuous sciatic nerve block for postoperative analgesia	• Cost of machine: not stated • Amortisation: 5 years • Procedures per year: 1000 • Cost per procedure: GBP6.50 (includes cost of sterile cover, gel, disinfectant towels)	Sterile cover, gel, disinfectant towels (included in US cost per procedure)	• Cost of machine: not stated • Amortisation: 5 years • Procedures per year: 1000 • Cost per procedure: GBP0.4	• Reduced time for catheter insertion: 0.5 min for physician and nurse, GBP0.7 • Reduced time for nurse postoperative: 18.7 minutes, GBP9.80 • Reduced need for medications for postoperative breakthrough pain: 14.8mL morphine and 15mL bupivacaine, GBP2.70	A cost saving of GBP7.10 per procedure with US. Higher success rate (effective sensory block in a 48 hour period post-surgery) with US (94% vs 79%). Likelihood of US being more effective and cheaper than NS was 84.7%.

GA: general anaesthesia; GBP: Great Britain pounds; NS: nerve stimulator; US: ultrasound; US$: United States dollars
Source: Sandhu 2004; Liu and John 2010; Ehlers 2012

Rationale for cost-effectiveness analysis

The benefits of using ultrasound compared with the landmark technique for vascular access include fewer failed cannulations and a reduction in the incidence of complications. The results of the cost-effectiveness analysis are presented as the incremental cost per failed cannulation avoided. The cost of the ultrasound procedure and the cost implications of treating pneumothorax and haemothorax events are considered.

The benefits of using ultrasound compared with nerve stimulation or the landmark technique for nerve blocks are varied and include reduced need for supplemental anaesthesia, improved postoperative analgesia, a lower dose of local anaesthetic and a reduction in the incidence of complications. Because the benefits cannot easily be

incorporated into a single effectiveness measure a cost analysis is presented for nerve blockade. The cost of the ultrasound and nerve stimulation procedures and the local anaesthetic, and the cost implications of improve postoperative pain control and treating LAST events, are considered.

Estimate of cost of ultrasound and electrical nerve stimulation

Average capital cost per procedure

Average capital costs per procedure are based on estimates of the purchase price of equipment, lifetime of equipment, maintenance and number of procedures performed per annum. These estimates were provided by the applicant and/or clinical experts. The opportunity cost of capital was included with the foregone capital return calculated using a 5 per cent discount rate. The estimated capital cost per ultrasound procedure and per nerve stimulation procedure is presented in Table 43 and Table 44, respectively.

Table 43 Calculation of average capital cost per procedure for ultrasound

	Base case	Lower	Upper	Source
Ultrasound machine (A)	$40,000	$25,000	$45,000	DAP, page18; Suppliers
Life time, years (B)	5	5	5	DAP, page18
Annual cost (C)	$8,000	$5,000	$9,000	A/B
Foregone capital return (5%), annual	$2,000	$1,250	$2,250	C x 0.05
Maintenance/insurance, annual	$1,000	$1,000	$1,000	DAP, page18
Total opportunity cost of capital, annual	$11,000	$7,250	$12,250	
Procedures per year	Capital cost per procedure: Base case	Capital cost per procedure: Lower estimate	Capital cost per procedure: Upper estimate	
100	$110	$73	$123	Lower estimate provided by Applicant[a]
250	$44	$29	$49	
500	$22	$15	$25	AURORA, Expert opinion
750	$15	$10	$16	
1000	$11	$7	$12	Sandhu 2004, Liu 2010, Ehlers 2012

a Range provided by Applicant is 100 to 150 procedures per machine per year.

Table 44 Calculation of average capital cost per procedure for nerve stimulation

	Estimate	Source
Nerve stimulator (A)	$1,000	Expert Opinion, Liu 2010
Life time, years (B)	5	Liu 2010
Annual cost (C)	$200	A/B
Foregone capital return (5%), annual	$10	C x 0.05
Total opportunity cost of capital, annual	$210	

Procedures per year	Capital cost per procedure	
100	$2.10	As for ultrasound
250	$0.84	
500	$0.42	
750	$0.28	
1000	$0.21	As for ultrasound, Liu 2010

The capital cost per ultrasound procedure is sensitive to the cost of the ultrasound machine and the total number of procedures performed (which is the product of the machine life time and number of procedures per year).

It is stated in the DAP (page 18) that the cost of an ultrasound machine could range from $25,000 to $90,000. The wide range reflects different machine capabilities. For vessel and nerve location a small portable real-time device with colour Doppler and a 7.5MHz or higher frequency transducer is considered adequate. The specific machines used in the identified clinical trials are specified inTable 86 and Table 91. Suppliers have indicated the list prices for these machines (including image processor, transducer, and trolley) are $30,000 to $45,000, although the machines may be sold for less than the list prices. Consistent with the Application a cost of $40,000 is used for the base case analysis. Lower and upper estimates of $25,000 and $45,000 are used in the sensitivity analyses.

A machine life time of 5 years (DAP, page 18) is consistent with the estimates in previous economic analyses (Table 41).

The applicant noted the number of procedures per year per ultrasound machine varies depending on individual practice profiles, and estimated 100-150 procedures per year (Application Part Di, page 5). This is substantially lower than used in previous economic analyses (780-1000 procedure per year; Table 42, Table 41), and possibly does not consider that the ultrasound machine may be used for other procedures (eg. pleural drainage, arterial line placements, transesophageal studies, Calvert et al. (2004), Liu et al. (2010), Sandhu et al (2004)). Data are available from 12 hospitals (10 located in Australia, 1 in New Zealand and 1 in Malaysia) on the number of peripheral nerve blocks performed from June 2011 through to February 2012 (Table 45). These data suggest on average substantially more than 100 nerve block procedures may be performed per year. Based on the nerve block data and considering the machine can also be used for vascular access as well as other procedures, 500 procedures are assumed per year for each ultrasound machine in the base case analysis. The Applicant's lower estimate (100 procedures per year) and the estimate included in previous economic analyses (1000 procedures per year) are tested in sensitivity analyses.

Table 45 Number of peripheral nerve block procedures and estimated number of procedures per ultrasound machine by hospital

Hospital	Nerve blocks Jun 11-Feb 12	Nerve blocks Annualised
Ballarat	74	99
Mater Adult Hospital	105	140
St Vincent's Private Hospital, Melbourne	109	145
Royal Brisbane Women's Hospital	137	183
Welllington Regional Hospital (New Zealand)	207	276
University Malaya Medical Centre (Malaysia)	238	317
Princess Alexandra Hospital	270	360
Northern Rivers Anaesthesia Service	413	551
Lismore based Hospital	444	592
Gold Coast Hospital	448	597
Geelong Hospital	533	711
St Vincent's Hospital	1135	1513
Mean	Not calculated	457
Median	Not calculated	339

Source: AURORA

To be eligible for the payment of Medicare benefits, practices providing diagnostic imaging services must be accredited through the Department of Health Diagnostic Imaging Accreditation Scheme. Prior to the 1 November 2012 ultrasound guidance was claimed by anaesthetists using MBS item 55054, and as this item is listed under the diagnostic section of the Medicare Benefits Schedule (MBS), practice accreditation was required. Practice accreditation on the Department of Health Diagnostic Imaging Accreditation Scheme will not be a requirement if the MBS items for ultrasound guidance are listed in the Schedule as therapeutic items (under Category 3) as proposed; however, accreditation may be considered appropriate by anaesthetists or the Department of Health. Therefore, the impact of including this cost has been tested in the sensitivity analyses for the scenario without a MBS benefit. The Applicant estimated the cost of accreditation to be $2,000 (Application Part Di, page 5). This is consistent with NATA's published accreditation fees ($1,650-$3,300, July 2013-June 2014) (NATA 2014). Accreditation is usually required every three years, and hence the cost per ultrasound procedure for accreditation is estimate to be $1.53 ($2,000 + $300 foregone return = $2300/1500 procedures = $1.53).

Additional costs

It is stated on page 9 of the DAP that anaesthetists who are to use ultrasound guidance need training and experience specific to ultrasonography, and that the specialist training curriculum of the Fellowship of the Australian and New Zealand College of Anaesthetists (FANZCA) includes compulsory training in the use of ultrasound. The applicant estimated the cost of continuing medical education and skills maintenance to be $800 per year (Application Part Di, page 5). Specific two days course on the use of ultrasound for anaesthetists cost approximately $1,500 (5th Australian Regional Anaesthesia and Cadaveric Ultrasound Seminar, February 2014, cost $1,400-$1,500; Ultrasound Training Solutions, Introductory Ultrasound for Anaesthetists, January 2014, cost $1,675) (Ultrasound Training Solutions 2014; University of Western Australia 2014). In addition, ongoing and hands-on training would be required. Assuming one

anaesthetist performs the 500 ultrasound procedures per machine per year, and apportioning the estimated training cost of $800 per year over these procedures, results in a training cost of $1.60 per procedure ($800 / 500). Assuming the 500 procedures are performed by five anaesthetists, the training cost per procedure would be $8 ($800 x 5 / 500). Given this estimate is highly uncertain, training is already incorporated into the Fellowship program and hence is not an incremental cost associated with the proposed MBS listing, and training would also be required for nerve stimulation, a cost for training has not been included in the base case analysis. The impact of excluding this cost, for the scenario without a MBS benefit, is tested in the sensitivity analyses.

The Applicant estimated the cost of consumables to be up to $20 per procedure (DAP, page 18). Suppliers have indicated the list price of a sterile transducer cover and gel to be $16, although this price may be discounted. A cost of $16 is assumed for the base case analysis. Specific echogenic needles may be used for ultrasound procedures. A cost for these needles has not been included as a recent international consensus statement notes there is little evidence for their superiority over standard cannulation needles (Lamperti et al 2012), and echogenic needles were not used in the identified clinical trials (see Table 86 and Table 91).

The Applicant has proposed a MBS fee of $58.35 for ultrasound guidance for both vascular access and neural blockade (DAP, page 12). This is based on three Relative Value Guide (RVG) units to align it with the fees and units allocated to the existing AMA/ASA RVG ultrasound items. The Applicant states this fee includes a professional component ($29.20) and a practice component ($29.15) and that the allocation of three RVG units is based on a comparison of the nature of the service to other services of similar complexity and skill, already funded by the items of Group T10. The 75% MBS benefit based on the proposed fee is $43.76. According to the DAP (page 8), the pre-service component of ultrasound includes an explanation to the patient about use of ultrasound, its benefits, the procedure and preparation and checking of the device. According to the Applicant, pre-service takes approximately 10-15 minutes. The scan itself takes another 5-10 minutes. Following feedback from the Department of Health and noting that the procedures for which ultrasound guidance is proposed already have existing MBS items, the MSAC may wish to consider if an additional fee is appropriate for the ultrasound procedure and the level of reimbursement. Therefore the results of the economic analysis are presented with and without the inclusion of the proposed fee.

Average patient co-payments were provided by the Department of Health for MBS item 55054 for anaesthetist-related claims. An anaesthetist-related claim was defined as a claim by a Provider with one of the following registered specialties current on date of service or derived specialty for the quarter of service being one of these specialties : Anaesthetics-specialist (051), Anaesthetics-intensive care (060), Resuscitation (075), Anaesthetics-non-specialist (216) and Anaesthetics-trainee (400). The co-payment component is calculated as the MBS fee charged minus the MBS benefit paid plus any additional specialist fees. The co-payment may not be the exact patient contribution, since it may also include some insurance contribution (up to 25% of the MBS fee). To avoid double counting, the 25 per cent insurance contribution is not included as a separate cost. The average patient co-payment for anaesthetist-related claims for MBS item 55054 for the 2012/2013 financial year was $64.75. It is unknown if the average patient co-payment for the proposed MBS items will be the same as for item 55054, however, for the analyses presented in this report the patient co-payment is assumed to be the same (i.e. $65).

Total cost per ultrasound procedure

The total cost per ultrasound procedure is summarised in Table 46 based on 100 to 1000 procedures per machine per year, an ultrasound machine cost of $25,000 to $45,000 and with and without the proposed MBS fee including patient co-payment.

Table 46 Ultrasound cost per procedure by procedures per year and machine cost

Procedures per machine per year	Machine cost: $25,000 - proposed MBS fee	Machine cost: $25,000 + proposed MBS fee[a]	Machine cost: $40,000 - proposed MBS fee	Machine cost: $40,000 + proposed MBS fee[a]	Machine cost: $45,000 - proposed MBS fee	Machine cost: $45,000 + proposed MBS fee[a]
100	$89	$197	$126	$235	$139	$247
500	$31	$139	$38	$147	$41	$149
1000	$23	$132	$27	$136	$28	$137

a Proposed MBS fee is $58.35, therefore the 75% MBS benefit is $43.76. The assumed patient co-payment is $65.

For the base case analysis, assuming an ultrasound machine cost of $40,000 and 500 procedures per machine per year, the cost per ultrasound procedure is $38 excluding the proposed MBS fee ($22+$16) and $147 ($38+$43.76+$65) including the proposed fee and patient co-payment.

Assuming 500 procedures per year, the cost per nerve stimulation procedure is $0.42 (Table 44). For 1000 and 100 procedures per year, the cost per procedure is $0.21 and $2.10, respectively. For nerve stimulation there are no additional costs for consumables and there is no relevant MBS item.

Vascular access economic analysis

A total of 34 RCTs were identified comparing ultrasound guidance and the landmark technique for vascular access (Table 88, Appendix M). In 30 of these trials access was via a vein, with arterial access in 2 trials and PICC access in 2 trials. Given the majority of evidence is for venous access, specifically for IJV and SCV access, this is the focus for the economic analysis.

Effectiveness

The effectiveness outcomes reported in the RCTs comparing ultrasound guidance and the landmark technique for vascular access included the mean time to cannulate the vessel, the mean number of attempts required to cannulate the vessel, the number of failed cannulations and failure at first attempt. In the meta-analyses (Figure 10, Figure 11,

Figure 12 and Figure 13) a statistically significant reduction in all of these outcomes was observed with ultrasound guidance compared with the landmark technique.

The use of ultrasound was associated with an average of 1.2 fewer attempts to successfully cannulate the vessel and a 48% reduction in the risk of failure on the first attempt compared with the landmark technique (Figure 11). However, the overall reduction in the mean cannulation time with ultrasound was only 0.8 minutes (Figure 10). Although statistically significant, this small reduction in time is unlikely to be of clinical significance. The number of needle pass attempts has been shown to correlate with the

incidence of complications (Calvert et al 2004; Palepu et al 2009) and the associated cost implications are explored below.

The number of failed cannulation attempts was reported in 32 RCTs, although the definition of failed attempt varied across the trials. In general, to be defined as a failed attempt the cannula could not be placed with 3 to 7 attempts (most commonly 3 attempts), with some trials also specifying a time limit for the cannulation and the requirement of no inappropriate vascular puncture. The risk of failed cannulation with ultrasound guidance was significantly lower compare with the landmark technique (RR 0.26, 95% CI: 0.19-0.37, P<0.001,

Figure 12, Table 28). The risk was significantly lowered when access was via the IJV (RR 0.22, 95% CI: 0.13-0.35, P<0.001, Table 28) and the SCV (RR 0.11, 95% CI 0.03-0.45, P=0.002, Table 28). With the landmark technique for IJV access, cannulation failure was reported for 11% (186/1629) of patients. Applying the risk ratio of 0.22 from the meta-analysis, the risk of a failed attempt with ultrasound guidance would be 2% (0.11 x 0.22), or nine percentage points less than with the landmark technique. With the landmark technique for SCV access, cannulation failure was reported for 16% (42/256) of patients. Applying the risk ratio of 0.11 from the meta-analysis, the risk of a failed attempt with ultrasound guidance would be 2% (0.16 x 0.11), or 14 percentage points less than with the landmark technique.

In the trials, the primary reasons for unsuccessful cannulation were considered to be thrombosis and anatomical variation of the veins (Fragou et al 2011; Karakitsos et al 2006). The presence of thrombus can be detected by ultrasound imaging and when present an alternative site cannulated. For patients in the landmark group, thrombosis was generally detected by ultrasound following an unsuccessful cannulation using the landmark technique. Similarly anatomical variations can generally be detected by ultrasound but not with the landmark technique. In the trials, failed cannulation attempts usually led to the use of ultrasound to cannulate an alternative vessel. The associated time implications were not reported. In the Calvert et al. (2004) economic analysis, a failed insertion was assumed to result in surgery being delayed by 10 minutes, and the cost for this delay was calculated assuming the procedure was undertaken in an operating theatre staffed by a consultant surgeon, a consultant anaesthetist, a senior house officer, a medical technical officer and a nurse. In the analysis presented in this report a cost has not been assigned for potential delays in surgery as the extent and staffing implications of the delay are highly uncertain. This is discussed further below.

Complications

The complications reported in the RCTs comparing ultrasound guidance and the landmark technique for vascular access included inappropriate vascular puncture, haematoma, catheter misplacement or malfunction, nerve damage or paraethesia, infection, pneumothorax and haemothorax. In the meta-analyses (Figure 6, Figure 7, Figure 8, Figure 9) a statistically significant reduction in the incidence of inappropriate vascular puncture, haematoma, pneumothorax and haemothorax was observed with ultrasound guidance compared with the landmark technique. No difference in the incidence of catheter related adverse events, nerve damage and infections was observed although data were reported for only a small number of trials.

Although haematoma may cause discomfort for the patient, there are generally no clinical sequelae and hence a cost has not been assigned.

Inadvertent or unrecognised arterial cannulation may, although rare, have serious consequences for the patient. Patients should therefore be kept under observation by nursing and/or clinical staff for at least 24 hours if accidental arterial puncture occurs (Boland et al 2003). In Calvert et al. (2004) a cost of GBP40 (2002 prices) was assigned to each arterial puncture. This was based on the analysis by Boland et al. (2003) in which approximately 20% of patients were outpatients and hence, an additional overnight stay was required for monitoring the patients. Anaesthetists are expected to perform vascular access procedures on inpatients undergoing major surgery and hence there would be no additional cost for overnight stays. A cost has therefore not been assigned for vascular puncture in the current analysis. Sensitivity analyses demonstrate excluding this cost has minimal impact on the cost-effectiveness results (see below). A cost has also not been applied for the very rare but serious consequences of arterial puncture as the impact of ultrasound on these events cannot be quantified.

Costs are assigned to the pneumothorax and haemothorax events.

Pneumothorax

The incidence of pneumothorax was reported in 12 RCTs (including 5 trials in which no pneumothorax was reported for either group). The puncture site was the IJV in eight of the trials, the SCV in one trial, either the IJV or SCV in two trials and either the IJV or femoral vein in one trial. A statistically significant reduction in the incidence of pneumothorax was observed with ultrasound compared with the landmark technique in Karakitsos et al. (2006) in IJV cannulations (0/450 vs 11/450 events, RR 0.04, 95% CI 0.00, 0.74), and in Fragou et al. (2011) in SCV cannulations (0/200 vs 10/201, RR 0.05, 95% CI 0.00, 0.81). In the other, generally smaller, trials, the reduction in the incidence of pneumothorax was not statistically significant. In the meta-analysis (Figure 8) ultrasound guidance significantly reduced the risk of pneumothorax compared to the landmark technique (RR 0.21, 95% CI: 0.06-0.71, P=0.01, Figure 8, Table 24). The risk of pneumothorax was lowered with ultrasound use for access via the IJV (RR 0.19, 95% CI: 0.03-0.89, P=0.093, Table 24), the SCV (RR 0.41, 95% CI: 0.03-5.64, P=0.506, Table 24) and when the access site was mixed (RR 0.09, 95% CI: 0.01-3.70, P=0.209, Table 24), although the reductions were not statistically significant. Given the reduction in risk of pneumothorax is similar for the different access sites, and the heterogeneity across all trials was low (I^2 statistic of 9.8%), the risk ratio of 0.21 is assumed for both IJV and SCV access.

The incidence of mechanical complications, including pneumothorax, has been reported to be higher with the SCV route compared with other routes (Fragou et al. (2011)). In the two trials using either the SCV or IJV route, the incidence of pneumothorax was higher with the SCV route (Cajozzo et al 2004): 4/96 [4.2%] vs 0/100 [0%]; Palepu et al. (2009): 1/45 [2.2%] vs 0/399 [0%]). Across all studies, with the use of the landmark technique the average incidence (weighted by sample size) of pneumothorax for the SCV route was 4.37% (10 events in 229 patients). Applying the risk ratio of 0.21 from the meta-analysis, the incidence of pneumothorax with ultrasound guidance would be 0.92% (4.37 x 0.21). Thus, ultrasound guidance for the SCV route results in 3.45 (4.37-0.92) fewer pneumothorax events for every 100 patients. Across all studies, with the use of the landmark technique the average incidence (weighted by sample size) of pneumothorax for the IJV route was 1.25% (14 events in 1123 patients). Applying the risk ratio of 0.21 from the meta-analysis, the incidence of pneumothorax with ultrasound guidance would be 0.26% (1.25 x 0.21). Thus, ultrasound guidance for the IJV route results in 0.98 (1.25-0.26) fewer pneumothorax events for every 100 patients.

A pneumothorax may resolve spontaneously, or if symptomatic or progressive can be treated by insertion of an intercostal tube (chest drain) (Boland et al. (2003)). In Fragou et al. (2011) in which the SCV was cannulated, a total of 10 pneumothorax events were report (all in the landmark group). Eight of these events (80%) required chest drainage. The mechanical complications in this trial led to a significant increase in the time of hospitalisation. In Karakitisos et al (2006), a total of 11 pneumothorax events were reported (all in the landmark group), of which 4 (36%) required therapeutic intervention.

The cost of treating a pneumothorax event was estimated in the Calvert et al (2004) economic analysis to be GBP316 (1999/2000 prices) based on a review of medical records for patients who suffered a pneumothorax during a trial assessing Hickman line insertions in cancer patients (Boland et al (2003)). A total of nine events occurred, of which one (11%) required a chest drain. The resources utilised included consumables (for the drain; 1 set), overnight hospital stay (11 nights), nursing time (10 hours), specialist registrar time (1 hour) and chest X-rays (23). Applying current Australian costs to this resource use results in a cost of $642 per pneumothorax event (Table 47). This is potentially an underestimate of the cost of treating pneumothorax following IJV or SCV access as a chest drain was required in only 11% of events. Assuming a chest drain is required in 36% of events as per Karakitisos et al (2006) (IJV access) the cost of treating a pneumothorax event is $782 (only the costs associated with insertion of the chest drain have been adjusted). Assuming a chest drain is required in 80% of events as per Fragou 2011 (SCV access) the cost of treating a pneumothorax event is $1,027.

Table 47 Cost of treating pneumothorax based on resource use collected by Boland 2003

Resource	Unit cost	Source	Units[a]	Cost
Insertion of chest drain				
Consumables	$425	Prostheses List, Product subgroup 3.7.1.1, billing code NG065, August 2013	0.11	$47
Medical Officer	$134	MBS item 38806, 1 November 2013	0.11	$15
Over-night hospital stay	$343	Hotel cost for AR-DRG E68Z (pneumothorax), Private Hospital v5.1, Round 12 (2007/08)	1.22	$418
Nursing time, hours	$37	5th year registered nurse weekly salary, $1302.30, NSW Award Rates 2011	1.11	$41
Chest x-ray	$47	MBS item 58503, 1 November 2013	2.56	$121
Total cost per event				$642

a Units as reported by Boland 2003 in which a chest drain was used in 11% of pneumothorax events.

The cost of treating a pneumothorax event was estimated in the Kinsella and Young economic analysis to be US$134.49 (2006 prices) based on the assumption of 2.5 chest x-rays and placement of a thoracostomy tube in 20% of patients (Kinsella and Young 2009). Applying current Australian costs to this resource use results in a cost of $230 per pneumothorax event ($47 x 2.5 + 0.2 x ($425+$134); see Table 47 for unit costs). This is considered a potential underestimate of the cost of treating pneumothorax following IJV or SCV access as the costs associated with additional over-night hospital stays have not been included and Fragou 2011 reported a statistically significant increase in the duration of hospitalisation due to mechanical complications. The impact of using this lower cost is tested in the sensitivity analyses below.

Applying a cost of $782 per pneumothorax event for IJV access, the saving associated with avoiding 0.98 events per 100 cannulation with the use of ultrasound is $8 (0.98/100 x $782).

Applying a cost of $1,027 per pneumothorax event for SCV access, the saving associated with avoiding 3.45 events per 100 cannulation with the use of ultrasound is $35 (3.45/100 x $1027).

Haemothorax

The incidence of haemothorax was reported in 6 RCTs (including 3 trials in which no haemothorax was reported for either group). The puncture site was the IJV in five of the trials and the SCV in one trial. A statistically significant reduction in the incidence of haemothorax was observed with ultrasound compared with the landmark technique in Fragou et al (2011) in SCV cannulations (0/200 vs 9/201, RR 0.05, 95% CI 0.00, 0.90). In the other trials, either no haemothorax events were reported or the reduction was not statistically significant.

In the meta-analysis (Table 25) ultrasound guidance significantly reduced the risk of haemothorax compared to the landmark technique (RR 0.10, 95% CI: 0.02-0.56, P=0.009, Table 25). The heterogeneity across the trials reporting haemothorax with other aggregate adverse events was moderate (I^2 statistic of 41%), and hence the risk ratio of 0.10 is assumed for both IJV and SCV access.

As noted above, the incidence of mechanical complications has been reported to be higher with the SCV route compared with other routes. Across the five IJV studies, with the use of the landmark technique the average incidence (weighted by sample size) of haemothroax was 1.15% (9 events in 784 patients). Applying the risk ratio of 0.10 from the meta-analysis, the incidence of haemothorax with ultrasound guidance would be 0.12% (1.15 x 0.10). Thus, ultrasound guidance for the SCV route results in 1.03 (1.15-0.12) fewer haemothorax events for every 100 patients. In the SCV study, the incidence of haemothorax with the use of the landmark technique was 4.48% (9 events in 201 patients). Applying the risk ratio of 0.01 from the meta-analysis, the incidence of haemothorax with ultrasound guidance would be 0.45% (4.48 x 0.01). Thus, ultrasound guidance for the IJV route results in 4.03 (4.48-0.45) fewer haemothorax events for every 100 patients.

In Fragou et al (2011) in which the SCV was cannulated, a total of 9 haemothorax events were reported (all in the landmark group). Five of these events required thoracotomy. In Karakitsos et al (2006), a total of 8 haemothorax events were reported (all in the landmark group), of which 4 required therapeutic intervention.

The cost of treating haemothorax was not included in the published economic analyses. Based on Fragou 2011 and Karakitsos 2006 it is assumed that a thoracotomy is required in 50% of events. The cost of a thoracotomy is estimated to be $1,407 (MBS items 38656 [thoracotomy or median sternotomy for post-operative bleeding]; 51303 [assistant]; 20540 [initiation of management of anaesthesia for thoracotomy procedures]; MBS 1 November 2013). Therefore, the cost of treating a haemothorax event is $704 ($1407 x 0.5).

Applying a cost of $704 per haemothorax event for IJV access, the saving associated with avoiding 1.03 events per 100 cannulation with the use of ultrasound is $7 (1.03/100 x $704).

Applying a cost of $704 per haemothorax event for SCV access, the saving associated with avoiding 4.03 events per 100 cannulation with the use of ultrasound is $28 (4.03/100 x $704).

Cost effectiveness

The incremental cost per failed cannulation avoided is summarised in Table 48 for IJV and SCV access. Sensitivity analyses are also presented in this table.

For SCV cannulations, the savings due to fewer pneumothorax and haemothorax events ($63) with ultrasound is greater than the ultrasound capital and consumable costs ($38). Ultrasound also results in fewer failed cannulation attempts and hence is the dominant procedure. A threshold analysis has been conducted to determine the minimum number of procedures required per machine per year for ultrasound to be dominant assuming the cost of the ultrasound machine is $40,000. Ultrasound is dominant if more than 235 procedures are performed per machine per year. A threshold analysis has also been conducted to determine the maximum cost of the ultrasound machine assuming 500 procedures are performed per machine per year. Ultrasound is dominant if the ultrasound machine costs less than $90,000. If the proposed MBS benefit ($43.76 per procedure) and patient co-payment are included, the cost of the ultrasound procedure ($147) is greater than the savings due to fewer complications ($63), and the incremental cost per failed cannulation avoided is $600.

The incidence of complications with IJV cannulations is lower than for SCV cannulations and the savings due to the avoidance of complications with ultrasound is less ($15 versus $63). Without the proposed MBS benefit, the incremental cost per failed cannulation avoided is $256. Including the proposed MBS benefit ($43.76) and patient co-payment ($65) increases the incremental cost per failed cannulation avoided to $1,467.

The sensitivity analyses demonstrate the results are sensitive to the assumed number of procedures performed per ultrasound machine per year. For SCV cannulations the results are also sensitive to the cost of treating pneumothorax events.

Table 48 Incremental cost per failed cannulation avoided with the use of ultrasound vs landmark technique for vascular access

	IJV access without MBS benefit	IJV access with MBS benefit[a]	SCV access without MBS benefit	SCV access with MBS benefit[a]
Base case analysis				
Cost of ultrasound procedure (A)	$38	$147	$38	$147
Cost savings from complications avoided with ultrasound vs landmark				
Pneumothorax (B)	$8	$8	$35	$35
Haemothorax (C)	$7	$7	$28	$28
Total cost (A – B – C)	$23	$132	-$25	$84
Reduction in failed cannulation attempts with ultrasound vs landmark	0.09	0.09	0.14	0.14
Incremental cost per failed cannulation avoided	$256	$1,467	Dominant	$600
Sensitivity analyses, incremental cost per failed cannulation avoided				
US machine cost				
$40,000 → $25,000	$178	$1,378	Dominant	$543
$40,000 → $45,000	$289	$1,489	Dominant	$614
Number of procedures per US per year				
500 → 1000	$133	$1,344	Dominant	$521
500 → 100	$1,233	$2,444	$450	$1,229
Inclusion of accreditation cost				
$0 → $1.53 per procedure	$273	NA	Dominant	NA
Inclusion of training cost				
$0 → $8 per procedure	$344	NA	Dominant	NA
Inclusion of accreditation and training cost				
$0 → $9.53 per procedure	$361	NA	Dominant	NA
Cost of treating pneumothorax				
$1,027 and $782 → $230	$319	$1,531	$15	$793
Inclusion of cost for vascular puncture				
$0 → $69 per event[b]	$206	$1,418	Dominant	$576

NA, not applicable
a Proposed MBS fee is $58.35, therefore the 75% MBS benefit is $43.76. The assumed patient co-payment is $65.
b Based on an overnight hospital stay for 20% of patients as per Calvert et al (2003).

The resource and clinical implications of avoiding a failed cannulation attempt are difficult to quantify, but potentially include avoidance of delays starting surgery and reducing the risk of complications. Calvert 2004 notes that the resource implications due to failed cannulations can be substantial as the majority of insertions are performed in high cost theatre and ICU environments, where delays may have significant cost and clinical implications, and estimated the cost of a failed cannulation due to a 10 minute delay to surgery to be GBP73 (2002 prices). From the data shown in Table 48, the use of ultrasound for IJV cannulations would be cost neutral if each failed cannulation attempt cost $256 (where there is no additional MBS fee for ultrasound guidance).

The economic analysis considers the cost of treating pneumothorax and haemothorax events but not the clinical implications for the patient. Further, other complications such as nerve damage, infections and catheter-related venous thrombosis may be avoided with the use of ultrasound (Lamperti 2012); however, there are insufficient data to quantify

the impact of ultrasound on these events. The clinical implications of these events are generally short-term however in rare cases can be serious and even fatal (Cook 2011).

Nerve block economic analysis

The Australian and New Zealand Registry of Regional Anaesthesia (AURORA) captures data on all peripheral nerve blocks performed by all practitioners on all patients at enrolled hospitals. Based on data for the period June 2011 through to February 2012, 3% of blocks are for intraoperative anaesthesia, 59% are for postoperative analgesia and 37% are for both anaesthesia and analgesia (the remaining 1% of blocks are for analgesia unrelated to surgery, rescue blocks and chronic pain) (AURORA). Therefore, analgesia is the aim for close to 100% of blocks. In 40% of blocks the aim is anaesthesia, primarily together with analgesia.

Based on the AURORA data, in 2006-2008 ultrasound alone, ultrasound plus nerve stimulation, nerve stimulation alone and the landmark technique was used in 13%, 50%, 30% and 7% of blocks, respectively. In 2011-2012 the corresponding percentages were 59%, 28%, 7% and 6% of blocks. The substantial increase in the use of ultrasound alone, and the corresponding reduction in use of nerve stimulation, both alone and together with ultrasound, suggests that ultrasound has replaced nerve stimulation, rather than been added to nerve stimulation, in Australian clinical practice. Therefore, the main focus of the economic analysis for nerve blockade is a comparison of ultrasound and nerve stimulation.

A total of 58 RCTs were identified for nerve blocks. In 39 of these trials the comparator was nerve stimulation, in 12 trials the comparator was the landmark technique, in 6 trials ultrasound together with nerve stimulation were compared with nerve stimulation alone and in 1 trial the comparator was a transarterial method.

Effectiveness

The effectiveness outcomes reported in the nerve block RCTs included the mean time to administer the block, the mean number of needle redirects and skin punctures required, the number of failed blocks, the block onset time, the block duration and the amount of time until analgesia is required. In the meta-analyses (Figure 18, Figure 19, Figure 20, Figure 21) a statistically significant reduction in the mean time to administer the block, the mean number of needle redirects and the number of failed blocks was observed with ultrasound guidance compared with nerve stimulation. For ultrasound guidance compared with the landmark technique, a significant increase in the mean time to administer the block and a reduction in the number of failed blocks was observed.

Compared with nerve stimulation, the use of ultrasound was associated with 1.5 fewer needle redirects and a reduction of approximately 2 minutes to administer the block. Compared with the landmark technique, the use of ultrasound did not result in a reduction in the number of needle redirects and increased the time to administer the block by approximately 1 minute. For blocks performed for anaesthesia, the time to block onset is relevant as surgery cannot commence prior to this. With the use of ultrasound the mean time to block onset was reduced by approximately 3-4 minutes compared with using nerve stimulation or the landmark technique. Thus, when using ultrasound rather than nerve stimulation the procedure and block onset time are faster. When using ultrasound rather than the landmark technique the procedure appears to be

marginally slower, although this may be offset by a faster block onset time. Overall the differences are small and unlikely to be of clinical significance.

Block failure was reported in 42 RCTs (Figure 21, Table 39), although the definition of failure varied across the trials, in part reflecting whether the primary aim of the block was for anaesthesia or postoperative analgesia, and for some trials included procedural failure. For procedures in which the nerve block is being used to provide anaesthesia, a reduction in the rate of block failures may reduce the need for supplemental nerve blocks or general anaesthesia. For procedures in which the nerve block is being used to provide postoperative analgesia, a reduction in the rate of block failures may lead to a reduced use of rescue pain medication (generally opioids), reduced nursing time to administer pain medication, a reduction in adverse events associated with opioids, and ultimately a shorter hospital stay.

Reduced need for supplemental anaesthesia

In some individual trials a reduction in the need for supplemental analgesia was demonstrated. For example, a reduction in the need for a general anaesthesia with the use of ultrasound compared with nerve stimulation was shown in Danelli 2009 (0% vs 18%, P-value not reported), Perlas 2008 (8% vs 24%, P=0.06), Sauter 2008 (0% vs 5%, P-value not reported) and Williams 2003 (0% vs 8%, P=0.12) (Perlas et al 2008; Sauter et al 2008; Williams et al 2003). In Strub 2011, a reduction in the need for additional anaesthesia with ultrasound compared with the landmark technique was demonstrated (20% vs 47%, P=0.0012), with the difference being driven by a reduction in the need for additional local anaesthetic (17% vs 45%, P=0.00049). In the meta-analysis a reduction in the need for additional anaesthesia or analgesia was demonstrated although the difference was not statistically significant (P=0.282). Similarly, the Cochrane review of peripheral nerve blockade (Walker et al. (2011)) concluded the rate of block success, defined as surgical anaesthesia without supplementation or conversion to general anaesthesia, was similar with ultrasound (range 72% to 99%) and nerve stimulation (range 58% to 93%). As a reduced need for additional local or general anaesthesia has not been consistently demonstrated in the RCTs, the cost implications associated with this has not been calculated; any reduction in additional anaesthesia would decrease the incremental cost for ultrasound.

Better postoperative pain control

A systematic review undertaken by Choi and Brull (2011) evaluated the effect of ultrasound guidance for nerve blocks on acute pain outcomes. Twelve RCTs were identified comparing ultrasound and nerve stimulation in which early (<24 hour) pain control was assessed. In 4 of the trials postoperative pain control was improved with ultrasound guidance. In the remaining 8 trials no difference in pain control was reported. Of the 12 RCTs, 7 reported opioid consumption. Reduced opioid consumption with the use of ultrasound was demonstrated in 3 of the trials (and these 3 trials also showed improved pain control), with no difference in consumption reported for the remaining 4 trials. Two of the RCTs compared the differences in length of stay in hospital between ultrasound guidance and nerve stimulation and did not find any difference. Choi and Brull (2011) concluded that there is insufficient evidence to define the effect of ultrasound guidance on acute pain control.

The Ehlers et al (2012) economic analysis was conducted alongside a randomised trial comparing ultrasound and nerve stimulation, and data for the use of postoperative pain medication, as well as the nurse's time for postoperative care, were collected

prospectively. A reduction of 14.8 mL of 1% morphine, 15 mL of 0.25% bupivacaine and 19 minutes of nurses' time were observed with ultrasound compared with nerve stimulation. The cost of 14.8 mL of 1% morphine is approximately $3 ($21.24 for 100 mL; Australian private hospital; cost of 14.8 mL = $21.24 / 100 x 14.8). The cost of 15 mL of 0.25% bupivacaine is approximately $5 ($30.23 for 5 x 20 mL ampules; Australian private hospital; cost of 15 mL = $30.23 / 100 x 15). The cost of 19 minutes of a nurse time is approximately $12 assuming a 5th year registered nurse (NSW award rates 2011, weekly salary $1,302.30). Thus, the total cost saving associated with reduced postoperative pain medications and nurse postoperative care is $20.

Reduced dose of local anaesthetic

The use of ultrasound has also been reported to reduce the dose of local anaesthetic required. In most of the RCTs the same dose of local anaesthetic was used in both treatment arms. However, in six of the trials comparing ultrasound and nerve stimulation the dose of local anaesthetic was not prescribed. In three of these trials, the volume of the injected local anesthetic was varied for consecutive patients based on an up-and-down method, according to the response of the previous patient (McNaught 2011; Ponrouch 2010 and Danelli 2009). In McNaught 2011 the minimum effective analgesic volume (MEAV) of 0.5% ropivacaine required to provide effective analgesia was significantly (P=0.034) reduced to 0.9 mL in the ultrasound group from 5.4 mL in the nerve stimulation group (McNaught et al 2011). In Ponrouch 2010 the MEAV of 1.5% mepivacaine was significantly lower in the ultrasound group than in the nerve stimulation group for the median nerve (2 mL vs 4 mL, P=0.017) but not the ulnar nerve (2 mL vs 2.4 mL). In Danelli 2009 the mean MEAV of 1.5% mepivacaine for sciatic nerve block was 12 mL in the ultrasound group and 19 mL in the nerve stimulation group (P<0.001).

In van Geffen 2009, the anaesthesiologist was asked to inject the smallest amount of local anaesthetic (lignocaine 1.5% with adrenaline 5 μg/mL) that his or her clinical experience judged to be necessary in order to obtain a successful block, but with a maximum of 40 mL. Significantly less local anaesthestic was injected in the ultrasound group compared to the nerve stimulation group (17 vs 37 mL, P<0.001), while the overall success rate was increased (100% vs 75%, P=0.017).

In Oberndorfer 2007 and Willschke 2005, the blocks were performed using an ultrasound-guided multiple injection technique until the nerves were surrounded by levobupivacaine (0.5% in Oberndorfer 2007 and 0.25% in Willschke 2005) (Oberndorfer et al 2007; Willschke et al 2005), or by nerve stimulator guidance using a predefined dose of 0.3 mL per kg of levobupivacaine. Both of these trials were conducted in children. In Willschke et al (2005), the volume of anaesthetic in sciatic and femoral nerve blocks was reduced with ultrasound compared with nerve stimulator guidance (0.2 vs 0.3 mL per kg, P<0.001 and 0.15 vs 0.3 mL per kg, P<0.001, respectively). Similarly in Oberndorfer et al (2007), the volume of anaesthetic in ilioinguinal/iliohypogastric blocks was reduced with ultrasound compared with nerve stimulator guidance (0.19 mL vs 0.3 mL per kg P<0.0001).

In one RCT comparing ultrasound and the landmark technique the dose of local anaesthetic was not prescribed (Strub et al. (2011)). In this study an axillary block was performed using bupivacaine hydrochloride (5 mg/ml) with 0.5% adrenaline and mepivacaine hydrochloride (10 mg/ml) in a ratio of 1:1. In the landmark group 40 mL of anaesthetic was administered to each patient. In the ultrasound group the anaesthetic

was injected until a perineural ring of fluid was observed in the ultrasound image, and the volume was reduced to 12 mL.

Data on the dose of local anaesthetic has been collected as part of the AURORA registry. In 2006-2008 the mean dose of ropivacaine used for single blocks was 2.0 mg/kg. This decreased to 1.7 mg/kg in 2008-2011, and to 1.4 mg/kg in 2011-2012. The reduction in dose may be due to the increased use of ultrasound, and is consistent with the results from the RCTs.

