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Ultrasound guidance versus landmark method for peripheral venous cannulation in adults (Review)

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[Intervention Review]

Ultrasound guidance versus landmark method for peripheral venous cannulation in adults

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ABSTRACT

Background

Peripheral intravenous cannulation is one of the most fundamental and common procedures in medicine. Securing a peripheral line is occasionally difficult with the landmark method. Ultrasound guidance has become a standard procedure for central venous cannulation, but its efficacy in achieving peripheral venous cannulation is unclear.

Objectives

To evaluate the effectiveness and safety of ultrasound guidance compared to the landmark method for peripheral intravenous cannulation in adults.

Search methods

We used standard, extensive Cochrane search methods. The latest search date was 29 November 2021.

Selection criteria

We included randomised controlled trials (RCTs) and quasi-RCTs (RCTs in which participants are systematically allocated based on data such as date of birth or recruitment) comparing the effects of ultrasound guidance to the landmark method for peripheral intravenous cannulation in adults.

Data collection and analysis

We used standard Cochrane methods. Our primary outcomes were first-pass success of cannulation, overall success of cannulation, and pain. Our secondary outcomes were procedure time for first-pass cannulation, procedure time for overall cannulation, number of attempts, patient satisfaction, and overall complications. We used GRADE to assess the certainty of the evidence.

Placing a peripheral intravenous line in individuals can be classed as 'difficult', 'moderate', or 'easy'. We use the terms 'difficult participants', 'moderate/moderately difficult participants' and 'easy participants' as shorthand to characterise the difficulty level in placing a peripheral line using the landmark method. We used the original studies' definitions of difficulty levels of peripheral intravenous cannulation with the landmark method. We analysed the results in these subgroups: 'difficult participants', 'moderate participants', and 'easy participants'.

We did this because we expected the effect of ultrasound-guided peripheral venous cannulation to be largest in participants classed as 'difficult' and smaller in participants classed as 'moderate' and 'easy'.

Main results

We included 14 RCTs and two quasi-RCTs involving 2267 participants undergoing peripheral intravenous cannulation. Participants were classed as 'difficult' in 12 studies (880 participants), 'moderate' in one study (401 participants), and 'easy' in one study (596 participants). Two studies (390 participants) did not restrict by landmark method difficulty level. The overall risk of bias assessments ranged from low to high. We judged studies to be at high risk of bias mainly because of concerns about blinding for subjective outcomes.

In difficult participants, ultrasound guidance increased the first-pass success of cannulation (risk ratio (RR) 1.50, 95% confidence interval (95% CI) 1.15 to 1.95; 10 studies, 815 participants; low-certainty evidence), and the overall success of cannulation (RR 1.40, 95% CI 1.10 to 1.77; 10 studies, 670 participants; very low-certainty evidence). There was no clear difference in pain (mean difference (MD) -0.20, 95% CI -1.13 to 0.72; 4 studies, 323 participants; very low-certainty evidence; numerical rating scale (NRS) 0 to 10 where 10 is maximum pain). Ultrasound guidance increased the procedure time for first-pass cannulation (MD 119.9 seconds, 95% CI 88.6 to 151.1; 2 studies, 219 participants; low-certainty evidence), and patient satisfaction (standardised mean difference (SMD) 0.49, 95% CI 0.07 to 0.92; 5 studies, 333 participants; very low-certainty evidence; NRS 0 to 10 where 10 is maximum satisfaction). Ultrasound guidance decreased the number of cannulation attempts (MD -0.33, 95% CI -0.64 to -0.02; 9 studies, 568 participants; very low-certainty evidence). Ultrasound guidance showed no clear difference in the procedure time for overall cannulation (MD -24.9 seconds, 95% CI -323.1 to 273.3; 8 studies, 413 participants; very low-certainty evidence) and overall complications (RR 0.64, 95% CI 0.37 to 1.10; 5 studies, 431 participants; low-certainty evidence).

In moderate participants, ultrasound guidance increased the first-pass success of cannulation (RR 1.14, 95% CI 1.02 to 1.27; 1 study, 401 participants; moderate-certainty evidence). No studies assessed the overall success of cannulation. There was no clear difference in pain (MD 0.10, 95% CI -0.47 to 0.67; 1 study, 401 participants; low-certainty evidence; NRS 0 to 10 where 10 is maximum pain). Ultrasound guidance increased the procedure time for first-pass cannulation (MD 95.2 seconds, 95% CI 72.8 to 117.6; 1 study, 401 participants; high-certainty evidence). Ultrasound guidance showed no clear difference in overall complications (RR 0.83, 95% CI 0.38 to 1.82; 1 study, 401 participants; moderate-certainty evidence). No studies assessed the procedure time for overall cannulation, number of cannulation attempts, or patient satisfaction.

In easy participants, ultrasound guidance decreased the first-pass success of cannulation (RR 0.89, 95% CI 0.85 to 0.94; 1 study, 596 participants; high-certainty evidence). No studies assessed the overall success of cannulation. Ultrasound guidance increased pain (MD 0.60, 95% CI 0.17 to 1.03; 1 study, 596 participants; moderate-certainty evidence; NRS 0 to 10 where 10 is maximum pain). Ultrasound guidance increased the procedure time for first-pass cannulation (MD 94.8 seconds, 95% CI 81.2 to 108.5; 1 study, 596 participants; high-certainty evidence). Ultrasound guidance showed no clear difference in overall complications (RR 2.48, 95% CI 0.90 to 6.87; 1 study, 596 participants; moderate-certainty evidence). No studies assessed the procedure time for overall cannulation, number of cannulation attempts, or patient satisfaction.

Authors' conclusions

There is very low- and low-certainty evidence that, compared to the landmark method, ultrasound guidance may benefit difficult participants for increased first-pass and overall success of cannulation, with no difference detected in pain. There is moderate- and low-certainty evidence that, compared to the landmark method, ultrasound guidance may benefit moderately difficult participants due to a small increased first-pass success of cannulation with no difference detected in pain. There is moderate- and high-certainty evidence that, compared to the landmark method, ultrasound guidance does not benefit easy participants: ultrasound guidance decreased the first-pass success of cannulation with no difference detected in overall success of cannulation and increased pain.

PLAIN LANGUAGE SUMMARY

Is ultrasound guidance a good option for peripheral intravenous cannulation in adults?

What is peripheral intravenous cannulation?

Placing a peripheral intravenous line is one of the most essential procedures in medicine. It involves putting a thin, flexible tube (known as a catheter or cannula) into a vein using a needle. This process is known as 'cannulation'. It is necessary when administering fluids, drugs, and drawing blood samples.

Peripheral intravenous cannulation is usually carried out by seeing and touching a target vein in the hand or arm. This is known as the landmark method. Placing a peripheral intravenous line is sometimes difficult, requiring multiple needle punctures if healthcare providers cannot find a suitable vein. If peripheral intravenous cannulation fails with the landmark method, a central venous line in the neck or chest is often the next step. However, central venous line placement can have serious complications, such as infection, thrombosis (blood clots), and pneumothorax (collapsed lung). It is also more time-consuming and costly. Therefore, the insertion of a central venous line should be a last resort.

How can ultrasound guidance (USG) help?