The cost of 5 x 100mg/10mL ampules of ropivacaine (500mg) at an Australian private hospital is $44.85. Based on a dose reduction of 0.6 mg/kg and an average patient weight of 80kg as reported in the AURORA registry, the saving associated with the reduced dose of local anaesthetic is estimated to be approximately $4 (0.6 x 80 x 44.85/500). This saving may not be realised as the ampules are single use and hence a reduction in dose may lead to increased wastage rather than a reduction in the number of ampules used. However, as anaesthetists gain confidence with using lower doses of local anaesthetic when using ultrasound, the dose may be further reduced as reductions of greater than 50% were observed in some of the RCTs.

Complications

The complications reported in the RCTs comparing ultrasound guidance and nerve stimulation or the landmark technique for nerve block included inappropriate vascular puncture, haematoma, paraesthesia and nerve injury. In the meta-analyses (Figure 14, Figure 15, Figure 16, Figure 17) a statistically significant reduction in the incidence of inappropriate vascular puncture and nerve injury was observed with ultrasound guidance compared with nerve stimulation or the landmark technique. A reduction in the incidence of paraesthesia was observed with ultrasound guidance however, the difference was not statistically significant.

Although haematoma may cause discomfort for the patient, there are generally no clinical sequelae and hence a cost has not been assigned. Further the incidence of haematoma was less than 10% in all studies in which it was reported.

Vascular puncture and hence injection of local anaesthetic into the vascular system may in rare cases result in local anaesthetic systemic toxicity (LAST). The incidence of LAST is too low to be assessed in RCTs, however data have been collected as part of the AURORA database which includes 25,336 peripheral nerve blocks. Ultrasound guidance significantly reduced the incidence of LAST compared with no ultrasound guidance (0.59 vs 2.1 per 1000 blocks, p=0.004). There were 22 episodes of LAST (13 minor, 8 major and 1 cardiac arrest). There were 12 episodes of LAST (8, minor; 4, major) with ultrasound (n = 20,401) and 10 episodes of LAST (5, minor; 4, major; 1, cardiac arrest) without ultrasound (n = 4,745). Seizure was the clinical symptom reported for 6 of the 8 major LAST events. Based on the costs weights for AR-DRG B76A (seizure with CSCC) and B76B (seizure without CSCC) weighted by number of separations, the inpatient cost of treating a seizure is assumed to be $3,311 (private sector, Round 12 (2007-2008, v5.1). The savings associated with the reduced incidence of major LAST events is therefore approximately $2 ($3311 x (4/4745-4/20401)). This is potentially an underestimate of the savings due to a reduced incidence of complications as only the costs associated with treating major LAST events have been considered.

The incidence of nerve injury following a nerve block is low. In 7,000 blocks included in the AURORA database in 2006-2008, there were three cases of nerve injury giving an incidence of 0.4 per 1,000 blocks. Data are not available assessing the impact of ultrasound on nerve injury (Neal et al. (2010)).

The lower dose of local anaesthetic required with the use of ultrasound may reduce the incidence of hemidiaphragmatic paresis (HDP). The use of ultrasound and low doses of anaesthetic has been shown to reduce the incidence of HDP defined based on spirometric measures of pulmonary function (Neal et al. (2010)). However, the impact of ultrasound on symptomatic HDP is unknown as the incidence is low (1% based on 510 supraclavicular blocks, Neal 2010).

Cost analysis

A summary of the potential cost offsets with ultrasound guidance compared with nerve stimulation for nerve blockade is presented in Table 49. Approximately three-quarters of the cost offsets relate to improved postoperative pain control and the associated reduction in rescue pain medication and nursing care. The reduced resource use was sourced from the Ehlers 2012 economic analysis in which resource use was collected prospectively as part of a RCT. The RCT was conducted in Denmark and hence the applicability of the resource use to Australian clinical practice is uncertain. Further, patients in the RCT received a continuous sciatic nerve block. Based on the 2011/2012 AURORA data, sciatic blocks were the second most common block type, however a catheter for a continuous block is used in approximately one-quarter of blocks with the remaining being single-shot blocks.

Table 49 Potential cost offsets associated with using ultrasound for peripheral nerve blocks

Resource	Units	$/unit	Cost	% of cost
Reduced dose of local anaesthetic, mg	48	$0.09	$4	15%
Reduced dose of postoperative morphine, mL	14.8	$2.39	$3	12%
Reduced dose of postoperative local anaesthetic, mg	6.25	$0.10	$5	19%
Reduced nursing time postoperative, minutes	19	$0.63	$12	46%
Reduced incidence of major LAST, events per 1000 blocks	0.65	$3.31	$2	8%
Total cost savings with ultrasound	-	-	$26	100%

LAST, local anaesthetic systemic toxicity

A summary of the overall cost implications of using ultrasound compared with nerve stimulation for nerve blockade is presented in Table 50. Sensitivity analyses are also presented in this table.

Without inclusion of the proposed MBS benefit, the additional cost per procedure with ultrasound compared with nerve stimulation is $12. A threshold analysis has been conducted to determine the minimum number of procedures required per machine per year for the cost of ultrasound to be less than nerve stimulation assuming the cost of the ultrasound machine is $40,000. Ultrasound is less expensive if more than 1,100 procedures are performed per machine per year. A threshold analysis has also been conducted to determine the maximum cost of the ultrasound machine assuming 500 procedures are performed per machine per year. Ultrasound is less expensive if the ultrasound machine costs less than $16,000.

With the inclusion of the proposed MBS benefit and assumed patient co-payment, the additional cost per procedure with ultrasound compared with nerve stimulation is $121 ($12 plus the proposed MBS benefit of $43.76 and assumed patient co-payment of $65). The proposed MBS benefit for the ultrasound procedure ($43.76) is greater than the estimated cost offsets ($26) and hence for this scenario ultrasound is more expensive than nerve stimulation regardless of the number of procedures performed per year or the cost of the ultrasound machine.

Sensitivity analyses demonstrate the results are sensitive to the assumed number of procedures performed per ultrasound machine per year, and the cost offset for improved postoperative pain management.

Table 50 Incremental cost with the use of ultrasound vs nerve stimulation for nerve blockade

	Without MBS benefit	With MBS benefit[a]
Base case analysis		
Cost of ultrasound procedure (A)	$38	$147
Cost of nerve stimulation procedure (B)	$0.42	$0.42
Incremental cost of procedure (A - B = C)	$38	$147
Potential cost offsets (D)	$26	$26
Incremental cost per procedure with ultrasound (C - D)	$12	$121
Sensitivity analyses, incremental cost per procedure with ultrasound		
Ultrasound machine cost		
$40,000 → $25,000	$4	$113
$40,000 → $45,000	$14	$123
Number of procedures per ultrasound per year		
500 → 1000	$1	$109
500 → 100	$100	$208
Inclusion of accreditation cost		
$0 → $1.53 per procedure	$14	NA
Inclusion of training cost		
$0 → $8 per procedure	$20	NA
Inclusion of accreditation and training cost		
$0 → $9.53 per procedure	$22	NA
No cost offsets associated with improved postoperative pain control	$32	$141

NA, not applicable
a Proposed MBS fee is $58.35, therefore the 75% MBS benefit is $43.76. The assumed patient co-payment is $65.

In summary, without inclusion of the proposed MBS benefit, the additional cost per procedure for ultrasound compared with nerve stimulation for performing nerve blocks is $12. The potential clinical benefits from using ultrasound compared with nerve stimulation include:

- reduced need for supplemental analgesia, and in particular general anaesthesia which may be associated with adverse events;
- better postoperative pain control,
- reduced use of opioids which may lead to reduced adverse events;
- reduced dose of local anaesthetic which may enable the patient to be mobile sooner after surgery; and

- fewer complication, including LAST.

However, the clinical data to support these benefits are limited.

Financial implications

Vascular access procedures can be claimed under MBS items:

- 22020: Central venous catheterisation in association with anaesthesia, and
- 22015: Right heart/pulmonary arterial catheterisation in association with anaesthesia.

The number of services for items 22020 and 22015 for the 2008/2009 – 2012/2013 financial years are presented in Table 51. The Applicant notes close to 100% of these services are expected to be for anaesthetists' services. Prior to the 1 November 2012, ultrasound guidance was claimed by anaesthetists using MBS item 55054. Data provided by the Department of Health indicate approximately 8% of item 55054 anaesthetist-related services were claimed together with vascular access items 22020 and 22015 (Table 52). An anaesthetist-related claim was defined as a claim by a Provider with one of the following registered specialties current on date of service or derived specialty for the quarter of service being one of these specialties: Anaesthetics-specialist (051), Anaesthetics-intensive care (060), Resuscitation (075), Anaesthetics-non-specialist (216) and Anaesthetics-trainee (400). Vascular access procedures can also be claimed under MBS items 13815 (central venous catheterisation as a standalone procedure) and 13818 (right heart/pulmonary arterial catheterisation as a standalone procedure). Only a proportion of claims for items 13815 and 13818 are expected to be made by anaesthetists as other specialists such as intensive care and emergency medicine physicians also perform these procedures. As only approximately 1-3% of item 55054 anaesthetist-related claims were in combination with items 13815 or 13818 (Table 53) these items are not considered when estimating the financial impact of the proposed MBS items.

Nerve block procedures for postoperative pain management can be claimed under MBS items:

- 22040: Peri-operatively performed nerve block for the control of postoperative pain via the femoral or sciatic nerves, in conjunction with hip, knee, ankle or foot surgery
- 22045: Peri-operatively performed nerve block for the control of postoperative pain via the femoral and sciatic nerves, in conjunction with hip, knee, ankle or foot surgery
- 22050: Peri-operatively performed nerve block for the control of postoperative pain via the brachial plexus in conjunction with shoulder surgery

The number of services for these items are presented in Table 51. The Applicant notes close to 100% of these services are expected to be for anaesthetists' services. Approximately 55% of item 55054 anaesthetist-related services were claimed together with postoperative pain management nerve block MBS items (Table 52). The Applicant notes that a small number of nerve block procedures may be claimed by Anaesthetists under MBS items 18254, 18262, 18266, 18268, 18270, 18272 and 18278 (MSAC Eligibility Form, Question 26). Only approximately 1% of item 55054 anaesthetist-

related claims were in combination with these items (Table 53), and hence they are not considered when estimating the financial impact of the proposed MBS items.

Nerve block procedures for anaesthesia can be claimed under general anaesthesia MBS items. There are a large number of general anaesthesia items and data are not available on the number of anaesthetist-related claims for item 55054 in combination with these items. It is likely that the majority of item 55054 services not in combination with vascular access items or nerve blocks for postoperative pain items (i.e. approximately 35% of item 55054 services), were for nerve blocks for anaesthesia. Based on the AURORA data, 3 per cent of peripheral nerve blocks are for anaesthesia and 37 per cent are for anaesthesia and postoperative analgesia (AURORA). The number of nerve block procedures for anaesthesia has been estimated assuming 40 per cent of all nerve block procedures are for anaesthesia. Thus it is assumed that the 37 per cent of blocks performed for anaesthesia and analgesia are all claimed under the anaesthesia items and hence, the total number of nerve block procedures may be overestimated.

Overall, in 2011/2012 and 2012/2013 approximately 10 per cent of anaesthetist-related claims for item 55054 were for vascular access, 55 per cent were for nerve blocks for postoperative pain management, and 35 per cent were not for either of these services and hence were likely for nerve blocks for anaesthesia (Table 52).

Table 51 MBS services for vascular access procedures (MBS items 22015 and 22020) and nerve block procedures for postoperative analgesia (MBS items 22040, 22045 and 22050), and estimated number of services for nerve block procedures for anaesthesia

Financial year	Item 22015 (vascular access)	Item 22020 (vascular access)	Item 22040 (analgesia)	Item 22045 (analgesia)	Item 22050 (analgesia)	Nerve blocks for anaesthesia	Total	Growth
2008/2009	5062	19866	20638	6327	14379	27563	93835	
2009/2010	4937	20528	22338	6619	15992	29966	100380	7.0%
2010/2011	4946	20892	22878	6904	16417	30799	102836	2.4%
2011/2012	4964	21787	23789	6651	17286	31817	106294	3.4%
2012/2013	5303	22294	24668	6645	18110	32949	109969	3.5%

Source: MBS statistical reports (http://www.medicareaustralia.gov.au/statistics/mbs_item.shtml)
Number of services for nerve blocks procedures for anaesthesia estimated as 40% of the total nerve block procedures.

Table 52 Anaethetist-related MBS services for ultrasound guidance (MBS item 55054) for financial years 2011/2012 and 2012/2013 and co-claimed MBS items for vascular access and nerve block procedures

	2011/2012		2012/2013[a]	
Total anaesthetist-related services for 55054	32041	100%	13205	100%
55054 services in combination with:				
Vascular access MBS items 22015 and/or 22020	2564	8.0%	1023	7.7%
Vascular access MBS items 13815 and/or 13818	362	1.1%	410	3.1%
Nerve block MBS items 22040/22045/22050	17831	55.7%	6940	52.6%
Nerve block MBS items 18254/18262/18266/18268/18270/18272/18278	190	0.6%	160	1.2%
Vascular access and nerve block MBS items	183	0.6%	48	0.4%
None of the above MBS items	10911	34.1%	4624	35.0%

Source: Data provided by Department of Health. An anaesthetist-related claim was defined as a claim by a Provider with one of the following registered specialties current on date of service or derived specialty for the quarter of service being one of these specialties: Anaesthetics-specialist (051), Anaesthetics-intensive care (060), Resuscitation (075), Anaesthetics-non-specialist (216) and Anaesthetics-trainee (400).
a Ultrasound guidance was able to be claimed by anaesthetists prior to 1 November 2012.

The number of anaesthetist-related claims for item 55054 for the 2008/2009 – 2011/2012 financial years, and July to October 2012 are presented inTable 53. In 2008/2009 ultrasound was used in 9% of vascular access and nerve block procedures, and this increased to 30% in 2011/2012, and to 34% in the period July to October 2012.

Table 53 Anaethetist-related MBS services for ultrasound guidance (MBS item 55054) and use as a percentage of vascular access and nerve block procedures

Year	Total services for vascular access and nerve blocks (A)	Anaesthesia related claims for Item 55054[a] (B)	Use of ultrasound (B/A)
2008/2009	93835	8744	9%
2009/2010	100380	19094	19%
2010/2011	102836	27290	27%
2011/2012	106294	32041	30%
July-Oct 2012	38319	13205	34%

Source: MBS statistical reports (http://www.medicareaustralia.gov.au/statistics/mbs_item.shtml)
a Data provided by Department of Health. An anaesthetist-related claim was defined as a claim by a Provider with one of the following registered specialties current on date of service or derived specialty for the quarter of service being one of these specialties: Anaesthetics-specialist (051), Anaesthetics-intensive care (060), Resuscitation (075), Anaesthetics-non-specialist (216) and Anaesthetics-trainee (400).

The annual growth in the number of services for nerve block and vascular access procedures for 2011/2012 and 2012/2013 was similar (Table 51), and therefore an annual growth rate of 3.4% has been assumed for the next 3 years. The proposed MBS fee for ultrasound guidance is $58.35, and as this is an inpatient procedure the MBS benefit is $43.76 ($58.35 x 0.75). Assuming the proportion of vascular access and nerve block procedures in which ultrasound guidance is used increases to 60%, the estimated MBS benefit in 2014/2015 and 2015/2016 is $3.1m and $3.2m, respectively (Table 54). Assuming the proportion of procedures in which ultrasound guidance is used increases to 90%, the estimated MBS benefit in 2014/2015 and 2015/2016 is $4.6m and $4.8m, respectively. The use of ultrasound in 90% of procedures is consistent with the AURORA data for nerve blocks in which ultrasound was used in 87% of procedures in 2011/2012 (AURORA), although it should be noted that hospitals participating in the AURORA registry were ensured access to an ultrasound machine.

Based on patient co-payment data for anaesthetist-related claims for MBS item 55054, the assumed patient co-payment is $65 per procedure. Thus, the total patient co-payment in 2015/2016 with the use of ultrasound guidance in 60% and 90% of procedures would be $4.7m and $7.1m, respectively.

Table 54 Estimated MBS services and benefits for ultrasound guidance

Year	Estimate total services for nerve block and vascular access[a]	60% use of ultrasound: Services	60% use of ultrasound: MBS benefit	90% use of ultrasound: Services	90% use of ultrasound: MBS benefit
2013/2014	113708	68225	$2,985,507	102337	$4,478,260
2014/2015	117574	70544	$3,087,014	105816	$4,630,521
2015/2016	121571	72943	$3,191,972	109414	$4,787,959

a Assuming a 3.4% annual increase in the number of services

The capital and consumable costs for each ultrasound guided procedure is estimated to be $38 (equipment = $22, consumables = $16). Based on 72,943 services (use in 60% of procedures) in 2015/2016, the capital and consumable cost is approximately $2.8m. Based on 109,414 services (use in 90% of procedures) in 2015/2016, the capital and

consumable cost is approximately $4.2m. The potential reductions in health care costs due to reduced postoperative care, reduced use of local anaesthetic and pain medications, and a reduced incidence of complications have not been quantified for the financial forecasts as the cost savings are uncertain and may not be realisable.

Implication to the extended Medicare safety net

If MBS funding is granted for ultrasound guidance for nerve blocks and major vascular access, it is unlikely to impact the extended Medicare safety net. This is because the proposed MBS service is provided in the inpatient setting.

Discussion

Limitations of the evidence

The body of evidence that has been identified and included in this assessment of the safety, effectiveness and cost effectiveness of ultrasound guided central venous access and percutaneous neural blocks draws from an international base; many of the reports describe studies performed either in North America or Europe. This should be considered when generalising outcomes of this assessment to the Australian context with respect to patient populations as well as proceduralists' training and skill level in the included studies.

The assessment of the body of evidence for ultrasound guidance in vascular access and percutaneous nerve block are detailed Table 55 and Table 56. Overall, the evidence base is of good quality and where discrepancy occurs it can be explained; for example, differences related to access site for vascular access, location of nerve, or use of different comparators. Broadly speaking these issues are reflective of variability in clinical practice. Given the large numbers of studies in the evidence base and the clinical scenarios that are encapsulated, the evidence should have direct relevance to the Australian context. The caveat to this statement in terms of the information in the current evidence base is the predominance of specific vascular access sites (such as internal jugular vein) or specific nerve blocks (such as the brachial nerve) within the literature. However, this weighting to specific conditions most likely mirrors clinical practice within Australia and is simply a reflection of the more common procedures performed. The overall clinical impact may be considered moderate. Although the evidence is supportive of statistical significance differences including for a number of adverse events, the effect size for some effectiveness outcomes may be considered small and not of clinical significance in all cases.

The identified literature on ultrasound guided central vascular access and percutaneous nerve block showed a large range of studies. Many systematic reviews and RCTs that addressed the use of ultrasound for these procedures were retrieved for this assessment. However, many trials had different research questions, for example investigated targeted provider populations which are not relevant to this assessment, or used inappropriate comparators such as alternative techniques of ultrasound guidance. Further to these, more recent RCTs address refinement of the ultrasound technique rather than investigate efficacy in comparison with alternate guidance techniques.

A total of 18 systematic reviews and 88 RCTs met the inclusion criteria to inform the PICO of this assessment and were deemed through the use of appraisal tools to be of appropriate methodological quality. The included evidence reported on multiple outcomes associated with safety and effectiveness of ultrasound guidance for both central venous access and percutaneous neural blockades. Synthesising the large volume of evidence represented by the included studies was performed by identifying overlap between systematic reviews and the identified RCTs. Any RCTs previously reported within included systematic reviews were excluded from primary data extraction and the study information was not summarised in this assessment report. For percutaneous nerve block a recent Cochrane review clearly presented individual study data (Walker et al., 2011). For vascular access the most recent systematic review did not provide clear and extractable data from the RCTs, therefore data from all primary studies was

extracted independently for the purposes of this assessment (Wu et al., 2013). This approached avoided the potential bias of study duplication in both the narrative synthesis and meta-analysis of the evidence. All included RCTs not represented by the identified systematic reviews were appraised, extracted and presented within this assessment report. This included studies published since the search date of the systematic reviews together with studies published on indications not reflected in the systematic reviews, such as central arterial access.

Table 55 Body of evidence assessment matrix for ultrasound guidance for major vascular access

Component	A Excellent	B Good	C Satisfactory	D Poor
Evidence base [a]		one or two level II studies with low risk of bias or a systematic review/several level III studies with low risk of bias		
Consistency [b]		most studies consistent and inconsistency may be explained		
Clinical impact			moderate	
Generalisability	population/s studied in body of evidence are the same as the target population			
Applicability	directly applicable to Australian healthcare context			

a Level of evidence determined from the NHMRC evidence hierarchy (Table 18).
b If there is only one study, rank this component as 'not applicable'.
c For example, results in adults that are clinically sensible to apply to children OR psychosocial outcomes for one cancer that may be applicable to patients with another cancer.
Source: NHMRC (2009).

Table 56 Body of evidence assessment matrix for ultrasound guidance for percutaneous neural blockade

Component	A Excellent	B Good	C Satisfactory	D Poor
Evidence base [a]		one or two level II studies with low risk of bias or a systematic review/several level III studies with low risk of bias		
Consistency [b]		most studies consistent and inconsistency may be explained		
Clinical impact			moderate	
Generalisability	population/s studied in body of evidence are the same as the target population			
Applicability	directly applicable to Australian healthcare context			

a Level of evidence determined from the NHMRC evidence hierarchy (Table 18).
b If there is only one study, rank this component as 'not applicable'.
c For example, results in adults that are clinically sensible to apply to children OR psychosocial outcomes for one cancer that may be applicable to patients with another cancer.
Source: NHMRC (2009).

The intended use of ultrasound imposed limitations on RCT study design. Typically, included studies were performed using a small size that was powered to achieve statistical significance for outcomes of primary effectiveness. Safety issues associated with the procedures of central venous access and percutaneous neural blocks are relatively rare as evidenced in the reporting of such events in the included RCTs. Safety event data were often only included if an adverse event occurred and this may have introduced a reporting bias with respect to safety. The issue of small sample size and infrequent reporting was redressed, in part, by the meta-analysis which is able to provide data regarding the occurrence of adverse events across a larger patient population.

Blinding of the proceduralists to intervention technique is impossible for ultrasound guided vascular access and percutaneous neural blockade. However, outcome measures should be conducted by assessors blinded to the intervention. The use of appropriately blinded assessor was not explicitly reported for all of the included studies. Also, blinding of patients to the intervention was rarely reported and patient knowledge may have influenced the results. The potential impact on reported outcomes could not be assessed. The other methodological issue was related to poor descriptions of patient flow through the trials both with regard to numbers that were withdrawn and reasons of drop-out. However, given that most studies focused on immediate effects of the procedure a significant number of studies had a 100 per cent patient retention across the trial period.

Overall, the evidence base for effectiveness can be consider good to excellent and comprises of a large number of NHMRC level I and II evidence (Table 55, Table 56). The risk of bias was considered minimal and between-study inconsistency could be explained. However, the effectiveness focus of the literature is a limitation in addressing the safety of ultrasound use for the both vascular access and placement of neural blocks. The volume of evidence and paucity of reporting of adverse events in the literature indicates that the procedures of vascular and neural blockade are established within clinical practice and are considered safe with a low risk of adverse events when performed by the experienced practitioner. Importantly, reports did provide statements on lack of adverse events and when events did occur they were reported and the impact of the intervention was assessed.

In Australia, the need for, and use of, ultrasound in the context of anaesthesia is reflected in the compulsory training for Fellowship. Ongoing research and recent published RCTs focus on refining the ultrasound technique to improve imaging, refining how ultrasound is used, assessing anaesthetic agent requirements and extending the application of ultrasound to specific clinical settings or patient populations.

Characteristics of evidence base

The extracted data from RCTs together with the high level of congruence between the results and conclusions of existing systematic reviews is confirmatory of the existing level I evidence. Where possible, data from RCTs reported in SRs were abstracted and combined with the RCT evidence independently identified in this assessment and subjected to meta-analysis.

Is it safe?

Vascular access

Based on the crude number of RCTs that reported safety events, the overall frequency of occurrence in decreasing order was; inappropriate vascular puncture, haematoma, pneumothorax, haemothorax, catheter related events, infection and nerve injury.

Assessing the impact of ultrasound on the reported adverse events is limited by their infrequent occurrence in RCTs which have been primarily designed to assess effectiveness outcomes. This is especially true for serious adverse events requiring clinical intervention. This is further compounded by small sample sizes associated with most of the include RCTs.

Variability in the effect size for any specified adverse event associated with ultrasound use observed between studies may reflect variation in the clinical and technical difficulty of gaining vascular access for a given site or patient population. As such, the utility of ultrasound to guide vascular access to reduce adverse events may vary and clinical judgment is required to assess need and use on a case by case basis. In addition, the current evidence base mainly addresses central venous access with the limited evidence for arterial access and PICC line placement. Although there does appear to be congruency in the evidence for different access sites caution should be exercised in extrapolating evidence from central venous studies to arterial access and PICC line placement.

The evidence synthesis in this assessment demonstrated statistically significant reductions in the risk of adverse events for inappropriate vascular puncture (predominantly arterial), haematoma, pneumothorax and haemothorax. Of note is the 80 to 90 per cent reduction in the risk of pneumothorax and haemothorax occurring when vascular access in guided by ultrasound as compared to a landmark technique. A reduction in the risk of such adverse events occurring is clinically significant for the both patients and the healthcare system.

Overall, the procedures of central venous access, central arterial access and placement of PICC lines are part of normal clinical practice. These procedures are considered safe and the evidence from the included studies in this assessment suggests that ultrasound guidance will reduce the incidence of adverse effects.

Percutaneous neural blockade

Of the 58 RCTs included in this assessment, adverse events are rarely reported and in most cases the absence of adverse events is reported by variations of the statement 'no minor or serious adverse events associated with neural block placement were recorded'. The evidence base is dominated by upper (brachial) and lower (sciatic) extremity neural blocks. In the three RCTs on truncal blocks no adverse events were reported. Studies most commonly compared ultrasound with ENS guidance (39 trials), with fewer studies comparing ultrasound with either anatomical landmark (12 trials) or a combination of ultrasound and ENS (6 trials). One trial included a comparator of the transarterial route.

Four main adverse events were reported in a quantitative manner. Based on the number of RCTs reporting adverse events, the frequency of occurrence in decreasing order was; inappropriate vascular puncture, nerve injury, paraesthesia and haematoma. The serious

adverse event of pneumothorax was not reported in any of the included RCTs on upper extremity nerve blocks. The use of the ultrasound modality to guide nerve block placement to reduce the risk of adverse events occurring was confirmed, with risks ratio ranging from 0.27 to 0.62. These reductions were statistically significant with the exception of paraesthesia. The benefit of ultrasound in reducing nerve injury over ENS was reinforced in the sub-group analysis. In studies that evaluated ultrasound plus ENS with ENS alone the risk reduction associated with ultrasound use was negated. If selection of guidance technique is to be based on reducing the risk of nerve injury, the evidence suggests that an ultrasound only technique should be the preferred choice.

One of the identified RCTs was specifically designed to assess the adverse event of diaphragmatic paraesthesia and the associated respiratory depression when nerve blocks were placed using either the ultrasound or ENS methods. Under the conditions of this study, the use of ultrasound significantly reduced the occurrence of respiratory depression from 90 per cent to 13 per cent of patients. This study highlights both the impact of ultrasound on adverse events as well as the issue of identifying and quantitating harm effects from RCTs designed to assess effectiveness.

Overall, the procedure of neural blockade is normal practice and is considered safe. The evidence from the studies included in this assessment suggests that ultrasound guidance will reduce the incidence of adverse effects.

Is it effective?

Vascular access

Seven systematic reviews and 33 RCTs addressed the effectiveness question of this assessment. Effectiveness of the guidance techniques was assessed by time to complete the procedure, the number of attempts to gain access, failure on first attempt and failure to access at a given site. For all four effectiveness outcomes the combined evidence favoured ultrasound over anatomical landmark methods and these differences were statistically significant.

In the majority of studies time to complete cannulation was considered skin-to-skin. Although statistically significant, the mean difference between techniques is less than one minute. The clinical impact of this time efficiency is minimal for most clinical scenarios. There was no evidence regarding the pre-procedure preparation time and only limited evidence on the impact of imaging on the overall procedure time. As such, the impact of these parameters on the overall time to perform ultrasound guided vascular access cannot be assessed from the available evidence.

A major benefit of the use of ultrasound is the significant reduction in risk of failed attempts to cannulate any given blood vessel. Failure is variously defined in the included RCTs but generally included the dimensions of time or number of attempts. If predetermined limits for these parameters were exceeded then vascular access at the original site was considered to have failed. Although not explicitly stated, failure may require access to be gained at an alternative site. Such failures will increase the overall time to affect the procedure and have a potential negative effect on patient comfort.

Other effectiveness indicators were the number of attempts needed to gain access and the number of cannulations completed successfully on first attempt. The use of ultrasound positively affected both of these effectiveness metrics. Such improvements

will have a positive impact on the aggregate time to perform multiple procedures as well as positively impact patient comfort.

Overall, the use of ultrasound appears to improve both the safety and effectiveness for central vascular access and placement of PICC lines. Although the reduction in time to gain access was only marginally reduced by ultrasound, the significant reduction in number of failed attempts will have a time saving impact over the course of multiple procedures. This should translate into an improved efficiency in readying patients for surgery. In addition, the observed improvements associated with the use of ultrasound should have a positive impact on patient comfort; however, no or only limited evidence of patient related impacts was extractable from the evidence base available for this assessment.

Percutaneous neural blockade

Ten systematic reviews and 58 RCTs were identified and formed the evidence base for the assessment of ultrasound effectiveness in performing percutaneous blocks. Nine of the identified effectiveness measures were subjected to a meta-analysis and included measures of procedural efficiency and block characteristics. Of the nine effectiveness measures subjected to meta-analysis five achieved statistical significance. Across the included studies a range of anaesthetic agents were used. Drug use regimes were reported as being those used in clinical practice to affect appropriate levels and duration of anaesthesia. As such the choice of anaesthetic agent was not considered in the assessment of ultrasound effectiveness when compared to landmark and electrical nerve stimulation guidance methods.

The evidence base is dominated by RCTs investigating the impact of ultrasound in the upper and lower extremities, and represented by brachial plexus and sciatic nerve block. Only three of the 58 RCTs addressed truncal nerve blocks. Given the diversity in anatomy the effectiveness of ultrasound to guide placement of neural blocks may vary and anatomical location was included as a sub-group within the meta-analysis. In addition, the evidence base includes both landmark and ENS comparators with interventions including ultrasound alone or in combination with ENS. Differences in comparators and interventions were investigated by sub-groups. Unless significant inter study variation was observed the effectiveness of ultrasound was assessed by combining all studies irrespective of anatomical location or comparator method.

Two of the three procedural measures achieved statistical significance. The use of ultrasound resulted in a statistically significant reduction in the skin-to-skin time for placement of nerve blocks when compared with ENS. In contrast, ultrasound extended the time for placement when compared with a landmark method. However, the observed differences in procedure time were less than 3 min for the ENS comparator and 1 min for landmark techniques. The clinical significance of these differences is considered low but is not assessable from the current evidence base. The procedural metric of needle redirects was defined by the need to retract the needle by a defined distance and then readvance without breaking the skin. Ultrasound reduced the need for needle redirects and this reflects the direct visual identification of the anatomy and ability to visually monitor placement in real-time. The impact of this should reduce the potential physical damage associated with repositioning of the needle and improve patient comfort.

Three of the block characteristics outcomes achieved statistical significance. The risk of failed blocks was reduced by the use of ultrasound. Failed blocks were defined by a total or partial failure to induce either sensory or motor block, need for rescue anaesthesia or exceed a predetermined time to locate the nerve and place anaesthetic agent. In the subgroup analysis the requirement of additional anaesthesia and analgesia did not reach statistical significance but there was a trend for ultrasound to reduce the need. The onset time for anaesthesia was significantly reduced when ultrasound was the guidance method and this in combination with improved procedural times for placement may translate to reducing the time taken to ready patients for surgery. This was confirmed in two RCTs that reported readiness for surgery, with a time saving of up to 20 min.

The outcome of required volume of anaesthetic agent to induce a surgical block was assessed in three RCTs in a step-down, step-up protocol. Across these RCTs the impact of ultrasound was to reduce the Mean Effective Anaesthetic Volume (50%) by 50 to 80 per cent. The clinical impact of this is a reduced injected volume of fluid and a reduction in associated potential tissue damage as well as reducing the overall impact of systemic anaesthetic toxicity if inadvertent vascular injection occurs.

Although neuroaxial blocks were not a specified intervention within the PICO, the assessment team conducted a focused search of the literature to inform on the use of ultrasound in this type of regional anaesthesia. Appendix O details the methods, results and discussion for the neuroaxial assessment. The evaluation of the neuraxial literature was limited to NHMRC level I evidence and identified systematic reviews on general, paediatric and obstetric patient populations. Three of the identified reviews were assessed as being of good methodological quality and provided information on the target populations. Overall, the impact of ultrasound to guide neuroaxial blocks is aligned with the evidence pertaining to peripheral nerve blocks. Specifically, ultrasound guidance reduced the number of skin punctures and risk of block failure.

Overall, the use of ultrasound for guiding the placement of neural blockade is at least equivalent, if not better than comparator techniques. Furthermore, the improvement in block characteristics should have a positive benefit for patients and patient flow through a surgical unit.

What are the economic considerations?

Capital cost per procedure

The capital cost per ultrasound procedure is sensitive to the cost of the ultrasound machine and the total number of procedures performed. Under the base case assumptions (assuming an ultrasound machine cost of $40,000 and 500 procedures per machine per year), the capital cost per ultrasound procedure is $22. Including costs for consumables ($16), the total cost per procedure is $38 (Table 57). With the most conservative assumptions (i.e. $45,000 machine cost and 100 procedures per year) the figure rises to $139; under the most optimistic assumptions (i.e. $25,000 machine cost and 1,000 procedures per year) the figure falls to $23 (Table 57).

Table 57 Capital and consumable cost per ultrasound procedure by procedures per year and machine cost

Procedures per machine per year	Ultrasound machine cost, $25,000	Ultrasound machine cost, $40,000	Ultrasound machine cost, $45,000
100	$89	$126	$139
500	$31	$38	$41
1000	$23	$27	$28

Based on the proposed MBS fee, the additional MBS benefit per procedure is $43.76. Following feedback from the Department of Health and noting that the procedures for which ultrasound guidance is proposed already have existing MBS items, the MSAC may wish to consider if an additional fee is appropriate for the ultrasound procedure and the level of reimbursement. The associated patient co-payment is assumed to be $65 based on the average patient co-payment for MBS item 55054 for anaesthetist-related claims for the 2012/2013 financial year.

Training costs

The above costs do not specifically consider training to perform the procedures or practice accreditation. The training costs are uncertain, and in order to apportion the cost over the procedures performed, an additional assumption regarding the number of anaesthetists using each ultrasound machine is required. Introductory training courses cost approximately $1,500, but there are potential additional costs for travel and the anaesthetists' time. Further, ongoing and hands-on training would be required, and additional training is likely to be required for using ultrasound guidance with neonates and children (Lamperti 2012). Training for ultrasound guidance is part of the specialist curriculum of the Fellowship of the Australian and New Zealand College of Anaesthetists (FANZCA). Practice accreditation on the Department of Health Diagnostic Imaging Accreditation Scheme will not be a requirement if the MBS items for ultrasound guidance are listed in the Schedule as therapeutic items (under Category 3) as proposed; however, accreditation may be considered appropriate by anaesthetists or the Department of Health. Accreditation would be required every three years and fees average up to approximately $2,000.

Cost offsets

The potential cost offsets associated with using ultrasound are highly uncertain and may not be realised in practice. For vascular access the costs associated with avoiding pneumothorax and haemothorax events have been estimated as part of the evaluation. The resource use, and hence costs, associated with treating these events are based on a single study conducted in the United Kingdom. For nerve blockade the costs associated with improved postoperative pain control, a reduced dose of local anaesthetic and avoidance of major local anaesthetic systemic toxicity (LAST) events have been estimated. Choi and Brull (2011) conducted a systematic review and concluded that there is insufficient evidence to define the effects of ultrasound guidance on acute pain outcomes. Further, the reduced resource use associated with improved pain management is from a single trial conducted in Denmark in which patients received a continuous sciatic nerve block. The applicability of the results from this study to Australian clinical practice is unknown. There is evidence that the dose of local anaesthetic can be reduced with ultrasound guidance, although the optimal dose is

currently unknown and will vary by nerve location. LAST events are rare, and hence the impact of ultrasound guidance on these events can only be assessed in large registries, such as AURORA.

Four of the economic evaluations identified in the literature assessing the use of ultrasound guidance included a cost offset associated with time savings for clinicians and nurses. Calvert et al. (2004) included a cost offset for a 10 minute delay starting surgery for every failed cannulation avoided. Sandhu et al. (2004), Liu et al. (2010) and Ehlers et al. (2012) included a cost offset due to reduced procedure time (5, 5 and 0.5 minutes, respectively). Sandhu et al. (2004) and Liu et al. (2010) assessing blocks for anaesthesia also included a cost offset due to a reduction in the block onset time (16 and 5 minutes, respectively). The results of the meta-analyses conducted as part of this assessment indicate that the time savings are likely to be less (total of 1 to 5 minutes), although only skin-to-skin time information was presented in the studies, and the associated resource implications are unknown. Further countering any potential time savings is the potential for delays waiting for shared ultrasound scanners that are being used elsewhere (Hessel 2009) However, more certainty with procedure time and block onset time with ultrasound guidance may lead to improved efficiency for the operating theatres, especially where dedicated ultrasound machines are available.

Synthesising costs and benefits

The additional costs of using ultrasound guidance need to be considered in light of the clinical benefits. The benefits of using ultrasound could not be assessed using utility measures and hence the standard economic measure quality adjusted life years (QALY) could not be calculated. Therefore the individual benefits need to be considered separately. The patient benefits of using ultrasound guidance include less discomfort resulting from reduced failed attempts and reduced procedure time, and the reduced risk of complications. In rare cases the complications can be serious and potentially lethal. Statistically significant reductions of 0.98 pneumothorax and 1.03 haemothorax events per 100 IJV cannulations, and 3.45 pneumothorax and 4.03 haemothorax events per 100 SCV cannulations were demonstrated with ultrasound guidance compared with the landmark technique. There were a total of 26 claims recorded by the UK NHS Litigation Authority (NHSLA) relating to anaesthetists and central venous access between 1995 and 2009 (Cook and MacDougall-Davis 2012). Of these, 14 claims related to arterial punctures, of which five included death, two non-fatal strokes and one brain damage. Overall, claims relating to central venous access were noted to represent a small proportion of claims against anaesthetists, but were marked by high severity. Based on data collected as part of the AURORA registry, a statistically significant reduction of 1.5 LAST events per 1000 blocks was demonstrated with ultrasound guidance compared with no ultrasound guidance (Barrington 2013). Approximately 40% of these LAST events were classified as major and included clinical symptoms such as seizures and cardiac arrest. Data from the American Society of Anesthesiologists Closed Claims database indicates that LAST is a significant source of morbidity and mortality following nerve blocks, being associated with 7 of 19 claims involving death or brain damage (Lee et al 2008).

For vascular access separate economic analyses have been conducted for IJV and SCV access and the cost offsets have been shown to vary by site. There is insufficient clinical evidence to enable reliable analyses for other access sites, and the cost offsets for these sites may be greater or less than estimated for IJV and SCV access. For the nerve blockade analysis, separate costings have not been undertaken for different nerves. In

general the meta-analyses demonstrate consistent results for blocks performed in the upper and lower extremities, however, the clinical and economic benefits may be greater or less for specific nerves. Similarly, there is insufficient evidence to enable specific analyses based on patient characteristics such as age and obesity.

Conclusions

Safety

Adverse events for central vascular access and percutaneous nerve blockade are relatively rare although can be serious and life-threatening. Comparative data shows that ultrasound guidance significantly improves a number of safety outcomes for ultrasound-guided compared to anatomical landmark techniques for both these procedures.

For central vascular access there were statistically significant improvements with ultrasound guidance for inappropriate vascular puncture, haematoma, pneumothorax and haemothorax.

For percutaneous nerve blockade there were significant reductions in the adverse events of inappropriate vascular puncture, nerve injury and haematoma. A reduction in diaphragmatic paraesthesia did not reach statistical significance, although one study that was specifically designed to assess this adverse event found a significant reduction in the occurrence of respiratory depression from 90 per cent of patients with the landmark technique to 13 per cent using ultrasound guidance.

Effectiveness

Trial data provided evidence for a range of effectiveness outcomes for both vascular access and percutaneous nerve block.

Ultrasound is shown to statistically improve a number of measures for central venous access including time to complete the procedure, the number of attempts to gain access, failure on first attempt and failure to access at a given site. Effectiveness is also improved for central arterial access, and for the placement of PICC lines.

For percutaneous nerve blockade, ultrasound is shown to improve procedural outcomes including fewer needle redirects and a reduction in skin-to-skin procedural time of three minutes when compared to ENS. Ultrasound extended the time for placement when compared with a landmark method by one minute. In terms of block characteristics, ultrasound reduces the number of failed blocks, reduces the onset time to anaesthesia, and reduces the mean effective anaesthetic volume.

Economic considerations

Vascular access

- For SCV cannulations, the savings due to fewer pneumothorax and haemothorax events ($63) with ultrasound is greater than the ultrasound capital and consumable costs ($38). Ultrasound also results in fewer failed cannulation attempts and hence is the dominant procedure. If the proposed MBS benefit and patient co-payment are included, the cost of the ultrasound procedure ($147) is greater than the savings due to fewer complications ($63), and the incremental cost per failed cannulation avoided is $600.
- For IJV cannulations the savings due to the avoidance of complications with ultrasound is $15. Without the proposed MBS benefit, the incremental cost per

failed cannulation avoided is $256. Including the proposed MBS benefit and patient co-payment increases the incremental cost per failed cannulation avoided to $1,467.

Nerve blockade

Without inclusion of the proposed MBS benefit, the additional cost per procedure with ultrasound compared with nerve stimulation is $12. With the inclusion of the proposed MBS benefit and patient co-payment, the additional cost per procedure with ultrasound compared with nerve stimulation is $121.

The potential cost offsets associated with using ultrasound are highly uncertain and may not be realised in practice. For vascular access the resource use costs associated with avoiding pneumothorax and haemothorax events are based on a single study conducted in the United Kingdom. For nerve blockade the costs associated with improved postoperative pain control, a reduced dose of local anaesthetic and avoidance of major local anaesthetic systemic toxicity (LAST) events have been estimated. The reduced resource use associated with improved pain management is from a single trial conducted in Denmark in which patients received a continuous sciatic nerve block. The applicability of the results from this study to Australian clinical practice is unknown. There is evidence that the dose of local anaesthetic can be reduced with ultrasound guidance, however the optimal dose is currently unknown and will vary by nerve location. LAST events are rare, and hence the impact of ultrasound guidance on these events can only be assessed in large registries, such as AURORA.

Advice

MSAC advised …

- The Minister for Health noted this advice on <*date*>… -

Appendix A MSAC terms of reference and membership

The Medical Services Advisory Committee (MSAC) is an independent scientific committee comprising individuals with expertise in clinical medicine, health economics and consumer matters. It advises the Minister for Health on whether a new medical service should be publicly funded based on an assessment of its comparative safety, effectiveness, cost-effectiveness and total cost, using the best available evidence. In providing this advice, MSAC may also take other relevant factors into account. This process ensures that Australians have access to medical services that have been shown to be safe and clinically effective, as well as representing value for money for the Australian healthcare system.

MSAC is to:

- Advise the Minister for Health on medical services including those that involve new or emerging technologies and procedures, and, where relevant, amendment to existing MBS Items, in relation to:
    - the strength of evidence in relation to the comparative safety, effectiveness, cost-effectiveness and total cost of the medical service;
    - whether public funding should be supported for the medical service and, if so, the circumstances under which public funding should be supported;
    - the proposed Medicare Benefits Schedule (MBS) Item descriptor and fee for the service where funding through the MBS is supported;
    - the circumstances, where there is uncertainty in relation to the clinical or cost-effectiveness of a service, under which interim public funding of a service should be supported for a specified period, during which defined data collections under agreed clinical protocols would be collected to inform a re-assessment of the service by MSAC at the conclusion of that period;
    - other matters related to the public funding of health services referred by the Minister.
- Advise the Australian Health Ministers' Advisory Council (AHMAC) on health technology assessments referred under AHMAC arrangements.

MSAC may also establish sub-committees to assist MSAC to effectively undertake its role. MSAC may delegate some of its functions to its Executive sub-committee.

The membership of MSAC at the 61st meeting held April 2014 comprised a mix of clinical expertise covering pathology, nuclear medicine, surgery, specialist medicine and general practice, plus clinical epidemiology and clinical trials, health economics, consumers, and health administration and planning:

Member *(Executive listed first followed by members in alphabetical order)*	**Expertise or affiliation**
Professor Robyn Ward (Chair)	Medical oncology
Dr Frederick Khafagi (Deputy Chair)	Nuclear medicine
Professor Jim Butler (Chair, Evaluation Sub-committee)	Health economics
Associate Professor John Atherton	Cardiology
Associate Professor Michael Bilous	Anatomical pathology
Janette Donovan	Consumers' Health Forum representative
Associate Professor Kirsty Douglas	General practice/research
Professor Kwun Fong	Thoracic medicine
Professor Paul Glasziou	Evidence-based health care
Mr Scott Jansson	Medical scientist pathology
Professor David Little	Orthopaedic surgery
Mr Russell McGowan	Consumer's Health Forum Representative
Associate Professor Bev Rowbotham	Haematology
Dr Graeme Suthers	Genetic pathology
Dr Christine Tippett	Obstetrics/gynaecology
Dr Simon Towler	WA Chief Medical Officer, part-time intensivist
Associate Professor David Winlaw	Paediatric cardiothoracic surgery
Dr Meegan Keaney	Ex-Officio (Department of Health, Medical Benefits Division)

Appendix B Health Expert Standing Panel members and evaluators

Health Expert Standing Panel members

Dr Michael Barrington, Specialiat anaesthesiologist

Dr Christopher Nixon, Anaesthetist

Evaluators

Name	Organisation
Dr David Tivey	Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S)
Dr Joanna Duncan	ASERNIP-S
Dr Alun Cameron	ASERNIP-S
Dr Meegan Vandepeer	ASERNIP-S
Mr Ning Ma	ASERNIP-S
Dr Yasoba Atukorale	ASERNIP-S
Ms Robyn Lambert	ASERNIP-S
Ms Stefanie Gurgacz	ASERNIP-S
Ms Deanne Forel	ASERNIP-S
Ms Jenny Houltram	Centre for Health Economics Research and Evaluation (CHERE)
Dr Richard Norman	CHERE

Appendix C Search strategies

Databases and websites searched

Table 58 Bibliographic databases searched

Database	Period covered
Cochrane Library – including Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, the Cochrane Central Register of Controlled Trials, the Health Technology Assessment Database, and the NHS Economic Evaluation Database	Inception–10/2013
PubMed (incorporating Medline)	Inception–10/2013
Web of Science (Current Contents)	Inception–10/2013
EMBASE	Inception–10/2013
The University of York Centre for Reviews and Dissemination – including NHS Economic Evaluation Database (NHS EED)/Database of Abstracts of Reviews of Effect (DARE)/Heath Technology Assessment (HTA) Database	Inception–10/2013

Table 59 Electronic internet databases searched

Database	Internet location
Scirus – for Scientific Information Only	http://www.scirus.com
TRIP database	http://www.tripdatabase.com
National Health Service (NHS) Evidence	http://www.evidence.nhs.uk/
NICE (NHS)	http://www.nice.org.uk/aboutnice/whatwedo/niceandthenhs/nice_and_the_nhs.jsp
National Guideline Clearinghouse	http://www.guideline.gov/
NZ Guideline Group	http://www.health.govt.nz/about-ministry/ministry-health-websites/new-zealand-guidelines-group
Guidelines International Network	http://www.g-i-n.net/
BMJ best practice	http://bestpractice.bmj.com/best-practice/welcome.html
Canadian Medical Association	http://www.cma.ca/index.php/ci_id/54316/la_id/1.htm
Current Controlled Trials metaRegister	http://controlled-trials.com/
Australian New Zealand Clinical Trials Registry	http://www.anzctr.org.au/
ClinicalTrials.gov	http://clinicaltrials.gov/
World Health Organization International Clinical Trials Registry Platform	http://apps.who.int/trialsearch/

Search strategies

Vascular access search strategy

Table 60 PubMED search strategy

#27	Search (#24 AND #25 AND #26)
#26	Search (#14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23)
#25	Search (#8 OR #9 OR #10 OR #11 OR #12 OR #13)
#24	Search (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7)
#23	Search metaanalys*
#22	Search meta-analys*
#21	Search meta (analys*)
#20	Search meta-analysis[MeSH Terms]
#19	Search systematic (review*)
#18	Search control*
#17	Search trial
#14	Search randomized controlled trial[MeSH Terms]
#15	Search random*
#16	Search random allocation[MeSH Terms]
#13	Search ultrasonic
#12	Search ultrasound
#11	Search sonograph*
#10	Search ultrasonograph*
#9	Search doppler ultrasonography[MeSH Terms]
#8	Search ultrasonography, interventional[MeSH Terms]
#7	Search catheterization, pulmonary artery[MeSH Terms]
#6	Search catheterization, swan ganz[MeSH Terms]
#5	Search PICC
#4	Search (peripheral*) (insert*) central (catheter*)
#3	Search central line (insertion*)
#2	Search central venous (line*)
#1	Search catheterization, central venous[MeSH Terms]

Table 61 Ovid EMBASE search strategy

1	exp central venous catheterization/
2	exp Swan Ganz catheter/
3	exp pulmonary artery catheter/
4	central venous line*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
5	central line insertion*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
6	central line*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
7	PICC.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
8	exp peripherally inserted central venous catheter/
9	peripheral* insert* central catheter*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
10	peripherally inserted central venous catheter.mp. [mp=title, abstract, subject headings, heading word, drug trade name,

1	exp central venous catheterization/
	original title, device manufacturer, drug manufacturer, device trade name, keyword]
11	pulmonary artery catheter*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
12	swan ganz catheter*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
13	exp ultrasound/
14	exp intravascular ultrasound/
15	exp Doppler flowmetry/
16	ultrasonograph*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
17	sonograph*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
18	ultrasound.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
19	ultrasonic.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
20	exp randomization/
21	randomized controlled trial/
22	random*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
23	RCT.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
24	trial.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
25	control*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
26	systematic review*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
27	exp "systematic review"/
28	meta analysis/
29	meta analysis/
30	meta analy*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
31	metaanaly*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
32	meta-analy*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
33	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12
34	13 or 14 or 15 or 16 or 17 or 18 or 19
35	20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32
36	central venous cather*.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
37	exp central venous catheter/
38	exp vascular access/
39	33 or 36 or 37 or 38
40	34 and 35 and 39

Table 62 York CRD search strategy

	Searches
1	MeSH DESCRIPTOR Catheterization, Central Venous EXPLODE ALL TREES

	Searches
2	(central venous line*)
3	(central line insertion*)
4	(peripherally inserted central catheter)
5	(PICC)
6	MeSH DESCRIPTOR Catheterization, Swan-Ganz EXPLODE ALL TREES
7	MeSH DESCRIPTOR Ultrasonography, Interventional EXPLODE ALL TREES
8	MeSH DESCRIPTOR Ultrasonography, Doppler EXPLODE ALL TREES
9	(ultrasonograph*)
10	(sonograph*)
11	(ultrasound)
12	(ultrasonic)
13	MeSH DESCRIPTOR Random Allocation EXPLODE ALL TREES
14	(random*)
15	MeSH DESCRIPTOR Randomized Controlled Trial EXPLODE ALL TREES
16	(trial)
17	(control*)
18	(systematic review*)
19	MeSH DESCRIPTOR Meta-Analysis EXPLODE ALL TREES
20	(meta analys*)
21	(meta-analys*)
22	(metaanalys*)
23	(central ve*)
24	(swan ganz)
25	(swan-ganz)
26	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #23 OR #24 OR #25
27	#7 OR #8 OR #9 OR #10 OR #11 OR #12
28	#13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22
29	#26 AND #27 AND #28

Table 63 Cochrane search strategy

ID	Search
#1	MeSH descriptor: [Catheterization, Central Venous] explode all trees
#2	central venous (line*)
#3	central line (insertion*)
#4	(peripheral*) (insert*) central (catheter*)
#5	PICC
#6	MeSH descriptor: [Catheterization, Swan-Ganz] explode all trees
#7	swan-ganz
#8	swan ganz
#9	MeSH descriptor: [Ultrasonography, Interventional] explode all trees
#10	MeSH descriptor: [Ultrasonography, Doppler] explode all trees
#11	ultrasonograph*
#12	sonograph*
#13	ultrasound
#14	ultrasonic

ID	Search
#15	MeSH descriptor: [Random Allocation] explode all trees
#16	random*
#17	MeSH descriptor: [Randomized Controlled Trial] explode all trees
#18	trial
#19	control*
#20	systematic review*
#21	MeSH descriptor: [Meta-Analysis] explode all trees
#22	meta analys*
#23	meta-analys*
#24	metaanalys*
#25	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8
#26	#9 or #10 or #11 or #12 or #13 or #14
#27	#15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24
#28	#25 and #26 and #27
#29	#1 or #2 or #4 or #5 or #6 or #7 or #8
#30	#29 and #26 and #27
#31	central line (insertion*)
#32	"central line*"

Percutaneous neural blockade search strategy:

Table 64 PubMED search strategy

1	Ultrasonography (MeSH) OR ultrasonograph* OR sonograph*
2	Nerve block (MeSH) OR nerve block* OR neural block* OR anesthesia conduction/methods (MeSH) OR analgesia/methods (MeSH)
3	Vascular access* OR venous access*
4	Catheterization (MeSH) OR catheterization, central venous (MeSH) OR catheter* OR cannula*
5	#3 AND #4
6	#2 OR #5
7	#1 AND #6

Note: an analogous strategy was used for the Cochrane and York CRD databases

Table 65 Ovid EMBASE search strategy

1	echography (MeSH) OR ultrasonograph* OR sonograph* OR echograph*
2	Nerve block (MeSH) OR nerve block* OR neural block* OR anesthesia/drug administration (MeSH) OR analgesia (MeSH)
3	Vascular access* OR venous access*
4	Catheterization (MeSH) OR catheterization OR catheter* OR cannula*
5	#3 AND #4
6	#2 OR #5
7	#1 AND #6

Table 66 Current contents search strategy

1	Topic=(ultrasonograph*) OR Topic=(sonograph*) DocType=All document types; Language=All languages

1	Topic=(ultrasonograph*) OR Topic=(sonograph*) DocType=All document types; Language=All languages
2	Topic=(nerve block*) OR Topic=(neural block*) OR Topic=(analgesi*) OR Topic= (anesthetic*) DocType=All document types; Language=All languages
3	Topic=(vascular access*) OR Topic=(venous access*) DocType=All document types; Language=All languages
4	Topic=(catheter*) OR Topic=(catheteri$ation) OR Topic=(cannula*) DocType=All document types; Language=All languages
5	#3 AND #4 DocType=All document types; Language=All languages
6	#2 OR #5 DocType=All document types; Language=All languages
7	#1 AND #6 DocType=All document types; Language=All languages

Clinical trials search strategy:

Table 67 Clinical trials, ultrasound vascular access and nerve block. Included search terms

Databases	Search terms
ANZCTR (www.anzctr.org.au)	vascular access, central venous access, ultrasound, guidance nerve block, ultrasound, guidance
Clinicaltrials.gov (www.clinicaltrials.gov)	Search terms: vascular OR venous OR arterial OR vein OR artery Conditions: cathete* OR cannula* OR "central venous" OR PICC Intervention: Ultrasound OR ultrasonograph* OR sonograph* OR echograph*) Search terms: Anaesthesia OR Anesthesia Condition: "nerve block" OR "neural block" OR OR analgesia OR anaesthesiology OR anesthesiology Intervention: Ultrasound OR ultrasonograph* OR sonograph* OR echograph
Current controlled trials (www.controlled-trials.com)	(Ultrasound OR ultrasonograph* OR sonograph* OR echograph*) AND (vascular OR venous OR arterial OR vein OR artery) AND (cathete* OR cannula* OR "central venous") metaRegister all dataset excluding clincialtrials.gov (Ultrasound OR ultrasonograph* OR sonograph* OR echograph*) AND ("nerve block" OR "neural block" OR anaesthesia OR anesthesia OR analgesia OR anaesthesiology OR anesthesiology) metaRegister all dataset excluding clincialtrials.gov

Clinical practice guidelines search strategy

No.	database	Topic	Keywords
1	National Guideline Clearinghouse	ultrasound	(Ultrasound OR ultrasonograph* OR sonograph* OR echograph*) restricted to Anesthesiology
2		Vascular access	(vascular OR venous OR arterial OR vein OR artery) restricted to Anesthesiology
3		Neural block	("nerve block" OR "neural block" OR anaesthesia OR anesthesia OR analgesia OR anaesthesiology OR anesthesiology) restricted to Anesthesiology
4		catheterization	(cathete* OR cannula* OR "central venous") restricted to Anesthesiology
5		combined	1 AND 2 restricted to Anesthesiology

No.	database	Topic	Keywords
6		combined	1 AND 2 AND 4 restricted to Anesthesiology
7		combined	1 AND 3 restricted to Anesthesiology
8		combined	1 AND 3 AND 4 restricted to Anesthesiology
9	NZ Guideline group	Searched listing on screen	
10	GIN	1,2	English language only; guidelines only
		1,3	English language only; guidelines only
11	NICE (NHS)	CGuidlines	Hand searched
		Guidance pathway	Ultrasound OR ultrasonograph* OR sonograph* OR echograph* (then hand searched)
12	NHS evidence	Filters: clinical, guidelines	Ultrasound guidance AND vascular access AND catheter (then hand searched)
			Ultrasound guidance AND (nerve block OR neural) (then hand searched)

Appendix D Studies included in the review

Ultrasound guidance for major vascular access and percutaneous neural blockade

Systematic reviews

Vascular access

Calvert, N., D. Hind, et al. (2003). The effectiveness and cost-effectiveness of ultrasound locating devices for central venous access: a systematic review and economic evaluation.

Hind, D., N. Calvert, et al. (2003). "Ultrasonic locating devices for central venous cannulation: Meta-analysis." British Medical Journal 327 (7411): 361-364.

Keenan, S. P. (2002). "Use of ultrasound to place central lines." Journal of Critical Care 17 (2): 126-137.

Krstenic, W. J., S. Brealey, et al. (2008). "The effectiveness of nurse led 2-D ultrasound guided insertion of peripherally inserted central catheters in adult patients: A systematic review." JAVA - Journal of the Association for Vascular Access 13 (3): 120-125.

Mehta, N., W. W. Valesky, et al. (2013). "Systematic review: Is real-time ultrasonic-guided central line placement by ED physicians more successful than the traditional landmark approach?" Emergency Medicine Journal 30 (5): 355-359.

Randolph, A. G., D. J. Cook, et al. (1996). "Ultrasound guidance for placement of central venous catheters: A meta- analysis of the literature." Critical Care Medicine 24 (12): 2053-2058.

Sigaut, S., A. Skhiri, et al. (2009). "Ultrasound guided internal jugular vein access in children and infant: A meta-analysis of published studies." Paediatric Anaesthesia 19 (12): 1199-1206.

Wu, S. Y., Q. Ling, et al. (2013). "Real-time two-dimensional ultrasound guidance for central venous cannulation: A meta-analysis." Anesthesiology 118 (2): 361-375.

Percutaneous neural blockade

Abrahams, M., M. Aziz, et al. (2009). "Ultrasound guidance compared with electrical neurostimulation for peripheral nerve block: a systematic review and meta-analysis of randomized controlled trials." British Journal of Anaesthesia 102(3): 408-417.

Bhatia A & Brull R (2013) Review article: is ultrasound guidance advantageous for interventional pain management? A systematic review of chronic pain outcomes. *Anesth Analg* 117 (1):236-251.

Choi S & Brull R (2011) Is ultrasound guidance advantageous for interventional pain management? A review of acute pain outcomes. *Anesth Analg* 113(3):596-604 (in eng).

Gelfand HJ, et al. (2011) Analgesic efficacy of ultrasound-guided regional anesthesia: A meta-analysis. *J. Clin. Anesth.* 23 (2):90-96.

Liu SS, Ngeow J, & John RS (2010) Evidence basis for ultrasound-guided block characteristics: onset, quality, and duration. *Reg Anesth Pain Med* 35(2 Suppl):S26-35

McCartney CJ, Lin L, & Shastri U (2010) Evidence basis for the use of ultrasound for upper-extremity blocks. (Translated from eng) *Reg Anesth Pain Med* 35(2 Suppl):S10-15 (in eng).

Neal JM (2010) Ultrasound-Guided Regional Anesthesia and Patient Safety An Evidence-Based Analysis. *Regional Anesthesia and Pain Medicine* 35(2):S59-S67

Rubin K, S. D. S. S. (2009). "Are peripheral and neuraxial blocks with ultrasound guidance more effective and safe in children?" Pediatric Anesthesia 19(2): 92-96.

Walker KJ, McGrattan K, Aas-Eng K, & Smith AF (2009) Ultrasound guidance for peripheral nerve blockade. *Cochrane Database Syst Rev* (4):CD006459 (in eng).

Yuan JM, et al. (2012) Ultrasound guidance for brachial plexus block decreases the incidence of complete hemi-diaphragmatic paresis or vascular punctures and improves success rate of brachial plexus nerve block compared with peripheral nerve stimulator in adults. *Chin Med J (Engl)* 125(10):1811-1816

Comparative studies not reported in the included systematic reviews

Level II: Vascular access

Airapetian N, et al. (2013) Ultrasound-guided central venous cannulation is superior to quick-look ultrasound and landmark methods among inexperienced operators: A prospective randomized study. Intensive *Care Medicine* 39 (11):1938-1944.

de Carvalho Onofre PS, da Luz Goncalves Pedreira M, & Peterlini MA (2012) Placement of peripherally inserted central catheters in children guided by ultrasound: a prospective randomized, and controlled trial. *Pediatr Crit Care Med* 13(5):e282-287

Dudeck O, et al. (2004) A randomized trial assessing the value of ultrasound-guided puncture of the femoral artery for interventional investigations. *International Journal of Cardiovascular Imaging* 20 (5):363-368.

Hayashi H & Amano M (2002) Does ultrasound imaging before puncture facilitate internal jugular vein cannulation? Prospective randomized comparison with landmark-guided puncture in ventilated patients. *J Cardiothorac Vasc Anesth* 16(5):572-575 (in eng).

Iwashima S, Ishikawa T, & Ohzeki T (2008) Ultrasound-guided versus landmark-guided femoral vein access in pediatric cardiac catheterization. *Pediatric Cardiology* 29 (2):339-342.

Killu K, et al. (2011) Utility of Ultrasound Versus Landmark-Guided Axillary Artery Cannulation for Hemodynamic Monitoring in the Intensive Care Unit. ICU Director 2 (3):54-59.

Li J, et al. (2013) A randomised, controlled trial comparing the long-term effects of peripherally inserted central catheter placement in chemotherapy patients using B-mode ultrasound with modified Seldinger technique versus blind puncture. Eur J Oncol Nurs

Miller AH, et al. (2002) Ultrasound guidance versus the landmark technique for the placement of central venous catheters in the emergency department. *Acad Emerg Med* 9(8):800-805

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Appendix E Excluded studies

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Inappropriate population

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Inappropriate comparator

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Inappropriate indication

Vascular access (n= 12)

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Inappropriate intervention

Vascular access (n= 2)

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Incorrect outcomes

Vascular access (n= 4)

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Neural blockade (n=1)

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Inappropriate study design

Vascular access

Wrong study type type (n= 18)

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Simulation (n= 5)

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Technique (n= 2)

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Trainee (n= 2)

Martin M.J., Husain F.A., Piesman M., Mullenix P.S., Steele S.R., Andersen C.A., Giacoppe G.N. (2004) Is routine ultrasound guidance for central line placement beneficial? A prospective analysis. Current Surgery 61 (1):71-74.

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Neural blockade

Studies focused on technique (n=5)

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Trainee focus (n=3)

Dolan J., Lucie P., Geary T., Smith M., Kenny G.N. (2009) The rectus sheath block: accuracy of local anesthetic placement by trainee anesthesiologists using loss of resistance or ultrasound guidance. Reg Anesth Pain Med 34:247-50. DOI: 10.1097/AAP.0b013e31819a3f67.

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Inappropriate publication

Vascular access

Case report (n= 1)

Glenn B.J. (2007) Single-Incision Method for the Placement of an Implantable Chest Port or a Tunneled Catheter. Journal of Vascular and Interventional Radiology 18 (1):137-140.

Conference (n= 26)

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Medicine Brussels Belgium. Conference Start: 20090324 Conference End: 20090327. Conference Publication: (var.pagings). 13:S80.

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Brantley H., Jones C., Daggu-Bati R. (2013) Ultrasound-guided femoral access outcomes in myocardial infarction: Understanding the strategy (ultrafamous) trial. Catheterization and Cardiovascular Interventions Conference: 36th Annual Scientific Sessions of the Society for Cardiovascular Angiography and Interventions', SCAI Orlando, FL United States. Conference Start: 20130508 Conference End: 20130511. Conference Publication: (var.pagings). 81:S170.

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Appendix F Current clinical trials for the use of ultrasound guidance

Table 68: Vascular access: Current clinical trials registered with ClinicalTrials.gov, Current Controlled Trials ISRCTN and ANZCTR

Study identifier	Title	Sponsor/Collaborators	Age Groups	Enrolment	Recruitment
NCT01660724	Ultrasound Guided Arterial Puncture: a Prospective, Blinded, Randomised Controlled Trial	Odense University Hospital, Denmark	Adult | Senior	238	Completed
NCT01543360	Comparison of Axillary Versus Subclavian Vein Strategies for Central Venous Catheterization Under Continuous Ultrasound Guidance	Centre Hospitalier Universitaire deNimes, France	Adult | Senior	132	Completed
NCT01966354	Comparison of Three Techniques for Ultrasound-guided Internal Jugular Cannulation	Fundacion Miguel Servet | Mikel Batllori | Instituto de Salud Carlos III, Spain	Adult | Senior	220	Completed
NCT01561196	Conventional vs. Ultrasound Guided Arteria Cannulation, With and Without Local Anesthesia	University of Aarhus, Denmark	Adult | Senior	20	Completed
NCT01680666	A Prospective Trial of Ultrasound Versus Landmark Guided Central Venous Access in the Pediatric Population	Stanford University, USA	Child | Adult	150	Completed
NCT01439113	Single-operator Ultrasound-guided IV Placement by Emergency Nurses	Tufts Medical Center |Baystate Medical Center, USA	Adult | Senior	50	Completed
NCT00882297	Subclavian Vein Ultrasound Guided Cannulation in Adult	University Hospital, Bordeaux, France	Adult | Senior	100	Completed
NCT00464828	Ultrasound Imaging of Neck Blood Vessels in Pregnant and Non-Pregnant Women	Samuel Lunenfeld Research Institute, Mount Sinai Hospital, USA	Adult	156	Completed

NCT00330837	Ultrasound Scanning of Vascular Access Sites	University of Pittsburgh, USA	Adult | Senior	100	Completed
NCT00330590	Central Venous Access Catheter Placement Using the Sonic Flashlight	University of Pittsburgh | National Institute of Health (NIH), USA	Adult | Senior	150	Completed
NCT00692549	Ultrasound Guidance for Intravenous Cannulation in Emergency Department Patients.	University of California, USA	Adult | Senior	60	Completed
NCT00557154	Ultrasound Assisted Peripheral Venous Access in Young Children	University of California, Davis | Children's Miracle Network, USA	Child	44	Completed
NCT01527175	Ultrasound-guided Subclavian Venous Catheterization in Children	Seoul National University Hospital, Tiawan	Child	98	Completed
ACTRN12610000101088	Comparing the success rate of ultrasound-guided axillary vein approach to the subclavian vein versus traditional infraclavicular subclavian vein cannulation for central venous access: a prospective randomised pilot study in intensive care patients	The Northern Hospital, Australia	> 18 yr	80	Completed
NCT01931969	Central Landmark vs USG for IJV Catheterization	Ankara University, Republic of Turkey	Adult | Senior	30	Not yet recruiting
NCT01888094	SUBclavian Central Venous Catheters Guidance and Examination by UltraSound	University Hospital, Clermont-Ferrand, France	Adult | Senior	300	Not yet recruiting
NCT01584193	Ultrasound-guided Subclavian Vein Puncture Versus Cephalic Vein Dissection for Venous Access Port Implantation	University of Lausanne Hospitals, Switzerland	Adult | Senior	172	Not yet recruiting
NCT01584193	Ultrasound-guided Subclavian Vein Puncture Versus Cephalic Vein Dissection for Venous Access Port Implantation	University of Lausanne Hospitals, Switzerland	Adult | Senior	172	Not yet recruiting

ACTRN12611000489998	A comparison of transradial versus transfemoral and standard versus ultrasound-guided approaches in reducing bleeding rates in patients undergoing coronary angiography or angioplasty	Liverpool Hospital, Australia	>18 yr	1388	Not yet recruiting
NCT01859559	A Randomized Controlled Trial To Compare The Initial Success Rate of Ultrasound Guided Versus Landmark Approach For Placement of Peripheral Intravenous Access Lines in Emergency Department Patients	George Washington University & Johns Hopkins University, USA	Adult | Senior	6314	Recruiting
NCT01914705	Landmark vs. Ultrasound Guided SCVC in the ED	Maimonides Medical Center, USA	Adult | Senior	100	Recruiting
NCT01919528	Ultrasound-guided Catheterization of the Axillary Vein	Publiczny Samodzielny Zaklad Opieki Zdrowotnej Wojewodzkie Centrum Medyczne, Poland	Adult | Senior	100	Recruiting
NCT01602133	Assessment of Ultrasound-guided Inserted Peripheral Intravenous Catheter	Prodimed SAS, France	Adult | Senior	29	Recruiting
NCT01870661	Ultrasound Guided Peripheral Intravenous Catheter Insertion in the Hospitalized Patient: Long vs. Short Axis Placement	Beth Israel Medical Center, USA	Adult | Senior	100	Recruiting
NCT01927185	Long-versus Short-Axis Ultrasound Guidance for Subclavian Vein Cannulation	Azienda Ospedaliero-Universitaria di Parma, Italy	Adult | Senior	100	Recruiting
NCT01510743	Ultrasound Guided Central Vein Catheterization and Complications	Seoul National University Bundang Hospital, Taiwan	Child | Adult | Senior	1484	Recruiting

NCT01877031	Needle Guidance With Virtual Reality Augmented Ultrasound Versus Ultrasound Guidance Alone For Central Line Insertion: A Randomized Trial.	Lawson Health Research Institute University of Western Ontario, Canada	Adult | Senior	192	Recruiting
NCT01690416	Conventional vs Ultrasound Guided Arteria Cannulation	Aarhus University Hospital Skejby, Denmark	Adult | Senior	50	Recruiting
NCT01605292	Radial Artery Access With Ultrasound Trial	University of California, Irvine | Lenox Hill Hospital |Jamaica Hospital Medical Center | Oklahoma City VA Medical Center, USA	Adult | Senior	400	Recruiting
NCT01599299	Comparison of the Right and Left Internal Jugular Vein Using Ultrasound	Catharina Ziekenhuis Eindhoven, Netherlands	Adult | Senior	100	Recruiting
NCT00859846	Ultrasound Guided Arterial Line Placement in Long Axis Versus Short Axis in Pediatric Patients	University of Oklahoma, USA	Child	74	Recruiting
NCT01154465	A Trial to Study the Influence of Ultrasound Guidance on the Complications of Central Catheter	Centre Hospitalier Universitaire, Amiens, France	Adult | Senior	450	Recruiting
NCT00639197	UGIST: Ultrasound Guided Internal Jugular Short-Term Central Venous Catheters Tunneling	McMaster University | Hamilton Health Sciences Corporation, Canada	Adult | Senior	20	Recruiting
NCT01742416	Ultrasound Assisted Arterial Cannulation in Small Children	The Hospital for Sick Children, Canada	Child	50	Recruiting
ACTRN12606000223538	Comparison of success rate, speed of insertion and acute complication rates of central venous catheter (CVC) insertion between using ultrasound guidance technique and traditional anatomical landmark technique in elective surgery	Hospital St Vincent's Hospital , Australia	>18yr	190	Recruiting

NCT00207883	Ultrasound Guided Vascular Access in Pediatric Intensive Care Patients	Children's Healthcare of Atlanta	Child	250	unknown

CVC, central venous catheter

Table 69: Nerve Block: Current clinical trials registered with ClinicalTrials.gov, Current Controlled Trials ISRCTN and ANZCTR

Study identifier	Title	Sponsor/ Collaborators	Age Groups	Enrolment	Recruitment
ACTRN12609000318280	Optimising Ultrasound Guided Infraclavicular Brachial Plexus Block for Ambulatory Hand Surgery: single vs. triple point injection	Dr Michael Fredrickson Anaesthesia Institute, NZ	No limit	100	closed, follow-up completed
NCT01339273	Transversus Abdominis Plane (TAP) Block for Postoperative Analgesia After Laparoscopic Colonic Resection	Oxford University Hospitals NHS Trust	Adult | Senior	72	Completed
NCT01815372	Ultrasound-guided Nerve Blocks for the Sciatic and Saphenous Nerves: Characteristics of the Single Penetration Dual Injection (SPEDI) Technique	Bispebjerg Hospital	Adult | Senior	60	Completed
NCT01492660	Echogenic Versus Stimulating Needle and Catheter for Sciatic Blocks	Lawson Health Research Institute|The Physicians' Services Incorporated Foundation	Adult | Senior	70	Completed
NCT01999647	Efficacy of Ultrasound-Guided Local Anesthetic Injection Into or Around the Sciatic Nerve for Lower Limb Anesthesia	University of Parma	Adult | Senior	64	Completed
NCT01440400	Ultrasound Guided Spinal Anesthesia in Non Obese Obstetric Patients	Corniche Hospital	Child | Adult | Senior	150	Completed
NCT01643616	Ultrasound Guided Distal Sciatic Nerve Block - a Comparison With Nerve Stimulator Technique	Helios Research Center	Adult | Senior	250	Completed
NCT01699373	A Trial on Ultrasound-assisted Spinal Anaesthesia	Changi General Hospital	Adult | Senior	170	Completed
NCT01421914	Determining the Minimum Effective Volume of Local Anesthetic for Ultrasound-guided Axillary Brachial Plexus	Federal University of Sao Paulo	Adult	19	Completed

Study identifier	Title	Sponsor/ Collaborators	Age Groups	Enrolment	Recruitment
	Block				
NCT01244932	Minimum Effective Volume of Local Anesthetic Using Ultrasound for Brachial Plexus Block	Federal University of Sao Paulo	Adult	33	Completed
NCT00988234	Comparison of Two Position for Ultrasound Guided Lumbar Plexus and Sciatic Nerve Block	Huazhong University of Science and Technology	Adult | Senior	200	Completed
NCT01719237	Trial Comparing the Onset and Duration of Ultrasound Guided Supraclavicular Nerve Blocks Using Ropivacaine Versus Ropivacaine-Chloroprocaine Mixture	University of New Mexico VA Palo Alto Health Care System	Adult | Senior	60	Completed
NCT00825786	Ultrasound Guided Supraclavicular Nerve Block	Outcomes Research Consortium	Adult | Senior	120	Completed
NCT01309360	Ultrasound-guided Axillary Plexus Block - Dose Reduction of Prilocaine	Helios Research Center	Adult | Senior	120	Completed
NCT01334619	Ropivacaine Volume for Ultrasound-guided Retrograde Infraclavicular Brachial Plexus Block	Beijing Jishuitan Hospital	Adult | Senior	30	Completed
NCT01010412	Ultrasound Visualization Versus Electrical Nerve Stimulation	Allentown Anesthesia Associates, SonoSite, Inc.	Adult | Senior	158	Completed
NCT00702416	Ultrasound Guidance for Interscalene Brachial Plexus Block	University of Parma	Adult | Senior	50	Completed
NCT00497276	Comparison of Ultrasound and Nerve Stimulation Technique for Continuous Sciatic Nerve Block	University of Aarhus | National Board of Health, Denmark	Adult | Senior	100	Completed
NCT00877266	Ultrasound Guidance Versus Electrical Stimulation for Perineural Catheter Insertion	University of California, San Diego	Adult | Senior	180	Completed

Study identifier	Title	Sponsor/ Collaborators	Age Groups	Enrolment	Recruitment
NCT00699244	Comparison of Central Versus Peripheral Placement of Local Anesthetic	Vanderbilt University	Adult | Senior	218	Completed
NCT00956683	Dual Endpoint Nerve Stimulation Versus Ultrasound in Infraclavicular Block for Hand Surgery	University Health Network, Toronto	Adult | Senior	106	Completed
NCT00166699	A Trial of the Use of Ultrasound to Aid the Insertion of Combined Spinal Epidural Anaesthesia	NHS Greater Glasgow and Clyde	Child | Adult | Senior	42	Completed
NCT00221884	Use of Ultrasound in Upper Extremity Blocks.	University Health Network, Toronto | Canadian Anesthesiologists' Society | The Physicians' Services Incorporated Foundation	Adult | Senior	NR	Completed
NCT00221910	Use of Ultrasound in Lower Extremity Blocks.	University Health Network, Toronto | University of Toronto	Adult | Senior	NR	Completed
NCT00497354	Does a Low Volume Ultrasound-Guided Technique Reduce Common Complications of Interscalene Brachial Plexus Block?	Sunnybrook Health Sciences Centre	Adult | Senior	38	Completed
NCT00321425	Ultrasound Guidance Vs. Electrical Nerve Stimulation for Infraclavicular Brachial Plexus Block	Rikshospitalet University Hospital	Adult | Senior	80	Completed
ACTRN12610000201077	Ultrasound guided interscalene catheter placement effectiveness: the optimum distance for catheter advancement in patients requiring continuous interscalene analgesia following elective shoulder surgery	Dr Michael Fredrickson Anaesthesia Institute, NZ	> 16 yr	150	Completed

Study identifier	Title	Sponsor/ Collaborators	Age Groups	Enrolment	Recruitment
ACTRN12609000689279	Fascia Iliaca Block with and without ultrasound for knee surgery	Royal Melbourne Hospital, Australia	> 18 yr	40	Completed
ACTRN12609000074291	Landmark and ultrasound guidance as methods for ankle block placement in patients having elective minor/moderate ankle surgery: A comparison of two endpoints for correct needle tip position	Dr Michael Fredrickson Anaesthesia Institute, NZ	> 16 yr	80	Completed
ISRCTN15749962	Evaluation of mepivacaine ED95 for peripheral nerve blocks using ultrasound guidance	University of Bern, Switzerland	> 18 < 70 yr	20	Completed
NCT00213954	Ultrasound Guidance in Nerve Block Anaesthesia	University Hospital, Strasbourg, France	Adult | Senior	1002	Not yet recruiting
NCT01605929	Clinical Evaluation of the Ultrasound-Guided Retroclavicular Brachial Plexus Block	Brigham and Women's Hospital, USA	Adult | Senior	60	Not yet recruiting
NCT01734954	Comparison of Two Techniques of Sciatic Nerve Block With Levobupivacaine 0.5% in Orthopedic Surgery	CES University | Hospital Pablo Tobon Uribe | Clinica CES	Adult | Senior	66	Not yet recruiting
NCT01322126	Comparison of Safety And Efficacy of Neuraxial Anesthesia, Palpation Versus Ultrasound	Hadassah Medical Organization	Adult | Senior	120	Not yet recruiting
NCT01122693	Comparison Between Two Ultrasound Technologies for Ultrasound-guided Catheter Placement in Regional Anesthesia	Charite University, Berlin, Germany	Adult | Senior	90	Not yet recruiting
NCT00696150	Can the Femoral Nerve Block be Improved by Ultrasound Guidance?	NHS Greater Glasgow and Clyde | Golden Jubilee National Hospital, UK	Adult | Senior	269	Not yet recruiting

Study identifier	Title	Sponsor/ Collaborators	Age Groups	Enrolment	Recruitment
ACTRN12613000392763	In adult patients undergoing bilateral ultrasound-guided transversus abdominis plane (TAP) blocks, does the use of a needle guidance device compared to a free-hand technique when performing the TAP block increase needle tip visibility and reduce procedural time?	Royal Melbourne Hospital, Australia	> 18 yr	20	Not yet recruiting
ACTRN12612000923864	Changes in the onset time of the sensory and motor blockade and changes in the duration of analgesia after warming local anesthetic solution during ultrasound guided axillary brachial plexus block in patients underwent upper arm surgery.	Tunisian Military Hospital, Tunisia	> 18 < 75 yr	80	Not yet recruiting
ACTRN12611001274965	Pattern of skin anaesthesia in healthy volunteers with ultrasound-guided lateral femoral cutaneous nerve of thigh blockade linked to the usual location of surgical incision for hip surgery	Dr Adam Crossley Fremantle Hospital, Australia	> 18 yr	20	Not yet recruiting
ACTRN12611000433909	Effect of altering ropivacaine concentration on interscalene block duration for arthroscopic shoulder surgery	Dr Jason Koerber Flinders Medical Centre, Australia	> 18 < 80 yr	120	Not yet recruiting
ACTRN12610000925044	In patients undergoing popliteal nerve blocks for foot surgery, is ultrasound guided administration of the block as good as or better than a	Mr Harvinder Bedi Orthosport, Epworth Eastern Hospital, Australia	> 18 < 100 yr	150	Not yet recruiting

Study identifier	Title	Sponsor/ Collaborators	Age Groups	Enrolment	Recruitment
	nerve stimulator for providing intraoperative and postoperative pain relief?				
ACTRN12612000401853	Does the addition of hyaluronidase to ultrasound-guided fascia iliaca compartment block improve the time to onset and extent of anaesthesia in patients undergoing unlilateral knee arthroplasty?	Dr Andrew Kenneth Royal Prince Alfred Hospital, Australia	> 18 < 80 yr	100	Not yet recruiting
ACTRN12610000153011	Ultrasound visibility of the Sonoplex needle: a randomised control trial in patients undergoing femoral and/or sciatic nerve block.	Sir Charles Gairdner Hospital, Australia	> 18 yr	60	Not yet recruiting
NCT01583179	Duration of Analgesic Effect for Ultrasound Guided Supraclavicular Blocks With the Addition of Buprenorphine to Local Anesthetic Solution	University of Wisconsin, USA	Adult | Senior	74	Recruiting
NCT01877330	Optimal Location of Local Anesthetic Injection for Ultrasound Guided Interscalene Block	University of California, USA	Adult | Senior	100	Recruiting
NCT01949480	Ultrasound-Assisted Paravertebral Block v. Traditional Paravertebral Block For Pain Control	University of Pittsburgh, USA	Adult | Senior	40	Recruiting
NCT01763814	Three Different Approaches for Ultrasound Guided Femoral Nerve Block for Patients Undergoing Total Knee Arthroplasty	Chicago Anesthesia Pain Specialists, USA	Adult | Senior	120	Recruiting