Ultrasound can find target veins invisible to the eye. Ultrasound also allows healthcare providers to see the needle and important surrounding structures that should not be damaged when inserting the tube. Ultrasound guidance is often used to help central venous cannulation, but the usefulness for peripheral venous cannulation remains unclear.

What did we want to find out?

We wanted to find out if ultrasound guidance was useful and safe compared to the landmark method for peripheral intravenous cannulation in adults. We also wanted to find out if using ultrasound guidance was different in people when cannulation was classed as difficult, moderately difficult, or easy.

What did we do?

We systematically searched for studies comparing the effects of ultrasound guidance to the landmark method on peripheral intravenous cannulation in adults. We combined the studies' results, and rated our confidence in the evidence, based on factors such as study methods and sizes.

What did we find?

We found 16 studies with 2267 participants comparing peripheral intravenous cannulation using ultrasound guidance to the landmark method. The effect of ultrasound guidance was dependent on the difficulty levels of cannulating people using the landmark method. The largest effect was seen in people classed as 'difficult' to cannulate, and the effect became smaller as the difficulty decreased.

- In 'difficult' patients, ultrasound guidance may increase the first-pass success of cannulation (that is, successful insertion of the tube on the first attempt), overall success of cannulation, and did not have a clear effect on people's pain.

- In 'moderately difficult' patients, ultrasound guidance probably increased the first-pass success of cannulation, and there was no clear effect on people's pain. No studies assessed the overall success of cannulation.

- In 'easy' patients, ultrasound guidance decreased the first-pass success of cannulation and probably increased people's pain. No studies assessed the overall success of cannulation.

What are the limitations of the evidence?

We are not very confident in this evidence because studies did not always measure outcomes in reliable ways. In addition, the studies varied in how they defined difficulty levels with the landmark method and 'puncture failure'.

How up to date is this evidence?

This evidence is up to date to November 2021. We identified six ongoing studies. We will include results from these studies in future updates.

Key messages

In people where peripheral intravenous cannulation using the landmark method is difficult, ultrasound guidance may increase the first-pass and overall success of cannulation and has no clear effect on pain. In moderately difficult patients, ultrasound guidance probably increases the first-pass success of cannulation slightly and may have no clear effect on pain. In easy patients, ultrasound guidance reduces the first-pass success of cannulation and probably increases pain slightly.

The lack of common definitions amongst the included studies for difficulty levels with the landmark method and puncture failure undermined the results. Future studies should use common definitions.

Summary of findings 1. Ultrasound guidance versus landmark method for peripheral venous cannulation in adults classed as difficult

Patient or population: adults undergoing peripheral venous cannulation classed as difficult[a]

Settings: emergency department, ICU, operating room

Intervention: USG

Comparison: LM

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with LM	Risk with USG				
First-pass success of cannulation Follow-up: immediately after the procedure	**358 per 1000**	**537 per 1000** (421 to 698)	**RR 1.50** (1.15 to 1.95)	815 (10 RCTs)	⊕⊕⊖⊖ **Low**[b]	
Overall success of cannulation Follow-up: immediately after the procedure	**575 per 1000**	**806 per 1000** (633 to 1000)	**RR 1.40** (1.10 to 1.77)	670 (10 RCTs)	⊕⊖⊖⊖ **Very low**[c]	
Pain NRS: from 0 to 10, where 10 is maximum pain Follow-up: immediately after the procedure	The mean pain score was **3.97**	**MD 0.20 lower** (1.13 lower to 0.72 higher)	-	323 (4 RCTs)	⊕⊖⊖⊖ **Very low**[d]	
Procedure time for first-pass cannulation (seconds) Follow-up: immediately after the procedure	The mean procedure time for first-pass cannulation was **130.5 seconds**	**MD 119.9 seconds longer** (88.6 longer to 151.1 longer)	-	219 (2 RCTs)	⊕⊕⊖⊖ **Low**[e]	
Number of cannulation attempts Follow-up: immediately after the procedure	The mean number of cannulation attempts was **2.15**	**MD 0.33 lower** (0.64 lower to 0.02 lower)	-	568 (9 RCTs)	⊕⊖⊖⊖ **Very low**[f]	

Patient satisfaction NRS from 0 to 10 or 4-step Likert scale The higher the score, the higher the level of satisfaction Follow-up: immediately after the procedure	The mean patient satisfaction score was **5.61**	**SMD 0.49 higher** (0.07 higher to 0.92 higher)	-	333 (5 RCTs)	⊕⊖⊖⊖ **Very low**[g]
Overall complications Follow-up: immediately after the procedure	**121 per 1000**	**78 per 1000** (45 to 133)	**RR 0.64** (0.37 to 1.10)	431 (5 RCTs)	⊕⊕⊖⊖ **Low**[h]

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **ICU:** intensive care unit; **LM:** landmark method; **MD:** mean difference; **NRS:** numeric rating scale; **RCTs:** randomised controlled trials; **RR:** risk ratio; **SMD:** standardised mean difference; **USG:** ultrasound guidance

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]Participants were classified according to the original studies' definitions.
[b]We downgraded by a total of two levels to low certainty due to risk of bias concerns (quasi-randomised trials, lack of blinding of the outcome assessors) and substantial inconsistency. There was minimal risk of publication bias (one small study was asymmetrical but would have had little impact).
[c]We downgraded by a total of three levels to very low certainty due to risk of bias concerns (quasi-randomised trials, lack of blinding of the outcome assessors) and serious inconsistency due to the lack of a standardised definition of failure. There was minimal risk of publication bias (two quasi-randomised trials were asymmetrical).
[d]We downgraded by a total of three levels to very low certainty due to risk of bias concerns (a quasi-randomised trial, lack of blinding of the outcome assessors, and incomplete outcome data), substantial inconsistency, and imprecision.
[e]We downgraded by a total of two levels to low certainty due to risk of bias concerns (a quasi-randomised trial, lack of blinding of the outcome assessors), and imprecision.
[f]We downgraded by a total of three levels to very low certainty due to risk of bias concerns (quasi-randomised trials, lack of blinding of the outcome assessors, and incomplete outcome data) and inconsistency due to heterogeneity and the lack of a standardised definition of failure.
[g]We downgraded by a total of three levels to very low certainty due to risk of bias concerns (a quasi-randomised trial, lack of blinding of the outcome assessors, and incomplete outcome data), substantial inconsistency, and imprecision.
[h]We downgraded by a total of two levels to low certainty due to risk of bias concerns (quasi-randomised trials, lack of blinding of the outcome assessors), and imprecision.