Study identifier	Title	Sponsor/ Collaborators	Age Groups	Enrolment	Recruitment
NCT01759940	Influence of the Concentration of the Local Anesthetic Ropivacaine on the Quality of a Ultrasound Guided Intermediate Cervical Block.	Salzburger Landeskliniken, Germany	Adult | Senior	46	Recruiting
NCT01386320	Ultrasound Guided Ankle Block Versus Medial Forefoot Block for Forefoot Surgery	Hull and East Yorkshire Hospitals NHS Trust, UK	Adult | Senior	60	Recruiting
NCT01956617	The Mininimum Effective Anaesthetic Volume of Local Anaesthetic in Ultrasound-guided \Shamrock\" Lumbar Plexus Block"	Oslo University Hospital, Norway	Adult | Senior	30	Recruiting
NCT01871181	US-guided Ilioinguinal Blocks Versus Local Infiltration	University of Alberta, Canada	Adult | Senior	60	Recruiting
NCT01449214	Ultrasound-Guided Technique for Thoracic Epidural Insertion	Samuel Lunenfeld Research Institute, Mount Sinai Hospital, USA	Adult | Senior	60	Recruiting
NCT01570491	A Real-Time Ultrasound Guided Approach For Spinal Anesthesia	The Cleveland Clinic, USA	Adult | Senior	400	Recruiting
NCT02020096	Ultrasound Plus Nerve Stimulator Versus Nerve Stimulator Guided Lumbar Plexus Block	Huazhong University of Science and Technology, China	Adult | Senior	46	Recruiting
NCT01865955	Comparison Between Palpatory and Preprocedural Ultrasound Guided Techniques on Performance of Spinal Anesthesia	Samuel Lunenfeld Research Institute, Mount Sinai Hospital, USA	Adult	90	Recruiting
NCT01459523	Optimizing Catheter Insertion Technique for Ultrasound-guided Continuous Peripheral Nerve Blocks	VA Palo Alto Health Care System, USA	Adult | Senior	200	Recruiting
NCT01842698	Ultrasound-guided PVB	Centre Jean Perrin, France	Adult | Senior	60	Recruiting

Study identifier	Title	Sponsor/ Collaborators	Age Groups	Enrolment	Recruitment
NCT01693900	A Study to Compare the Ultrasound-guided Fascia Iliaca Compartment Block (FICB) to Surgeon-placed Fascia Iliaca Compartment Block for Post-operative Pain Control in Patients Undergoing an Anterior Hip Replacement Surgery.	William Beaumont Hospitals, USA	Adult	50	Recruiting
NCT01680913	Does Ultrasound Guidance Improve Time to Perform a Spinal or Number of Attempts in Obese Patients?	University of Saskatchewan, Canada	Adult | Senior	110	Recruiting
NCT01761175	Comparison of Ultrasound-Guided Infraclavicular Block and Ultrasound-Guided Axillary Block	Centre Hospitalier Universitaire de Quebec, Canada	Adult | Senior	224	Recruiting
NCT01217593	Ultrasound vs. Predetermined Distance Techniques for Paravertebral Nerve Block in Patients Having Breast Surgery	Ochsner Health System, USA	Adult | Senior	60	Recruiting
NCT01603680	Distribution Circumferential Versus Non Circumferential of Mepivacaine in the Median and Ulnar Nerves	Complexo Hospitalario Universitario de A Corua, Spain	Adult | Senior	124	Recruiting
NCT01583010	Improvement of Needle Visibility in Ultrasound Guided Regional Anaesthesia	Medical University of Vienna, Austria	Adult | Senior	100	Recruiting
NCT00523055	Ultrasound-guided Supraclavicular Brachial Plexus Blockade	University of Manitoba, Canada	Adult | Senior	30	Recruiting
NCT01554722	Needle Nerve Contact in Ultrasound Guided Femoral Block	Hospital Clinic of Barcelona, Spain	Adult	44	Recruiting
NCT00992810	Medial Versus Lateral Approach in Ultrasound (US)-Guided Supraclavicular Block	University Health Network, Toronto	Adult | Senior	78	Recruiting

Study identifier	Title	Sponsor/ Collaborators	Age Groups	Enrolment	Recruitment
NCT00956137	Ultrasound-assisted Spinal Anaesthesia in Patients With Difficult Anatomical Landmarks	University Health Network, Toronto	Adult | Senior	180	Recruiting
NCT00731146	Effects of Technique on the Local Anesthetic Dose Required for Interscalene Brachial Plexus Block	Sunnybrook Health Sciences Centre, Canada	Adult | Senior	80	Recruiting
ACTRN12612000549820	In women receiving ultrasound guided transversus abdominis plane blocks for gynaecological or obstetric surgery is there a difference in the needle tip visibility when an echogenic needle is used compared to a non-echogenic needle.	King Edward Memorial Hospital for Women, Australia	> 18 yr	21	Recruiting
ACTRN12610000094077	A randomised, double blind, pilot study to evaluate the distribution and duration of the sensory block after a standard and refined ultrasound guided transversus abdominis plane (TAP) block.	Mater Health Services, Australia	> 18yr	20	Recruiting
ACTRN12609000526279	Ultrasound guided femoral nerve block using 1% ropivacaine as a method of pain control in patients who present to emergency with a fractured hip.	St Vincent's Hospital, Australia	> 18yr	46	Recruiting
ACTRN12605000671662	Ultrasound guided regional anaesthesia: an audit of practice. That the use of ultrasound to guide needle placement during nerve block insertion improves the success of the procedure and reduces complications	Auckland City Hospital, NZ	NR	400	Recruiting

Study identifier	Title	Sponsor/ Collaborators	Age Groups	Enrolment	Recruitment
NCT00923494	Effectiveness of Ultrasound (US) Guided Supraclavicular Block	Baylor College of Medicine, USA	Adult	30	Suspended
NCT01325012	Ultrasound-Guided Continuous Sciatic Nerve Blocks: Popliteal Versus Subgluteal Catheters	University of California, USA	Adult | Senior	2	Terminated
ACTRN12607000646448	Examination of a newly developed needle which is more echo-genic than standard needles for use in peripheral nerve blockade. The outcome of this trial will be an assessment of the performance of these new needles when being used for a sciatic nerve block.	St Vincent's Hospital, Australia	> 18 yr	15	Unknown

Appendix G Australian Register of Therapeutic Goods listing

Table 70 details 46 of the 60 ultrasound systems (imaging, general-purpose) currently listed on the Australian Register of Therapeutic Goods (ARTG) that were deemed appropriate for ultrasound guided vascular access and percutaneous neural blockade. Fit-for-purpose was based on the publically available intended purpose statement for individual items, with the minimum requirement being diagnostic imaging. Of the 46 devices, 17 have vascular imaging stated in their intended purpose. Furthermore, four of these 17 (ARTG items; 141585, 168137, 175610, 180918) have an explicit statement regarding vascular access. Finally, the intended purpose for ARTG item 116584 indicates that this instrument is for use with an anaesthesia setting.

Ultrasound transducers are devices that generate, transmit and receive sound of an appropriate frequency and pulse rate. Sound is then processed by an ultrasound processor to generate on-screen images. Table 71 details 21 ultrasound transducers designed for extracorporeal use, and are hand-held. Again, fit-for-purpose was based on the publically available intended purpose statements for the individual items, with the minimum requirement being an indication that the transducer can be used for diagnostic imaging.

Examples of ancillary equipment necessary to perform ultrasound guided vascular access and percutaneous neural blockade are present in Table 72. Eight needle guides are detailed; these devices are typical attached to an ultrasound transducer to facilitate the introduction of the needle at given angle and orientation to the ultrasound image. The objective is improved needle visibility and precision of needle placement. Item 218385 is an example of an ultrasonic/electromagnetic-guided needle kit that can be used in the placement of a percutaneous neural blockade. Such kits are provided in sterile packs and are complete with the necessary ancillary devices to perform the procedure. The final group of devices pertain to central venous access. Again, these are complete kits and contain disposables and catheter lines that are necessary to perform a vascular access procedure.

Examples of available instrumentation necessary for electrical nerve stimulation are detailed in Table 72. Such devices deliver electric pulses of defined voltage, current and duration to elicit motor nerve response when an insulated is advance towards and nerve or nerve plexus.

In summary, the necessary specialize devices required to perform ultrasound guided vascular access as well as neural blocks guided by either ultrasound or electric nerve stimulation are registered with the ARTG and are potentially available to practitioners.

Table 70 Australian Register of Therapeutic Goods listings for ultrasound systems and their intended purpose

Sponsor	Manufacturer	ARTG number	Intended purpose
AMA Services WA Pty Ltd T/A AMA Medical Products	Edan Instruments Inc, China - Peoples Republic of	194451	A general-purpose diagnostic ultrasound imaging system designed exclusively for use in a wide variety ofboth extracorporeal and/or intacorporeal (endosonography or endoscopic) body imaging procedures. A general-pupose system supports a wide variety of transducers and related application software packages allowing for the collection, display and analysis of ultrasound information. Usages are, e.g. general-purpose imaging, cardiac, OB/GYN, endoscopy, breast, prostate, vascular, intra-surgical, Doppler r colour Doppler, depending on the operating system specific software packages and compatible ultrasound transducers.
Ausmedic Australia Pty Ltd Patterson Medical ANZ	Shenzhen Mindray Bio Medical Electronics Co ltd China - Peoples Republic of	122152	A general purpose diagnostic ultrasound imaging unit used for the collection, display and analysis of ultrasound information relating to a wide range of body imaging procedures.eg. general purpose imaging, vascular and muscle imaging.
Australian Medical Supplies Pty Ltd	NewTech Medical Limited China - Peoples Republic of	169107	A general purpose diagnostic ultrasound imaging unit used for the collection, display and analysis of ultrasound information relating to a wide range of body imaging procedures.eg. general purpose imaging, vascular and muscle imaging
Australian Medical Systems Pty Ltd	Chison Medical Imaging Co Ltd, China - Peoples Republic of	204930	A general-purpose diagnostic ultrasound imaging system designed exclusively for use in a wide variety of both extracorporeal and/or intracorporeal body imaging procedures. It is a general-purpose system which supports a wide variety of transducers and related application software packages allowing for the collection, display and analysis of ultrasound information. Usages are, e.g. general-purpose imaging, cardiac, OB/GYN, endoscopy, breast, prostate, vascular, Doppler or colour Doppler, depending on the operating system specific software packages and compatible ultrasound transducers.
AVNET Technology Solutions Australia Ltd	Shenzhen Mindray Bio Medical Electronics Co ltd China - Peoples Republic of	123159	Diagnostic ultrasound equipment for general ultrasound imaging
Bard Australia Pty Ltd	Bard Access Systems Inc USA	141585	Intended to provide ultrasound guidance for placement of needles and catheters in vascular structures Ultrasound guidance may occur intraoperatively or percutaneously. Ultrasound imaging of vascular structures, various organs and structures of the body may also be performed
C R Kennedy & Co Pty Ltd	Hitachi Med Corp Japan	139484	General Purpose Ultrasound imaging scanner for use with a wide variety of transducers to enable visualization of muscles, tissue and internal organs, their size, structures and possible pathologies or lesions as well as embryos.

Sponsor	Manufacturer	ARTG number	Intended purpose
C.R. Kennedy Pty Ltd supply Hitachi products	Chison Medical Imaging Co Ltd China - Peoples Republic of	165285	For use in a wide variety of both extracorporeal and/or intracorporeal (endosonography or endoscopic) body imaging procedures allowing for the collection, display and analysis of ultrasound information, including general-purpose imaging, cardiac, OB/GYN, endoscopy, breast, prostate, vascular, intra-surgical, Doppler or colour Doppler, which supports a wide variety of transducers and related application software packages.
Device Technologies Australia Pty Ltd	Mediwatch UK Ltd United Kingdom	150314	A diagnostic ultrasound imaging system used to provide various intracorporeal body images. The system allows for the collection, display and analysis of the ultrasound information.
Device Technologies Australia Pty Ltd	Esaote Europe BV Netherlands	197103	A diagnostic system used to provide various ultrasound images of the body. The system allows for the collection, display and analysis of the ultrasound information.
Device Technologies Australia Pty Ltd	Esaote SPA Italy	197356	A diagnostic system used to provide various ultrasound images of the body. The system allows for the collection, display and analysis of the ultrasound information.
Device Technologies Australia Pty Ltd	Esaote SPA Italy	198758	A diagnostic system used to provide various ultrasound images of the body. The system allows for the collection, display and analysis of the ultrasound information.
Device Technologies Australia Pty Ltd	Hitachi Med Corp Japan	208902	A diagnostic system used to provide various ultrasound images of the body. The system allows for the collection, display and analysis of the ultrasound information.
Fujifilm Australia Pty Ltd	Fujifilm Corporation Japan	183753	FUJIFILM FAZONE CB is a software-based ultrasound diagnostic imaging equipment, it is compact and portable. The FUJIFILM FAZONE CB obtains and displays images for diagnosis in B, M, Color Doppler and Pulsed Wave Doppler Modes.
Fujifilm Sonosite Australasia Pty Ltd	Sonosite Inc USA	118714	The indication for use is: Medical Diagnostic Ultrasound. The Ultrasound System is intended for diagnostic ultrasound imaging or fluid flow analysis of the human body.
Fujifilm Sonosite Australasia Pty Ltd	Sonosite Inc USA	193635	The SonoSite Edge Ultrasound system is a general purpose ultrasound system intended for use by a qualified physician for evaluation by ultrasound imaging or fluid flow analysis of teh human body. Featal - OB/GYN, Abdominal intraoperative (abdominal organs and vascular), Intra-operative (Neuro), Paediatric, Small Organ (Breast, thyroid, testicle, prostate), Neonatal Cephalic, Adult cephalic, Trans-rectal, Trans-vaginal, Musculoskeletal (conventional, Musculoskeletal (Superficial), Cardiac Adult , Cardiac Paediatric, Trans-oesophageal (cardiac), Peripheral vessel.
Fujifilm Sonosite Australasia Pty Ltd	Sonosite Inc USA	215880	The indication for use is: Medical Diagnostic Ultrasound. The Ultrasound System is intended for diagnostic ultrasound imaging or fluid flow analysis of the human body.
GE Healthcare Australia Pty Ltd	Wipro GE Healthcare India	92889	Diagnostic ultrasound imaging
GE Healthcare Australia Pty Ltd	GE Ultrasound Korea, Korea - Republic of	93418	Ultrasound diagnostic imaging

Sponsor	Manufacturer	ARTG number	Intended purpose
GE Healthcare Australia Pty Ltd	GE Medical Systems (China) Co Ltd, China - Peoples Republic of	123899	This general-purpose diagnostic ultrasound system imaging system is intended exclusively for use in a wide variety of both extracorporeal and/or intracorporeal body imaging procedures. This general purpose system supports a wide variety of transducers and related application software packages allowing for the collection, display and analysis of ultrasound information
GE Healthcare Australia Pty Ltd	GE Healthcare Austria GmbH & Co OG Austria	123902	This general-purpose diagnostic ultrasound system imaging system is intended exclusively for use in a wide variety of both extracorporeal and/or intracorporeal body imaging procedures. This general purpose system supports a wide variety of transducers and related application software packages allowing for the collection, display and analysis of ultrasound information.
GE Healthcare Australia Pty Ltd	GE Healthcare Japan Japan	125536	This general-purpose diagnostic ultrasound system imaging system is intended exclusively for use in a wide variety of both extracorporeal and/or intracorporeal body imaging procedures. This general purpose system supports a wide variety of transducers and related application software packages allowing for the collection, display and analysis of ultrasound information.
GE Healthcare Australia Pty Ltd	GE Medical Systems Ultrasound and Primary Care Diagnostics LLC, USA	126295	This general-purpose diagnostic ultrasound system imaging system is intended exclusively for use in a wide variety of both extracorporeal and/or intracorporeal body imaging procedures. This general purpose system supports a wide variety of transducers and related application software packages allowing for the collection, display and analysis of ultrasound information.
GE Healthcare Australia Pty Ltd	GE Ultrasound Korea Korea - Republic of	198951	General purpose radiology imaging and analysis system providing digital acquisition, processing and display capability
GE Healthcare Australia Pty Ltd	GE Vingmed Ultrasound AS, Norway	166229	This general-purpose diagnostic ultrasound imaging system is intended for use in a wide variety of both extracorporeal and/or intracorporeal (endosonography or endoscopic) body imaging procedures. This general-purpose system is intended to support a wide variety of transducers and related application software packages allowing for the collection, display and analysis of ultrasound information. Usages are, e.g. general-purpose imaging, cardiac, OB/GYN, endoscopy, breast, prostate, vascular, intra-surgical, Doppler or colour Doppler, depending on the operating system specific software packages and compatible ultrasound transducers.
Innologic Pty Ltd	Alpinion Medical Systems Co Ltd Korea - Republic of	217445	System designed to be used with attached ultrasound transducers for the imaging, measurement, calculation and recording of anatomic structures and blood flow.
Insight Oceania Pty Ltd	Medison Co Ltd Korea - Republic of	153916	A general purpose, mobile, software controlled diagnostic Ultrasound systems. Its function is to acquire ultrasound data and to display the data as 2D mode, M mode, Color doppler imaging, power Doppler imaging, harmonic imaging and PW Spectral doppler mode on the LCD display. The system also provides for the measurement of anatomical structures and for analysis packages that provide information used for clinical diagnostic purposes by qualified health care professionals. The clinical applications include abdomen, OB, Gynecology, contrast agent, small parts, vascular, muscular-skeletal, pediatric abdomen, adult cardiac, pediatric cardiology, TCD, urology, cardiac applications.

Sponsor	Manufacturer	ARTG number	Intended purpose
Insight Oceania Pty Ltd	Zonare Medical Systems Inc USA	156146	A general purpose, mobile, software controlled diagnostic Ultrasound systems. Its function is to acquire ultrasound data and to display the data as 2D mode, M mode, Color doppler imaging, power doppler imaging, harmonic imaging and PW Spectral doppler mode on the LCD display. The system also provides for the measurement of anatomical structures and for analysis packages that provide information used for clinical diagnostic purposes by qualified health care professionals. The clinical applications includeabdomen, OB, Gynecology, contrast agent, small parts, vascular, muscular-skeletal, pediatric abdomen adult cardiac, pediatric cardiology, TCD, urology, cardiac applications
M4 Healthcare	Chison Medical Imaging Co Ltd China - Peoples Republic of	196925	A general-purpose diagnostic ultrasound imaging system designed exclusively for use in a wide variety of both extracorporeal and/or intracorporeal body imaging procedures. The Sonotouch 20 is a general-purpose system which supports a wide variety of transducers and related application software packages allowing for the collection, display and analysis of ultrasound information. Usages are, e.g. general-purpose imaging, cardiac, OB/GYN, endoscopy, breast, prostate, vascular, intra-surgical, Doppler or colour Doppler, depending on the operating system specific software packages and compatibleultrasound transducers
Medical Technologies Aust Pty Ltd	Xuzhou Kaixin Electronic Instrument Co Ltd China - Peoples Republic of	163364	Ultrasound for external observation of tissue, organs and bone
Medical Technologies Pty Ltd	Hitachi Aloka Medical Ltd Japan	132538	Ultrasound imaging of anatomical structures and blood flow.
Mediquip Pty Ltd	Bionet Co Ltd Korea - Republic of	217565	Ultrasound diagnostic imaging system for general purpose imaging
Medtel Pty Ltd no US device on website	Shenzhen Biocare Electronics Co Ltd China - Peoples Republic of	165735	To collect, display and analyse ultrasound information through the use of various body imaging procedures
Olympus Australia Pty Ltd	Hitachi Aloka Medical Ltd 6-22-1 Japan	173992	Ultrasound imaging of anatomical structures and blood flow.
Philips Electronics Australia Ltd	Philips Ultrasound Inc USA	93851	Diagnostic Cardiovascular & General Purpose Ultrasound Imaging machine with peripherals and transducers

Sponsor	Manufacturer	ARTG number	Intended purpose
Philips Electronics Australia Ltd	Philips and Neusoft Medical Systems Co Ltd China - Peoples Republic of	152112	To use sound waves to image and diagnose patients
Philips Electronics Australia Ltd	SuperSonic Imagine SA France	204980	A general-purpose diagnostic ultrasound imaging system designed exclusively for use in a wide variety of both extracorporeal and/or intracorporeal (endosonography or endoscopic) body imaging procedures. A general-purpose system supports a wide variety of transducers and related application software packages allowing for the collection, display and analysis of ultrasound information. Usages are, e.g. general-purpose imaging, cardiac, OB/GYN, transesophageal, breast, prostate, vascular, intra-surgical, Doppler or colour Doppler, depending on the operating system specific software packages and compatible ultrasound transducers
Scanmedics Pty Ltd	B-K Medical AS Denmark	161442	General purpose Ultrasound system for imaging
Shimadzu Medical Systems Oceania Pty Ltd	Shimadzu Corp Japan	139798	For use as a general-purpose diagnostic ultrasound imaging in a variety of fields including both extracorporeal and/or intracorporeal (endosonography or endoscopic) body imaging procedures. Usages are, e.g. general-purpose imaging, cardiac, OB/GYN, endoscopy, breast, prostate, vascular, intra-surgical, Doppler or colour Doppler, depending on the operating system specific software packages and compatible ultrasound transducers.
Siemens Ltd	Siemens Medical USA	137563	A general-purpose diagnostic ultrasound imaging system designed exclusively for use in a wide variety of both extracorporeal and/or intracorporeal (endosonography or endoscopic) body imaging procedures. Usages are, e.g. general-purpose imaging, cardiac, OB/GYN, endoscopy, breast, prostate, vascular, intra-surgical, Doppler or colour Doppler, depending on the operating system specific software packages and compatible ultrasound transducers
Sportstek	Chison Medical Imaging Co Ltd China - Peoples Republic of	215539	To be used as a diagnostic ultrasound imaging system for use in a variety of body imaging procedures. Depending on the probe selected, the system can be used in ultrasound diagnostic examinations in areas such as Abdomen, Cardiology, Obstetrics, Gynaecology, Small Parts, musculoskeletal, PT Nerve and Peripheral vascular
Toshiba Australia Pty Ltd	Toshiba Medical Systems Corporation, Japan	94738	The systems provide high-quality ultrasound images in all its modes of 2D(B)mode,M mode and CDI(Colour Doppler Imaging)mode (blood-flow imaging),and Doppler (blood-flow spectrum).
Ultramedix Australasia Pty Ltd	Shantou Institute of Ultrasonic Instruments Co China - Peoples Republic of	168137	This high-end laptop-design B & W ultrasound imaging system employing digital technology and five frequency broadband probe technology and is intended for use in ultrasound exams such as bedside checkup, in-office consultation and field work. The wide variety of probes are typically used for imaging of the abdomen (kidney, liver, gall bladder, abdominal aorta, uterus , bladder), vascular access, foreign body localisation, thyroid and carotid carotid plaque imaging.

Sponsor	Manufacturer	ARTG number	Intended purpose
Ultramedix Australasia Pty Ltd	Shantou Institute of Ultrasonic Instruments Co China - Peoples Republic of	175610	This is high-end portable B & W ultrasound with Colour 4D imaging capability employing digital technology and multi frequency broadband probe technology. It is intended for use in ultrasound exams such as bedside checkup, and in-office consultation. The wide variety of probes are typically used for imaging of the abdomen (kidney, liver, gall bladder, abdominal aorta, obstetrics,uterus,bladder), vascular access, foreign body localisation, thyroid and carotid plaque imaging.
Ultramedix Australasia Pty Ltd	Shantou Institute of Ultrasonic Instruments Co China - Peoples Republic of	180918	This is high-end portable Colour doppler ultrasound with Colour 4D imaging capability employing digital technology and multi frequency broadband probe technology. It is intended for use in ultrasound exams such as bedside checkup, and in-office consultation. The wide variety of probes are typically used for imaging of the abdomen (kidney, liver, gall bladder, abdominal aorta, obstetrics,uterus,bladder), vascular access, foreign body localisation, thyroid and carotid plaque imaging.
Ultramedix Australasia Pty Ltd eZono 3000 Apogee 1200 Touch	EZono AG Germany	166584	Portable diagnostic ultrasound for anaesthesia and intensive care

Table 71: Australian Register of Therapeutic Goods listings for Transducer assembly, ultrasound, diagnostic, extracorporeal, hand-held and their intended purpose

Sponsor	Manufacturer	ARTG number	Intended purpose
Active Lifestyle Physiotherapy	Wuxi Belson Imaging Technology Co Ltd, China - Peoples Republic of	205084	An ultrasound probe, supplied separately, to be used with the Belson Ultrasound System for the purposes of diagnostic imaging. This probe is intended for application to image musculoskeletal areas of the body on intact skin.
Alcon Laboratories Australia Pty Ltd	Alcon Laboratories Inc, USA	146746	It is a held-hand device moved from location to location on a patient's body during imaging applications.
AVNET Technology Solutions Australia Ltd	Shenzhen Mindray Bio Medical Electronics Co Ltd, China - Peoples Republic of	146555	An ultrasound transducer assembly specifically designed to be positioned on the intact surface of a patient's body that can convert electric voltages into an ultrasound beam. It steers, focuses, and detects the ultrasound beam and resulting echoes either mechanically or electronically.
Bard Australia Pty Ltd	Bard Access Systems Inc, USA	143642	Intended to produce sound waves that bounce off body tissue, receive the ultrasonic echoes, and transmit the ultrasonic echoes to the ultrasound unit, which interprets the signals into a two-dimensional image.
C R Kennedy & Co Pty Ltd	Hitachi Med Corp, Japan	139485	Extracorporeal hand-held ultrasound transducer to enable visualization of muscles, tissue and internal organs as well as observing embryonic and fetal development
Fujifilm Sonosite Australasia Pty Ltd	Sonosite Inc, USA	118863	The indication for use is: Medical Diagnostic Ultrasound. The SonoSite dianostic ultrasound system transducers are intended for diagnostic ultrasound imaging or fluid flow analysis of the human body
GE Healthcare Australia Pty Ltd	GE Healthcare Austria GmbH & Co OG, Austria	123896	This extracorporeal ultrasound transducer assembly is a hand-held device intended to be moved from location to location on the intact surface of a patient's body during imaging applications. It includes single or multiple element transducer assembly configurations that convert electric voltages into an ultrasound beam.
GE Healthcare Australia Pty Ltd	GE Healthcare Japan Corporation, Japan	124215	This extracorporeal ultrasound transducer assembly is a hand-held device intended to be moved from location to location on the intact surface of a patient's body during imaging applications. It includes single or multiple element transducer assembly configurations that convert electric voltages into an ultrasound beam.
GE Healthcare Australia Pty Ltd	GE Medical Systems Ultrasound and Primary Care Diagnostics LLC, USA	126296	This extracorporeal ultrasound transducer assembly is a hand held device intended to be moved from location to location on the intact surface of a patient's body during imaging applications. It includes single or multiple element transducer assembly configurations that convert electric voltages into an ultrasound beam.

Sponsor	Manufacturer	ARTG number	Intended purpose
GE Healthcare Australia Pty Ltd	GE Vingmed Ultrasound AS, Norway	146318	This extracorporeal ultrasound transducer assembly is a hand held device intended to be moved from location to location on the intact surface of a patient's body during imaging applications. It includes single or multiple element transducer assembly configurations that convert electric voltages into an ultrasound beam.
GE Healthcare Australia Pty Ltd	Parallel Design Sas, France	154665	This extracorporeal ultrasound transducer assembly is a hand held device intended to be moved from location to location on the intact surface of a patient's body during imaging applications. It includes single or multiple element transducer assembly configurations that convert electric voltages into an ultrasound beam.
Innologic Pty Ltd	Alpinion Medical Systems Co Ltd, Korea - Republic of	217446	Ultrasound transducer designed to be used with Ultrasound System for the imaging, measurement, calculation and recording of anatomic structures and blood flow
Medical Technologies Pty Ltd	Hitachi Aloka Medical Ltd, Japan	132539	Ultrasound Imaging transducer for anatomical structures & blood flow.
Olympus Australia Pty Ltd	Hitachi Aloka Medical Ltd, Japan	213219	The ultrasonic probe is a held-hand device moved from location to location on the intact surface of a patient's body during imaging applications. It includes single or multiple element transducer assembly configurations that convert electric voltages into an ultrasound beam. It steers, focuses and detects the ultrasound beam and resulting echoes mechanically or electronically. Typically used with coupling gels to ensure adequate contact with the patient.
Orthotic & Prosthetic Centre Pty Ltd	Esaote Europe BV, Netherlands	148583	Use with ultrasound imaging unit for musculoskeletal imaging and diagnostic purposes.
Philips Electronics Australia Ltd	Philips and Neusoft Medical Systems Co Ltd, China - Peoples Republic of	158748	To be used with Ultrasound imaging systems to diagnose patients.
Philips Electronics Australia Ltd	Philips Ultrasound Inc, USA	99934	To be used with Ultrasound imaging systems to diagnose patients.
Philips Electronics Australia Ltd	Philips and Neusoft Medical Systems Co Ltd, China - Peoples Republic of	158748	To be used with Ultrasound imaging systems to diagnose patients.
Scanmedics Pty Ltd	B-K Medical AS, Denmark	196198	An extracorporeal ultrasound transducer assembly that is a held-hand device, moved from location to location on the intact surface of a patient's body during diagnostic ultrasound imaging applications.

Sponsor	Manufacturer	ARTG number	Intended purpose
Siemens Ltd	Siemens Medical Solutions USA Inc, USA	141676	The extracorporeal ultrasound transducer is designed to transmit and receive ultrasonic soundwaves from a converted electrical voltage using a hand held probe assembly that is placed against a patient's skin with a conductive gel.
SonoLogic Pty Ltd	SonoScape Co Ltd, China - Peoples Republic of	160039	Ultrasound transducer designed to be used with Ultrasound System for the imaging, measurement, calculation and recording of anatomic structures and blood flow.

Table 72 Australian Register of Therapeutic Goods listings for ancillary devices used in the ultrasound guided vascular access or percutaneous neural blockade and their intended purpose. [1]

Sponsor	Manufacturer	ARTG number	Intended purpose
			Needle guide
Bard Australia Pty Ltd	Bard Access Systems Inc, USA	136490	An instrument designed to lead a needle into a specific structure when performing an ultrasound-guided, intraoperative or percutaneous punctures
Emergo Asia Pacific Pty Ltd T/a Emergo Australia	Civco Medical Instruments Co Inc DBA CIVCO and CIVCO Medical Solutions, USA	191487	Disposable needle guide intended to attach to a bracket and provide physicians with a tool to keep an instrument in-plane during ultrasound procedures.
Endocorp Pty Ltd	AS Medizintechnik GmbH, germany	189959	An instrument intended to lead a needle into its proper course when performing a clinical and/or surgical procedure.
Fujifilm Sonosite Australasia Pty Ltd	Sonosite Inc, USA	118886	Medical Diagnostic Ultrasound Accessory (Sterile, Single Use) -- Attaches to the L25 transducer via a bracket through a sterile sheath to facilitate proper needle placement to various depths in vascular or other anatomical structures from the transducer surface.
JLM Accutek Health Care Pty Ltd	Protek Medical Products Inc, USA	212300	For guiding a needle or catheter during a diagnostic ultrasound procedure in order to perform a biopsy or precise needle placement
Medical Logistics Australia Pty Ltd	AprioMed AB, Sweden	181031	A passive guide for guided access to tissue that is to be examined or treated.
Rocket Medical Pty Ltd	Rocket Medical Plc, UK	216399	A sterile device designed to lead a needle into its proper course when performing a clinical and/or surgical procedure
Scanmedics Pty Ltd	B-K Medical AS, denmark	197955	An instrument designed to lead a needle into its proper course when performing ultrasound-guided punctures, biopsies and nerve blocks.
			Ultrasonic/electromagnetic-guided needle kit
Fujifilm Sonosite Australasia Pty Ltd	Soma Access Systems LLC, USA	218385	The AxoTrack I Sterile Procedure Kit is intended to provide physicians with tools for electromagnetic tracking instruments with respect to image data.
			Catheterization kit, central venous
Bard Australia Pty Ltd	Bard Access Systems Inc, USA	198806	Intended for short or long term peripheral access to the central venous system for intravenous therapy and power injection of contrast media

Sponsor	Manufacturer	ARTG number	Intended purpose
CMD TEC AUST Pty Ltd	Beijing Target Medical Technologies Ltd, China - Peoples Republic of	186598	The single and multiple-lumen catheters permit venous access to the adult and paediatric central circulation for the administration of medicines, blood sampling and pressure monitoring
Emergo Asia Pacific Pty Ltd T/a Emergo Australia	Navilyst Medical Inc, USA	215419	The BioFlo™ PICC with ENDEXO™ Technology with Stainless Steel Guidewire is indicated for short or long-term peripheral access to the central venous system for intravenous therapy, including but not limited to, the administration of fluids, medications, nutrients; the sampling of blood; for central venous pressure monitoring and for power injection of contrast media.
GSE Pty Ltd	Arrow International Inc, USA	196742	Intended to allow short term access (<30 days) to the central vascular system. This catheter is intended for multiple procedures through a single access site such as fluid infusion, blood sampling, medication administration and central venous monitoring. The kit contains a Central Venous Catheter, and other components such as a spring wire guide, introducer needle, and other devices to assist insertion depending on the selected insertion site.
The Critical Group Pty Ltd	Biosensors International Pte Ltd, Singapre	208697	Central Venous Catheters are designed for use in critical care patients to monitor central venous pressures; sample blood; and administer drugs and solutions intravenously. Multiple lumen catheters provide multiple access channels to the central venous circulation through a single insertion site, permitting several functions to be performed simultaneously. The CVC Kit contains accessories (Dilator, Introducer Needle, Guide wires) which are used to assist in the process.

1 items listed are for illustrative purposes only. Data is not inclusive of all available ancillary items that may be used in ultrasound guided vascular access and percutaneous neural blockade.

Table 73: Australian Register of Therapeutic Goods listings for nerve stimulators used to locate peripheral nerves to facilitate placement of neural blockades 1

Sponsor	Manufacturer	ARTG ID	Intended purpose
LMA PacMed Pty Ltd	Te Me Na SAS, USA	157039	Peripheral nerve stimulation. The device allows the peripheral nerve to be located quickly prior to an injection of local anaesthetic. Muscle reflex is activated and observed by the electrical stimulation. After the actual current is transmitted to the patient it can be checked simultaneously.
Globus Medical Australia Pty Ltd	Globus Medical Inc, USA	190999	A device designed to intermittently locate a nerve to monitor the nerve's position relative to a surgical instrument

1 items listed are for illustrative purposes only. Data is not inclusive of all appropriate and available electric nerve stimulators.

Appendix H Clinical practice guidelines

Twelve clinical practice guidelines and HTA reports of direct relevance to the current assessment were identified from database searches of the National Guideline Clearinghouse, NZ Guideline group, GIN, NICE (NHS) and NHS evidence. Searches were performed according the strategies defined in Appendix C and were not dated limited. Guidelines indicated that ultrasound should/must be made available to anaesthetists to assist in either the placement of central lines or percutaneous neural blocks and the technology should be appropriate for patient population. For vascular access, the use of ultrasound is reported to reduce the risk of procedural, mechanical and infection complications, (American Society of Anesthesiologists Task Force on Central Venous Access 2012; Lamperti et al 2012; Troianos et al 2011) and increase the success rate of catheter placement (Troainos et al (2011)). There are limited guidance notes for use of ultrasound in the placement of nerve blocks; these being NICE procedure guidance note 249 and 285. The identified guidelines and HTA reports provide a span-shot of the available evidence and are broadly aligned with the findings of the current assessment.

Table 74 Current clinical practice guidelines for ultrasound guided vascular access and percutaneous nerve block

Author	Title	Key statement
National Institute for Health and Clinical Excellence (2008)	Interventional procedure guidance 249 Ultrasound-guided catheterisation of the epidural space	Evidence based summary, including selected summaries of primary research "The Specialist Advisers stated that the key efficacy outcomes include patient comfort during catheterinsertion, success rate for entering the epidural space on the first attempt, success in patients in whom the conventional technique has failed, identification of the interspinous space by ultrasound and correlation of depth measured by ultrasound with depth on needle insertion. "
National Institute for Health and Clinical Excellence (2009)	Interventional procedure guidance 285 Ultrasound-guided regional nerve block	Evidence based summary, including selected summaries of primary research "The Specialist Advisers considered key efficacy outcomes to include success of the blocks, volume of anaesthetic required, speed of onset of analgesia, pain score and number of needle passes"
Wee et al (2013) www.rcoa.ac.uk/gpas2013	Guidelines for the provision of anaesthetic services: Obstetric anaesthesia (Chapter 9)	Ultrasound imaging equipment should be available for central vascular access, transversus abdominis plane (TAP) blocks and epidural cannulation of parturients as well as high risk and morbidly obese women (pg 5)
Wilkinson et al (2013) www.rcoa.ac.uk/gpas2013	Guidelines for the provision of anaesthetic services: Paediatric anaesthesia (Chapter 10)	Equipment must be appropriate for use in babies and children of all sizes and ages and include: : ultrasound devices (for central venous and nerve identification).(pg 3)
Merchant et al (2013) J Can Aesth 60:60 - 84.	Guidelines to the Practice of Anesthesia Revised Edition 2013	For the placement of central venous catheters, dedicated ultrasound capability must be provided.(pg 65)
Australian and New Zealand College of Anaesthetists and faculty of Pain Medicine.	Acute pain management: scientific evidence (Third Edition, 2010)	Ultrasound guidance reduces the risk of vascular puncture during the performance of regional blockade (N) (Level I).(pg xxvi) Blocks performed using ultrasound guidance are more likely to be successful, faster to perform, with faster onset and longer duration compared with localisation using a peripheral nerve stimulator (N) (Level I).(pg xxxii)
Bishop etal (2007) Int. Jnk Lab Hem 29:291-278	Guidelines on the insertion and management of central venous access devices in adults	Ultrasound guided insertion is recommended for all routes of central venous catheterization. The use of ultrasound is also recommended for the insertion of PICC when the peripheral veins are not visible or palpable (pg 262)
National Institute for Clinical Excellence (2005)	Technology Appraisal No. 49 Guidance on the use of ultrasound locating devices for placing central venous catheters	HTA assessment: specific evaluation of the use of ultrasound of vascular access.

Author	Title	Key statement
Calvert et al (2003) Health Technol Assess 7 (12)	The effectiveness and cost effectiveness of ultrasound locating devices for central venous access: a systematic review and economic evaluation	HTA assessment: specific evaluation of the use of ultrasound of vascular access.(full report)
Developed by the American Society of Anesthesiologists Task Force on Central Venous Access (2012) Anesthesiology 116: 539 - 73	Practice Guidelines for Central Venous Access A Report by the American Society of Anesthesiologists Task Force on Central Venous Access	Evidence based; Recommends the use of ultrasound to prevent mechanical trauma during the catheter placement.
Lamperti et al (2012) Intensive Care med 38: 1105 - 1117	International evidence-based recommendations on ultrasound-guided vascular access	Recommendation based on evidence review and expert consensus. "Ultrasound guidance can be used not only for central venous cannulation but also in peripheral and arterial cannulation" (pg 1106) This technique allows the reduction of infectious and mechanical complications. (pg 1106)
Troainos et al (2011) J Am Soc Echocardiogr 24;1291-1318	Guidelines for Performing Ultrasound Guided Vascular Cannulation: Recommendations of the American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists	Evidence based review The authors conclude: Ultrasound should be used whenever possible to increase cannulation success and reduce the incidence of complications. Recommend the use of ultrasound for LJ and FV cannulation in paediatric patients Obese and coagulopathic patients: ultrasound screening of the SC vein should be performed before cannulation. Training in ultrasound use is essential to realise the clinical outcomes reported in the literature. Training should also focus on an understanding of the limitation of ultrasound.

Appendix I Quality appraisal tools

AMSTAR guide

1. Was an *a priori* design approved?

Yes: if the research question and the inclusion criteria are clearly stated in the abstract, introduction or methods section of the review

No: no statement on question or inclusion criteria

Cannot answer: the research question and inclusion criteria are vague/unclear, or they are stated/described in other sections of the review

2. Was there duplicate study selection and data extraction?

Yes: two reviewers for selection and extraction and a consensus procedure

No: at least one of the above is a "no" (e.g., one reviewer for selection, two for extraction, and a consensus procedure in place)

Cannot answer: if at least one of the above is not mentioned in the study and thus can't be determined whether it was done in duplicate or not

3. Was a comprehensive literature search performed?

Yes: all four elements are there (two electronic sources, years and databases, key words or MeSH terms, additional sources)

No: if any of the four elements are missing

4. Was the status of publication (e.g., grey literature) used as an inclusion criterion?

Yes: clear statement about publication type and language

No: no statement on publication type or language

Cannot answer: statement is unclear

5. Was a list of studies (included and excluded) provided?

Yes: both included and excluded are presented (tables or lists), or only included studies are presented but it is mentioned that a list of excluded studies is available on request or there are links to a list of excluded studies

No: no tables or lists with information on both of these elements

6. Were the characteristics of the included studies provided?

Yes: tables of included studies with all three elements (interventions, outcomes and participants) for each study. Information on participants must include at least age and sex to receive a yes.