Summary of findings 2. Ultrasound guidance versus landmark method for peripheral venous cannulation in adults classed as moderately difficult

Patient or population: adults undergoing peripheral venous cannulation classed as moderately difficult[a]

Settings: emergency department

Intervention: USG

Comparison: LM

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with LM	Risk with USG				
First-pass success of cannulation Follow-up: immediately after the procedure	**714 per 1000**	**813 per 1000** (728 to 906)	**RR 1.14** (1.02 to 1.27)	401 (1 RCT)	⊕⊕⊕⊖ **Moderate**[b]	
Overall success of cannulation Follow-up: immediately after the procedure	See comment	-	-	-	-	None of the studies included moderately difficult participants
Pain NRS: from 0 to 10, where 10 is maximum pain Follow-up: immediately after the procedure	The mean pain score was **3.20**	**MD 0.10 higher** (0.47 lower to 0.67 higher)		401 (1 RCT)	⊕⊕⊖⊖ **Low**[c]	
Procedure time for first-pass cannulation (seconds) Follow-up: immediately after the procedure	The mean procedure time for first-pass cannulation was **122.6 seconds**	**MD 95.2 seconds longer** (72.8 longer to 117.6 longer)		401 (1 RCT)	⊕⊕⊕⊕ **High**	
Number of cannulation attempts Follow-up: immediately after the procedure	See comment	-	-	-	-	None of the studies included moderately difficult participants
Patient satisfaction NRS from 0 to 10 or 4-step Likert scale The higher the score the higher the level of satisfaction Follow-up: immediately after the procedure	See comment	-	-	-	-	None of the studies included moderately difficult participants

Overall complications Follow-up: immediately after the procedure	**65 per 1000**	**54 per 1000** (25 to 119)	**RR 0.83** (0.38 to 1.82)	401 (1 RCT)	⊕⊕⊕⊖ **Moderate**[d]

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **LM:** landmark; **MD:** mean difference; **NRS:** numeric rating scale; **RCTs:** randomised controlled trials; **RR:** risk ratio; **USG:** ultrasound guidance

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]Participants were classified according to the original studies' definitions.
[b]We downgraded by one level to moderate certainty due to imprecision.
[c]We downgraded by a total of two levels to low certainty due to risk of bias concerns (lack of blinding of the outcome assessors) and imprecision.
[d]We downgraded by one level to moderate certainty due to imprecision.

Summary of findings 3. Ultrasound guidance versus landmark method for peripheral venous cannulation in adults classed as easy

Patient or population: adults undergoing peripheral venous cannulation classed as easy[a]

Settings: emergency department

Intervention: USG

Comparison: LM

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with LM	Risk with USG				
First-pass success of cannulation Follow-up: immediately after the procedure	**966 per 1000**	**859 per 1000** (821 to 908)	**RR 0.89** (0.85 to 0.94)	596 (1 RCT)	⊕⊕⊕⊕ **High**	
Overall success of cannulation Follow-up: immediately after the procedure	See comment	-	-	-	-	None of the studies included easy participants

Pain NRS: from 0 to 10, where 10 is maximum pain Follow-up: immediately after the procedure	The mean pain score was **2.30**	**MD 0.60 higher** (0.17 higher to 1.03 higher)		596 (1 RCT)	⊕⊕⊕⊖ **Moderate**[b]	
Procedure time for first-pass cannulation (seconds) Follow-up: immediately after the procedure	The mean procedure time for first-pass cannulation was **89.7 seconds**	**MD 94.8 seconds longer** (81.2 longer to 108.5 longer)		596 (1 RCT)	⊕⊕⊕⊕ **High**	
Number of cannulation attempts Follow-up: immediately after the procedure	See comment	-	-	-	-	None of the studies included easy participants
Patient satisfaction NRS from 0 to 10 or 4-step Likert scale The higher the score, the higher the level of satisfaction Follow-up: immediately after the procedure	See comment	-	-	-	-	None of the studies included easy participants
Overall complications Follow-up: immediately after the procedure	**17 per 1000**	**43 per 1000** (15 to 118)	**RR 2.48** (0.90 to 6.87)	596 (1 RCT)	⊕⊕⊕⊖ **Moderate**[c]	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **LM:** landmark; **NRS:** numeric rating scale; **RCTs:** randomised controlled trials; **RR:** risk ratio; **USG:** ultrasound guidance

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]Participants were classified according to the original studies' definitions.
[b]We downgraded by one level to moderate certainty due to risk of bias concerns (lack of blinding of the outcome assessors).
[c]We downgraded by one level to moderate certainty due to imprecision.

BACKGROUND

Description of the condition

Placing a peripheral intravenous line is one of the most essential procedures in hospitals. It is necessary when administering fluids and drugs, and drawing blood. It is usually performed using the landmark method, comprising visualisation and palpation of the veins (Moureau 2019; Sadud 2019; Troianos 2012). Placing a peripheral intravenous line is occasionally difficult. The first attempt is unsuccessful in as many as 14% to 21% of adults in the emergency department (Carr 2016; Sebbane 2013), and in 9% to 26% of adults in the prehospital setting (Jones 1989; Lapostolle 2007; Minville 2006). About 10% of surgical patients or those in emergency departments require three or more attempts (Civetta 2019; Davis 2021; Fields 2012). This is mainly due to factors including obesity, chronic illness, intravenous drug use, dehydration, and shock (Mills 2007; Ortega 2008; Sebbane 2013). The failure rate at the first attempt is much higher in people with difficult intravenous access, reported as being between 34% and 93% (McCarthy 2016; Sebbane 2013; Van Loon 2016). Multiple punctures lead to discomfort, anxiety, delay in subsequent interventions, and return of test results (Davis 2021). If a peripheral intravenous line cannot be placed with the landmark method, a central venous line is often the next step in those with difficult intravenous access. However, central venous line placement is costly, time-consuming, and exposes people to more pain and discomfort. In addition, central venous line placement can cause serious complications, such as infection, thrombosis, and pneumothorax, which are reported to occur in more than 15% of people (McGee 2003). Hence, the insertion of a central venous line should be considered as a last resort. Placing a peripheral intravenous line with ultrasound guidance may be an alternative for people with difficult intravenous cannulation.

Description of the intervention

Ullmann and Stoelting first reported the use of ultrasound for intravenous cannulation in 1978 (Ullman 1978). Since then, ultrasound guidance has been widely used for cannulation of central veins, and it has become the standard of care in recent years. Keyes and colleagues first reported ultrasound-guided peripheral intravenous cannulation in 1999 (Keyes 1999). There are two techniques for ultrasound guidance: short-axis (out-of-plane) and long-axis (in-plane). The short-axis technique uses the short-axis image of a targeted vein and has two methods: a static method and a dynamic method. In the static method, ultrasound is used to determine the location and the diameter of the vein and to evaluate important surrounding structures, such as arteries and nerves. Because cannulation is attempted without real-time ultrasound guidance, the location of the targeted vein can be missed. In the dynamic method, the entire procedure is performed under real-time ultrasound guidance, enabling operators to visualise both the vein and the important surrounding structures. However, there is a risk of puncturing the posterior wall because it is occasionally difficult to identify and visualise the needle tip throughout the procedure. The long-axis technique uses a long-axis image of the targeted vein and needle. Because it can visualise the entire length of the needle, the risk of puncturing the posterior wall is theoretically low. However, it is difficult for operators to maintain the needle and targeted vein within the narrow width of the ultrasound beam, and they cannot visualise important surrounding structures. Two randomised controlled trials (RCTs) compared short- and long-axis techniques, and in neither trial was there a significant overall difference in success between the two techniques (Mahler 2011; Privitera 2021).

Although evidence about the longevity of functional catheters placed with ultrasound guidance versus the landmark methods is mixed, the target vein's depth and the appropriate needle length are probably important factors. Using 4.8 cm or 6.35 cm catheters, 53% to 75% of catheters placed under ultrasound guidance were still functional at 24 hours, compared with 74% to 99% of catheters placed by the landmark method. (Dargin 2010; Dillon 2008). However, another study showed a similar proportion of functional catheters for ultrasound guidance and the landmark method at 72 hours: 73% and 78%, respectively (Shokoohi 2019). Of note, long needles were used more often in the ultrasound guidance group than in the landmark method group (40% versus 1%) (Shokoohi 2019). Furthermore, using a 4.8 cm catheter, the proportion of functional catheters placed with ultrasound guidance at 48 hours was 100% for veins at less than 0.4 cm depth, 62% for veins that were at 0.41 cm to 1.19 cm depth, and 29% for veins at 1.2 cm depth or greater (Fields 2012). Therefore, ultrasound guidance requires a longer needle appropriate for the vein's depth because ultrasound guidance targets deeper veins than the landmark method.

The length of the catheter in the vein is also important for the longevity of functional catheters. At 72 hours, 100% of intravenous lines failed if the length of the catheter in the vein was less than 30% of the total catheter length, 32% failed if it was between 30% and 64%, and none failed if it was greater than 65% (Pandurangadu 2018). It is occasionally difficult to visualise the needle tip or needle when the subcutaneous tissue between the skin surface and the target vein is thin. The ideal depth of the target vein could be at least 0.5 cm, using a 4.57 cm catheter (Avila 2019). Therefore, when using a usual intravenous catheter of up to about 5 cm, it may be desirable to select a vein with a depth of approximately 0.5 cm to 1 cm and place a catheter roughly half the length into the vein. Longer catheters (approximately 6 cm to 20 cm), such as midline catheters, may be a better option, especially for veins that are at a subcutaneous depth of approximately 1 cm or more because long catheters survive longer and have a similar success of cannulation compared to usual catheters (Bahl 2019; Bahl 2020; Elia 2012). However, the Seldinger technique is used for midline catheters, which are more costly (Adams 2016; Seldinger 1953). The usefulness of longer catheters is beyond the scope of this review. The Michigan Appropriateness Guide for Intravenous Catheters offers a method for selecting catheters (Chopra 2015).

How the intervention might work

If the targeted peripheral vein is visible or palpable, cannulation is usually straightforward with the landmark method and will be successful at the first attempt in over 95% of cases (McCarthy 2016). However, the location and diameter of peripheral veins differ substantially between people. It is often difficult to cannulate deep peripheral veins that are not visible and palpable from the skin surface. Ultrasound can help the operator to: visualise the local anatomy of interest; identify the size and direction of veins and important surrounding structures, such as arteries and nerves; and clarify the diameter and route of these important structures. Furthermore, in the dynamic method, where the needle is visualised with ultrasound, the operator can see the spatial relationships between the vein, surrounding structures, and the needle. Thus, ultrasound guidance may facilitate successful

cannulation and prevent complications, especially in people with difficult intravenous access who would otherwise be candidates for central venous line placement. Shokoohi and colleagues reported data from a cohort study, where the number of central venous lines placed decreased by 80% during the six years after the introduction of ultrasound-guided peripheral intravenous cannulation (Shokoohi 2013).

Why it is important to do this review

The efficacy of ultrasound guidance for central venous cannulation has been established (Brass 2015a; Brass 2015b; Wu 2013). The National Institute for Health and Care Excellence and the American Society of Anesthesiologists recommend using ultrasound guidance for central venous cannulation (ASA Task Force 2012; NICE 2002), and it is currently the standard of care. However, the efficacy of ultrasound guidance for peripheral intravenous cannulation has not been well established. Several meta-analyses have been conducted (Egan 2013; Heinrichs 2013; Liu 2014; Stolz 2015; Van Loon 2018; Tran 2021), and the results have shown a fairly consistent increase in the overall success with ultrasound guidance in people with difficult intravenous cannulation. However, there are several weaknesses in the synthesised evidence on this topic to date. Most of the included studies had fewer than 60 participants and larger studies (1189 participants) have since been published (McCarthy 2016). Older studies did not always use appropriate methodology and seldom evaluated the first-pass success (successful cannulation at first attempt), reporting the overall success instead. Even if the overall success improves, it may not be beneficial if it subjects individuals to more skin punctures. Furthermore, because peripheral intravenous cannulation with the landmark method is usually straightforward for people with easy intravenous access, the efficacy of ultrasound guidance for peripheral intravenous cannulation varies according to the difficulty of intravenous access. However, previous studies were unclear in their definition of the difficulty or did not take into account the impact of the difficulty. This methodologically rigorous meta-analysis assesses the influence of intravenous access difficulty, reports the current evidence for patient-relevant outcomes, and hopes to aid decision-making for placing peripheral intravenous cannulation.

OBJECTIVES

To evaluate the effectiveness and safety of ultrasound guidance compared to the landmark method for peripheral intravenous cannulation in adults.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials (RCTs), including cluster-randomised controlled trials, cross-over trials, and quasi-RCTs (RCTs in which participants are allocated based on data such as date of birth, date of recruitment, or medical record number).

Types of participants

We included all adult participants (≥ 18 years old) with any clinical characteristics, in any setting, who required a peripheral intravenous line, irrespective of the difficulty of cannulation. We defined a peripheral intravenous line as a catheter placed in a peripheral vein. We excluded central lines, intraosseous lines, and peripherally inserted central lines. We excluded children because the effect of ultrasound guidance would be different for them, due to smaller veins and extremities, and a possible lack of cooperation.

Placing a peripheral intravenous line in individuals can be classed as ‘difficult’, ‘moderate’, or ‘easy’. We use the terms ‘difficult participants’, ‘moderate/moderately difficult participants’ and ‘easy participants’ as shorthand to characterise the difficulty level in placing a peripheral line using the landmark method. We used the original studies’ definitions of difficulty levels of peripheral intravenous cannulation with the landmark method. We analysed the results in these subgroups: ‘all participants’, ‘difficult participants’, ‘moderate participants’, and ‘easy participants'. We did this because we expected the effect of ultrasound-guided peripheral venous cannulation to be the largest in participants classed as 'difficult' and smaller in participants classed as 'moderate' and 'easy' (see Subgroup analysis and investigation of heterogeneity).

Types of interventions

We included studies comparing ultrasound-guided peripheral intravenous cannulation with the landmark method, irrespective of the profession of the operators, number of operators (one- or two-person method), methods (short-axis or long-axis, static or dynamic), or the sites of the peripheral veins, and all studies using ultrasonography, irrespective of the manufacturer or generation of the ultrasound machine. We excluded studies on peripherally inserted central catheters.

Types of outcome measures

We did not use outcome measures as a criterion for excluding studies. All outcome measures below would be reported at the time of cannulation.

Primary outcomes

- First-pass success of cannulation
- Overall success of cannulation
- Pain

We defined the overall success of cannulation as the success of cannulation irrespective of the number of attempts and procedure time. We defined successful cannulation as stated by the study authors. A cutaneous puncture was counted as one attempt, irrespective of the duration of subcutaneous exploration. We anticipated that studies would use different pain intensity scales, with most studies using standard subjective scales, such as a numerical rating scale (NRS) or a visual analogue scale (VAS).

Secondary outcomes

- Procedure time for first-pass cannulation
- Procedure time for overall cannulation
- Number of cannulation attempts
- Patient satisfaction
- Overall complications (including arterial puncture, haematoma, and nerve injury)

Studies could report patient satisfaction results as either continuous or dichotomous data. Scales of patient satisfaction

included Likert scales and validated instruments, such as the Client Satisfaction Questionnaire-18 (Attkisson 1982).