No: no tables with information on these elements or tables with information on only one or two of the three elements

7. Was the scientific quality of the included studies assessed and documented?

Yes: if tool or checklist/tool for formal critical appraisal is mentioned/used, *and* critical appraisal is documented in tables or text

No: no mention of a tool/checklist, or critical appraisal not documented in tables or text

8. Was the scientific quality of the included studies used appropriately in formulating conclusions?

Yes: if results of the methodological rigour and scientific quality considered in the conclusions/discussion of the review

No: no reference to quality of evidence made in the conclusions/discussion or studies only mentioned by level of evidence

9. Were the methods used to combine the finding of studies appropriate?

Yes: for quantitative analysis, tests for homogeneity/heterogeneity must be done

No: no test for homogeneity/heterogeneity done, or not mentioned.

Not applicable: qualitative analysis

10. Was the likelihood of publication bias assessed?

Yes: if anything mentioned on publication bias (graphical aids not required, but a statement is required)

No: no statement on publication bias

11. Was the conflict of interest stated?

Yes: comment is made regarding whether there are/are not conflicts of interest with respect to *both* the review and the included studies

No: no comment is made regarding conflicts of interests with respect to the review and the included studies, or comment is made regarding the review but not the individual studies or vice versa

Table 75 Critical appraisal tool for randomised controlled trials

	Study characteristic		Answer[a]
Patient selection	Q1	Were the eligibility criteria specified?	Y, N,U, NA
Patient selection	Q2a.	Was randomisation performed adequately?	
Patient selection	Q2b.	Was treatment allocation concealed?	
Patient selection	Q3.	Were the groups similar at baseline?	
Interventions	Q4.	Were the index and control interventions explicitly described?	
Interventions	Q5	Were co-interventions avoided or comparable?	
Interventions	Q6.	Was the patient blinded to the intervention?	
Interventions	Q7	Was the provider blinded to the intervention?	
Outcome measurement	Q8	Was the outcome assessor blinded to the intervention?	
Outcome measurement	Q9	Were the outcome measures relevant?	
Outcome measurement	Q10	Were adverse events described?	
Outcome measurement	Q11	Was the withdrawal/dropout rate described and acceptable?	
Outcome measurement	Q12a	Was a short-term follow-up measurement performed?	
Outcome measurement	Q12b.	Was a long-term follow-up measurement performed?	
Outcome measurement	Q13.	Was the timing of the outcome assessment comparable in both groups?	
Statistics	Q14	Was the sample size for each group described?	
Statistics	Q15	Did the analysis include an intention-to-treat analysis?	
Statistics	Q16.	Were point estimates and measures of variability presented for the primary outcome measures?	

[a]Answer key: Yes = Y No = N; Unclear = N; Not applicable or not possible because of the nature of the intervention = NA

Internal validity criteria: Q2a & b, 5, 6, 7, 8, 9, 11, 13, 16; External validity criteria: Q1, 3, 4, 10, 12a & b; Statistical criteria: Q14, 16

Critical appraisal of vascular access randomised controlled trials

Table 76 Methodological quality appraisal of randomised control trials on ultrasound guidance for vascular access[a]

Study	Q1	Q2a	Q2b	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12a	Q12b	Q13	Q14	Q15	Q16
(Hayashi and Amano 2002)	Y	U	U	Y	Y	Y	U	NA	Y	Y	Y	U	Y	N	Y	Y	N	Y
(Kaye et al 2011)	N	U	U	Y	Y	U	U	NA	U	Y	Y	Y	Y	N	Y	Y	N	Y
(de Carvalho Onofre et al 2012)	Y	Y	U	Y	Y	U	N	NA	U	Y	N	Y	Y	N	Y	Y	N	Y
(Iwashima et al 2008)	N	N	N	Y	Y	U	U	NA	U	Y	Y	Y	Y	N	Y	Y	N	N
(Miller et al 2002)	Y	N	N	N	Y	U	N	NA	N	N	Y	Y	Y	N	N	Y	N	N
(Ray et al 2013)	Y	N	U	Y	Y	Y	Y	NA	U	Y	Y	Y	Y	N	Y	Y	Y	Y
(Li et al 2013a)	Y	Y	Y	Y	Y	Y	N	NA	N	N	Y	U	Y	N	Y	Y	U	Y
(Dudeck et al 2004)	Y	U	U	Y	Y	Y	N	NA	N	Y	Y	Y	Y	N	Y	Y	U	Y
(Killu et al 2011)	Y	U	U	U	Y	Y	N	NA	N	Y	Y	U	Y	N	Y	Y	U	Y
(Airapetian et al 2013)	Y	Y	Y	Y	Y	Y	N	NA	N	Y	Y	Y	Y	N	Y	Y	U	Y
Summary																		
Y	8	3	2	8	10	6	0	0	1	8	9	7	10	0	8	9	0	7
N	2	3	2	1	0	0	7	0	5	2	1	0	0	10	1	0	5	2
U	0	4	7	1	0	4	3	0	4	0	0	3	0	0	0	0	4	0
NA	0	0	0	0	0	0	0	10	0	0	0	0	0	0	0	0	0	0

[a] Assessment toot adapted from (Van Tulder MW 1997) Downs and Black (1998)

[b] Description of assessment questions (Table 75)

Critical appraisal of nerve block randomised controlled trials

Table 77 Methodological quality appraisal of randomised controlled trials on ultrasound guidance for percutaneous neural blockade [a]

Study	Q1	Q2a	Q2b	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12a	Q12b	Q13	Q14	Q15	Q16
Antonakakis et al (Antonakakis et al 2010)	Y	Y	Y	Y	Y	U	Y	NA	Y	Y	Y	U	Y	N	Y	Y	N	N
Aveline, (Aveline et al 2011)	Y	Y	Y	Y	Y	Y	Y	NA	Y	Y	Y	Y	Y	Y	Y	Y	N	Y
Bendtsen et al (Bendtsen et al 2011)	Y	Y	Y	Y	Y	Y	N	NA	Y	Y	Y	Y	Y	N	Y	Y	Y	Y
Bloc et al (Bloc et al 2010)	Y	Y	Y	Y	Y	U	N	NA	Y	Y	Y	N	Y	N	U	Y	N	N
Brull et al	Y	Y	N	Y	Y	Y	Y	NA	Y	Y	Y	U	Y	N	Y	Y	Y	Y
Danelli et al	Y	Y	U	U	Y	NA	U	NA	Y	Y	Y	Y	Y	N	Y	Y	Y	Y
Danelli et al	Y	Y	Y	Y	Y	Y	N	NA	Y	Y	Y	Y	Y	N	Y	Y	N	Y
Faraoni et al	Y	Y	U	Y	Y	Y	N	NA	Y	Y	Y	Y	Y	N	Y	Y	U	Y
Fredrickson and Danesh-Clough	Y	Y	Y	Y	Y	Y	Y	NA	Y	Y	Y	Y	Y	N	Y	Y	U	N
Gorthi et al	Y	U	U	Y	Y	U	N	NA	N	Y	Y	U	Y	N	Y	Y	N	Y
Gurkan et al (Gurkan et al 2008)	Y	U	U	Y	Y	Y	N	NA	Y	Y	Y	Y	Y	N	Y	Y	Y	Y
Kent et al[c]	Y	Y	Y	NA	Y	Y	N	NA	Y	Y	Y	Y	Y	N	Y	Y	NA	Y
Ko et al	Y	Y	Y	Y	Y	Y	Y	NA	Y	Y	Y	Y	Y	N	Y	Y	N	Y
Liu et al	Y	Y	Y	Y	Y	Y	U	NA	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

Study	Q1	Q2a	Q2b	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12a	Q12b	Q13	Q14	Q15	Q16
Maalouf et al	Y	Y	Y	Y	Y	Y	Y	NA	Y	Y	U	Y	Y	N	Y	Y	N	Y
Min et al	Y	Y	U	Y	Y	Y	U	NA	Y	Y	Y	Y	Y	N	Y	Y	Y	Y
O'Sullivan	Y	U	Y	Y	Y	Y	U	NA	Y	Y	Y	Y	Y	N	Y	Y	U	Y
Ponde et al	Y	Y	U	Y	Y	Y	U	NA	Y	Y	N	U	Y	N	Y	Y	N	Y
Ponde and Diwan	Y	U	Y	Y	Y	Y	N	NA	Y	Y	Y	Y	Y	N	Y	Y	U	Y
Ponrouch et al	Y	Y	N	Y	Y	Y	Y	NA	Y	Y	Y	Y	Y	N	Y	Y	U	Y
Redborg et al	N	Y	Y	Y	Y	U	Y	NA	Y	Y	Y	U	Y	N	Y	Y	N	Y
Reid et al[c]	Y	N	N	Y	Y	Y	N	NA	N	Y	Y	Y	Y	N	Y	Y	Y	Y
Renes et al	Y	Y	N	Y	Y	Y	N	NA	N	Y	Y	N	Y	N	Y	Y	Y	Y
Sala-Blanch et al	U	U	Y	Y	Y	Y	N	NA	Y	Y	Y	Y	Y	U	Y	Y	U	Y
Salem et al	Y	Y	U	Y	Y	Y	U	NA	U	Y	Y	Y	Y	N	Y	N	Y	Y
Strub et al	Y	Y	U	Y	Y	Y	N	NA	N	Y	Y	Y	Y	U	Y	Y	U	Y
Trabelsi et al	Y	U	Y	Y	Y	Y	U	NA	Y	Y	U	Y	Y	N	Y	Y	U	Y
Tran et al	Y	Y	Y	Y	Y	U	N	NA	Y	Y	Y	N	Y	N	Y	Y	N	Y
Zencirci	Y	N	N	Y	N	Y	N	NA	N	Y	Y	Y	Y	N	Y	Y	U	Y

Summary

Study	Q1	Q2a	Q2b	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12a	Q12b	Q13	Q14	Q15	Q16
Y	27	22	16	27	28	23	8	0	23	29	26	21	29	2	28	28	9	26
N	1	1	5	0	1	0	14	0	5	0	1	3	0	25	0	1	10	3
U	1	6	8	1	0	5	7	0	1	0	2	5	0	2	1	0	9	0
NA	0	0	0	1	0	1	0	29	0	0	0	0	0	0	0	0	1	0

[a] Assessment toot adapted from (Van Tulder MW 1997) and Downs and Black (1998)

[b] Description of assessment questions (Table 75)

[c] Level of evidence, III-1 pseudoRCT.

Appendix J RCTs included in the systematic reviews

Overlap of included RCTs with identified systematic reviews is shown in Table 78 and Table 79.

Table 78 Overlap of RCTs identified in our search with included systematic reviews – venous access

RCT	Wu 2013	Calvert 2003	Keenan 2002	Randolph 1996	Mehta 2013	Sigaut 2009
Agarwal 2008	✓	×	×	×	×	×
Aiapetian 2013	×	×	×	×	×	×
Aouad 2010	✓	×	×	×	×	×
Cajozzo 2004	✓	×	×	×	×	×
Chuan 2005	×	×	×	×	×	✓
Fragouu 2011	✓	×	×	×	×	×
Gilbert 1994	×	✓	✓	×	×	×
Gratz 1994	×	✓	✓	✓	×	×
Grebenik 2004	✓	×	×	×	×	✓
Gualteri 1995	✓	✓	✓	✓	×	×
Hayashi 2002	×	×	×	×	×	×
Hilty 1997	✓	✓	✓	×	×	×
Iwashima 2008	×	×	×	×	×	×
Karakitsos 2006	✓	×	×	×	×	×
Kaye 2011	×	×	×	×	×	×
Lefrant 1998	×	✓	✓	×	×	×
Leung 2006	✓	×	×	×	✓	×
Mallary 1990	✓	✓	✓	✓	×	×
Milling Jr 2005	✓	×	×	×	×	×
Palepu 2009	✓	×	×	×	×	×
Shrestha 2011	✓	×	×	×	×	×
Slama 1997	✓	✓	✓	×	×	×
Soyer 1993	✓	✓	×	×	×	×
Sulek 2000	✓	✓	×	×	×	×
Teichgraber 1997	✓	✓	✓	×	×	×
Troianos 1991	✓	✓	✓	✓	×	×
Turker 2009	✓	×	×	×	×	×
Verghese 1999	✓	✓	✓	×	×	✓
Verghese 2000	✓	✓	✓	×	×	✓
RCTs included in the systematic reviews missing from our search	1 missing - Ovezov	1 missing: Alderson	1 missing: Denys 1993	None missing	None missing	1 missing: Alderson

Table 79 Overlap of RCTs identified in our search with included systematic reviews – percutaneous nerve block

RCT	Bhatia and Brull 2013	Yuan 2012	Walker 2011	Gelfand 2011	Choi and Brull 2011	Liu 2010	McCartney 2010	Neal 2010	Abrahams 2009	Rubin 2008
Abdellatif 2012	×	×	×	×	×	×	×	×	×	×
Ali 2003	×	×	×	×	×	×	×	×	×	×
Antonakakis 2010	×	×	×	×	×	×	×	×	×	×
Aveline 2010	×	×	×	×	✓	×	×	×	×	×
Aveline 2011	×	×	×	×	×	×	×	×	×	×
Bendtsen 2011	×	×	×	×	×	×	×	×	×	×
Bloc 2010	×	×	×	×	×	×	×	×	×	×
Brull 2009	×	✓	×	×	×	×	✓	×	×	×
Casati 2007	×	×	✓	×	×	×	×	✓	×	×
Casati 2007 b	×	✓	✓	✓	×	✓	✓	✓	✓	×
Cataldo 2012	×	×	×	×	×	×	×	×	×	×
Chan 2007	×	✓	✓	✓	×	✓	✓	✓	✓	×
Danelli 2012	×	×	×	×	×	×	×	×	×	×
Danelli 2009a	×	×	✓	✓	×	×	×	✓	×	×
Danelli 2009 b	×	×	×	×	×	×	×	×	×	×
Dhir 2008	×	×	✓	×	×	✓	✓	×	×	×
Dolan 2008	×	×	✓	×	×	×	×	×	×	×
Dolan 2009	×	×	×	×	×	×	×	×	×	×
Domingo-Triado 2007	×	×	✓	×	✓	✓	×	✓	✓	×
Dufour 2008	×	×	✓	×	✓	✓	×	✓	×	×
Elnour 2009	×	×	×	×	×	×	×	×	×	×
Faraoni 2010	×	×	×	×	✓	×	×	×	×	×
Fredrickson 2009a	×	×	×	×	✓	×	×	×	×	×

RCT	Bhatia and Brull 2013	Yuan 2012	Walker 2011	Gelfand 2011	Choi and Brull 2011	Liu 2010	McCartney 2010	Neal 2010	Abrahams 2009	Rubin 2008
Fredrickson 2009b	×	✓	×	×	✓	✓	×	✓	×	×
Gorthi 2010	×	×	×	×	×	×	×	×	×	×
Grau 2001	×	×	×	×	✓	×	×	×	×	×
Grau 2002	×	×	×	×	✓	×	×	×	×	×
Grau 2004	×	×	×	×	×	×	×	×	×	×
Gurkan 2008	×	×	×	×	×	✓	✓	✓	×	×
Gurkan 2010	×	×	×	×	×	×	×	×	×	×
Jee 2013	×	×	×	×	×	×	×	×	×	×
Kapral 2008	×	✓	✓	✓	✓	✓	✓	✓	✓	×
Kent 2013	×	×	×	×	×	×	×	×	×	×
Ko 2013	×	×	×	×	×	×	×	×	×	×
Li 2011	×	×	×	×	×	×	×	×	×	×
Liu 2005	×	✓	✓	✓	×	✓	✓	✓	✓	×
Liu 2009	×	✓	×	✓	×	✓	✓	✓	×	×
Maalouf 2012	×	×	×	×	×	×	×	×	×	×
Macaire 2008	×	×	✓	✓	×	✓	✓	✓	✓	×
Manassero 2012	×	×	×	×	×	×	×	×	×	×
Marhofer 1997	×	×	×	×	×	×	×	✓	✓	×
Marhofer 1998	×	×	✓	×	×	×	×	✓	✓	×
Marhofer 2004	×	×	✓	✓	✓	×	✓	✓	✓	✓
Mariano 2009 b	×	×	×	×	✓	×	×	×	×	×
Mariano 2009a	×	✓	×	×	✓	✓	×	✓	×	×
Mariano 2010	×	✓	×	×	✓	×	×	×	×	×

RCT	Bhatia and Brull 2013	Yuan 2012	Walker 2011	Gelfand 2011	Choi and Brull 2011	Liu 2010	McCartney 2010	Neal 2010	Abrahams 2009	Rubin 2008
McNaught 2011	×	×	×	×	✓	×	×	×	×	×
Na 2010	×	×	×	×	×	×	×	×	×	×
Nash 1996	×	×	×	×	×	×	×	×	×	×
O'Sullivan 2011	×	×	×	×	×	×	×	×	×	×
Oberndorfer 2007	×	×	×	✓	✓	×	×	✓	✓	✓
Perlas 2008	×	×	✓	✓	✓	✓	×	✓	✓	×
Ponde 2009	×	×	×	✓	✓	×	✓	×	×	×
Ponde 2013	×	×	×	×	×	×	×	×	×	×
Ponrouch 2010	×	×	×	×	×	×	×	×	×	×
Redborg 2009	×	×	×	×	×	✓	×	✓	×	×
Reid 2009	×	×	×	×	×	×	×	×	×	×
Renes 2009	×	✓	×	×	×	×	×	×	×	×
Sahin 2011	×	×	×	×	×	×	×	×	×	×
Sala-blanch 2012	×	×	×	×	×	×	×	×	×	×
Salem 2012	×	×	×	×	×	×	×	×	×	×
Sauter 2008	×	✓	✓	✓	×	✓	✓	✓	✓	×
Sites 2006	×	×	✓	✓	×	✓	✓	✓	×	×
Soeding 2005	×	×	✓	✓	✓	✓	✓	✓	×	×
Stone 2008	×	×	×	×	×	×	×	×	×	×
Strub 2011	×	×	×	×	×	×	×	×	×	×
Taboada 2009	×	✓	×	×	✓	✓	✓	✓	×	×
Tedore 2009	×	×	×	×	×	✓	×	✓	×	×
Thomas 2011	×	✓	×	×	×	×	×	×	×	×

RCT	Bhatia and Brull 2013	Yuan 2012	Walker 2011	Gelfand 2011	Choi and Brull 2011	Liu 2010	McCartney 2010	Neal 2010	Abrahams 2009	Rubin 2008
Trabelsi 2013	×	×	×	×	×	×	×	×	×	×
Tran 2010	×	×	×	×	×	×	×	×	×	×
Tran de 2008	×	×	×	×	×	×	×	×	×	×
Van Geffen 2009	×	×	×	✓	✓	✓	×	×	×	×
Williams 2003	×	×	✓	×	×	✓	✓	✓	✓	×
Willschke 2005	×	×	×	×	✓	×	×	✓	×	✓
Zencirci 2011	×	✓	×	×	×	×	×	×	×	×
	0 studies identified – chronic pain focus here	missing Yu 2007 (excluded language)	Missing none	Missing Yu 2007 (excluded language)	Missing Willschke 2006 (epidural)	Missing Marhofer 2005 – not RCT and Marhofer 2007 - Narrative	Missing Morros 2009 – language, Yu 2007 – language, Dingemans 2007 – excluded comp	Missing Dingemans 2007 – excluded comp, Yu 2007 – excluded language		Missing 8 studies — all epidural or caudal

Appendix K Safety and effectiveness data from the systematic reviews: vascular access

Table 80 Systematic reviews: Safety of ultrasound compared with landmark for guidance of major vascular access

Review	Vascular puncture	Hematoma	Pneumothorax	Haemothorax	Placement complications
(Wu et al 2013) Broad review of patients undergoing CVC including separate outcomes reported for adults, children, and IJV, SCV and FV access sites	Relative risk 0.25 (95% CI 0.15-0.42) Favours ultrasound[c] Subpopulations: IJV, SV, both favour ultrasound, FV[ns] Children:0.34 (95% CI 0.05-2.60)[ns]	Relative risk 0.30 (95% CI 0.19-0.46) Favours ultrasound[c] Subpopulations: IJV, SV, both favour ultrasound, FV [ns] Children:0.13 (95% CI 0.01-2.62)[ns]	Relative risk 0.21 (95% CI 0.06-0.73) Favours ultrasound[a] Subpopulations: IJV favour ultrasound, SC[ns] Children:0.40 (95% CI 0.02-9.61)[ns]	Relative risk 0.10 (95% CI 0.02-0.54) Favours ultrasound[b] Subpopulations: IJV[ns], SV favours ultrasound Children:0.40 (95% CI 0.02-9.61)[ns]	NR
(Calvert et al 2003b) Broad review of patients undergoing CVC including separate outcomes reported for adults, children, and IJV, SCV and FV access sites	NR	NR	NR	NR	Subpopulations: IJV: 57% reduction with ultrasound[a] SV:90% reduction with ultrasound[a] Children: IJV73% reduction with ultrasound[a]

Review	Vascular puncture	Hematoma	Pneumothorax	Haemothorax	Placement complications
(Keenan 2002) Broad review of patients undergoing CVC including outcomes reported for IJV, SCV and FV access sites	Risk difference 7% (95% CI 3-10%) Favours ultrasound[c] Subpopulations: IJV and FV favour US, SV[ns]	NR	NR	NR	NR
(Randolph et al 1996) Broad review of patients undergoing CVC including outcomes reported for IJV and SCV access sites	NR	NR	NR	NR	Relative risk 0.22 (95% CI 0.10-0.45)
(Mehta et al 2013) Review of CVC specific to procedures performed on adults in the emergency department	NR	NR	NR	NR	NR
(Sigaut et al 2009a) Review of CVC specific to procedures performed in children where access was via the internal jugular vein	Children: odds ratio 0.32 (95% CI 0.08-1.62)[ns]	Children: odds ratio 0.19 (95% CI 0.04-0.90) favours ultrasound[a]	NR	NR	NR
(Krstenic et al 2008) Review of PICC placement by nurses in adult patients	NR	NR	NR	NR	NR

Abbreviations: CI, confidence interval. CVC, central venous catheter. IJV, internal jugular vein. SCV, subclavian vein. FV, femoral vein. NR, not reported
Significant difference ([I] vs [C]) indicated by superscript a, b, c or ns for $p < 0.05$, $p < 0.01$, $p < 0.001$ and not significant respectively

Table 81 Systematic reviews: Effective of ultrasound compared with landmark for guidance of major vascular access

Review	Failure rate	Number of attempts	Time	Success rate
(Wu et al 2013) Broad review of patients undergoing CVC including separate outcomes reported for adults, children, and IJV, SCV and FV access sites	Relative risk 0.18 (95% CI 0.1-0.32) Favours ultrasound[c] Subpopulations: IJV, SV, FV all favour ultrasound Children: 0.26 (95% CI 0.03-2.55)[ns]	NR	NR	NR
(Calvert et al 2003b) Broad review of patients undergoing CVC including separate outcomes reported for adults, children, and IJV, SCV and FV access sites	Subpopulations: IJV: 86% reduction in failures[c] SCV: 86% reduction[b] FV: 71% reduction[ns]	Subpopulations: IJV: 1.5 fewer attempts Favours ultrasound[b] FV: 2.7 fewer attempts Favours ultrasound[a]	Subpopulations: IJV: US 20.47 seconds faster[ns] FV: 3.2 seconds faster[ns]	NR
(Keenan 2002) Broad review of patients undergoing CVC including outcomes reported for IJV, SCV and FV access sites	Risk reduction 0.16 (95% CI 0.09-0.23) Favours ultrasound[c]	Risk reduction 1.41 (95% CI 1.15 – 1.67) Favours ultrasound	6.56 seconds faster (95% CI -44.02-57.14)[ns]	NR
(Randolph et al 1996) Broad review of patients undergoing CVC including outcomes reported for IJV and SCV access sites	Relative risk of failure 0.32 (95% CI 0.18-0.55) Favours ultrasound	NR	9 seconds faster (95% CI -80.1 – 62.2)[ns]	NR
(Mehta et al 2013) Review of CVC specific to procedures performed on adults in the emergency department	NR	NR	NR	Relative rate[1] 3.5 (95% CI 1.22-10.07) Favours ultrasound[a]
(Sigaut et al 2009a) Review of CVC specific to procedures performed in children where access was via the internal jugular vein	Odds ratio 0.28 (95% CI 0.05-1.47)[ns]	0.81 fewer attempts (95% CI -1.1 - -0.52) Favours ultrasound[c]	1.4 minutes faster (95% CI -2.85 – 0.04)[ns]	NR
(Krstenic et al 2008) Review if PICC placement by nurses in adult patients	Risk ratio 0.4 (95% CI 0.33-0.48) Favours ultrasound[c]	NR	NR	NR

Abbreviations: CI, confidence interval. CVC, central venous catheter. IJV, internal jugular vein. SCV, subclavian vein. FV, femoral vein. NR, not reported
Significant difference ([I] vs [C]) indicated by superscript a, b, c or ns for $p < 0.05$, $p < 0.01$, $p < 0.001$ and not significant respectively

[1] failure defined as the inability to locate or puncture the vein or the inability to feed the guide wire. Success defined as venous puncture and guide wire insertion within three attempts.

Appendix L Safety and effectiveness data from the systematic reviews: percutaneous nerve blockade

Table 82 Summary of systematic review data: safety of ultrasound guided percutaneous neural blockade

Review	Number of included RCTs (# patients)	Vascular puncture	Paraesthesia	Nerve injury	Neurological symptoms	Major complications	Overall complications	Other
Abrahams et al 2009 Broad review of peripheral nerve block	13 (946 patients)	Risk ratio 0.16 (0.05-0.47) favours US[c]	No significant difference	NR	No significant difference	No major complication reported in any study	NR	NR
(Bhatia and Brull 2013) Nerve block for chronic pain treatment	1 relevant RCT (50 patients)	[I] 0 incidences [C] 2 incidences	NR	[I] 0 incidences [C] 3 incidences	NR	Pneumothorax [I] 0 incidences [C] 0 incidences	NR	NR
(Choi and Brull 2011) Nerve block for the management of acute pain	23 (1,674 patients)	3 trials significantly favour US	NR	NR	NR	NR	20 studies found no significant difference	Headaches: 3 studies favour US
(Gelfand et al 2011) Peripheral nerve blocks conducted for a surgical procedure	16 (1,264 patients)	NR	NR	NR	NR	NR	NR	NR

Review	Number of included RCTs (# patients)	Vascular puncture	Paraesthesia	Nerve injury	Neurological symptoms	Major complications	Overall complications	Other
Liu et al 2010 Broad review of peripheral nerve block	24	NR	NR	NR	NR	NR	NR	NR
McCartney et al 2010 Upper extremity nerve block	19	2 trials favour US, 0 trials favour [C]	NR	NR	NR	NR	NR	Pain: 1 study favours US, 0 studies favour [C]
Neal 2010 Broad review of nerve block	22 (1,863 patients)	2 trials favour US 10 trials report no statistically significant difference, 1 trial favours ENS	2 studies favour US, 20 studies not significant	1 study favours US, 5 studies not significant, 1 study favours [C]	NR	NR	NR	NR
(Walker et al 2011) Broad study reporting nerve block outcomes in adult patients	18 (1.344 adults)	8 trials favour ultrasound (10 NR)	1 trial favours US, 1 trial favours [C]	NR	NR	No major complication reported in any study	1 trial favours US	Haematoma: 8 trials favour US
Yuan et al 2012 Brachial plexus block in adults	16 (1,321 adults)	Risk ratio of 0.13 (95% CI 0.06-0.27) favours ultrasound[c]	NR	NR	Risk ratio 0.87 (95% CI 0.58 – 1.30)[ns]	NR	NR	Hemidiaphragmatic paralysis Complete paralysis: Risk ratio 0.09 .95% CI (0.03-0.31) favours ultrasound[c] Partial paralysis: risk ratio 0.25 (95% CI 0.03-2.14)[ns]
Rubin et al 2009	3 relevant RCTs	NR	NR	NR	NR	NR	NR	NR

Abbreviations: CI. NR, not reported Significant difference ([I] vs [C]) indicated by superscript a, b, c or ns for $p < 0.05$, $p < 0.01$, $p < 0.001$ and not significant respectively

Table 83 Summary of systematic review data: effectiveness of ultrasound guided percutaneous neural blockade

Study	Time to perform block	Block onset time	Block success	Block duration	Co-administered drugs	Needle passes and/or skin punctures	Pain or discomfort	Other
Abrahams et al 2009	Mean difference -1 minute faster (95 % CI 0.4 – 1.7) favours ultrasound[b]	29% difference (95% CI 12-45%) favours ultrasound[c]	Risk of failure 0.41 (95% CI 0.26 – 0.66) – favours ultrasound[c]	Mean difference 25% (95% CI 12-38%) favours ultrasound[c]	Risk of rescue block 0.52 (95% CI 0.26 – 1.04)[ns]	NR	NR	Block completeness at 30 minutes ratio 1.23 (95% CI 1.07-1.41) favour ultrasound[b]
Bhatia and Brull 2013	NR	NR	NR	NR	NR		US: pain scores 45% below base line [C] no difference with baseline	NR
Choi and Brull 2011	NR	NR	NR	3 studies favour ultrasound, 5 studies not significant	Opioid consumption: 3 studies favour ultrasound, 4 studies not significant		Pain at rest: 8 studies favour ultrasound, 8 studies not significant. Pain at movement: 1 study favours ultrasound, 3 studies not significant	Patient satisfaction: 2 studies favour ultrasound, 3 studies not significant. Length of hospital stay: 2 studies not significant.
Gelfand et al 2011	NR	NR	Success risk ratio 1.11 (1.05 – 1.17) – favours US[c]	NR	NR		NR	NR
Liu et al 2010	5 studies favour ultrasound (range of means 4-14 mins faster) 5 studies not significant, 1 study favours comparator (mean 2 mins faster)	14 studies favour ultrasound, 7 studies not significant, 1 study favours comparator	13 studies favour ultrasound, 5 studies not significant, 0 studies favour comparator	1 study favour ultrasound, 8 studies not significant	Rescue anaesthesia: 3 studies favour ultrasound, 14 studies not significant. Supplement analgesia: 1 study favours ultrasound, 12 studies not significant	NR	NR	Block completeness: 6 studies favour ultrasound, 6 studies not significant.

Study	Time to perform block	Block onset time	Block success	Block duration	Co-administered drugs	Needle passes and/or skin punctures	Pain or discomfort	Other
McCartney et al 2010	4 studies favour ultrasound, 4 studies not significant. 3 studies favour comparator.	Sensory: 6 studies favour ultrasound, 1 study favours comparator. Motor: 1 study favours ultrasound, 0 studies favour comparator.	8 studies favour ultrasound, 0 favour comparator	2 studies favour ultrasound, 0 favour comparator	NR	Needle passes: 3 studies favour ultrasound, 0 favour comparator.	Pain: 1 study favours ultrasound, 0 favour comparator.	NR
Neal 2010	NR	NR	NR	NR	NR	NR	NR	NR
Rubin et al 2009	NR	1 RCT favours US,	2 studies favour US, 1 study NS	2 studies favour US	NR	NR	NR	NR
Walker et al 2011	5 studies favour US (between 1.5 and 4.5 minutes faster) 5 studies not significant	NR	3 trials favour ultrasound, 10 trials not significant difference	NR	NR	Number of skin punctures and/or needle passes: 4 studies favour ultrasound	1 study favours ultrasound, 5 studies not significant	
Yuan et al 2012	Mean difference -2.25 min (95% CI -4.56 – 0.06)^{ns}	Sensory: mean difference: -3.32 min (95% CI -7.01 – 0.37)^{ns} Motor: mean difference: -2.35 min (95% CI -6.41 – 1.72)^{ns}	NR	NR	NR		NR	NR

Abbreviations: CI. NR, not reported
Significant difference ([I] vs [C]) indicated by superscript a, b, c or ns for $p < 0.05$, $p < 0.01$, $p < 0.001$ and not significant respectively

Appendix M Study information, safety and effectiveness data from the randomised controlled trials: vascular access

Table 84 Study information: Ultrasound guided arterial, venous or PICC vascular access

Study	Country	N	Type of vascular access	Location of access	Reason for access	Proceduralist
(Dudeck et al 2004)	Germany	112	Arterial	Femoral artery	NR	Two interventional radiologists with extensive experience
(Killu et al 2011)	USA	33	Arterial	Axillary artery	Haemodynamic monitoring or arterial blood gas sampling	Postgraduate year 1 or 2 surgical anaesthesiology residents or postgraduate year 4-5 critical care medicine fellows under supervision
(Airapetian et al 2013)	France	118	Venous	Femoral or jugular vein at discretion of attending	Septic shock or sepsis n=43, respiratory distress n=30, acute renal failure n=29, hypovolemic shock n=9, deliberate overdose n=4, cardiac arrest n=1, multiple trauma n=1 and coma n=1	Inexperienced residents who had not inserted more than five venous catheters
(Hayashi and Amano 2002)	Japan	240	Venous	Right internal jugular vein	Elective surgery	Six anaesthesiologists (2 residents and 4 attending physicians) familiar with US and LM guided cannulation
[a] (Iwashima et al 2008)	Japan	87	Venous	Femoral vein	Heart disease (congenital or other)	Two operators with assistant
[a] (Miller et al 2002)	USA	122	Venous	Various (internal jugular, subclavian, femoral and peripheral)	NR but reasons included hypertension, need for blood product or dehydration where peripheral access could not be obtained	Emergency medicine residents and faculty or residents in postgraduate years 1-3, various experience levels
(Ray et al 2013)	India	120	Venous	Internal jugular vein	NR	NR

Study	Country	N	Type of vascular access	Location of access	Reason for access	Proceduralist
(de Carvalho Onofre et al 2012)	Brazil	42	PICC	NR (peripheral veins)	IV therapy for ≥ 7 days	Two nurses with more than 2 years of experience in PICC insertion
(Li et al 2013a)	China	100	PICC	Right basilica vein	Chemotherapy (and half also for total parental nutrition)	PICC specialist

Abbreviations: N, number of patients in trial; PICC, peripherally inserted central catheter; LM: landmark; US: ultrasound; NR: not reported. Superscript (a) indicates pseudo-RCTs (NHMRC level of evidence III-1) all other studies are randomised controlled trials

Table 85 Characteristics of patient / volunteer populations for included RCTs evaluating ultrasound guided vascular access

Study	Indication description	Number: [I] [C]	M/F: [I] [C]	Age, [I] [C]	Inclusion criteria	Exclusion criteria	Number of patients excluded
(Dudeck et al 2004)	Interventional radiology patients requiring diagnostic or therapeutic trans-arterial procedures	56 56	36/24 36/18	60 yr ± 15 60 yr ± 13	Consecutive patients referred for diagnostic or therapeutic transarterial procedures	Patients with abnormal anticoagulation parameters, those who received anti-coagulatives pre or peri-procedural	24
(Killu et al 2011)	ICU patients undergoing haemodynamic monitoring or arterial blood gas sampling	18 15	19/14[1]	55.9 yr ± 18.5[1]	ICU patients undergoing arterial line placement for haemodynamic monitoring or frequent blood gas sampling	Patients who were pregnant, younger than 18 and those with no obtainable consent were excluded	NR
(Airapetian et al 2013)	ICU patients requiring a jugular or femoral central venous cannula	36 82	26/10 UM 28/16 LM 25/13	63 yr ± 15 UM 65 yr ± 15 LM 67 yr ±16	Patients who need for a jugular or femoral central cannula (as determined by attending physician). Patients < 18 yr	Patients requiring a subclavian catheter	445 patients were admitted to ICU, of these 257 were not randomised
(Hayashi and Amano 2002)	Patients requiring RIJV catheter placement under GA for elective surgery	$US_{3.75\ MHz}$: 60 $US_{7.5\ MHz}$: 60 [C]120	$US_{7.5\ MHz}$: 32/28 $US_{3.75\ MHz}$: 35/25 [C]: 77/4	$US_{7.5\ MHz}$: 62 yr ± 14 $US_{3.75\ MHz}$: 59 yr ± 13 [C]: 62 yr ± 12	Patients requiring RIJV catheter placement under general endotracheal anaesthesia determined on clinical criteria	Patients with a history of previous neck surgery or RIJV cannulation were excluded	NR
(Iwashima et al 2008)	Paediatric patients who require cardiac catheterisation	43 44	19/24[ns] 19/25	2 yr (0.08– 18)[ns] 1 yr (0.17 – 19)	Patients with congenital heart disease or other heart disease	NR	NR
(Miller et al 2002)	Patients presenting to ED with an acute medical or surgical problem	51 71	20/31[a] 41/30	49.1 yr ± 12.3[a] 43.8 yr ± 12.3	All patients presenting to the ED with an acute medical or surgical problem that necessitated CVA, where peripheral access could not be obtained	children (less than 14 year old), pregnant women	NR

Study	Indication description	Number: [I] [C]	M/F: [I] [C]	Age, [I] [C]	Inclusion criteria	Exclusion criteria	Number of patients excluded
Ray et al (2013)	Patients scheduled for elective or emergency surgery or staying in ICU who require internal jugular vein catheterisation	40 40 40	24/16 28/12 25/12	41.6 yr ±17.52 41.1 yr ± 15.29 44.2 yr ± 13.32	All patients aged 15-65, scheduled for elective or emergency surgery or staying in ICU who required IJV catheterisation	Patients with a history of neck surgery, head and neck mass or cancer, superior vena cava syndrome, coagulopathy, infection at the cannulation site were excluded	NR
(de Carvalho Onofre et al 2012)	Paediatric patients requiring IV therapy for ≥ 7 days	21 21	15/6 11/10	2.3 yr (0.1-16.3) 3.5 yr (0.1-15.8)	Children > 18 yr who are eligible for intravenous therapy administration by PICC	Infiltrations and hematomas on the chosen puncture site. Failure to provide consent	27 due to impairment of peripheral veins
Li et al. (2013)	Patients requiring a PICC line for chemotherapy	50 50	35/15 37/11	≥60 yr (n=7, 14%) 50-59 yr (n=8, 16%) 40-49 yr (n=20, 40%) 30-39 yr (n=11; 22%) ≤29 yr (n=4, 8%) ≥60 yr (n=5, 10%) 50-59 yr (n=16, 33%) 40-49 yr (n=16, 33%) 30-39 yr (n=9; 19%) ≤29 yr (n=2, 4%)	Age between 18 and 75 years, had completed at least a primary school education, would receive chemotherapy, was undergoing PICC insertion for the first time and would receive catheter maintenance at the same hospital	Contraindication of PICC placement	4 excluded prior to randomisation (2 declined to participate and 2 did not meet inclusion criteria)

Abbreviations: I: intervention; C: comparator; GA: general anaesthesia; ICU: intensive care unit; LM: landmark; UM: ultrasound marking; US, ultrasound CVA: central venous access; PICC: peripherally inserted central catheter; RIJV: right internal jugular vein.

Significant difference ([I] vs [C]) indicated by superscript a, ns for $p < 0.05$ and not significant, respectively. Comparison without superscripts, statistical significance was either not reported or not performed.

Data: NR: not reported; mean ± SD; mean [95% CI or range]; median (range or percentile or IQR)

Table 86 Ultrasound devices transducer frequency settings and landmark technique for guided major vascular access

Study	Location of access	Ultrasound probe (setting) and device	Needle	Landmark	Needle
(Dudeck et al 2004)	Femoral artery	7.5 MHz linear transducer with transportable US unit (Ecoscan EVB-405)	Needle: 18G.	Femoral artery palpation	NR
(Killu et al 2011)	Axillary artery	Bard-Dymax Site Rite II US scanner with a 7.5 MHz transducer and 4cm depth capacity (Access Systems, Inc. Salt Lake City, UT)	Needle: 20G 12cm catheter (Arrow International. Inc. Reading, PA)	Axillary artery palpation	NR
(Airapetian et al 2013)	Femoral or jugular vein at discretion of attending	7.5 MHz transducer (Site-Rite, Dymax Corp. USA)	18G, 10 cm long needle	LM: anatomic (4 cm below the angle of the mandible at the level of thyroid cartilage, lateral to common cratoid artery). UM: US was used to locate the internal jugular or femoral vein. Visible skin indentation were made along the course of the vessel to guide the needle entry point (needle was entered without US guidance)	LM: 19G 10 cm needle. UM: NR
(Hayashi and Amano 2002)	Right internal jugular vein	Either a 7.5 MHz (PLF-703NT, Toshiba, Tokyo, Japan) or 3.75 MHz (PSH-37LT, Toshiba, Tokyo, Japan) scanning probe connected to an US imaging system (SSH-140A, Toshiba, Tokyo, Japan)	18G catheter	respiratory jugular venodilation	18G catheter
(Iwashima et al 2008)	Femoral vein	12 MHz transducer attached to an US imaging system (Toshiba SSA-550A, Tokyo, Japan)	NR	Femoral artery palpation and localisation of the femoral triangle	NR
(Miller et al 2002)	Various (internal jugular, subclavian, femoral and peripheral)	7.5 MHz linear probe connected to a GE LOGIQ 400 MD US machine.	NR	NR	NR
Ray et al (2013)	Internal jugular vein	7.5 MHz transducer probe connected to a SIteRite USG system (Bard access system, Inc. Salt Lake City, USA)	Catheter: Certofix Trio V, 7F 20cm triple lumen central venou pressure catheter (B Braun, Melsungen, AG, Germany)	LM: Visualisation of the triangle formed by the two heads of the sterocleidomastoid muscle UM: US was used to locate and mark the internal jugular vein. Needle insetion was withour US guidance	LM: 18 G introducer needle (catheter as for US group) UM: needle NR Catheter as for US group

Study	Location of access	Ultrasound probe (setting) and device	Needle	Landmark	Needle
(de Carvalho Onofre et al 2012)	Peripheral veins specific location NR	10 – 15 MHz linear array transducer that reaches a 4 cm depth connected to an Ilook25 (SonoSite Bothell, WA) US machine	Catheter size of 1.9 – 3.0F	Landmark visualisation and palpation of the peripheral venous system	Catheter size of 1.9 – 3.0F
Li et al. (2013)	Right basilica vein	5-10 MHz linear array transducer connected to a uniform B-mode ultrasound (Bard, USA0)	21G micropuncture needle	NR	14G puncture needle

Abbreviations: G: gauge; LM: landmark; NR: not reported; UM: ultrasound mark; US: ultrasound; MHz: megahertz.