Search methods for identification of studies

Electronic searches

The Cochrane Vascular Information Specialist conducted systematic searches of the following databases for RCTs and controlled clinical trials without language, publication year, or publication status restrictions:

- the Cochrane Vascular Specialised Register via the Cochrane Register of Studies (CRS-Web);
- the Cochrane Central Register of Controlled Trials (CENTRAL) via the Cochrane Register of Studies Online (CRSO);
- MEDLINE (Ovid MEDLINE Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE Daily and Ovid MEDLINE);
- Embase Ovid;
- CINAHL (Cumulative Index to Nursing and Allied Health Literature) EBSCO;
- LILACS (Latin American and Caribbean Health Science Information) Bireme.

We developed search strategies for other databases from the search strategy designed for MEDLINE. Where appropriate, they were combined with adaptations of the highly sensitive search strategy designed by Cochrane for identifying randomised controlled trials and controlled clinical trials (as described in the *Cochrane Handbook for Systematic Reviews of Interventions* Chapter 4, Lefebvre 2021). Search strategies for major databases are provided in Appendix 1.

We searched the following trials registries:

- the World Health Organization International Clinical Trials Registry Platform (who.int/trialsearch);
- ClinicalTrials.gov (clinicaltrials.gov).

The most recent searches were carried out on 29 November 2021.

Searching other resources

Four review authors (MT, TM, CT, NY) checked the reference lists of all identified studies and review articles to find additional studies. We contacted trial authors, experts in this field, and manufacturers of ultrasound machines to identify unpublished studies.

Data collection and analysis

Selection of studies

We used the reference management software Mendeley to collate the results of searches and to remove duplicates (Mendeley). We used Rayyan software to screen the results of the search (Ouzzani 2016). Four review authors (MT, TM, CT, NY) independently and in duplicate checked titles and abstracts of the results of the search and identified potentially relevant studies. We obtained full texts of all potentially relevant studies if any of the authors judged them to be relevant or potentially relevant. We excluded only the clearly irrelevant articles at this stage. Four review authors (MT, TM, CT, NY) independently and in duplicate assessed the full papers for eligibility using a pre-designed checklist. We compared the results and resolved disagreements through discussion. If we were unable to reach a consensus, we consulted the sixth review author (NW). We recorded the number of papers retrieved at each stage and reported this information using a PRISMA flowchart.

Data extraction and management

We used a Microsoft Excel data extraction sheet that we designed specifically for this study (Microsoft Excel 2020). Four review authors (MT, TM, CT, NY) independently and in duplicate extracted the data using the extraction form. We resolved disagreements through discussions. If we could not reach a consensus, we consulted the sixth review author (NW). If additional information was necessary, one review author (MT) contacted the corresponding author of the relevant studies. When we completed data extraction, one review author (MT) entered the data into Review Manager software and another review author (NY) checked the data (RevMan Web 2020).

Assessment of risk of bias in included studies

Four review authors (MT, TM, CT, NY) independently assessed the methodological quality of each included study using the Cochrane risk of bias 1 tool (Higgins 2011). We evaluated the following domains and rated them as at low, unclear, or high risk of bias:

- random sequence generation (selection bias);
- allocation concealment (selection bias);
- blinding (performance bias and detection bias);
- incomplete outcome data (attrition bias);
- selective outcome reporting (outcome reporting bias);
- other potential sources of bias;
- overall risk.

Due to the nature of the intervention, blinding the operators was not possible. This might have caused some performance bias, but it was unavoidable and not expected to be serious. It was also not possible to blind the participants, but this should not have affected objective outcomes, such as the success of cannulation. For this reason, we assessed performance and detection bias as one domain and assessed blinding separately for each outcome. We evaluated objective outcomes as low risk when a third person assessed the outcome. For subjective outcomes, such as pain and satisfaction, we evaluated them as high risk regardless of the outcome assessor. We also assessed incomplete outcome data and overall risk separately for each outcome.

We defined the overall risk of bias for each outcome as follows:

- low risk of bias: all domains rated as low risk;
- moderate risk of bias: one or more domains rated as being at unclear risk;
- high risk of bias: one or more domains rated as being at high risk.

We reviewed the assessments and resolved any disagreements through discussion. If needed, we consulted the sixth review author (NW).

Measures of treatment effect

We calculated dichotomous data as risk ratios (RR) with 95% confidence intervals (CIs). We calculated continuous data as mean differences (MDs) with 95% CIs when the outcomes of all studies

used the same scale. We used a standardised mean difference (SMD) with 95% CIs if different scales were used.

Unit of analysis issues

The unit of analysis was the individual participant. If we included any cluster-randomised trials, we planned to adjust the sample size by the trial's intracluster correlation coefficient, using the method described in the *Cochrane Handbook for Systematic Reviews of Intervention* (Higgins 2021a). We excluded any cluster-randomised trials which did not report the intracluster correlation coefficient.

Dealing with missing data

We contacted the study authors when possible to obtain missing data. We performed an intention-to-treat analysis when possible. We planned to impute data for binary outcomes using various scenarios, such as "best-case" and "worst-case" scenarios. For continuous outcomes, we used available case analysis. We calculated the standard deviation from P values, standard errors, or CIs according to the instructions given in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2021a). Otherwise, we imputed them from other studies in the meta-analysis according to the validated method (Furukawa 2006).

Assessment of heterogeneity

We assessed heterogeneity by inspecting forest plots visually and examined statistical heterogeneity by Chi^2 and I^2 statistics. We used P = 0.10 as the predefined significance level of heterogeneity for the Chi^2 test. We considered I^2 statistics of 25% or lower to indicate low heterogeneity, between 25% and 50% to indicate moderate heterogeneity, and 50% or more to indicate substantial heterogeneity. However, we interpreted this value in light of the size and direction of effect and the strength of the evidence for heterogeneity, based on the P value from the Chi^2 test (Higgins 2021a). If we identified substantial heterogeneity, we investigated and reported potential reasons for this.

Assessment of reporting biases

We tried to minimise the effect of publication bias by performing well-designed, comprehensive literature searches, by using trial registries, such as ClinicalTrials.gov, and by contacting the manufacturers of ultrasound machines. If we included a sufficient number of studies in a meta-analysis (that is, more than 10 studies; Higgins 2021a), we visually inspected funnel plots to evaluate small study effects and used contour-enhanced funnel plots to evaluate publication bias. We evaluated reporting bias by checking the protocol of the study if we could identify one from trial registries.

Data synthesis

We reviewed the data from the included studies and, if possible, synthesised and analysed data using Review Manager software (RevMan Web 2020). We used the random-effects model to pool data because we expected the definitions of participants and operators to vary to some extent amongst studies, and also because the random-effects model is more conservative than the fixed-effect model. If it was not possible to pool data, we provided clear reasons for this and reported results narratively.

Subgroup analysis and investigation of heterogeneity

We performed subgroup analyses of the following parameters for the primary outcomes if we found sufficient data from the included studies. For conditions other than the definition of the difficulty of intravenous access with the landmark method, we performed subgroup analyses using the original studies' definitions of the difficulty.