Table 87 Safety of ultrasound compared to landmark alone or landmark plus nerve for guidance of vascular access

Study	Adverse events on insertion – n with adverse event/N (%)	Adverse events on insertion – n with adverse event/N (%)	Procedural complication – n with complication /N (%)	Procedural complication – n with complication /N (%)	Hematoma – n with hematoma/N (%)	Hematoma – n with hematoma/N (%)	Pneumothorax – n with pneumothorax/N (%)	Pneumothorax – n with pneumothorax/N (%)	Nerve injury / neurological symptoms – n with nerve injuries/N (%)	Nerve injury / neurological symptoms – n with nerve injuries/N (%)
	[I]	[C]	[I]	[C]	[I]	[C]	[I]	[C]	[I]	[C]
(Dudeck et al 2004)	Femoral vein puncture 2/56 (3.6%)[ns]	Femoral vein puncture 5/56 (8.9%)	0/56 (0%)	0/56 (0%)	5/56 (8.9%)[ns]	5/56 (8.9%)	0/56 (0%)	0/56 (0%)	0/56 (0%)	0/56 (0%)
(Killu et al 2011)	Venous puncture 3/18 (16.7%)[ns]	Venous puncture 3/15 (20%)	Paraesthesia 0/18 (0%)[ns]	Paraesthesia 0/15 (0%)	1/18 (5.6%)[ns]	1/15 (6.7%)	NR	NR	0/18 (0%)[ns]	0/15 (0%)
(Airapetian et al 2013)	Arterial puncture 0/36 (0%)[b]	Arterial puncture LM: 5/38 (13%) UM: 11/44 (25%)	Catheter colonisation 9/36 (25%)[ns] Mechanical complications: 0/38 (0%)[c]	Catheter colonisation LM: 7/38 (18%) UM: 8/44 (18%) Mechanical complications LM: 9/38 (24%) UM: 16/44 (36%)	0/36 (0%)[b]	LM: 6/38 (16%) UM: 11/44 (25%)	0/36 (0%)	LM: 0/38 (0%) UM: 0/44 (0%)	0/0/36 (0%)	LM: 0/38 (0%) UM: 0/44 (0%)
(Hayashi and Amano 2002)	Arterial puncture $US_{3.75\ MHz}$: 2/60 (3.3%)[ns] $US_{7.5\ MHz}$: 1/60 (1.7%)[ns]	Arterial puncture 4/120 (3.3%)	NR	NR	NR	NR	NR	NR	NR	NR

Study	Adverse events on insertion – n with adverse event/N (%)	Adverse events on insertion – n with adverse event/N (%)	Procedural complication – n with complication /N (%)	Procedural complication – n with complication /N (%)	Hematoma – n with hematoma/N (%)	Hematoma – n with hematoma/N (%)	Pneumothorax – n with pneumothorax/N (%)	Pneumothorax – n with pneumothorax/N (%)	Nerve injury / neurological symptoms – n with nerve injuries/N (%)	Nerve injury / neurological symptoms – n with nerve injuries/N (%)
	[I]	[C]	[I]	[C]	[I]	[C]	[I]	[C]	[I]	[C]
(Iwashima et al 2008)	Femoral artery puncture 3/43 (7%)[b]	Femoral artery puncture 14/44 (32%)	NR	NR	NR	NR	NR	NR	NR	NR
(Miller et al 2002)	NR	NR	Overall complications[1] associated with the procedure 6/51 (12%)[ns]	Overall complications[1] associated with the procedure 10/71 (14%)						
(Ray et al 2013)	Carotid artery puncture 1/40 (2.5%)	Carotid artery puncture LM 3/40 (7.5%). UM 1/40 (2.5%)	NR	NR	0/40 (0%)	LM: 1/40 (2.5 %) UM: 0/40 (0%)	NR	NR	NR	NR
(de Carvalho Onofre et al 2012)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

Study	Adverse events on insertion – n with adverse event/N (%)	Adverse events on insertion – n with adverse event/N (%)	Procedural complication – n with complication /N (%)	Procedural complication – n with complication /N (%)	Hematoma – n with hematoma/N (%)	Hematoma – n with hematoma/N (%)	Pneumothorax – n with pneumothorax/N (%)	Pneumothorax – n with pneumothorax/N (%)	Nerve injury / neurological symptoms – n with nerve injuries/N (%)	Nerve injury / neurological symptoms – n with nerve injuries/N (%)
	[I]	[C]	[I]	[C]	[I]	[C]	[I]	[C]	[I]	[C]
Li et al. (2013)	NR	NR	Overall complications[2] 31/50 (62%)[ns]	Overall complications[2] 31/48 (64.6%)	NR	NR	NR	NR	NR	NR
			Mechanical phelebitis[2] 0/50 (0%)[c]	Mechanical phelebitis[2] 11/48 (22.9%)						
			Contact dermatitis[2] 18/50 (36%)[ns]	Contact dermatitis[2] 21/48 (43.8%)						
			Infection[2] 0/50 (0%)[ns]	Infection[2] 3/48 (6.3%)						
			Venous[2] thrombosis 0/50 (0%)[a]	Venous[2] thrombosis 4/48 (8.3%)						

Abbreviations: [C] comparator (landmark); [I], Ultrasound guided; LM: Landmark method; US: ultrasound

Data: mean ± SD; mean [95% CI or range]; median (range or percentile)

Significant difference ([I] vs [C]) indicated by superscript a, b, c or ns for $p < 0.05$, $p < 0.01$, $p < 0.001$ and not significant respectively

1 Overall complications included formation of a hematoma or the occurrence of a pneumothorax, cannulation of the artery, or improper cannulation into the thorax or soft tissues

2 Procedural complications were also reported for the first and second months

Table 88 Effectiveness of ultrasound compared to landmark for guidance of vascular access

Study	Needle redirects and/or skin punctures [I]	Needle redirects and/or skin punctures [C]	Success rate of placement n/N (%) [I]	Success rate of placement n/N (%) [C]	Time taken for needle placement [I]	Time taken for needle placement [C]	Other effectiveness outcomes [I]	Other effectiveness outcomes [C]
(Dudeck et al 2004)	Needle redirects: 1.93 ± 1.26[ns]	Needle redirects: 2.16 ± 1.62	NR	NR	3.46 min ± 2.06[ns]	3.28 min ± 2.75	NR	NR
(Killu et al 2011)	Needle redirects: 4.06 ± 2.86[ns] Skin punctures: 2.44 ± 1.72[ns]	Needle redirects: 10.00 ± 13.45 Skin punctures: 3.07 ± 2.96	18/18 (100%)[a]	11/15 (73%)	7.01 min ± 4.40[ns]	9.29 min ± 10.00	NR	NR
(Airapetian et al 2013)	Skin punctures: 1 ± 0	Skin punctures: LM: 3±1[c] UM: 3 ± 2[c]	36/36 (100%)[b]	LM: 28/38 (74%) UM: 32/44 (73%)	4 min ± 2[c]	LM: 8 min ± 7 UM: 10 min ± 9	NR	NR
(Hayashi and Amano 2002)	NR	NR	$US_{3.75\ MHz}$: 58/60 (96.7%)[ns] $US_{7.5\ MHz}$: 58/60 (96.7%)[ns] P($US_{3.75MHz}$ v $US_{7.5MHz}$)[NS]	112/120 (93.3%)	NR	NR	Access rate: $US_{3.75\ MHz}$: 51/60 (85%)[a] $US_{7.5\ MHz}$: 52/60 (86.7%)[a] P($US_{3.75MHz}$ v $US_{7.5MHz}$) [NS]	Access rate: 88/120 (73.3%)
(Iwashima et al 2008)	NR	NR	29/43 (67.4%)[ns]	26/44 (59.1%)	Time less than 5 min = 21/43 (48.8%)[ns]	Time less than 5 min = 21/44 (47.7%)	NR	NR
(Miller et al 2002)	Number of attempts 1.6 ±1.0[c]	Number of attempts 3.5 ± 2.7	NR	NR	1.91 min ± 3.05[c]	8.53 min ±11.63	NR	NR

Study	Needle redirects and/or skin punctures [I]	Needle redirects and/or skin punctures [C]	Success rate of placement n/N (%) [I]	Success rate of placement n/N (%) [C]	Time taken for needle placement [I]	Time taken for needle placement [C]	Other effectiveness outcomes [I]	Other effectiveness outcomes [C]
Ray et al 2013	NR	NR	38/40 (95%)[ns]	LM: 34/40 (85%), UM: 37/40 (92.5%)	Vascular access: 0.2 min (0.07-0.5)[a] Catheterisation 2.8 min (1.5-22.8)[a]	LM: Vascular access: 0.2 min (0.08-2.0) Catheterisation 3.8 min (1.5-41.3) UM: Vascular access: 0.2 min (0.07-1.0) Catheterisation 2.8 min (1.4-35.2)	NR	NR
(de Carvalho Onofre et al 2012)	NR	NR	18/21 (85.7%)[a]	11/21 (52.4%)	20 min (IQR 20-30)[c]	50 min (IQR 30-60)	Access rate 19/21 (90.5%)[b]	Access rate 10/21 (47.6%)

Study	Needle redirects and/or skin punctures [I]	Needle redirects and/or skin punctures [C]	Success rate of placement n/N (%) [I]	Success rate of placement n/N (%) [C]	Time taken for needle placement [I]	Time taken for needle placement [C]	Other effectiveness outcomes [I]	Other effectiveness outcomes [C]
Li et al. (2013)	NR	NR	50/50 (100%)	46/48 (96%)	NR	NR	Degree of comfort score Week 1 = 36.26 ± 5.23 [b] Month 1 =34.33 ± 4.92[c] Month 2 =33.21 ± 4.28[c] Month 3 32.18 ± 4.39[b] Unplanned catheter removal 2/50 (4%)[a] Tip malposition during placement 3/50 (6%)[ns] Tip malposition after placement 0/50 (0%)[ns]	Degree of comfort score Week 1 = 43.42 ± 7.4 Month 1 =40.35 ± 5.71 Month 2 =38.34 ± 6.26 Month 3 37.29 ± 5.97 Unplanned catheter removal 9/48 (18.7%) Tip malposition during placement 3/48 (6%) Tip malposition after placement 2/48 (4.2%)

Abbreviations: [C]; comparator (landmark); [I], Ultrasound guided; LM, landmark technique; NR, not reported; NS, not significant; Data: mean ± SD; mean [95% CI or range]; median (range or percentile or IQR)
Significant difference ([I] vs [C]) indicated by superscript a, b ,c or ns for $p < 0.05$, $p < 0.01$, $p < 0.001$ and not significant, respectively.

1 Needle redirects/skin punctures was not defined

2 Success rate of placement was defined as successful puncture and PICC placement ; 2 insertion attempts allowed, if 3rd = unsuccessful then considered a failure Li et al (2013). Failures included procedures aborted at discretion of operator when failure to cannulate and significant time had passed

3. Patients with successful cannulation were older and heavier: Success median weight = 15 kg (range 2.9-84.2) and age 4 years (range 2 months-18 years Unsuccessful: median weight 8.1 kg (range 4-18) and age 4 months (range 1 month – 5 years)

4 Time taken for needle placement was variably defined. Time taken from skin penetration until needle placement (ie setup time of US not included) Miller et al. (2002)(#161); time taken from when transducer applied to skin until placement of needle ; time taken from when fingers touched the skin to palpate for the artery until needle placement ; defined as time from skin preparation to placement of PICC .

Appendix N Study information, safety and effectiveness data from the randomised controlled trials: percutaneous nerve blockade

Table 89 Study information: Ultrasound guided nerve blocks performed peri-operative for anaesthesia / analgesia during surgery or as a procedure for pain management not related to surgery

Study	Country	Indication: PM = Pain MGMT PPO = Peri operative	N	Region / [nerve block]	Proceduralist	Population	Admin. (bolus or continuous infusion)	Comparator	Procedure / Surgery [Anaesthesia]
(Antonakakis et al 2010)	USA	Trial	36	Lower Limb [Deep peroneal nerve]	A single anaesthesiologist skilled in RA.	Adult	Bolus	LM	Procedure
(Bendtsen et al 2011)	Denmark	PPO	98	Lower Limb [Sciatic and Saphenous nerves]	Four staff anaesthesiologists with expertise in both nerve localisation techniques	Adults	Bolus	ENS	Surgery [RA with GA]
(Danelli et al 2009)	Italy	PPO	60	Lower Limb [Sciatic nerve]	Investigator with substantial expertise in RA techniques.	Adult	Bolus	ENS	Surgery [RA]
(Fredrickson and Danesh-Clough 2009)	New Zealand	PPO	45	Lower Limb [Sciatic nerve]	A single operator experienced in US guided RA.	Adult	Bolus	ENS	Surgery [RA with GA if RA not adequate to complete surgery]
(Kent et al 2013)[a]	USA	Trial	20	Lower Limb [Saphenous nerve]	Single procedurelist, experience not reported.	Adult	Bolus	LM	Procedure

Study	Country	Indication: PM = Pain MGMT PPO = Peri operative	N	Region / [nerve block]	Proceduralist	Population	Admin. (bolus or continuous infusion)	Comparator	Procedure / Surgery [Anaesthesia]
(Maalouf et al 2012)	USA	PPO	45	Lower Limb [Sciatic nerve at the posterior-medial (tibial component)]	NR	Adult	Bolus	ENS	Surgery [RA with S at discretion of anaesthetist]
(Min et al 2011)	China	PPO	120	Lower Limb [Femoral nerve]	Two anaesthesiologists experienced in ultrasound-guided peripheral nerve blocks and the use of nerve stimulators.	Adult	Bolus	ENS	Surgery [RA with GA]
(Ponde et al 2013)	India	PPO	60	Lower Limb [Sciatic block]	Anaesthesiologist with extensive experience in NS and US use.	Paediatric	Bolus	ENS	Surgery [RA plus GA]
(Redborg et al 2009)	USA	Trial	36	Lower Limb [Sural nerve]	NR	Adult	Bolus	LM	Procedure [RA]
(Reid et al 2009)[a]	Australia	PM	67	Lower Limb [Femoral nerve]	Emergency medicine specialists or senior registrars under direct supervision of the specialists.	Adult	Bolus	LM	Procedure [RA]
(Sala-Blanch et al 2012)	Spain	PPO	52	Lower Limb [Sciatic nerve]	NR	Adult	Bolus	ENS	Surgery [RA]
(Aveline et al 2011)	France	PPO	273	Trunk [TAP]	All blocks performed by three anaesthetists experienced in RA.	Adult	Bolus	LM	Surgery [GA plus RA]
(Faraoni et al 2010)	Belgium	PPO	40	Trunk [Dorsal penile nerve]	Anaesthesiologist experienced in US.	Paediatric	Bolus	LM	Surgery [GA plus RA]

Study	Country	Indication: PM = Pain MGMT PPO = Peri operative	N	Region / [nerve block]	Proceduralist	Population	Admin. (bolus or continuous infusion)	Comparator	Procedure / Surgery [Anaesthesia]
(O'Sullivan et al 2011)	Ireland	PPO	66	Trunk [Dorsal penile nerve]	All blocks performed or supervised by an experienced consultant (attending) anaesthetist.	Paediatric	Bolus	LM	Surgery [GA plus RA]
(Bloc et al 2010)	France	PPO	120	Upper Limb [Axillary fossa]	Four senior anaesthesiologists experienced in both techniques.	Adult	Bolus	ENS	Surgery [RA]
(Brull et al 2009)	Canada	PPO	103	Upper Limb [Infraclavicular brachial plexus]	All performed by one of four experienced regional anaesthesiologists.	Adult	Bolus	ENS	Surgery [RA]
(Danelli et al 2012)	Italy	PPO	50	Upper Limb [Interscalene brachial plexus]	Senior anaesthetists.	Adult	Bolus	ENS	Surgery [RA]
(Gorthi et al 2010)	South Korea	PM	50	Upper Limb [Suprascapular nerve]	All performed by one physician experience not reported.	Adult	Bolus	LM	Procedure
(Gurkan et al 2008)	Turkey	PPO	80	Upper limb [Sagittal infraclavicular block]	Either a specialist anaesthesiologist or senior resident with experience in lateral sagittal infraclavicular block	Adult	Bolus	ENS	Surgery [RA]
(Ko et al 2013)	Republic of Korea	PPO	42	Upper Limb [Suprascapular nerve]	NR	Adult	Bolus	ENS LM	Surgery [GA plus RA]
(Liu et al 2009b)	USA	PPO	230	Upper Limb [Brachial plexus]	Attending or trainee.	Adult	Bolus	ENS	Surgery [RA with S]

Study	Country	Indication: PM = Pain MGMT PPO = Peri operative	N	Region / [nerve block]	Proceduralist	Population	Admin. (bolus or continuous infusion)	Comparator	Procedure / Surgery [Anaesthesia]
(Ponde and Diwan 2009)	India	PPO	50	Upper Limb [Infraclaviular brachial block]	All blocks performed by 1st author (no detail on experience).	Paediatric	Bolus	ENS	Surgery [RA plus GA]
(Ponrouch et al 2010)	France	PPO	42	Upper Limb [Median and ulnar nerves]	Investigators who had substantial expertise in RA.	Adult	Bolus	ENS	Surgery [RA]
(Renes et al 2009)	Netherlands	PPO	30	Upper Limb [Interscalene Brachial plexus]	NR	Adult	Bolus	ENS	Surgery [RA plus GA]
(Salem et al 2012)	Germany	PPO	60	Upper Limb [Interscalene brachial plexus]	Anaesthetists with over 10 years' experience.	Adult	Bolus	ENS	Surgery [RA with or without S]
(Strub et al 2011)	Switzerland	PPO	141	Upper Limb [Axillary block for brachial plexus anaesthesia]	Non-anaesthesiologists all by same hand surgeon with training from experienced anaesthesiologist (>300 traditional procedures performed). 10 procedures performed before study started as basic experience.	Adult	Bolus	LM	Surgery [RA]
(Trabelsi et al 2013)	Tunisia	PPO	60	Upper Limb [Coracoid infraclavicular brachial plexus]	NR	Adult	Bolus	ENS	Surgery [RA]
(Tran et al 2010)	Canada	PPO	40	Upper Limb [Superficial cervical plexus]	Two experienced proceduralist who are familiar with both US and landmark technique.	Adult	Bolus	LM	Surgery [RA]

Study	Country	Indication: PM = Pain MGMT PPO = Peri operative	N	Region / [nerve block]	Proceduralist	Population	Admin. (bolus or continuous infusion)	Comparator	Procedure / Surgery [Anaesthesia]
(Zencirci 2011)	Turkey	PPO	60	Upper Limb [Axilliary brachial plexus]	Anaesthetist experience not reported.	Adult	Bolus	ENS	Surgery [RA]

Abbreviations: PM: pain management; PPO: perioperative; N: number of patients in trial; Admin: administration mode for anaesthetic agent; COMPTR: comparator; RA: regional anaesthesia; TAP: transversus abdominis plane; LM: landmark; ENS: electrical nerve stimulation; US: ultrasound; GA, general anaesthesia; NR: not reported; CS: conscious sedation; S: sedation.

Trial: these were randomised controlled trials conducted in healthy volunteers; as such the indication could not be considered surgery (PPO) or pain management (PM).

Superscript (a) indicates pseudo-RCTs (NHMRC LoE III-1) all other studies are of RCT design (NHMRC LoE II).

Table 90: Characteristics of patient / volunteer populations for include RCTs evaluating the ultrasound guided nerve blocks

Study	Indication description	Number: [I] [C]	M/F: [I] [C]	Age: [I] [C]	Inclusion criteria	Exclusion criteria	Number of patients excluded
Lower Limb							
(Antonakakis et al 2010)	Healthy volunteers	18 *	NR	36 yr (20 - 58)	Healthy volunteers with acceptance of written consent.	Abnormal sensory or motor examination result.	NA
(Bendtsen et al 2011)	patients scheduled for elective major foot and/or ankle surgery -	50	48	56.5 yr ± 14.7 56.2 yr ± 13.0	minimum age of 18 years, ASA physical status I-III, written informed consent, elective major foot or ankle surgery	neuropathy of the sciatic or femoral nerves, impaired sensory or motor function of the lower extremities, diabetic neuropathy, Charcot-Marie-Tooth disease, local infection in the popliteal fossa, systemic infection, coagulopathy, significant peripheral vascular disease, allergy to local anaesthetics, inability to comprehend the numeric rating scale, communicative disability, dementia, BMI greater than 35, need for bilateral surgery	2 after randomisation from the comparator group for protocol violation
(Danelli et al 2009)	Pain management for post-operative analgesia	30 30	21/9 18/12	46.3 yr ± 13.8 44.3 yr ± 12.1	ASA physical status I-II, aged between 18-80 and undergoing knee arthroscopy.	Coagulopahthy, infection at injection site, allergy to local anaesthetics, severe cardiopulmonary disease, body mass index >35, diabetes, neuropathies, opioid user for chronic pain.	NR
(Fredrickson and Danesh-Clough 2009)	Elective hamstring graft anterior cruciate ligament reconstruction (ACLR) and total knee joint replacement (TKJR).	21 24	13/8 15/9	49 yr ± 20.5 56 yr ± 20.5	All patients scheduled for elective hamstring graft anterior cruciate ligament reconstruction and total knee joint replacement by a single surgeon at a single centre from March to December 2008.	Patient refusal of femoral nerve block, known neuropathy involving the leg undergoing surgery, known allergy to amide local anaesthetic drugs, patients less than 85kg scheduled for bilateral TKJR.	2 elderly patients due to confusion during the post-operative period.

Study	Indication description	Number: [I] [C]	M/F: [I] [C]	Age: [I] [C]	Inclusion criteria	Exclusion criteria	Number of patients excluded
(Kent et al 2013)	Healthy volunteers	20*	20/0	> 18 years	Healthy males, ASA physical status I –II.	Patients aged < 18 years non-English speakers, history of chronic pain syndromes, central or peripheral neuropathies, and relative contraindications to regional anaesthesia, allergy to local anaesthetics, thyroid disease, and significant cardiopulmonary disease, not eligible for care at the treating military hospital.	NR
(Maalouf et al 2012)	Foot surgery	24 21	12/12 9/12	55 yr ± 13 54 yr ± 14)	ASA physical status I-III, patients undergoing major foot surgery with a planned hospital stay of more than 48 hours and requiring a sciatic nerve catheter.	ASA status greater than III, neurological deficit in the operative extremity, infection at site for block, allergy to local anaesthetics, pregnancy, diabetes, history of chronic opioid use.	9
(Min et al 2011)	Unilaterial total knee arthoplasty	60 60	17/43 [ns] 13/47	68 yr (57 - 75)[ns] 69 yr (55 - 74)	No clear inclusion criteria stated. However, all patients were 50 to 80 years old with an ASA physical status I – III.	Coagulation disorders, infection near the injection site, hypersensitivity or known allergy to any of the study drugs, difficulties in comprehending visual analogue scale pain scores, difficulty in using an intravenous patient-controlled analgesia device, pre-existing neurological disorders, patients receiving opioids for chronic analgesic therapy.	NR
(Ponde et al 2013)	NR	30 30	24/8** 19/11	11.7 mo ± 3.8 [ns] 12.2 mo ± 4.0	Written informed consent from patient's parents or guardians, children aged 6 months to 5 years with distal arthrogryposis multiplex congenita posted for surgical correction of congenital vertical talus.	Coagulopathies, cardiac and renal disorders.	None

Study	Indication description	Number: [I] [C]	M/F: [I] [C]	Age: [I] [C]	Inclusion criteria	Exclusion criteria	Number of patients excluded
(Redborg et al 2009)	Healthy volunteers to compare ultrasound-guided sural nerve bock with the landmark technique	18*	9/9	34 yr ± 9.6) years	Healthy volunteers with acceptance of written consent.	NR	NR
(Reid et al 2009)	Lower-limb fractures (neck of femur fracture n=42, shaft of femur fracture n=25)	34 33	13/21[ns] 8/25	81 yr (58 - 84)	Patients of any age presented to the Emergency Department with sustained acute extracapsular neck of femur fracture, femoral shaft and/or patella fractures with normal mental state.	Intracapsular neck of femur fractures, those unable to understand the consent or trial process, those with neurovascular injuries to the limb and those with allergies to bupivacaine.	NR
(Sala-Blanch et al 2012)	Hallus valgus repair	25 26	2/23 [ns] 1/25	58 yr ± 14[ns] 62 yr ± 12	ASA physical status I – III, scheduled outpatient hallux valgus repair surgery under sciatic popliteal block.	NR	1 withdrawn due to change in surgical intervention which required a perineural catheter for post-op PM.
Trunk							
(O'Sullivan et al 2011)	Circumcision	34 32	34/0[ns] 32/0	33.5 mo (22.5 - 81.0) [ns] 28.5 mo (24.0 - 42.0)	Written consent from parent, ASA physical status I-II, scheduled for day case circumcision.	Allergy to local anaesthetics, patients having an additional surgical procedure under the same GA as the circumcision.	None
(Aveline et al 2011)	Litchenstein technique - open repair of inguinal hernia with mesh	134 139	134/0[ns] 139/0	58 yr ± 13 [ns] 60 yr ± 12	Consecutive adults males of ASA physical status I-III, undergoing elective primary unilateral open inguinal hernia repair (with mesh) under combined GA US guided transversus adominis plane or ilioinguinal/iliohypogastric nerve block.	Inability to consent, age ≤ 18 years, body mass index ≥ 40, skin infection at the puncture site, contra-indication to ketoprofen, paracetamol or LA agents, chronic hepatic or renal failure, preoperative opioid or NSAID treatment for chronic pain.	2 after consent withdrawn

Study	Indication description	Number: [I] [C]	M/F: [I] [C]	Age: [I] [C]	Inclusion criteria	Exclusion criteria	Number of patients excluded
(Faraoni et al 2010)	Elective circumcision	20 20	20/0 20/0	2 yr (1 - 4) ns 2.25 yr(1 - 3.5)	Boys aged 1-14 years scheduled for elective circumcision in day case department.	Allergy to amino-amide local anaesthetics or a general contraindication for penile nerve block.	NR
Upper Limb							
(Bloc et al 2010)	Hand and distal arm surgery	40 US OOP 40 US IP 40 ENS	18/22 US OOP 19/21 US IP 22/18ENS	49 yr ± 12 USOOP 51 yr ± 14 USIP 46 yr ± 13 ENS	ASA physical status I–III, written consent.	Pregnancy, age ≤ 18 years, contraindication to regional anaesthesia, allergy to local anaesthetics, local infections at the site of puncture and treatment, coagulation abnormalities.	NR
(Brull et al 2009)	Hand Wrist or forearm surgery	52 51	33/19 34/17	46.8 yr ± 17.1 43.6 yr ± 15.7	Written consent, adults with ASA physical status I–III scheduled for elective elbow, forearm, wrist or hand surgery, patient of one of four hand surgeons at Toronto Western Hospital.	<18 years or >70 years, language barrier, contraindications to regional anaesthesia, weight >100 kg, pre-existing neurological deficit in the distribution to be anaesthetised, local infection, coagulopathy, chest or shoulder deformities, severe respiratory disease, clavicle fracture.	25 total (17 patients refused, 5 did not meet inclusion criteria, 3 excluded from analysis after randomisation as they did not receive the intervention)
(Danelli et al 2012)	Elective coracoacromial ligament repair	Total 50 Number per group NR	NR	50 yr [24 - 72][ns] 57 yr [32 – 79]	Written informed consent, ASA physical status I-III, patients undergoing elective coracoacromial ligament repair for rotator cuff disorders.	Patients < 18 years old or > 85 years old, inability to express informed consent, known allergy to study medications, chronic opioid use, ipsilateral upper limber neurological deficits, contraindications to continuous block placement.	None
(Gorthi et al 2010)	Chronic pain around the shoulder region	25 25	12/13 11/14	55.1 yr [40 - 72)] 51.6 yr [36 – 64]	Patients with pain around the shoulder area with normal range of movement and normal radiographs / MRIs.	Significant abnormalities such as rotator cuff tears, calcific tendonitis, wet bursitis and advanced adhesive capsulitis.	NR

Study	Indication description	Number: [I] [C]	M/F: [I] [C]	Age: [I] [C]	Inclusion criteria	Exclusion criteria	Number of patients excluded
(Gurkan et al 2008)	Elective hand wrist or forearm surgery	40 40	26/14 29/11	40 yr ± 16 37 yr ± 16	Patients scheduled for elective hand wrist and forearm surgery. ASA physical status I or II, ages 18-70	Patients who could not co-operate, those with a disease that could prevent sensory block assessment in the upper extremity, patients with coagulopathy, allergy to the study drugs, pregnancy, previous surgery or trauma preventing anatomic localisation of the injection point	NR
(Ko et al 2013)	Rotor cuff disease	21 US (15 analysed) 21 ENS (18 analysed) 21LM (19 analysed)	12/3 US[ns] 14/4 ENS 15/4 LM	42.8 yr ± 14.3 US ns 39.3 yr ± 14 ENS 40.8 yr ± 15.8 LM	Patients with rotor cuff disease diagnosed through MRI and scheduled for arthroscopic acromioplasty who refused or could not undergo interscalene block.	Coagulopathy, neurologic disorders, hypersensitivity to local anaesthetics, history of drug abuse, injection or antecedent surgery on the same shoulder, age > 18 years or < 75 years, ASA status above III, refusal to participate, inability to understand pain scale.	37 total (15 did not meet inclusion criteria, 21 declined participation, 1 was excluded for 'other reasons')
(Liu et al 2009b)	Shoulder surgery (5 diagnostic procedures; 81 rotator caff repairs, 17 stabilisations, 7 acromioclavicular joint resections, 16 debridements, 42 labral repairs, 46 decompressions, 5 'others')	115 115	NR	48 yr ±16 49 yr ±14)	Written informed consent, scheduled outpatient shoulder arthroscopy under interscalene block and sedation.	Aged < 18 years, > 75 years, typical contraindications to interscalene block (including: patient refusal, pregnancy, dementia, severe pulmonary disease, known pre-existing neurological disorders involving the operative limb).	169 total (36 requiring non-protocol treatment, 38 declined, 31 pre-existing neuropathy, 28 attending's contraindications, 36 excluded for 'other reasons'
(Ponde and Diwan 2009)	Radial club hand repair-centralisation of ulna	25 25	10/10** 14/6**	11.87 mo ± 0.19 [ns] 12.87 mo ± 1.19	ASA physical status I - II, children aged 1-2 years, scheduled for radial club hand repair (centraliation of the ulna).	Cardia, renal or neurological diseases and coagulopathies.	NR

Study	Indication description	Number: [I] [C]	M/F: [I] [C]	Age: [I] [C]	Inclusion criteria	Exclusion criteria	Number of patients excluded
(Ponrouch et al 2010)	Carpal tunnel release surgery	21 21	6/15 8/13	55 yr ± 17[ns] 56 yr ± 17	ASA status I –III, patients scheduled for ambulatory endoscopic or open pit carpal tunnel release surgery, aged 18 to 90 years.	Patients who did not cooperate, patients with psychological disorders or linguistic difficulties that might interfere with sensory block, coagulopathies, known allergy to trial drugs, infection at the puncture site, body mass index > 40, or < 19, diabetes mellitis or known neuropathies, patients who received opiates for chronic pain and cardiac conduction problems (third degree atrioventricular block).	4 total (2 with body mass index > 40, 1 with neuropathy, 1 who refused)
(Renes et al 2009)	Assessment of hemidiaphragmatic paresis	15 15	9/6 ns 5/10	50.3 [24 - 62] [ns] 51.9 [24 - 66]	Age 18 to 75, ASA physical status I to III.	Patients who refused or were unable to provide consent, hemidiaphragmatic dysfunction, coagulation disorders, neuropathy, pulmonary and / or cardiac disorders, body mass index over 35km/m2, pregnancy, allergy to local anaesthetics.	NR
(Salem et al 2012)	Shoulder surgery	30 30	19/11 14/16	56.5 (30-75) 60.5 (36 - 82)	Consecutive patients scheduled for shoulder surgery with written consent.	Patients with hypersensitivity to local anaesthetics, neurologic deficits, bleeding tendency, respiratory failure, local infection, non – compliance, refusal to participate in the study, request for general anaesthesia.	None
(Strub et al 2011)	Hand surgery	70 71	46/ 24 48/ 23	37 yr (16 - 89) 42 yr (17 - 88)	Scheduled for hand surgery distal to the elbow with estimated duration less than 2 hours	Declined consent Known allergy to any anaesthetic Infection in region of injection site Severe coagulopathy, Pathological enlargement of axillary lymph nodes Previous surgery on the axilla	None

Study	Indication description	Number: [I] [C]	M/F: [I] [C]	Age: [I] [C]	Inclusion criteria	Exclusion criteria	Number of patients excluded
(Trabelsi et al 2013)	NR	30 30	23/7 21/9	31 yr ±10 37 yr ±15	≥ 18 and ≤ 80 years ASA status I - III	No exclusion criteria reported	NR
(Tran et al 2010)	Pain suppression for post-operative analgesia	20 20	13 7 11 9	47 yr ± 18 46 yr ± 17	Age from 18 to 70 ASA status I – III BMI 20 to 35 Capacity of providing consent	Inability to consent Coagulopathy Hepatic or renal failure Allergy to local anaesthetics	NR
(Zencirci 2011)	NR	30 30	13 17 18 12	37. yr ± 16 40 yr ± 11	ASA status I – II Planned to undergo extremity operations through auxilliary brachial plexus block	Presence of cardiac, inspiratory Renal failure Pregnancy.	NR

* Healthy volunteers received both intervention and comparator blocks. Limb to receive each block was randomised.

**Male/Female numbers do not add up to total number of patients treated. Reason for this is unclear.

ASA Physical Status: grade I, a normal healthy patient; grade II, a patient with mild systemic disease; grade III, a patient with severe systemic disease, grade IV, a patient with severe systemic disease that is a constant threat to life; grade V, a moribund patient who is not expected to survive without the operation; grade VI, a declared brain-dead patient whose organs are being removed for donor purposes

Data: mean ± SD; mean [95% CI or range]; median (range or percentile

Significant difference ([I] vs [C]) indicated by superscript a, b, or ns for $p < 0.05$, $p < 0.01$, and not significant, respectively. Comparison without superscripts, statistical significance not reported or performed.

Table 91 Instrumentation type and settings used of ultrasound and electrical nerve stimulator guidance of percutaneous neural blockade

Study	Block location	Ultrasound probe, setting and device manufacturer [Ultrasound technique]	Needle	ENS device / settings	Needle
(Antonakakis et al 2010)	Lower	25 mm SLA 10MHz; SonoSite, SonoSite HFL, Bothell, WA, USA [Short axis image/out-of-plane]	1.5 inch, 22 gauge short-bevel needle, Precision Glide; Becton Dickinson, Franklin Lakes, NJ	NA	NA
(Bendtsen et al 2011)	Lower	General Electric's Logic E US machine, Jiangsu, China with a 12L-RS, large bandwidth, multifrequency linear probe 8-13 MHz [NR]	22G 100 mm insulated needle, Stimuplex A, B Braun Medical, Melsungen, Germany	Stimuplex HNZ 11. B Braun Medical stimulator set to deliver 1.5 mA current impulses of 0.1 ms duration at a frequency of 2 Hz. A distinct distal motor response at a current output ranging between 0.3-0.5 mA was sought in al patients	NR
(Danelli et al 2009)	Lower	Semiconvex 2 to 5 MHz probe LOGIQ e, GE Healthcare, Milan Italy [In-plane]	100mm 18 gauge , short bevel Teflon coated Tuchy needle, Locopex®	Plexygon nerve stimulator 1.5 mA 2 Hz	100mm 18 gauge , short bevel Teflon coated Tuchy needle Locopex®
(Fredrickson and Danesh-Clough 2009)	Lower	38mm 13-6 MHz linear US probe SonoSite HFL, Sonosite, Bothell, WA, USA with Sonosite Mturbo/MicroMax/180 Ultrasound [Coronal plane]	51mm insulated Tuohy needle, Contiplex Tuohy, B. Braun, Bathlehem, PA, USA	Nerve stimulator set at 1.0mA (pulse width 0.1ms). Pajunk Vario, Tucker, GA, USA	51mm insulated Tuohy needle. Contiplex Tuohy, B. Braun, Bathlehem, PA, USA.
(Kent et al 2013)	Lower	6 to 13 MHz linear probe M-turbo, Sonosite, Bothell, WA or Logiq E, GE Healthcare, San Francisco, CA [In-plane]	22G, 100mm Touchy needle	NA	NA

Study	Block location	Ultrasound probe, setting and device manufacturer [Ultrasound technique]	Needle	ENS device / settings	Needle
(Maalouf et al 2012)	Lower	Curvilinear 5-8 MHz probe ,SonoSite C11, SonoSite, Bothell, WA, USA NS 2.0Hz, 1mA, 0.1s to confirm placement [In-plane, ENS to confirm the US placement]	18G insulated needle, Contiplex Tuohy. B. Braunm Bethleham, PA, USA	Nerve stimulator, not reported Initial frequency of 1.0 mA and frequency of 2.0 Hz, pulse duration 0.1 ms. Planter flexion or inversion of the foot at a current less than 0.5 mA was accepted	18-G insulated needle. Contiplex Tuohy, B. Braunm Bethleham, PA, USA.
(Min et al 2011)	Lower	SonoSite 5cm HFL38e, 8-12-MHz linear probe, MicroMaxx; SonoSite, USA [Short axis out-of-plane]	19-G × 50mm stimulating needle, Stimulong Plus and 20-G × 50cm stimulating catheter, Plexolong Catheter Set, Pajunk, Germany	Stimplex HNS11. Braun, Germany Control: Initial stimulating current: set at 1 mA, 2 Hz, and 0.3 ms The needle was repositioned until the stimulating current was 0.5 mA or less. Intervention: US needle advance until quadriceps muscle contractions were elicited at a current of 0.5 mA or less.	Stimulong Plus Plexolong Catheter Set was used with a 19-G × 50-mm stimulating needle and 20-G × 50-cm stimulating catheter. Pajunk, Germany.
(Ponde et al 2013)	Lower	10 MHz high frequency probe, Sonosite Micromax [Transverse axis, in-plane]	NR	Stimuplex DIG RC. B Braun Sciatic block: A current of 1.5 mA was used to locate the nerve. Femoral nerve block: Quadricep contractions at 0.5 mA were taken as the endpoint	24 G, 5 cm insulated needle. Braun, Melsungen, Germany.
(Redborg et al 2009)	Lower	SonoSite, 25mm linear transducer SLA 13Mhz, SonoSite, Bothell WA [Short axis out-of-plane]	22 gauge b-beveled needle. Precision Glide, Becton Dickenson Frankin Lakes NJ	NA	NA

Study	Block location	Ultrasound probe, setting and device manufacturer [Ultrasound technique]	Needle	ENS device / settings	Needle
(Reid et al 2009)	Lower	Linear array probe 7-9MHz, with GE Logic 200 Pro Series, GE Healthcare, Chalfont, St. Giles, UK [Transverse axis]	22G short bevelled needle	NA	22G short bevelled needle
(Sala-Blanch et al 2012)	Lower	L38 linear transducer 6-13 MHz, Micromax, SonoSite, Bothell, WA [Out-of-plane, ENS to confirm placement]	22G 50mm short-bevel stimulating needle, Stimuplex D 50. B. Braun, Melsungen AG, Germany	Stimuplex HNS. B Braun, Melsungen AG, Germany Initially set to deliver 1.5mA (2Hz, 0.1 ms) stimulus. Plantar flexion between 0.2 and 0.5 mA considered successful	22G 50mm short-bevel stimulating needle, Stimuplex D 50. B. Braun, Melsungen AG, Germany.
(O'Sullivan et al 2011)	Thorax / Abdomen	SonoSite "hockey stick" probe 6-13 MHz, 25 mm with Sonosite M-Turbo, Sonosite, Bothell WA USA [In-plane]	23 G 1 1/4 inch hypodermic needle	NA	NR
(Aveline et al 2011)	Throax / abdomen	Linear array transducer probe 6-13 MHz connected to portable ultrasound unit, S-Nerve, SonoSite, Bothell, WA, USA [In-plane]	22G 80 mm short bevel needle. Uniplex Nanoline, Pajunk, Germany	NA	NR
(Faraoni et al 2010)	Throax / abdomen	Probe 13-6 MHz, 38 mm broadband linear array, SonoSite, Bothell, WA [In-plane]	23 G Terumo Neolus Needle 0.6x25 mm. Leuven, Belgium	NA	NR
(Bloc et al 2010)	Upper	Linear, 8 - 13MHz US probe, LOGIQe; GE Healthcare, Piscataway, NJ, USA [Out-of-plane, in-plane]	22G 50 mm, 30 degree bevel, insulated needle	Nerve stimulator with a stimulating frequency of 1Hz and pulse duration of 100 us. The intensity of the current was 1.5mA . Stimuplex HNS 12; B Braun	22 gauge, 30 degree bevel, 50 mm insulated needle

Study	Block location	Ultrasound probe, setting and device manufacturer [Ultrasound technique]	Needle	ENS device / settings	Needle
(Brull et al 2009)	Upper	Linear 7-13 MHz Philips/ATL HDI 5000 ultrasound, Philips Medical systems, Bothell, WA, USA or 5-12 MHz Philips HD11 Ultrasound (Philips Medical systems, Bothell, WA, USA) [In-plane]	22G 50-80 mm insulated needle, Stimuplex. B. Braune Medical, Bethleham, PA, USA	Nerve Stimulator. Stimuplex, Braun, Medical, bethlehem, PA USA Two of the following endpoints were sought: lateral cord stimulation (elbow flexion, finger flexion or Thumb opposition posterior cord stimulation (wrist extension) medial cord stimulation (finger flexion, thumb or wrist adduction) at a minimum threshold current of 0.3-0.5 mA	sterile 22 G 50 -80 mm insulated needle. Stimuplex, B. Braune Medical, Bethleham, PA, USA
(Danelli et al 2012)	Upper	5 cm linear 10-12 MHz probe LOGIQ E; GE Healthcare, Milan, Italy [Short axis]	18 G, 50 mm, short-bevel	Nerve stimulator, Not reported. Initially set up to deliver 1.0 mA intensity (2 Hz, 0.2 mg). Reduced to 0.5 mA.	18 G, 35 mm, short-bevel
(Gorthi et al 2010)	Upper	8-12MHz probe, Accuvix XQ® ,Medison, Seoul Korea [Long axis]	10cm long 23 gauge needle	NA	NR
(Gurkan et al 2008)	Upper	6-13 MHz linear transducer connected to a Micromaxx or M-turbo or ultrasound unit, Sonosite, Bothell, WA, USA	Contiplex catheter 20 G 400 mm. Braun Melsungen, Germany	Stimuplex HNS 12, Braun stimulator set to deliver 1.5 mA current initially then reduced to 0.5 mS current. Frequency 2 Hz, stimulation duration of 100 μs. If no response the needle was repositioned.	NR

Study	Block location	Ultrasound probe, setting and device manufacturer [Ultrasound technique]	Needle	ENS device / settings	Needle
(Ko et al 2013)	Upper	5-12 MHz linear array transducer, Philips Medical Systems, Eindhoven, The Netherlands [Transducer aligned with the long axis to supraspinatus muscle]	US group: 3.5 inch 20G spinal needle.	Nerve Stimulator, Medelec Synergy. Vickers medical, Surrey, England. Initial stimulation of 1 Hz, 0.2 ms and 5 mA used to locate nerve by monitoring the amplitude of motor action potential on the monitor where maximum motor action potential was achieved with an intensity of less than 0.5 mA.	NS/LM: 22G teflon covered double lumen inclined cannula. Myojet Disposable hypodermic Needle Electrode, TECA Accessories, Oxford, NY.
(Liu et al 2009b)	Upper	Linear Probe, 10-13 MHz ultrasound probe, manufacturer and model not reported [In-plane]	50mm, 22 g Stimuplex® insulated needle. B Braun Medical.	Nerve stimulator, Not reported Initial 0.6-1.5 mA at 2 Hz needle repositioned so a motor response was present at currents between 0.2 -0.5 mA only	50mm, 22 g Stimuplex® insulated needle. B Braun Medical Bethlehem, PA USA.
(Ponde and Diwan 2009)	Upper	5-10 MHz, 38 mm linear array probe with SonoSite Titam Ultrasound [Parasagital plane and in-plane]	24 G, 50mm insulated needle. Braun, Melsungen, Germany	Nerve stimulator. B Braun Stimuplex Dig RC Ser. No. 10218. Motor response at wrist elicited at current of 0.5mA (250 ms pulse duration)	24 G, 50mm insulated needle. Braun, Melsungen, Germany.
(Ponrouch et al 2010)	Upper	linear probe set to 12 MHz with Logic E Ultrasound (GE Healthcare machine) [Short axis in-plane]	50 mm 22G needle Uniplex nanoLine Facet. Pajunk, Germany	Nerve stimulator, MultiStim Sensor. Pajunk, Germany. Initially set at pulse duration 0.1 ms, intensity 1.5 mA at 2Hz.	50 mm 22G needle, Uniplex nanoLine Facet. Pajunk, Germany.
(Renes et al 2009)	Upper	SonoSite HFL, 38mm broadband 6-13MHZ linear array US probe, SonoSite, Bothell, Wash [Short axis in-plane]	5cm 22 guage insulated needle. Braun, Melsungen, Germany	Nerve Stimulator HNS11. Braun, Melsungen Germany. 0.2 to 0.5mA with a pulse duration of 0.1 millisecond at 2 Hz	5cm 22 guage insulated needle. Braun, Melsungen, Germany.

Study	Block location	Ultrasound probe, setting and device manufacturer [Ultrasound technique]	Needle	ENS device / settings	Needle
(Salem et al 2012)	Upper	NR	Simpulex D 55 mm 15° bevel, 22 G insulated needle	Nerve Stimulator - HNS 12. Braun, Melsungen Germany. Initial current intensity of 1.0 mA reduced to 0.2 to 0.3 mA, frequency of 2 Hz and impulse duration of 0.1 ms.	Simpulex D 55 mm 15° bevel, 22 G insulated needle
(Strub et al 2011)	Upper	5MHz linear transducer with mobile US device, SononSIte	20G 1.5 inch bevelled needle with 10 mL syringe	NA	NA
(Trabelsi et al 2013)	upper	10-12 MHz linear probe with Logiq 7, GE Healthcare USA [In-plane]	22G insulated needle, Echoplex D 50 mm, Vygon, France	Nerve Stimulator, Stimuplex DIG RC. Braun Melsungen, Germany. Initial current 1-1.5 mA, when brachial plexus reached at 6-8cm current decreased until desired response present at 0.3 mA or less. Twitches of triceps, forearm and hand muscles were acceptable	22G insulated needle, Echoplex D 50 mm. Vygon, France.
(Tran et al 2010)	upper	6 to 13 MHz linear probe SonoSite Turbo, SonoSite Inc, Bothell, Wash [Coronal plane and in-plane]	1.5 inch 22 gauge needle precision Glide. Becton Dickinson, Franklin Lakes NJ USA	NA	1.5 inch 22 gauge needle
(Zencirci 2011)	upper	Aloka SSD-4000, Japan, 10 MHz probe [NR]	22G insulated needle, Stimuplex D 50 mm. B.Braun, Germany	Nerve Stimulator Stimuplex DIG RC. Braun Melsungen, Germany. No settings reported	22G insulated needle, Stimuplex D 50 mm. B.Braun, Germany.

Table 92 Safety of ultrasound compared to landmark alone or landmark plus nerve stimulation for guidance of lower limb neural blockade

Study	Adverse events on insertion – n with adverse event/N (%) [I]	Adverse events on insertion – n with adverse event/N (%) [C]	Procedural complications – n with complication /N (%) [I]	Procedural complications – n with complication /N (%) [C]	Hematoma – n with hematoma/N (%) [I]	Hematoma – n with hematoma/N (%) [C]	Nerve injury / neurological symptoms – n with nerve injuries/N (%) [I]	Nerve injury / neurological symptoms – n with nerve injuries/N (%) [C]
(Antonakakis et al 2010)	Paraesthesia 3/18 (17%)	Paraesthesia 2/18 (11%)	NR	NR	NR	NR	NR	NR
(Bendtsen et al 2011)	Paraesthesia 0/50 (0%)	Paraesthesia 0/48 (0%)	Infection 0/50 (0%)	Infection 0/48 (0%)	0/50 (0%)	0/48 (0%)	NR	NR
(Danelli et al 2009)	NR	NR	NR	NR	NR	NR	0/30 (0%) [1]	0/30 (0%) [1]
(Fredrickson and Danesh-Clough 2009)	NR	NR	Cardiac toxicity 0/21 (0%) [1]	Cardiac toxicity 0/24 (0%) [1]	NR	NR	At 24h post-surgery Muscle weakness [2] 0/21 (0%)	At 24h post-surgery Muscle weakness [2] 2/24 (8.3%)
(Kent et al 2013)	0/20 (0%) [1]	0/20(0%) [1]	NR	NR	0/20 (0%) [1]	0/20 (0%) [1]	0/20 (0%) [1, 3]	0/20 (0%) [1, 3]
(Maalouf et al 2012)	NR	NR	NR	NR	NR	NR	NR	NR
(Min et al 2011)	Arterial puncture 1/60 (1.6%)[ns]	Arterial puncture 5/60 (8%)	NR	NR	0/60 (0%) [1]	0/60 (0%) [1]	0/60(0%) [1]	0/60 (0%) [1]
(Ponde et al 2013)	NR	NR	NR	NR	NR	NR	NR	NR
(Redborg et al 2009)	NR	NR	Dysesthesia 1/18 (5.5%) Pain [4] 1/18 (5.5%)	Dysesthesia 0/18 (0%) Pain [4] 3/18 (16.5%)	0/18 (0%)	1/18 (5.5%)	Dysfunction or paraesthesia at 1 week follow-up [5] 0/18 (0%)	Dysfunction or paraesthesia at 1 week follow-up [5] 0/18 (0%)

Study	Adverse events on insertion – n with adverse event/N (%) [I]	Adverse events on insertion – n with adverse event/N (%) [C]	Procedural complications – n with complication /N (%) [I]	Procedural complications – n with complication /N (%) [C]	Hematoma – n with hematoma/N (%) [I]	Hematoma – n with hematoma/N (%) [C]	Nerve injury / neurological symptoms – n with nerve injuries/N (%) [I]	Nerve injury / neurological symptoms – n with nerve injuries/N (%) [C]
(Reid et al 2009)	Vascular events 0/34 (0%) [1]	Vascular events 0/33 (0%) [1]	Infection 0/34 (0%) [1]	Infection 0/33 (0%) [1]	NR	NR	NR	NR
(Sala-Blanch et al 2012)	Paresthesia 1/25 (4%) Sensory (heat, cold or tingling) 7/25 (28%)[ns]	Paresthesia 2/ 26(8%) Sensory (heat, cold or tingling) 2/26 (8%)	NR	NR	NR	NR	Residual sensory-motor deficit or symptoms of neurologic injury at 24 h, 1 week and 30 days after surgery 0/25 (0%) [1]	Residual sensory-motor deficit or symptoms of neurologic injury at 24 h, 1 week and 30 days after surgery 0/26 (0%) [1]

Abbreviations: MB, motor block SB, sensory block; [C] comparator (nerve stimulation or landmark); [I], Ultrasound guided

Data: mean ± SD; mean [95% CI or range]; median (range or percentile)

Significant difference ([I] vs [C]) indicated by superscript a, b, c or ns for $p < 0.05$, $p < 0.01$, $p < 0.001$ and not significant respectively

[1] Numeric data inferred from textual reporting

[2] Patients suffered minor falls

[3] Post-block there was recovery of full motor function and no difficulty in ambulation

[4] Pain at injection site at 24h post-procedure

[5] Assessed by telephone follow-up

Table 93 Safety of ultrasound compared to landmark alone or landmark plus nerve stimulation for guidance of trunk neural blockade

Study	Adverse events on insertion – n with adverse event/N (%)	Adverse events on insertion – n with adverse event/N (%)	Procedural complications – n with complication/N (%)	Procedural complications – n with complication/N (%)	Hematoma – n with haematoma/N (%)	Hematoma – n with haematoma/N (%)	Nerve injury / neurological symptoms – n with nerve injuries/N (%)	Nerve injury / neurological symptoms – n with nerve injuries/N (%)
	[I]	[C]	[I]	[C]	[I]	[C]	[I]	[C]
(Aveline et al 2011)	NR	NR	0/134 (%) [1]	Femoral extension of the RA block [2] 1/139 (0.7%)	NR	NR	NR	NR
(Faraoni et al 2010)	NR	NR	0/20 (0%) [1]	0/20 (0%) [1]	NR	NR	NR	NR
(O'Sullivan et al 2011)	NR	NR	0/34(%) [1]	0/32(%) [1]	NR	NR	NR	NR

Abbreviations: [C] comparator (nerve stimulation or landmark); [I], Ultrasound guided; NR, not reported; RA, regional anaesthesia

[1] Numeric data inferred from textual reporting, authors state that no complications were recorded.

[2] Patient was admitted to surgical ward and discharge the following day after a complete recovery

Table 94 Safety of ultrasound compared to landmark alone or landmark plus nerve stimulation for guidance of upper limb nerve blocks

Study	Adverse events on insertion- n with adverse event/N (%) [I]	Adverse events on insertion- n with adverse event/N (%) [C]	Procedural complications – n with complication/N (%) [I]	Procedural complications – n with complication/N (%) [C]	Haematoma – n with haematoma/N (%) [I]	Haematoma – n with haematoma/N [C]	Nerve injury / neurological symptoms – n with nerve injuries/N (%) [I]	Nerve injury / neurological symptoms – n with nerve injuries/N (%) [C]
(Bloc et al 2010)	Vascular puncture 0/40 (0 %) [ns]	Vascular puncture 0/40 (0%)	On injection Transient paraesthesia 0/40 (0%) [ns]	On injection Transient paraesthesia 1/40(5%)	NR	NR	NR	NR
(Brull et al 2009)	Vascular puncture 3/52 (6%)[ns]	Vascular puncture 4/49(8%)	Skin infiltration 0/52 (0%)[ns] Tachycardia [2] 0/52 (0%)[ns]	Skin infiltration 1/49 (2%) Tachycardia [2] 1/49 (2%)	NR	NR	Paraesthesia 3/52 (6%)[c]	Paraesthesia 22/49 (45%)
(Danelli et al 2012)	NR	NR	Accidental aspiration of blood 0/25 (0 %)[a] [1] Rop toxicity 0/25 (0%) [1]	Accidental aspiration of blood 3/10 (30%)[3] Rop toxicity 0/25 (0%) [1]	NR	NR	Neurological deficits 0/25(0%) [1]	Neurological deficits 0/25 (0%) [1]
(Gorthi et al 2010)	None	None	NA	NA	0/25 (0%)[1]	2/25 (8%)	0/25 (0%)	Prolonged neurological effects at 2 months 3/25 (12%)
(Gurkan et al 2008)	Vascular puncture 0/40 (0%) Paraesthesia 0/40 (0%)	Vascular puncture 3/40 (7.5%) Paraesthesia 0/40 (0%)	Drug toxicity 0/40 (0%)	Drug toxicity 0/40 (0%)	0/40 (0%)	0/40 (0%)	NR	NR

Study	Adverse events on insertion- n with adverse event/N (%) [I]	Adverse events on insertion- n with adverse event/N (%) [C]	Procedural complications – n with complication/N (%) [I]	Procedural complications – n with complication/N (%) [C]	Haematoma – n with haematoma/N (%) [I]	Haematoma – n with haematoma/N [C]	Nerve injury / neurological symptoms – n with nerve injuries/N (%) [I]	Nerve injury / neurological symptoms – n with nerve injuries/N (%) [C]
(Ko et al 2013)	NR	NR	Serious complications [4] 0/15 (0%)	Serious complications [4] 0/19 (0%)	NR	NR	NR	NR
(Liu et al 2009b)	NR	NR	Post-operative pain at injection site 16/111 (14%) [ns]	Post-operative pain at injection site 23/108 (21%)	NR	NR	Post-operative neurological outcomes: At 1w 9/111 (8%) of patients reported moderately severe symptoms [ns] At 4w 7/111 (6%) of patients reported mildly severe symptoms [ns]	Post-operative neurological outcomes: At 1w 12/108 (11%) of patients reported moderately severe symptoms At 4w 8/108 (7%) of patients reported mildly severe symptoms
(Ponde and Diwan 2009)	NR	NR	No complications related to RA technique 0/20 (0%) [1]	No complications related to RA technique 0/20 (0%) [1]	NR	NR	NR	NR
(Ponrouch et al 2010)	NR	NR	Adverse events 0/21 (0%)	Adverse events 0/21 (0%)	NR	NR	NR	NR

Study	Adverse events on insertion- n with adverse event/N (%) [I]	Adverse events on insertion- n with adverse event/N (%) [C]	Procedural complications – n with complication/N (%) [I]	Procedural complications – n with complication/N (%) [C]	Haematoma – n with haematoma/N (%) [I]	Haematoma – n with haematoma/N [C]	Nerve injury / neurological symptoms – n with nerve injuries/N (%) [I]	Nerve injury / neurological symptoms – n with nerve injuries/N (%) [C]
(Renes et al 2009)[5]	NR	NR	Ventilatory function at 30min [6] FEV 2.3L ± 0.67 [c] FVC 2.9L ± 0.93 [c] PEF 304L/min ± 111.7 [c]	Ventilatory function at 30min [6] FEV 1.8L ± 0.46 FVC 2,1L ± 0.58 PEF 266L/min ± 86	NR	NR	Horner's Syndrome 3/15 (20%) [ns] Hemidiaphragmatic paresis 2/15 (13%) [c]	Horner's Syndrome, 7/14 (46%) Hemidiaphragmatic paresis 14/15 (93%)
(Salem et al 2012)	NR	NR	Bloody tap 0/30 (0%) [ns]	Bloody tap n/N 1/30 (3.3%)	NR	NR	Incidence of Horner's Syndrome, recurrent laryngeal nerve palsy, phrenic nerve stimulation of paraesthesia 5/30 (16%) [ns]	Incidence of Horner's Syndrome, recurrent laryngeal nerve palsy, phrenic nerve stimulation of paraesthesia 4/30 (13%)
(Strub et al 2011)	NR	NR	Overall complications 5/70 (7%) [ns]	Overall complications 9/71 (13%)	2/70 (3%)	5/71 (7%)	Upper arm pain 8/70(11%)[a] Prolonged axilla pain 1/70 (1.4%) Neuralgia (hand) 0/70 (0%)	Upper arm pain 20/71 (28%) Prolonged axilla pain 3/71 (4.3%) Neuralgia (hand) 2/71 (2.8%)
(Trabelsi et al 2013)	NR	NR	NR	NR	NR	NR	NR	NR

Study	Adverse events on insertion- n with adverse event/N (%) [I]	Adverse events on insertion- n with adverse event/N (%) [C]	Procedural complications – n with complication/N (%) [I]	Procedural complications – n with complication/N (%) [C]	Haematoma – n with haematoma/N (%) [I]	Haematoma – n with haematoma/N [C]	Nerve injury / neurological symptoms – n with nerve injuries/N (%) [I]	Nerve injury / neurological symptoms – n with nerve injuries/N (%) [C]
(Tran et al 2010)	Vascular puncture 0/20 (0%) [1]	Vascular puncture 0/20 (0%) [1]	RA toxicity 0/20 (0%) [1]	RA toxicity 0/20 (0%) [1]	NR	NR	Brachial plexus block 0/20 (0%) Horner Syndrome 0/20 (0%) Transient paraesthesia (cervical plexus region) at 1week follow-up 1/20 (5%) Hoarseness 1/20 (5%) Difficulty swallowing 1/20(5%)	Brachial plexus block 0/0(0%) Horner Syndrome 0/20 (0%) Transient paraesthesia (cervical plexus region) at 1week follow-up. 0/20 (0%) [1] Hoarseness 0/20 (0%) [1] Difficulty swallowing 0/20 (0%) [1]
(Zencirci 2011)	Vascular punctures 0/30 (0%) [1]	Vascular punctures 0/30 (0%) [1]	Cardiovascular side effects 0/30 (0%) [1]	Cardiovascular side effects 0/30(0%) [1]	NR	NR	Adverse neurological symptoms 0/30 (0%) [1]	Adverse neurological symptoms 0/30 (0%) [1]

Abbreviations: [C] comparator (nerve stimulation or landmark); [I], Ultrasound guided; RA, regional anaesthesia; Rop, ropivaciane

Significant difference ([I] vs [C]) indicated by superscript a, b, c or ns for $p < 0.05$, $p < 0.01$, $p < 0.001$ and not significant respectively

[1] Numeric data inferred from textual reporting

[2] Tachycardia; surrogated marker for intravascular injection of anaesthetic agent

[3] Author explicitly state that 3 patient (30%) had aspiration of blood. These data indicates that N=10, no explanation for this apparent loss of patients is reported.

[4] Serious complications defined as sizure, cardiovascular collapse or pneumothorax

[5] This study is an adverse event study focused on hemidiaphragmatic paresis

[6] Ventilatory functions: FEV, forced expiratory volume; FVC, forced vital capacity; PEF, peak expiratory flow

Table 95: Effectiveness of ultrasound compared to landmark alone or landmark plus nerve stimulation for guidance of lower limb nerve blocks

Study	Needle redirects and/or skin punctures	Needle redirects and/or skin punctures	Block failures - n with failure/N (%)	Block failures - n with failure/N (%)	Time taken for needle or catheter placement	Time taken for needle or catheter placement	Nerve block characteristics	Nerve block characteristics	Injected volume	Injected volume
	[I]	[C]	[I]	[C]	[I]	[C]	[I]	[C]	[I]	[C]
(Antonakakis et al 2010)	Needle redirects 3 (1-9)	Needle redirects 2 (1-7)	NR	NR	143 s [77 –243][b]	81 s [44–144]	Maximal block at 20 to 30 min at 10min • lack of sensation to cold SB[a] • loss of motor function[a]	Maximal block at 20 to 30 min at 10min • lack of sensation to cold SB • loss of motor function	5 mL 2-CHP	5 mL 2-CHP
(Bendtsen et al 2011)	1 (1-6)[c]	2 (1-10)	3/50 (6%)[a]	10/48 (20.8%)	NR	NR	NR	NR	30 mL Rop	30 mL Rop
(Danelli et al 2009)	Needle redirects 3 [0-9]	Needle redirects 3 [0-15]	NR	NR	3 min (1–20)	4 min (1– 20)	NR	NR	12 mL[b] $MEAV_{50}$ 0.5% Mep	19 mL $MEAV_{50}$ 0.5% Mep
(Fredrickson and Danesh-Clough 2009)	Needle redirects[1] 0/21 (0%)	Needle redirects[1] 5/24 (20.8%)	0/21 (0%)[2]	1/24 (4.2%)[2]	Needle time under skin: 58 s (51–86)[c]	Needle time under skin: 120 s (95–178)	NR	NR	At placement 20 mL Rop followed by infusion of Rop at 2 mL/h plus PCA 5 mL max/h	At placement 20 mL Rop followed by infusion at 2 mL/h plus PCA 5 mL max/h

Study	Needle redirects and/or skin punctures	Needle redirects and/or skin punctures	Block failures - n with failure/N (%)	Block failures - n with failure/N (%)	Time taken for needle or catheter placement	Time taken for needle or catheter placement	Nerve block characteristics	Nerve block characteristics	Injected volume	Injected volume
	[I]	[C]	[I]	[C]	[I]	[C]	[I]	[C]	[I]	[C]
(Kent et al 2013)	NR	NR	MVM 4/20 (20%)[b] PF 0/20 (0%)[c]	LM 14/20 (70%)	MVM 4.3 min PF 3.0 min[b]	LM 3.6 min	Sensory loss MVM 7.7 min (n=16) PF 5.9 min (n=20)	Sensory loss LM 10.0 min (n=6)	10 mL 1.5% Lid	10 mL 1.5% Lid
(Maalouf et al 2012)	NR	NR	0/24 (0%)[3]	0/21 (0%)[3]	NR	NR	Duration of block 3.5 h ± 1.6	Duration of block 4 h ± 1.7	At placement 30 mL 0.5% Bup with Epi Post-op 0.2% Rop Cumulative Rop use 50 mL in 48 h[c]	At placement 30 mL 0.5% Bup with Epi Post-op 0.2% Rop Cumulative Rop use 197 mL in 48 h
(Min et al 2011)	Needle redirects[4] 5.5±0.3[a]	Needle redirects[4] 8.0±0.7	NR	NR	Insertion of catheter 9.0 min (6.0–22.8)[a]	Insertion of catheter 13.5 min (6.0–35.9)	63.3% of patients had complete SB at 30 min[a]	3% of patients had complete SB at 30 min	At placement 20 mL 1.5 % Lid After 30 min: 0.2% Rop at 5mL /h for 48 h	At placement 20 mL 1.5% Lid After 30 min: 0.2% Rop at 5mL/h for 48 h

Study	Needle redirects and/or skin punctures	Needle redirects and/or skin punctures	Block failures - n with failure/N (%)	Block failures - n with failure/N (%)	Time taken for needle or catheter placement	Time taken for needle or catheter placement	Nerve block characteristics	Nerve block characteristics	Injected volume	Injected volume
	[I]	[C]	[I]	[C]	[I]	[C]	[I]	[C]	[I]	[C]
(Ponde et al 2013)	NR	NR	1/30 (3%)[a]	7/30 (23%)	NR	NR	Duration of analgesia 8.6 h ± 0.66[c]	Duration of analgesia 7.6 h ± 0.57	Sciatic nerve block 0.5 mL/kg of 0.25% Bup Femoral nerve block 0.7 mL/kg of 1% Lig	Sciatic nerve block 0.5 mL/kg of 0.25% Bup Femoral nerve block 0.7 mL/kg of 1% Lig
(Redborg et al 2009)	Needle redirects 1.6±1.3	Needle redirects 1.6±2.0	NR	NR	173 s ± 84[b]	71 s ± 22	At 10 min 78% of patients had sensory loss to cold[b] at 60 min 33% of patients maintain block[a]	At 10 min 28% of patients had sensory loss to cold at 60 min 6% of patients maintain block	5 mL 3% 2-CHP	5 mL 3% 2-CHP
(Reid et al 2009)	NR	NR	NR	NR	NR	NR	Degree of block at 15 min[a] none 26.5% partial 44.1% complete 29.4% Degree of block at 60 min[ns] none 12.5% partial 34.4% complete 53.1%	Degree of block at 15 min none 42.4% partial 51.5% complete 6.1% Degree of block at 60 min none 24.2% partial 48.5% complete 27.3%	0.5% Bup 0.3 mL/ kg up to a maximum dose of 20 mL Restricted on safety issues	0.5% Bup 0.3 mL/ kg up to a maximum dose of 20 mL Restricted on safety issues

Study	Needle redirects and/or skin punctures	Needle redirects and/or skin punctures	Block failures - n with failure/N (%)	Block failures - n with failure/N (%)	Time taken for needle or catheter placement	Time taken for needle or catheter placement	Nerve block characteristics	Nerve block characteristics	Injected volume	Injected volume
	[I]	[C]	[I]	[C]	[I]	[C]	[I]	[C]	[I]	[C]
(Sala-Blanch et al 2012)	Needle redirects 1/25 (4%)	Needle redirects 3/26 (12%)	NR	NR	NR	NR	At 30 min post injection surgical block: 100% At 15 min post injection SB complete: 80%[c] At 15 min post injection MB complete: 60%[c] Duration of block 301 min ± 44[ns]	At 30 min post injection surgical block: 100% At 15 min post injection SB complete: 4% At 15 min post injection MB complete: 8% Duration of block 312 min ± 49	20 mL 1.5% Mep	20 mL 1.5% Mep

Abbreviations: Bup, bupivacaine; [C], 2-CHP, 2-chloroprocaine; comparator (nerve stimulation or landmark); Epi, epinephrine; [I], Ultrasound guided; MB, block; Lid, lidocaine; Lig, lignocaine; LM, field block; $MEAV_{50}$, minimum effective anaesthetic volume to induce complete block in 50% of patients; Mep, mepivacaine; MVM, Modified Vastus Medialis; NR, not reported; NS, not significant; PF, periformal; Rop, ropivacaine; SB, sensory block; Data: mean ± SD; mean [95% CI or range]; median (range or percentile or IQR)

Significant difference ([I] vs [C]) indicated by superscript a, b ,c or ns for $p < 0.05$, $p < 0.01$, $p < 0.001$ and not significant, respectively. Comparison without superscripts, statistical significance not reported or performed.

[1] Redirect: if patient did not register a patellar response within four minutes the needle was directed towards superficial/anterior of the femoral nerve.

[2] One patient did not register a satisfactory patellar response after five minutes therefore ultrasound was used.

[3] Failed: if patients still perceived cold in the sciatic nerve distribution

[4] Needle pass: defined as the need to redirect the needle and labelled redirects

Table 96: Effectiveness of ultrasound compared to landmark alone or landmark plus nerve stimulation for guidance of trunk nerve blocks

Study	Needle redirects and/or skin punctures	Needle redirects and/or skin punctures	Failed attemptsBlock failures - n with failure/N (%)	Failed attemptsBlock failures - n with failure/N (%)	Time taken for needle placement (seconds)	Time taken for needle placement (seconds)	Nerve block characteristics	Nerve block characteristics	Injected volume	Injected volume
	[I]	[C]	[I]	[C]	[I]	[C]	[I]	[C]	[I]	[C]
(Aveline et al 2011)	NR	NR	NR	NR	NR	NR	Duration of surgery 48 min±12	Duration of surgery 51 min±13	0.5% LevoB	0.5% LevoB
(Faraoni et al 2010)	NR	NR	0/20[1] (0%)[ns]	2/20[1] (10%)	NR	NR	Duration of surgery[2] 41.2 min (35–50)[c]	Duration of surgery[2] 31.8 min (26–39)	0.75% Rop 1.35 mL (1.2-1.7)[ns] 24.1 mg (21–30)[ns]	0.75% Rop 1.5 mL (1.3–2) 27.7 mg (21–37.5)
(O'Sullivan et al 2011)	NR	NR	NR	NR	115 (100–136.3)[c]	40 (40–45)	NR	NR	0.5% Bup, 1-2 mL to 3 years additional 1 mL per 3 years of age to a max of 6 mL	0.5% Bup, 1-2 mL to 3 years additional 1 mL per 3 years of age to a max of 6 mL

Abbreviations: Bup, bupivacaine; [C] comparator (nerve stimulation and / or landmark); [I], Ultrasound guided; LevoB, levobupivacaine; NR, not reported; Rop, ropivacaine

Data: mean [95% CI or range]; median (range or percentile); mean ± SD.

Significant difference ([I] vs [C]) indicated by superscript a, b, c or ns for $p < 0.05$, $p < 0.01$, $p < 0.001$ and not significant, respectively

1 Ineffective block (failed block) defined as an intra-operative increase in heart rate and mean arterial pressure.

2 Duration of surgery defined by time of anaesthetic to recovery suite }

Table 97 Effectiveness of ultrasound guidance compared to landmark alone or landmark plus nerve stimulation for guidance of upper limb nerve blocks

Study	Needle redirects and/or skin punctures [I]	Needle redirects and/or skin punctures [C]	Block failures - n with failure/N (%) [I]	Block failures - n with failure/N (%) [C]	Time taken for needle placement [I]	Time taken for needle placement [C]	Nerve Block characteristics [I]	Nerve Block characteristics [C]	Injected volume [I]	Injected volume [C]
(Bloc et al 2010)	Block placed with 2 cutaneous punctures PP Max needle depth out of plane 32 mm ± 8[a] In plane 50 mm ± 12	Block placed with 2 cutaneous punctures PP Max needle depth 40mm ± 11	Out of plane 0/40 (0%) In plane 0/40 (0%)	0/40 (0%)	Out of plane 240 s (140–420)[a] In plane 300 s (180–600)[ns]	360 s (240–900)	SB evaluated 30–45 min after placement Block complete if pin-prick or cold sensation elicits reaction for the 5 major nerves of the arm and forearm	SB evaluated 30–45 min after placement Block complete if pin-prick or cold sensation elicits reaction for the 5 major nerves of the arm and forearm	5 mL 1.5% Mep Out of plane 27 mL (23–31)[a] In plane 32 mL (28–38)[ns]	5–7mL 1.5% Mep 40 mL

Study	Needle redirects and/or skin punctures	Needle redirects and/or skin punctures	Block failures - n with failure/N (%)	Block failures - n with failure/N (%)	Time taken for needle placement	Time taken for needle placement	Nerve Block characteristics	Nerve Block characteristics	Injected volume	Injected volume
	[I]	[C]	[I]	[C]	[I]	[C]	[I]	[C]	[I]	[C]
(Brull et al 2009)	NR	NR	4/52 (8%)[ns]	10/51 (20%)	5 min (5)[c]	10.5 min (6.8)	SB pin prick[a] 10 min = 62% 15 min = 87% 20 min = 92% 25 min = 92% 30 min = 92 % SB light touch[ns] 10 min = 12% 15 min = 21% 20 min = 50% 25 min = 50% 30 min = 50% Ready for surgery at 20 min = 85%[a]	SB pin prick 10 min = 45% 15 min = 65% 20 min = 80% 25 min = 80% 30 min = 80% SB light touch 10 min =12% 15 min = 20% 20 min = 37% 25 min = 37% 30 min = 37% Ready for surgery at 20 min = 65%	15 mL 2% Lid 15 mL 0.5% Bup with Epi	15 mL 2% Lid 15 mL 0.5% Bup with Epi

Study	Needle redirects and/or skin punctures [I]	Needle redirects and/or skin punctures [C]	Block failures - n with failure/N (%) [I]	Block failures - n with failure/N (%) [C]	Time taken for needle placement [I]	Time taken for needle placement [C]	Nerve Block characteristics [I]	Nerve Block characteristics [C]	Injected volume [I]	Injected volume [C]
(Danelli et al 2012)	Skin punctures 1 (1-2)[b] Needle redirects[1] 2 (1–4)[a]	Skin punctures 1 (1-4) Needle redirects[1] 3 (1–5)	NR	NR	First US scan until needle removal 5 min ± 3[b]	Identification of LM until needle removal 8 min ± 5	SB onset time: axillary nerve (14 min ± 7), radial nerve (16 min ± 9), musculocutaneous nerve (14 min ± 7) MB onset time: axillary nerve (13 min ± 7), radial nerve (20 min ± 7), musculocutaneous nerve (17 min ± 9) Ready for surgery 15 min ± 9	SB onset time: axillary nerve (15 min ± 6), radial nerve (16 min ± 6), musculocutaneous nerve (17 min ± 6) MB onset time: axillary nerve (14min ± 8), radial nerve (25min ±7), musculocutaneous nerve (17 min ± 9) Ready for surgery 18 min ± 7	20 mL 1% Rop	20 mL 1% Rop
(Gorthi et al 2010)	NR	NR	NR	NR	Range 45–75 s	Range 45–80 s	NR	NR	8 mL 12.5% dextrose, 2 mL 2% Lid	8 mL 12.5% dextrose, 2 mL 2% Lid
(Gurkan et al 2008)	NR	NR	Complete 0/40 (0%) Partial 2/40 (5%)	Complete 2/40 (5%) Partial 1/40 (2.5%)	7.1 min ± 1[a]	6.4 min ± 1	Block onset time 20 min (10-30)	Block onset time 20 min (10-30)	20 mL Levo (5 mg/mL) and 20 mL Lid (20 mg/mL) with 5 µg/mL epi	20 mL Levo (5 mg/mL) and 20 mL Lid (20 mg/mL) with 5 µg/mL epi

Study	Needle redirects and/or skin punctures [I]	Needle redirects and/or skin punctures [C]	Block failures - n with failure/N (%) [I]	Block failures - n with failure/N (%) [C]	Time taken for needle placement [I]	Time taken for needle placement [C]	Nerve Block characteristics [I]	Nerve Block characteristics [C]	Injected volume [I]	Injected volume [C]
(Ko et al 2013)	NR	NR	None success: scapular notch filling with RA	None success: reduction of VAS to 0 at 30 min	NR	NR	NR	NR	10 mL 0.375% Rop	10 mL 0.375% Rop
(Liu et al 2009b)	1 (1)[a]	3 (1)	NR	NR	5 min ± 3	5 min ± 3	MB at bicep enhanced in US compared to ENS at 5 min[a] MB at deltoid and median muscle equivalent between ENS and US at 5 min[ns]	MB at bicep enhanced in US compared to ENS at 5 min MB at deltoid and median muscle equivalent between ENS and US at 5 min	1.5% Mep with Epi <50 kg 45–55 mL, ≥50kg 55–65 mL	1.5% Mep with Epi < 50kg 45–55 mL, ≥50kg 55–65 mL
(Ponde and Diwan 2009)	NR	NR	1/25 (4%)[b] Block failure[2]	9 /25 (36%) Block failure[2]	NR	NR	NR	NR	0.5% Bup at 0.5 mL/kg BW	0.5% Bup at 0.5 mL/kg BW
(Ponrouch et al 2010)	NA[7]	NA[7]	NA[3]	NA[3]	NR	NR	NR	NR	1.5% Mep $MEAV_{50}$ Median nerve: 2mL ± 0.1 [a] Ulnar nerve: 2mL ± 0.1	1.5% Mep $MEAV_{50}$ Median nerve: 4mL ± 3.8 Ulnar nerve: 2.4 mL ± 0.6

Study	Needle redirects and/or skin punctures	Needle redirects and/or skin punctures	Block failures - n with failure/N (%)	Block failures - n with failure/N (%)	Time taken for needle placement	Time taken for needle placement	Nerve Block characteristics	Nerve Block characteristics	Injected volume	Injected volume
	[I]	[C]	[I]	[C]	[I]	[C]	[I]	[C]	[I]	[C]
(Renes et al 2009)	NR	NR	0/15 (0%)	1/15 (7%)	NR	NR	NR	NR	10 mL 0.75% Rop	10 mL 0.75% Rop
(Salem et al 2012)	13 on first attempt	29 on first attempt	NR[4]	1/30 (3%)[4]	Time to detect brachial plexus and placement of anaesthetic 3.3 min ± 1.4	Time to detect brachial plexus and placement of anaesthetic 3.9 min ± 4.0	5 min (2–12) Block success: complete 28 patients Plus analgesia 2 patients	4.5 min (1–25) Block success complete 27 patients Plus analgesia 2 patients	30 mL 1% prilocaine 2 h post placement PCA 0.2% Rop 3mL /h with 5mL bolus, 20 min lockout	30 mL 1% prilocaine 2 h post placement PCA 0.2% Rop 3 mL/h with 5 mL bolus, 20 min lockout
(Strub et al 2011)	NR	NR	NR	NR	7.5min (5–16)	7min (4–20)	Ready for surgery 8min (4–60)[c] Number of patients with complete block at 60 min for all nerves (median, radial, ulnar, musculocutaneous) / N (%) 52/70 (74%)[c] Number of anaesthetic non-responders/N (%) 18/70 (26%)	Ready for surgery 30min (4–110) Number of patients with complete block at 60 min for all nerves (median, radial, ulnar, musculocutaneous) / N (%) 31/71 (44%) Number of anaesthetic non-responders/N (%) 40/71 (56%)	Bup 5mg/mL with epi plus Mep 10 mg /mL (1:1 mix) mean 12mL	Bup 5mg/mL with epi plus Mep 10 mg /mL (1:1 mix) 40 mL

Study	Needle redirects and/or skin punctures [I]	Needle redirects and/or skin punctures [C]	Block failures - n with failure/N (%) [I]	Block failures - n with failure/N (%) [C]	Time taken for needle placement [I]	Time taken for needle placement [C]	Nerve Block characteristics [I]	Nerve Block characteristics [C]	Injected volume [I]	Injected volume [C]
(Trabelsi et al 2013)	NR	NR	NR	NR	220 s ± 130	281 s ± 134	Onset SB: radial nerve 10 (8–13)[b] ulnar nerve 10 min (10–15)[b] median nerve 8 min (6–11)[b] musculocutaneous nerve 6 min (6–9)[c] all nerves 10 min (10–15)[a] Complete SB: 40 min Onset MB: radial nerve 19 min (15–22)[a] ulnar nerve 21 min ± 10[a] median nerve 13 min (10–18)[a] musculocutaneous nerve 9 min (8–15) all nerves 20 min (15–26) Complete MB: 50min	Onset SB: radial nerve 20 min (10–25) ulnar nerve 18 min (10–25) median nerve 13 min (7– 25), musculocutaneous nerve 11 min (8–21) all nerves 14 min (12–25). Complete SB: 45 min Onset MB: radial nerve 27 min (16– 42) ulnar nerve 27 min ± 11, median nerve 20 min (14–33) musculocutaneous nerve 10 min (9–23) all nerves 23 min (16–32) Complete MB: 55min	15 mL 0.5% Bup	15 mL 0.5% Bup

Study	Needle redirects and/or skin punctures	Needle redirects and/or skin punctures	Block failures - n with failure/N (%)	Block failures - n with failure/N (%)	Time taken for needle placement	Time taken for needle placement	Nerve Block characteristics	Nerve Block characteristics	Injected volume	Injected volume
	[I]	[C]	[I]	[C]	[I]	[C]	[I]	[C]	[I]	[C]
(Tran et al 2010)	2 ± 0[ns]	2 ± 1	3/20 (15%)[5]	4/20 (20%)[5]	needling time 99 s ± 65[ns] performance time 119 s ± 67[c]	needling time 61 s ± 19 performance time 61 s ± 19	Onset time 7.1 min±3.6[ns] Total time 9.0 min ± 3.5[a]	Onset time 6.3 min ± 2.2 Total time 7.3 min ± 2.1	10 mL 1.5% Lid with Epi	10 mL 1.5% Lid with Epi
(Zencirci 2011)	NR	NR	NR	NR	7.3 min ± 2.6[ns] time includes imaging	6.4 min ± 3.9	Number of patients with complete SB / N (%) at 10 min: 13/30 (43%)[ns] 20 min:24/30 (80%)[ns] 30 min: 30/30 (100%)[ns] Number of patients with complete MB / N (%) at 30 min 30/30 (100%)[a]	Number of patients with complete SB / N (%) at 10 min: 9/30 (30%) 20 min: 17/30 (57%) 30 min: 26/30 (87%) Number of patients with complete MB / N (%) at 30 min 21/30 (76.6%)	40 mL 0.75% Rop	40 mL 0.75% Rop

Abbreviations: Bup, bupivacaine; BW, body weight; [C] comparator (nerve stimulation and / or landmark); ENS, electrical nerve stimulation; Epi, epinephrine; GA, general anaesthesia; [I], Ultrasound guided; Lid, lidocaine; LM, landmark; MB, Motor block; $MEAV_{50}$, minimum effective anaesthetic volume for successful nerve block in 50% of patients; Mep, mepivacaine; NA, not applicable; NR, not reported; PCA, patient controlled analgesia; PP, as per protocol; RA, regional anaesthesia; Rop, ropivacaine; SB, sensory block; US, ultrasound; VAS, visual analogue scale

Data: mean [95% CI or range]; median (range or percentile); mean ± SD.