The difficulty of obtaining intravenous access: 'difficult' versus 'moderately difficult' versus 'easy'

Because the effect of ultrasound guidance varied depending on the difficulty of obtaining intravenous access in each participant, we evaluated participants separately for each difficulty level, according to the following criteria:

- we used the definition of the difficulty of peripheral intravenous cannulation adopted by original studies;
- we defined the difficulty based on the first-pass success or the overall success of cannulation using the landmark method.

Because we expected the definition of the difficulty of peripheral intravenous cannulation to differ between studies (Egan 2013; Liu 2014), we also defined the difficulty based on the first-pass success and, where the first-pass success was not assessed, on the overall success of cannulation using the landmark method. As in previous studies, we classified success rates of lower than 60%, 60% to 80%, and higher than 80% as "difficult", "moderately difficult", and "easy", respectively (McCarthy 2016; Sebbane 2013; Van Loon 2016). For example, Aponte 2007 moves from 'difficult' venous access participants, based on the original study's definition, to 'easy' participants, based on the definition of the success rate with the landmark method. We performed a post hoc meta-regression analysis to assess the effect of the difficulty level on the primary outcomes if the test for subgroup difference was significant, and there were three or more subgroups and 10 or more studies in total. We performed the following post hoc subgroup analyses on difficult participants only, except for the type of ultrasound guidance, due to the small number of studies for moderately difficult and easy participants. We used the original studies' definitions of the difficulty for the subgroup analyses. We performed the meta-regression analyses with R (version 4.0.3) (R 2020).

Practical difficulties of obtaining intravenous access

We analysed participants separately where they satisfied the definition of a difficult case. A difficult case was defined as any of the following:

- the operator could not see and palpate the targeted vein;
- the operator identified a participant as a difficult case;
- the participant had a history of difficult intravenous access;
- the participant had multiple failed attempts.

Operators' skill and study setting

We analysed separately according to the following criteria:

- finished any kind of training programme for ultrasound-guided peripheral intravenous cannulation;
- had any clinical experience with ultrasound-guided peripheral intravenous cannulation;

- finished any kind of training programme for ultrasound-guided peripheral intravenous cannulation and had any clinical experience with ultrasound-guided peripheral intravenous cannulation;
- types of operators;
- study settings: emergency departments or intensive care units (ICUs) versus operating rooms.

Compared to participants in operating rooms, those in emergency departments or ICUs would be more likely to be in shock or dehydrated. Since these factors are associated with difficult intravenous cannulation, ultrasound guidance might be more effective in the setting of emergency departments or ICUs than in operating rooms.

Date of publication: 1999 to 2008 versus 2009 to 2019

Advances in machine technology have led to improved ultrasound image quality, improving the effectiveness of ultrasound guidance. Therefore, we stratified the studies by publication year into two groups: 1999 to 2008, and 2009 to 2019. If we included more than 10 studies, we also performed univariate meta-regression with R software, using publication year as a continuous covariate (R 2020).

Types of ultrasound guidance

We planned to analyse studies separately according to the type of ultrasound guidance:

- short-axis technique versus long-axis technique;
- dynamic method versus static method.

Sensitivity analysis

We performed sensitivity analyses for the following factors, using the original studies' definitions of the difficulty, if applicable.

- We limited the analysis to studies with a low overall risk of bias. We defined the low overall risk of bias as satisfying all the following domains: adequate allocation concealment, blinding of outcome assessment, and data analysis performed according to the intention-to-treat principle.
- We limited the analysis to RCTs only.

Summary of findings and assessment of the certainty of the evidence

We summarised the main findings of each relevant outcome, recording the magnitude of effect, total number of participants, and the number of relevant studies. We assessed the certainty of the evidence using the GRADE approach (GRADE 2004). We used the GRADEpro software to assist in the preparation of the summary of findings tables (GRADEpro GDT). We created one table each for each class of difficulty using the original studies' definitions of the difficulty. See Summary of findings 1; Summary of findings 2; Summary of findings 3. We included the following outcomes:

- first-pass success of cannulation;
- overall success of cannulation;
- pain;
- procedure time for first-pass cannulation;
- number of attempts before successful cannulation;
- patient satisfaction;
- overall complications (arterial punctures, haematoma formations, and nerve injuries).

We presented the results of the subgroup analyses in additional summary of findings tables where sufficient data were available. We considered the following subgroup analyses to be sufficiently clinically relevant to present as additional summary of findings tables:

- Operators had any clinical experience with ultrasound-guided peripheral intravenous cannulation (see Appendix 2);
- Setting (see Appendix 3).

RESULTS

Description of studies

Results of the search

The first search in October 2019 identified 2966 articles; the second update search in November 2020 identified 571 articles; the third update search in November 2021 identified a further 501 articles. We removed 67 duplicate articles and screened the remaining 3971 articles. We removed 3936 articles after title and abstract screening, and assessed the remaining 35 articles in full text. We included 16 studies (from 14 full-text articles) in the quantitative analysis and excluded 14 articles at full-text review. We identified six ongoing studies and listed one study as 'awaiting classification'. The inter-rater agreement for the full-text screening stage was substantial (κ = 0.82). See Figure 1 for the flow diagram and exclusion reasons.

Figure 1. Study flow diagram

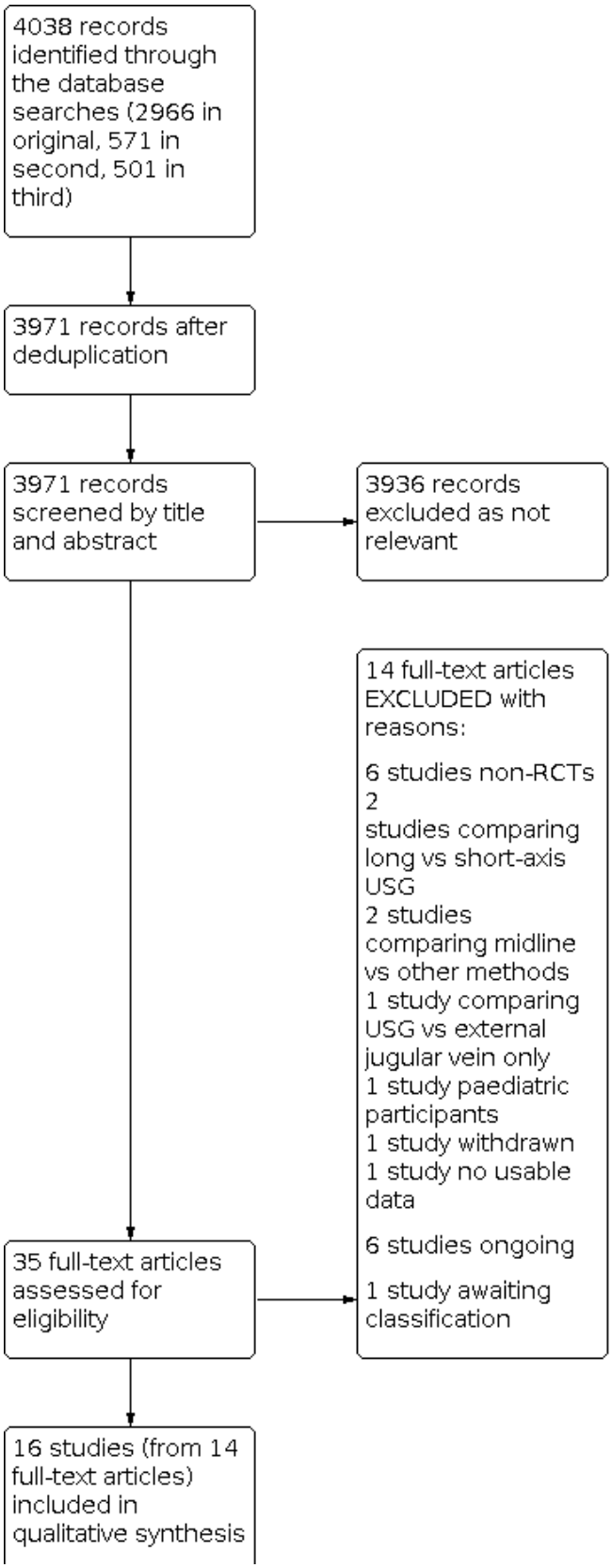
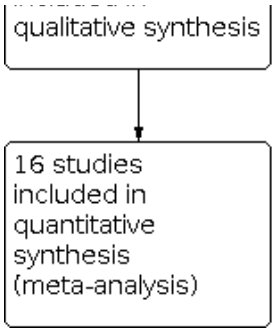