Significant difference ([I] vs [C]) indicated by superscript a, b or c for $p < 0.05$, p, 0.01 and $p < 0.001$ respectively

1 Number of needle redirections defined as any needle withdrawal of at least 10 mm with subsequent forward movement

2 Failed: if (a) 20% increase in heart rate and blood pressure above basal and/or (b) movement on surgical stimulus

3 Failed attempts not applicable, study designed to determine $MEAV_{50}$. As such, the intent is to generate failed blocks due to inadequate anaesthetic volume

3 Redirect required because after positioning nerve stimulation failed to elicit a motor response

4 Failed: if failed to get any response after 18 min moved to US

5 Failed: We considered a block to have fail if, at 15 mins, analgesia (patient can feel touch, not cold) is not achieved

Appendix O Focused systematic review on the use of ultrasound guidance for neuraxial blocks

Search strategy

A literature search was conducted in PubMed, EMBASE, the Centre for Reviews and Dissemination (CRD) of the University of York, and the Cochrane Library from database inception to December 2013. The search strategy and search terms used for PubMed are shown in Table 98. Similar search strategies were used for EMBASE, York CRD and the Cochrane Library.

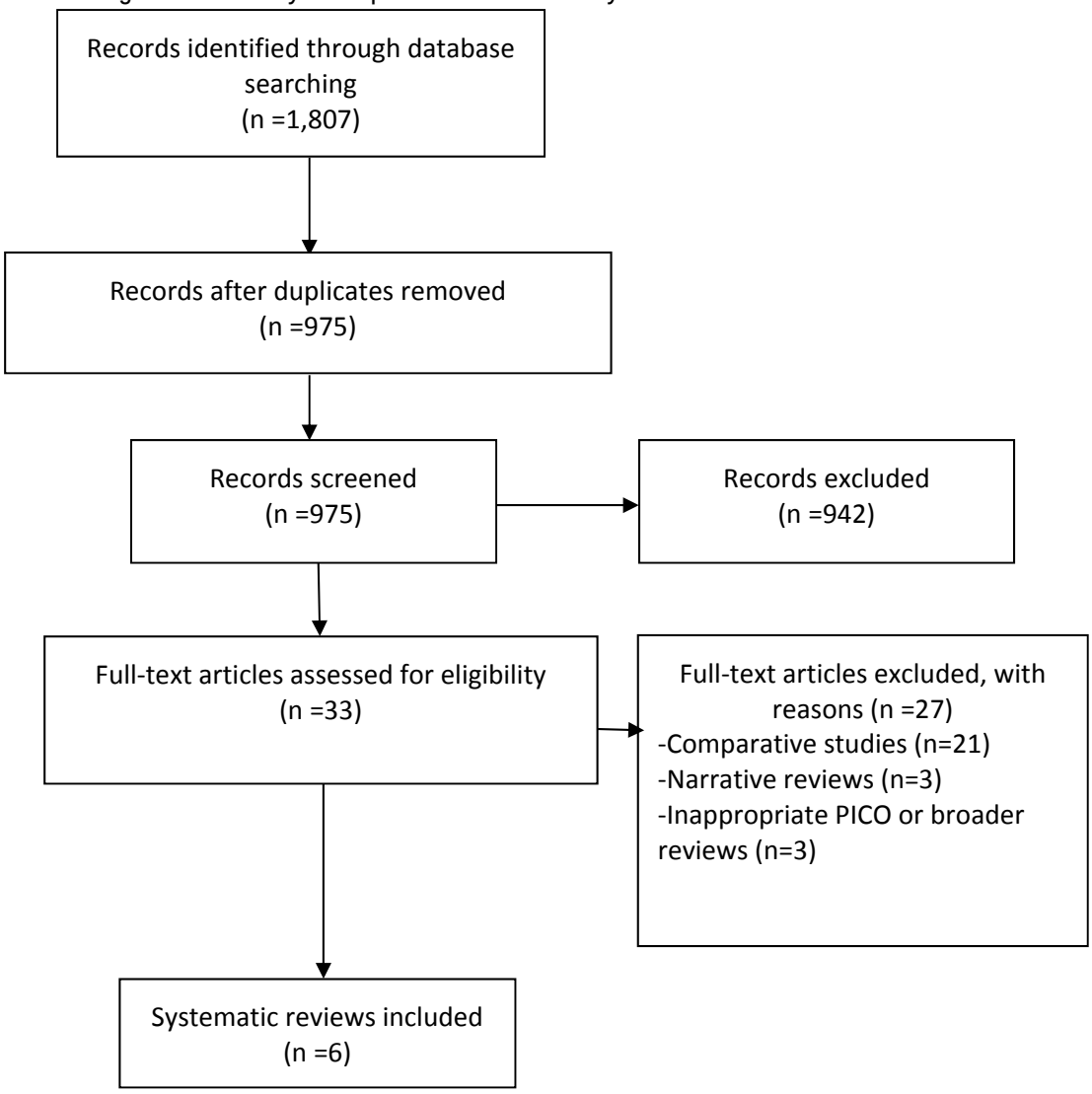
Table 98 PubMed search strategy for neuraxial anaesthesia

ID	Searches
#45	Search (#43 AND #44)
#44	Search (#24 AND #32)
#43	Search (#33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42)
#42	Search metaanalys*
#41	Search meta-analys*
#40	Search (meta) AND analys*
#39	Search (systematic) AND review*
#38	Search control*
#37	Search trial*
#36	Search random*
#35	Search meta analysis[MeSH Terms]
#34	Search randomized controlled trial[MeSH Terms]
#33	Search allocation, random[MeSH Terms]
#32	Search (#25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31)
#31	Search ultrasonograph*
#30	Search sonograph*
#29	Search ultrasound
#28	Search ultrasonic
#27	Search interventional ultrasonography[MeSH Terms]
#26	Search doppler ultrasonography[MeSH Terms]
#25	Search ultrasound[MeSH Terms]

ID	Searches
#24	Search (#23 OR #20)
#23	Search (#21 AND #22)
#22	Search (#15 OR #16 OR #17 OR #18 OR #19)
#21	Search (#7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14)
#20	Search (#1 OR #2 OR #3 OR #4 OR #5 OR #6)
#19	Search anesthe*
#18	Search anaesthe*
#17	Search analges*
#16	Search analgesia[MeSH Terms]
#15	Search anesthesia[MeSH Terms]
#14	Search neuraxial
#13	Search paravertebral
#12	Search subarachnoid
#11	Search intrathecal
#10	Search epidural
#9	Search spinal
#8	Search spine
#7	Search spine[MeSH Terms]
#6	Search epidural analgesia[MeSH Terms]
#5	Search epidural anesthesia[MeSH Terms]
#4	Search anesthesia, spinal[MeSH Terms]
#3	Search epidural injections[MeSH Terms]
#2	Search intrathecal injections[MeSH Terms]
#1	Search spinal injections[MeSH Terms]

The search results were processed according to the methods described in 'Approach to assessment'. However, in terms of study design the included studies were limited solely to systematic reviews. Patients considered were those who received neuraxial regional nerve blocks, including spinal, epideural, intrathecal, subaarachnoid or paravertebral anaesthesia. All other aspects of the inclusion criteria remained the same. The results of the study selection are provided in the following PRISMA flowchart (Figure 22).

Figure 22 Summary of the process used to identify and select studies for neuraxial anaesthesia



Adapted from Liberati et al (2009 (PRISMA 2014)).

Descriptive characteristics of included systematic reviews

Six systematic reviews were identified from the total of 1,807 articles imported to the Endnote library (Figure 1, Table 2). Characteristics of these reviews are provided in Table 2. Out of the six studies, two reviews investigated ultrasound guidance in children only (Rubin et al 2009; Tsui and Suresh 2010b) and another study in obstetrics only (Schnabel et al 2012). The remaining three studies included a mix population of children, adults and obstetric patients (Shaikh et al 2013, Lir et al 2009, Perlas 2010).

A total of 27 studies were excluded after reading the full text of the manuscript. The majority of these were comparative studies (n=21). Three studies (Baldi et al 2007; Narouze and Peng 2010; Tsui and Suresh 2010a) were excluded as being narrative reviews. Neal et al (2010) and Abrahams et al (2010) were broader reviews of percutaneous nerve blockade and have been included previously in this assessment. During the appraisal process, another study was excluded due to inappropriate research question (Heesen et al 2013). This study only focused on the postural puncture headache as a complication to the epidural analgesia in labouring women.

Critical appraisal of the systematic reviews

The systematic reviews were appraised in terms of their quality using the AMSTAR tool. The reviews were appraised for methodological quality by two reviewers independently (Table 3). Any disagreement was resolved through discussion. The median score of 6 was chosen to differentiate good quality systematic reviews (>6) from poor quality reviews (≤6) (CADTH 2006).

The overall quality of the identified studies was ranged from good to poor (Table 3). Most of the studies undertook a systematic search of the available literature with search strategies provided. However, none of the studies provided a list of excluded studies. The data extraction process varied across the systematic reviews. Some of the systematic reviews reported very robust review processes by independent reviewers for data extraction and resynthesis, whereas the extraction method was unclear in other studies. Two studies conducted the meta-analyses to quantitatively synthesise the evidence (Schnabel et al 2012; Shaikh et al 2013a) and the remaining studies were qualitative reviews. Publication biases and conflicts of interests were reported only by Shaikh et al. (2013) and Tsui and Pillay (2010) .

Three systematic reviews of good quality were identified to summarise the safety and effectiveness of ultrasound guided neuraxial, spinal and epidural anaesthesia (Schnabel et al 2012; Shaikh et al 2013b; Tsui and Suresh 2010b). These represented the three main patient populations of paediatrics only (Tsui and Pillay 2010), obstetrics (Schnabel et al 2012) and general population (Shaikh et al 2013). These three studies were appraised to be of high methodological quality and were the most recent in terms of literature search date. Both Schnabel et al (2012) and Shaikh et al (2013) included three RCTs published by Grau and colleagues (Grau et al 2001a; Grau et al 2001b; Grau et al 2002).

Two studies investigated the ultrasound guided neuraxial anaesthesia in paediatric population (Rubin et al 2009; Tsui and Suresh 2010a).The study produced by Tsui and Pillay (2010) is not a conventional systematic review. The study had the characteristic of a systematic review from the methodological aspect and reported the qualitative data from their included studies. However, it did not resynthesize the qualitative evidence to form a conclusion, but formulated guideline-like recommendations in the study and reported them individually. In contrast, the outcomes reported in Rubin et al (2009) included information regarding both peripheral and neuraxial anaesthesia. Neuraxial anaesthesia was reviewed by a single RCT included with relatively poor Jadad score. The safety and efficacy outcomes were also not explicitly reported. Only Tsui and Pillay's study was include in the assessment of paediatric patients, being the highest quality study among the two systematic reviews focused on this population.

Table 99: Systematic reviews for ultrasound assisted neuraxial nerve block: study characteristics

Review	Question of the review	Inclusion/exclusion criteria	Number of included studies	Intervention Comparator	Heterogeneity
Rubin et al., 2009	safety and efficacy of ultrasound guided neuraxial blocks in paediatric patients	All RCTs comparing USG neuraxial blocks or peripheral nerve blocks with other techniques in children were included. No explicit exclusion criteria were reported	9 studies including 1 RCT	Ultrasound Landmark	No meta-analysis was undertaken hence no heterogeneity information is provided.
Liu et al., 2009	safety and efficacy of ultrasound-guided regional anesthesia and analgesia	RCTs comparing ultrasound guidance to an alternative techniques, and some large prospective case series (patients number>100) were included. Studies were excluded if they were earlier than 1966. No language restriction was applied. The review only searched Medline database.	7 studies (both RCTs and case series) were included for USG epidural anaesthesia in adults and children	Ultrasound Landmark	The systematic review summarised the finding qualitatively hence the measurement of heterogeneity was not undertaken. No meta-analysis was performed
Schnabel et al., 2012	meta-analysis of efficacy and safety of ultrasound-guided neuraxial anaesthesia and analgesia in obstetrics. To	All RCTs, controlled clinical trials, and prospective cohort studies were included. No explicit exclusion criteria were reported, and there was no restriction on language of publication. Earliest publication dates vary across different databases.	6 RCTs were included in meta-analysis, 3 of them were RCTs and the other 3 were prospective cohort studies	Ultrasound Landmark	Meta-analyses were performed only on subgroup analyses –total number of puncture attempts and total number of puncture sites. Heterogeneity was not significant in both meta-analyses (I^2=0%).
Tsui and Pillay, 2010	safety and efficacy in ultrasound guided regional anaesthesia in paediatric patients	All systematic reviews/meta-analyses, RCTs, non-randomized clinical trials with control, and case series including at least 10 patients. There was no limit to the English language. Studies which use ultrasound for non-anaesthesia purposes were excluded.	12 studies, including 1 RCT, 10 comparative studies and 10 case series	Ultrasound Landmark	No meta-analysis was undertaken hence no heterogeneity information is provided.
Shaikh et al., 2013	meta-analysis of ultrasound guided lumbar punctures and epidural catheterisation in anaesthesia in the general population	All RCTs and quasi-randomised trials were included with certain criteria met –undertaking randomisation process; comparing ultrasound imaging with other techniques and reporting relevant outcomes.	14 studies were included, and 10 of them were used for meta-analysis	Ultrasound Landmark	Meta-analysis was performed. The heterogeneity was not significant (I^2=0%)
Perlas, 2010	evaluate evidence for use of ultrasound in neuraxial nerve blocks in a general population	No explicit inclusion criteria regarding to study types are identified from the studies. Any studies related to regional anaesthesia or acute pain practice were included. Letters, case reports and studies relating to chronic pain were excluded. No English language limit was applied.	17 studies were included, with no information of study type provided	Ultrasound Landmark and others	No meta-analysis was undertaken hence no heterogeneity information is provided.

Abbreviations: CI, confidence interval. IJV, internal jugular vein. SCV, subclavian vein. FV, femoral vein. NR, not reported

Table 100 Methodological quality appraisal of systematic reviews on ultrasound guidance for neuraxial block using the AMSTAR tool (Shea et al 2007)

Question	Review characteristics	Children	Children	Obstetrics	Obstetrics	General population)	General population
		(Rubin et al 2009)	(Tsui and Suresh 2010b)	(Schnabel et al 2012)	(Liu et al 2009a)	(Shaikh et al 2013b)	(Neal et al 2010)
1	Was an 'a priori' design provided?	Yes	Yes	Yes	Yes	Yes	Yes
2	Was there duplicate study selection and data extraction?	Yes	No	Yes	No	Yes	No
3	Was a comprehensive literature search performed?	Yes	Yes	Yes	No	Yes	Yes
4	Was the status of publication (i.e. grey literature) used as an inclusion criterion?	Yes	Yes	Yes	Yes	Yes	No
5	Was a list of studies (included and excluded) provided?	No	No	No	No	No	No
6	Were the characteristics of the included studies provided?	No	No	Yes	Yes	Yes	No
7	Was the scientific quality of the included studies assessed and documented?	Yes	Yes	Yes	No	Yes	Yes
8	Was the scientific quality of the included studies used appropriately in formulating conclusions?	No	Yes	Yes	No	Yes	No
9	Were the methods used to combine the findings of studies appropriate?	No	No	Yes	Yes	Yes	No
10	Was the likelihood of publication bias assessed?	No	Yes	Yes	No	Yes	No
11	Was the conflict of interest stated?	Yes	Yes	No	No	Yes	No
Totals	Yes	6	7	8	4	10	3
	No	5	4	2	7	1	8
	Cannot answer	-	-	1	-	-	-
	Not applicable	-	-	-	-	-	

NA: not applicable

Is it safe?

Adverse events reported in the three included studies following ultrasound guided neuraxial, spinal and epidural anaesthesia are shown in Table 101. In general, ultrasound reduced the number of overall complications (P=0.0005) and reduced the frequency of post-dural puncture headaches (P=0.0005).

Two studies reviewed the evidence of ultrasound guided neuraxial anaesthesia in a paediatric population. Besides the quantitative investigations on the safety outcomes of ultrasound guided neuraxial blockades, Tsui and Pillay (2010) queried technical aspects of the neuraxial blockades among paediatric patients. The review found evidence to show that ultrasound imaging was able to delineate the dura mater and observe the downward movement of the needle to confirm the epidural injection and improve the safety of the procedure (Tsui and Suresh 2010b). However, adverse events and placement complications were not reported in this study. The findings by Rubin et al (2009) were consistent with Tsui and Pillay (2010). It confirmed that ultrasound guidance would be able to provide better visualisations to the epidural and dura mater, suggesting that complications could be potentially avoided. Non-serious complications such as bloody tap were reviewed and reported by the review but these data were from non-RCT studies.

From the best evidence available, ultrasound guided neuraxial blocks show better safety profiles in terms of adverse events and placement complications. However, the safety outcomes across population groups not represented in this evidence base is unclear.

Table 101 Systematic reviews: Safety of ultrasound compared with landmark for guidance of neuraxial nerve block

Review	Adverse event on insertion	Placement complications	Overall complications
(Schnabel A 2012) Two studies investigated the parturient.	With the ultrasound guided nerve block, there are 0.4% for dural puncture and 2.0% for intravascular catheter placement among 250 patients No data was provided for the comparator	The risk ratio is lower in ultrasound guided nerve block in regard to post-dural puncture headache (RR=0.28, CI = 0.14~0.57, p = 0.0005)	NR
(Shaikh et al 2013b) A mix of obstetric patients and general adults	NR	NR	The study reported the traumatic procedures as the overall complications. Risk ratio = 0.27, 95% CI = (0.11, 0.67), p = 0.005; showing the ultrasound imaging reduced the risk of traumatic procedures
(Tsui and Suresh 2010b) Children	NR	NR	NR

Abbreviations: CI, confidence interval. NR, not reported. RR, risk ratio.

Is it effective?

The reported effectiveness outcomes are provided in Table 102. Ultrasound is associated with a reduced risk of failed procedure (P<0.001) (Shaikh et al 2013b). In general, the reviews reported ultrasound significantly reduces the number of attempts (P<0.001) (Schnabel et al 2012; Shaikh et al 2013b). Data were not reported in terms of the time of onset or duration of anaesthesia.

Tsui and Pillay's study (2010) reported the effectiveness outcomes narratively for the paediatric patients. It was argued that ultrasound offered a better visibility of a needle within the epidural space and provided improved detections of catheters advancement (Tsui and Suresh 2010b). This would lead to an increased success rate of the procedure and a reduction in the procedural time. However, Tsui and Pillay (2010) did not report any quantifiable effectiveness data which, therefore, could not be tabulated alongside with the other two included studies. A high success rate was also reported in by Rubin et al (2009) for children. A 100 per cent success rate of epidural catheter placement was reported in the review based on a single RCT. Other non-RCT studies included in this review also reported high success rate of the visualisation to catheters and neuraxial block placements. This is consistent with outcomes reported by Tsui and Pillay (2010).

The systematic reviews suggest that ultrasound guided neuraxial blocks can be performed more accurately and efficiently compared with anatomical landmark techniques.

Table 102 Systematic reviews: Effective of ultrasound compared with landmark for guidance of neuraxial nerve block

Review	Failure rate	Number of attempts	Time	Success rate
(Schnabel et al 2012) Two studies investigated the parturient.	NR	Mean difference = -0.92, 95% CI = (-1.11, -0.74), p < 0.001; showing ultrasound-guided neuraxial puncture was associated with lower total number of attempts.	NR	88.3% in the first puncture of intervertebral space in which ultrasound-guided or combined spinal epidural was performed Success rate for the comparator was not reported.
(Shaikh et al 2013b) A mix of obstetric patients and general adults	Risk ratio (RR) = 0.21, 95% CI = (0.10, 0.43), p <0.001, which indicates ultrasound imaging reduced the risk of failed procedures	Mean difference = -0.44, 94% CI = (-0.64, -0.24), p < 0.001; showing ultrasound-guided neuraxial puncture was associated with lower total number of attempts	NR	NR
(Tsui and Suresh 2010b) Children	NR	NR	NR	NR

Abbreviations: CI, confidence interval. RR, risk ratio. NA, not applicable NR, not reported

Discussion

Although the protocol did not specify a formal assessment of evidence in the use of ultrasound guided neuraxial, spinal and epidural anaesthesia, PASC acknowledged that ultrasound may play a role in this provision of this service. A targeted search was undertaken to identify high level systematic review evidence on this question. Although six systematic reviews were identified as a

result of these searches, three were excluded from data extraction due to the availability of more recent and methodologically more robust reviews.

The three included reviews provide evidence on paediatric, obstetric and general population settings of whether the ultrasound guided neuraxial blocks are safe and effective compared with landmark and other traditional techniques. Although no explicit PICO criteria was provided for neuraxial blocks it may be that certain relevant patient populations such as obese patients are not represented in this high level of evidence. The overall quality of the identified reviews varied across different studies. The quality of the three included studies was satisfactory, and most of the identified reviews report qualitative findings. RCTs which have been included in the reviews were diverse in terms of research questions and populations. Some reviews reported both on peripheral and neuraxial nerve blockade in their studies. Two quantitative analyses and meta-analyses were identified (Schnabel et al 2012; Shaikh et al 2013b).

Conclusions

Ultrasound guided insertions for neuraxial, spinal and epidural anaesthesia and analgesia appears to be safer compared with anatomical landmark guidance. The accuracy and efficiency of neuraxial nerve blocks is also improved with ultrasound guidance.

Appendix P MBS information

MBS item previously claimed for use of ultrasound guidance for anaesthesia services

Ultrasound guidance to facilitate vascular access and nerve blockade procedures in association with anaesthesia has been used in Australia in both public and private practice for the last decade. The service was claimed through MBS item 55054 (Table 103) until 1 November 2012. The number of claims made for the item from 2000 to 2011 follows in Table 104. There was a gradual increase in the number of services and number of anaesthesia-related claims between the 2000/2001 and 2010/2011 financial years. According to the Applicant private health insurance rebates were available during this period for the MBS item and the exact amount varied depending on the insurer.

MBS item 55026 has also been used in a smaller percentage of anaesthesia-related claims. This item is used for ultrasound devices which are over 10 years old.

Table 103 MBS item 55054

Category 5 Group I1,Subgroup 1 - Diagnostic Imaging services
MBS item 55054 Ultrasonic cross-sectional echography, in conjunction with a surgical procedure using interventional techniques, not being a service associated with a service to which any other item in this group applies. (See para DIQ of Explanatory Notes to this category) Fee: $109.10 Benefit: 75% = $81.85 85% = $92.75 Explanatory note DIQ: To provide an incentive to bulk-bill, for out-of-hospital services that are bulk-billed, the Schedule Fee is reduced by 5% and rebates provided at 100% of this revised fee (except for item 61369).

Item Start Date: 01-Jul-1993; Description Start Date: 01-Nov-1993; Schedule Fee Start Date: 01-Nov-2004.
Category 5: Diagnostic Imaging Services; Group I1: Ultrasound; Subgroup 1: General.

Table 104 Number of services claimed for MBS item 55054

Financial year	Number of services	Anaesthesia related claims*	Proportion of the total (%)
2000/2001	45,922	NR	NR
2001/2002	53,254	NR	NR
2002/2003	62,188	NR	NR
2003/2004	70,784	NR	NR
2004/2005	81,828	5	<0.001
2005/2006	96,431	108	0.1
2006/2007	107,688	274	0.2
2007/2008	120,093	1121	0.9
2008/2009	142,780	7222	5.1
2009/2010	163,585	17,291	10.6
2010/2011	187,417	26,363	14.1
2011/2012	206,701	32,041	15.5
2012/2013	208,881	13,205	6.3

*data provided by the Applicant; NR: not reported
Source: Australian Government Department of Health, https://www.medicareaustralia.gov.au/statistics/mbs_item.shtml, accessed 18 November 2013.

MBS items for anaesthetic services which may be associated with ultrasound guidance

MBS items which may be used in conjunction with ultrasound guidance are described in Table 105, Table 106, Table 107 and Table 108. Four MBS items are related to arterial cannulation, of which items 13818, 22015 and 22025 are relevant to the central arteries. There are three MBS items relevant to central vascular access (13815, 13319 and 22020) which are also available for peripherally inserted central catheters (PICC) (see Medicare note T1.6).

There are a number of items specific to local anaesthetic nerve blockade. For post-operative pain items 22040, 22045 and 22050 cover the use of percutaneous nerve blockade and items 22031 and 22036 cover intrathecal or epidural injection. The use of nerve blockade for perioperative anaesthesia is covered by the items related to the anaesthesia for the procedure (items in Group T10). Group T10 contains items relevant to anaesthesia organised within anatomical regions (Subgroups 1-18), time unit allocations reflecting the total time of the anaesthesia (items 23010-24136) and modifying units. As none of these items is specific to nerve blockade it is not possible to estimate from the MBS data how many services within Group T10 may be relevant to the review. In addition to these item numbers; Group T7 contains 44 items (item numbers 18234-18298) for nerve blockade. These are administered by a medical practitioner in the course of a surgical procedure undertaken by that practitioner, so would commonly be provided by specialties other than anaesthetists. There are also other items for intrathecal or epidural infusion of a therapeutic substance (18216, 18219, 18226 and 18227).

Table 105 Current MBS item descriptors used for arterial vascular access

MBS item 13818 Right heart balloon catheter, insertion of, including pulmonary wedge pressure and cardiac output measurement (Anaes.) Fee: $113.70 Benefit: 75% = $85.30 85% = $96.65 (See para T1.10 of explanatory notes to this Category) Item Start Date: 01-July-1993; Description Start Date: 01-May-1994; Schedule Fee Start Date: 01-Nov-2012. Category 3: Therapeutic procedures
MBS item 13842 Intraarterial cannulation for the purpose of taking multiple arterial blood samples for blood gas analysis Fee: $69.30 Benefit: 75% = $52.00 85% = $58.95 (See para T1.10 of explanatory notes to this Category) Item Start Date: 01-May-1994; Description Start Date: 01-May-1994; Schedule Fee Start Date: 01-Nov-2012. Category 3: Therapeutic procedures; Group T1: Miscellaneous therapeutic procedures; Subgroup 9: procedures associated with intensive care and cardiopulmonary support.
MBS item 22015 Right heart balloon catheter, insertion of, including pulmonary wedge pressure and cardiac output measurement, when performed in association with the administration of anaesthesia (6 basic units) Fee: $118.80 Benefit: 75% = $89.10 85% = $101.00 (See para T10.8 of explanatory notes to this Category)

MBS item 13818

Right heart balloon catheter, insertion of, including pulmonary wedge pressure and cardiac output measurement

(Anaes.)

Fee: $113.70 Benefit: 75% = $85.30 85% = $96.65

(See para T1.10 of explanatory notes to this Category)

Item Start Date: 01-July-1993; Description Start Date: 01-May-1994; Schedule Fee Start Date: 01-Nov-2012.

Category 3: Therapeutic procedures

Item Start Date: 01-Nov-2001; Description Start Date: 01-Nov-2001; Schedule Fee Start Date: 01-Nov-2012.

Category 3: Therapeutic procedures; Group T10: Relative value guide for anaesthesia; subgroup 19: Therapeutic and diagnostic services.

MBS item 22025

Intraarterial cannulation when performed in association with the administration of anaesthesia (4 basic units)

Fee: $79.20 Benefit: 75% = $59.40 85% = $67.35

(See para T10.8 of explanatory notes to this Category)

Item Start Date: 01-Nov-2001; Description Start Date: 01-Nov-2001; Schedule Fee Start Date: 01-Nov-2012.

Category 3: Therapeutic procedures; Group T10: Relative value guide for anaesthesia; subgroup 19: Therapeutic and diagnostic services.

Source: Australian Government Department of Health, http://www9.health.gov.au/mbs/search.cfm, accessed 18 November 2013.

Table 106 Current MBS item descriptors used for central venous access

MBS item 13815

Central vein catheterisation by percutaneous or open exposure not being a service to which item 13318 applies

(Anaes.)

Fee: $85.25 Benefit: 75% = $63.95 85% = $72.50

(See para T1.6 of explanatory notes to this Category)

Item Start Date: 01-Jul-1993; Description Start Date: 01-Jul-2012; Schedule Fee Start Date: 01-Nov-2012.

Category 3: Therapeutic procedures; Group T1: Miscellaneous therapeutic procedures; Subgroup 9: procedures associated with intensive care and cardiopulmonary support.

MBS item 13318

Central vein catheterisation - by open exposure in a person under 12 years of age

(Anaes.)

Fee: $227.45 Benefit: 75% = $170.60 85% = $193.35

(See para T1.6 of explanatory notes to this Category)

Item Start Date: 01-Dec-1991; Description Start Date: 01-Jul-2012; Schedule Fee Start Date: 01-Nov-2012.

Category 3: Therapeutic procedures; Group T1: Miscellaneous therapeutic procedures; Subgroup 4: Paediatric and neonatal.

MBS item 13319

Central vein catheterisation in a neonate via peripheral vein

(Anaes.)

Fee: $227.45 Benefit: 75% = $170.60 85% = $193.35

Item Start Date: 01-May-1997; Description Start Date: 01-May-1997; Schedule Fee Start Date: 01-Nov-2012.

Category 3: Therapeutic procedures; Group T1: Miscellaneous therapeutic procedures; Subgroup 4: Paediatric and neonatal.

MBS item 22020

Central vein catheterisation by percutaneous or open exposure, not being a service to which item 13318 applies, when performed in association with the administration of anaesthesia

(4 basic units)

Fee: $79.20 Benefit: 75% = $59.40 85% = $67.35

(See para T1.6, T10.8 of explanatory notes to this Category)

Item Start Date: 01-Nov-2001; Description Start Date: 01-Jul-2012; Schedule Fee Start Date: 01-Nov-2012.

Category 3: Therapeutic procedures; Group T10: Relative value guide for anaesthesia; subgroup 19: Therapeutic and diagnostic services.

Medicare note T1.6

T1.6 Peripherally Inserted Central Catheters

Peripherally inserted central catheters (PICC) are an alternative to standard percutaneous central venous catheter placement or surgically placed intravenous catheters where long-term venous access is required for ongoing patient therapy.

Medicare benefits for PICC can be claimed under central vein catheterisation items 13318, 13319, 13815 and 22020.

These items are for central vein catheterisation (where the tip of the catheter is positioned in a central vein) and cannot be used for venous catheters where the tip is positioned in a peripheral vein.

Related Items: 13318, 13815, 22020

Source: Australian Government Department of Health, http://www9.health.gov.au/mbs/search.cfm, accessed 18 November 2013.

Table 107 Current MBS item descriptors used for percutaneous nerve blockade

MBS Item 22040 Introduction of a regional or field nerve block peri-operatively performed in the induction room theatre or recovery room for the control of post-operative pain via the femoral OR sciatic nerves, in conjunction with hip, knee, ankle or foot surgery (2 basic units) Fee: $39.60 Benefit: 75% = $29.70 85% = $33.70 (See para T10.17, T10.21 of explanatory notes to this Category) Item Start Date: 01-Nov-2001; Description Start Date: 01-Nov-2003; Schedule Fee Start Date: 01-Nov-2012. Category 3: Therapeutic procedures; Group T10: Relative value guide for anaesthesia; subgroup 19: Therapeutic and diagnostic services.
MBS item 22045 Introduction of a regional or field nerve block peri-operatively performed in the induction room, theatre or recovery room for the control of post-operative pain via the femoral AND sciatic nerves, in conjunction with hip, knee, ankle or foot surgery (3 basic units) Fee: $59.40 Benefit: 75% = $44.55 85% = $50.50 (See para T10.17, T10.21 of explanatory notes to this Category) Item Start Date: 01-Nov-2001; Description Start Date: 01-Nov-2003; Schedule Fee Start Date: 01-Nov-2012. Category 3: Therapeutic procedures; Group T10: Relative value guide for anaesthesia; subgroup 19: Therapeutic and diagnostic services.
MBS item 22050 Introduction of a regional or field nerve block peri-operatively performed in the induction room, theatre or recovery room for the control of post-operative pain via the brachial plexus in conjunction with shoulder surgery (2 basic units) Fee: $39.60 Benefit: 75% = $29.70 85% = $33.70 (See para T10.17, T10.21 of explanatory notes to this Category) Item Start Date: 01-Nov-2001; Description Start Date: 01-Nov-2001; Schedule Fee Start Date: 01-Nov-2012. Category 3: Therapeutic procedures; Group T10: Relative value guide for anaesthesia; subgroup 19: Therapeutic and diagnostic services.

Source: Australian Government Department of Health, http://www9.health.gov.au/mbs/search.cfm, accessed 18 November 2013.

Table 108 Current MBS item descriptors used for intrathecal or epidural injection of regional anaesthetic agent for postoperative pain management

MBS item 22031 Intrathecal or epidural injection (initial) of a therapeutic substance or substances, with or without insertion of a catheter, in association with anaesthesia and surgery, for postoperative pain management, not being a service associated with a service to which 22036 applies (5 basic units) Fee: $99.00 Benefit: 75% = $74.25 85% = $84.15 (See para T10.19 of explanatory notes to this Category) Item Start Date: 01-Nov-2005; Description Start Date: 01-Nov-2005; Schedule Fee Start Date: 01-Nov-2012. Category 3: Therapeutic procedures; Group T10: Relative value guide for anaesthesia; subgroup 19: Therapeutic and diagnostic services.

MBS item 22036

Intrathecal or epidural injection (subsequent) of a therapeutic substance or substances, using an in situ catheter, in association with anaesthesia and surgery, for postoperative pain management, not being a service associated with a service to which 22031 applies

(3 basic units)

Fee: $59.40 Benefit: 75% = $44.55 85% = $50.50

(See para T10.20 of explanatory notes to this Category)

Item Start Date: 01-Nov-2005; Description Start Date: 01-Nov-2005; Schedule Fee Start Date: 01-Nov-2012.

Category 3: Therapeutic procedures; Group T10: Relative value guide for anaesthesia; subgroup 19: Therapeutic and diagnostic services.

Source: Australian Government Department of Health, http://www9.health.gov.au/mbs/search.cfm, accessed 18 November 2013.

The number of services claimed for MBS items numbers identified as being relevant to this review are detailed in Table 15,

Table 110, Table 111 and Table 112. Utilisation of all items (with the exception of item 22015) has increased over the past 10 years, both on an absolute and per capita basis. Item 22015, insertion of a right heart balloon catheter, has experienced a gradual decrease in utilisation over the past 10 years.

Table 109 Number of services claimed for MBS items relevant to central arterial vascular access

	MBS item 13842		MBS item 22015		MBS item 22025	
Financial year	Number of services	Number of services per 100,000 population	Number of services	Number of services per 100,000 population	Number of services	Number of services per 100,000 population
2003/2004	4,257	20	5,517	26	40,802	196
2004/2005	4,387	21	5,245	25	44,456	213
2005/2006	4,817	23	5,448	26	50,546	245
2006/2007	4,802	23	5,061	24	54,691	261
2007/2008	5,132	24	5,348	25	61,810	291
2008/2009	4,738	22	5,062	23	67,943	315
2009/2010	4,577	21	4,937	23	71,705	327
2010/2011	4,861	22	4,946	22	74,993	336
2011/2012	5,461	24	4,964	22	83,369	366
2012/2013	5,928	26	5,303	23	90,202	389

Source: Australian Government Department of Health, https://www.medicareaustralia.gov.au/statistics/mbs_item.shtml, accessed 18 November 2013.

Table 110 Number of services claimed for MBS items relevant to central venous vascular access (13815, 13318, 13319, 22015 and 22020)

	MBS item 13815		MBS item 13318		MBS item 13319		MBS item 22020	
Financial year	Number of services	Number of services per 100,000 population	Number of services	Number of services per 100,000 population	Number of services	Number of services per 100,000 population	Number of services	Number of services per 100,000 population
2003/2004	8,753	42	12	0	224	1	17,784	85
2004/2005	9,340	45	6	0	234	1	17,610	84
2005/2006	10,208	50	7	0	239	1	18,742	91
2006/2007	10,497	50	9	0	306	2	18,698	89
2007/2008	11,322	53	8	0	298	2	19,965	94
2008/2009	11,397	53	3	0	302	1	19,866	92
2009/2010	11,515	53	5	0	348	2	20,528	94
2010/2011	12,528	56	4	0	359	2	20,892	94
2011/2012	13,517	59	2	0	332	2	21,787	96
2012/2013	15,077	65	13	0	510	2	22,294	96

Source: Australian Government Department of Health, https://www.medicareaustralia.gov.au/statistics/mbs_item.shtml, accessed 18 November 2013.

Table 111 Number of services claimed for MBS items relevant to percutaneous nerve blockade for postoperative pain (22040, 22045 and 22050)

	MBS item 22040		MBS item 22045		MBS item 22050	
Financial year	Number of services	Number of services per 100,000 population	Number of services	Number of services per 100,000 population	Number of services	Number of services per 100,000 population
2003/2004	12,459	60	3,878	19	9,714	47
2004/2005	14,177	68	4,364	21	9,883	47
2005/2006	15,438	75	5,027	24	11,033	54
2006/2007	16,057	77	5,654	27	12,214	58
2007/2008	18,661	88	6,272	30	13,384	63
2008/2009	20,638	96	6,327	29	14,379	67
2009/2010	22,338	102	6,619	30	15,992	73
2010/2011	22,878	102	6,904	31	16,417	73
2011/2012	23,789	104	6,651	29	17,286	76
2012/2013	24,668	106	6,645	29	18,110	78

Source: Australian Government Department of Health, https://www.medicareaustralia.gov.au/statistics/mbs_item.shtml, accessed 18 November 2013.

Table 112 Number of services claimed for MBS items relevant to for intrathecal or epidural injection for postoperative pain (22031 and 22036)

	MBS item 22031		MBS item 22036	
Financial year	Number of services	Number of services per 100,000 population	Number of services	Number of services per 100,000 population
2005/2006	34,425	167	2,783	13
2006/2007	67,358	322	2,406	11
2007/2008	70,695	333	2,457	12
2008/2009	72,765	338	2,200	10
2009/2010	75,162	343	2,381	11
2010/2011	75,565	338	2,189	10
2011/2012	78,938	347	2,327	10
2012/2013	80,992	349	2,348	10

Source: Australian Government Department of Health, https://www.medicareaustralia.gov.au/statistics/mbs_item.shtml, accessed 18 November 2013.

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Shortened forms

AHMAC	Australian Health Ministers' Advisory Council
AIHW	Australian Institute of Health and Welfare
AMSTAR	Assessing the Methodological Quality of Systematic Reviews
AR-DRG	Australian Refined Diagnostic Related Group
ARTG	Australian Register of Therapeutic Goods
ASA	Australian Society of Anaesthetists
ASERNIP-S	Australian Safety and Efficacy Register of New Interventional Procedures – Surgical
AURORA	Australian and New Zealand Register of Regional Anaesthesia
CRD	Centre for Reviews and Dissemination (University of York)
CHERE	Centre for Health Economics Research and Evaluation
CI	confidence interval
DRG	diagnosis related group
ENS	electrical nerve stimulation
GBP	Great Britain pounds
HDP	hemidiaphramatic paresis
HTA	health technology assessment
ICER	incremental cost-effectiveness ratio
ICU	intensive care unit
IQR	interquartile range
ITT	intention to treat
IV	intravenous
LAST	local anaesthetic systemic toxicity
LOS	length of hospital stay
LYG	life year gained
MBS	Medicare Benefits Schedule

MEAV	minimum effective anaesthetic dosage
MSAC	Medical Services Advisory Committee
NATA	National Association of Testing Authorities
NHMRC	National Health and Medical Research Council
NHS	National Health Service
PASC	Protocol Advisory Sub-Committee
PICC	peripherally-inserter central catheters
PRISMA	preferred reporting items for systematic reviews and meta-analyses
QALY	quality-adjusted life year
RCT	randomised controlled trial
RR	risk ratio
SD	standard deviation
TGA	Therapeutic Goods Administration
TPN	total parenteral nutrition
UK	United Kingdom
US$	United States dollars
USA	United States of America
WTP	willingness-to-pay