Figure 1. (Continued)



Included studies

See Characteristics of included studies.

We identified 14 articles (2267 participants) that compared the efficacy of ultrasound guidance and the landmark method for peripheral intravenous cannulation (Aponte 2007; Bahl 2016; Bridey 2018; Costantino 2005; Glasin 2020; İsmailoğlu 2015; Kerforne 2012; McCarthy 2016; Nishizawa 2020; Pappas 2006; River 2009; Skulec 2019; Stein 2009; Weiner 2013). McCarthy 2016 randomised participants separately according to the difficulty of the landmark method (easy, moderate, and difficult). Because it is only possible to analyse two comparisons from any study in Review Manager at one time, we split the study according to the difficulty level and added the details for each level as a separate study, indicated by the study ID 'McCarthy 2016' plus A, B, or C (McCarthy 2016A; McCarthy 2016B; McCarthy 2016C). Therefore, in effect, we included 16 studies. Kerforne 2012 and River 2009 were conference reports, and Pappas 2006 was a report from the United States Air Force. Glasin 2020 has not been published yet, but the data were available owing to the courtesy of the study author. All other studies were published in peer-reviewed journals. Amongst the 16 studies, 14 were RCTs, and two were quasi-RCTs (Costantino 2005; İsmailoğlu 2015). Costantino 2005 allocated participants according to the day of presentation to the emergency department (odd day: ultrasound guidance, even day: landmark method), and İsmailoğlu 2015 allocated participants to each group alternately, in the order in which they were seen. Ten studies were conducted in the emergency department (Bahl 2016; Costantino 2005; Glasin 2020; İsmailoğlu 2015; McCarthy 2016A; McCarthy 2016B; McCarthy 2016C; River 2009; Stein 2009; Weiner 2013), three in the ICU (Bridey 2018; Kerforne 2012; Nishizawa 2020), two in the operating room (Aponte 2007; Pappas 2006), and one in the prehospital setting (Skulec 2019).

Most studies targeted participants with difficult intravenous cannulation with the landmark method (Aponte 2007; Bahl 2016; Bridey 2018; Costantino 2005; İsmailoğlu 2015; Kerforne 2012; McCarthy 2016A; Nishizawa 2020; Pappas 2006; River 2009; Stein 2009; Weiner 2013). The studies varied in how they defined 'difficulty', but all definitions were clinically valid. Three studies defined it as failing at least two or three times with the landmark method (Pappas 2006; River 2009; Stein 2009); three studies as no apparent or palpable veins (Bridey 2018; Kerforne 2012; McCarthy 2016A); and one study as a history of difficult intravenous cannulation (Bahl 2016). Aponte 2007 defined 'difficulty' as either a history of difficult intravenous cannulation or an operator's decision that a participant was difficult. Costantino 2005 defined it as a history of difficult cannulation and failing at least three times. İsmailoğlu 2015 defined it as a history or suspicion of difficult cannulation, and no apparent or palpable veins. Nishizawa 2020 defined it as either failing two times with the landmark method or an operator's decision based on the absence of palpable veins or a history of difficult intravenous cannulation. Weiner 2013 defined it as either failing two times with the landmark method or having a history of difficult intravenous cannulation.

One study defined 'moderately difficult' participants as those in whom the operators could visualise or palpate at least one vein but were expected to have difficulty with the landmark method (McCarthy 2016B). One study defined 'easy' participants as those in whom the operator could see or palpate at least one vein and thought intravenous access would be easy with the landmark method (McCarthy 2016C). Two studies did not limit by the landmark method difficulty (Glasin 2020; Skulec 2019). Glasin 2020 recruited participants with obesity (body mass index > 25 kg/m^2), and Skulec 2019 included all participants irrespective of the difficulty.

We expected that the varying definitions of 'difficulty' would cause heterogeneity. Therefore, we also redefined the difficulty by the first-pass success or the overall success of cannulation with the landmark method as planned in the protocol, with a success rate of lower than 60% defined as difficult, 60% to 80% as moderate, and higher than 80% as easy. As a result, nine studies were classified as difficult (Bahl 2016; Bridey 2018; Costantino 2005; İsmailoğlu 2015; Kerforne 2012; McCarthy 2016A; Nishizawa 2020; Stein 2009; Weiner 2013), four were classified as moderate (Glasin 2020; McCarthy 2016B; River 2009; Skulec 2019), and two were classified as easy (Aponte 2007; McCarthy 2016C). Pappas 2006 was unclassifiable because there were no success rate results.

Twelve studies employed dynamic ultrasound guidance (Aponte 2007; Costantino 2005; Glasin 2020; İsmailoğlu 2015; Kerforne 2012; McCarthy 2016A; McCarthy 2016B; McCarthy 2016C; Nishizawa 2020; Pappas 2006; Stein 2009; Weiner 2013), and one study had three arms comparing dynamic ultrasound guidance, static ultrasound guidance, and the landmark method (Skulec 2019). Three studies did not specify if they employed dynamic or static guidance (Bahl 2016; Bridey 2018; River 2009). Amongst the 13 studies employing dynamic guidance, five studies used short-axis ultrasound guidance (Costantino 2005; Glasin 2020; Nishizawa 2020; Skulec 2019; Weiner 2013), and eight studies did not specify if they used short- or long-axis ultrasound guidance (Aponte 2007; İsmailoğlu 2015; Kerforne 2012; McCarthy 2016A; McCarthy 2016B; McCarthy 2016C; Pappas 2006; Stein 2009). No study used only

long-axis ultrasound guidance. A variety of ultrasound machines were used, with the oldest being Site-Rite 3 (Aponte 2007; Pappas 2006), and the newest being x-Porte (Glasin 2020). Five studies used M-turbo (Bahl 2016; McCarthy 2016A; McCarthy 2016B; McCarthy 2016C; Weiner 2013); this machine was the most commonly used amongst the included studies.

In 10 studies, the operators were nurses (Aponte 2007; Bahl 2016; Bridey 2018; Glasin 2020; İsmailoğlu 2015; Kerforne 2012; Nishizawa 2020; Pappas 2006; River 2009; Weiner 2013); in two studies, the operators were physicians (Costantino 2005; Stein 2009); in three studies, the operators were technicians (McCarthy 2016A; McCarthy 2016B; McCarthy 2016C); and in one study, they were paramedics and physicians (Skulec 2019). The number of operators ranged from two to 33 (median 20). Five studies did not report the number of operators (Bridey 2018; İsmailoğlu 2015; Kerforne 2012; River 2009; Weiner 2013). The operators performed both ultrasound guidance and the landmark method in most studies, but Glasin 2020 had 17 operators, and only one operator performed ultrasound guidance. The operators had clinical experience (any) with ultrasound guidance before the trials in 10 studies (Aponte 2007; Bridey 2018; Costantino 2005; Glasin 2020; McCarthy 2016A; McCarthy 2016B; McCarthy 2016C; Pappas 2006; River 2009; Stein 2009), but not in three studies (Bahl 2016; Nishizawa 2020; Weiner 2013). In Skulec 2019, physicians had clinical experience (any), but paramedics did not. In 14 studies, the operators had finished a training programme for ultrasound guidance (Aponte 2007; Bahl 2016; Bridey 2018; Costantino 2005; Glasin 2020; İsmailoğlu 2015; McCarthy 2016A; McCarthy 2016B; McCarthy 2016C; Nishizawa 2020; River 2009; Skulec 2019; Stein 2009; Weiner 2013); the training consisted mainly of lectures and hands-on practice. Kerforne 2012 and Pappas 2006 did not specify whether they provided a training programme. Seven studies reported the number of ultrasound guidance cases or experiences before the studies started, ranging from three cases in Nishizawa 2020 to more than 200 cases in Skulec 2019 (median five). Three studies reported on the frequency of ultrasound guidance during the study period, with 39% of operators performing five or more ultrasound-guided procedures per day (McCarthy 2016A; McCarthy 2016B; McCarthy 2016C).

All studies used usual intravenous catheters. McCarthy 2016A, McCarthy 2016B, McCarthy 2016C, Nishizawa 2020, and Skulec 2019 used both short (approximately 30 mm) and long needles (approximately 45 mm), while Bridey 2018 and Costantino 2005 used only short needles. The other studies did not specify the length of the needles used.

Excluded studies

We excluded 14 studies for the following reasons: six were not randomised controlled trials (Bauman 2009; DRKS00013797; Evans 2013; Galen 2018; NCT01602133; Raio 2018); two compared long- and short-axis ultrasound guidance (Hill 2017; NCT04234347); two compared midline and other methods (NCT03440944; NCT03457259); one compared ultrasound guidance with external jugular vein only (Costantino 2010); one study was in children (Curtis 2015); one study was withdrawn (NCT02360163); and one study had no usable data (Troisi 2013). See Characteristics of excluded studies.

Ongoing studies

We identified six ongoing studies (NCT03745209; NCT03841864; NCT04218643; NCT04853290; NCT04856826; NCT05119985). See Characteristics of ongoing studies.

Studies awaiting classification

One study is awaiting classification (IRCT201408097751N4). It was registered in 2015, but its status is unknown. See Characteristics of studies awaiting classification.

Risk of bias in included studies

To assess risk of bias, we considered each outcome separately for blinding (performance and detection bias), incomplete outcome data, and for overall bias. See Figure 2 and Figure 3. Of the high-risk assessments across the 16 studies, 78% were from the blinding domain, 15% were from the incomplete outcome data domain, and 7% were from the random sequence and allocation domain.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies

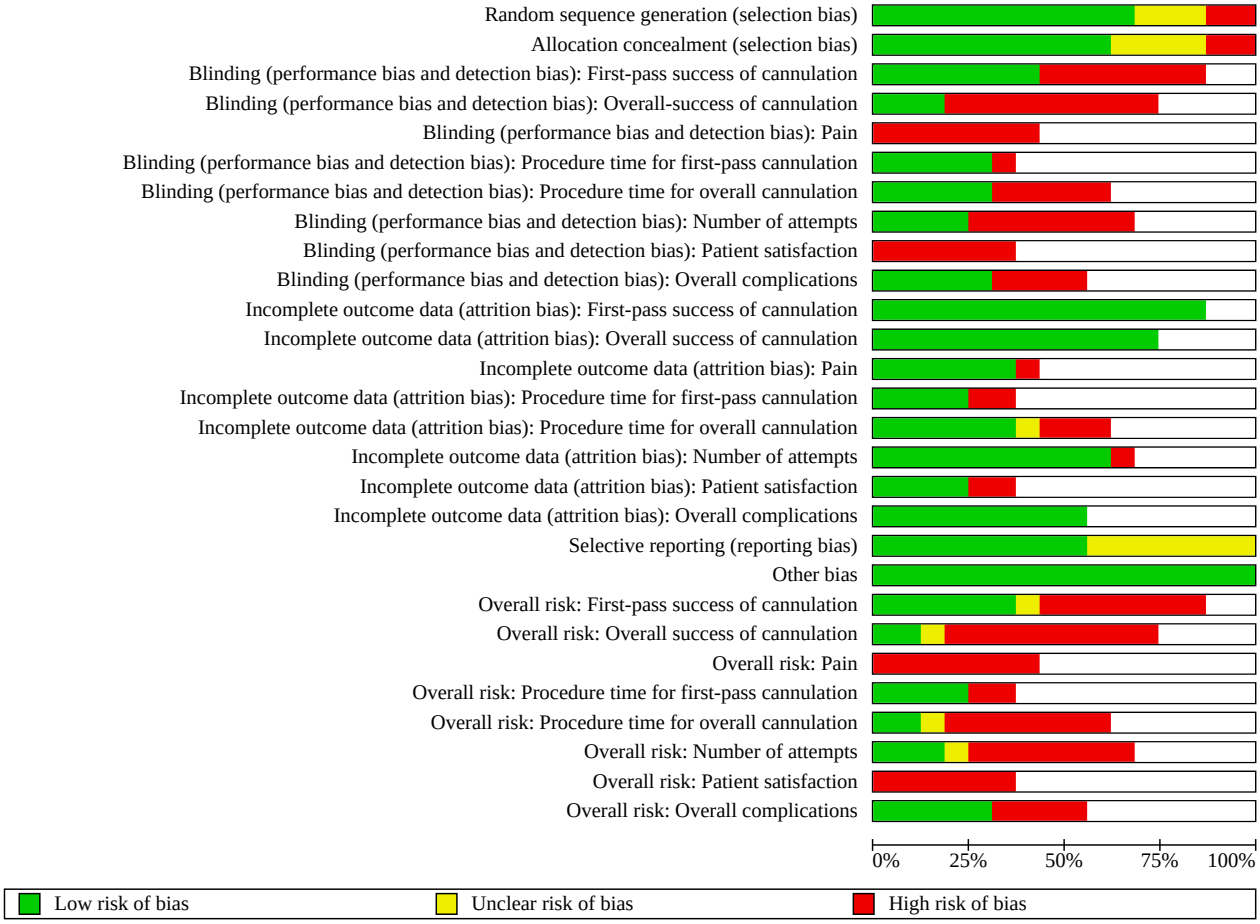
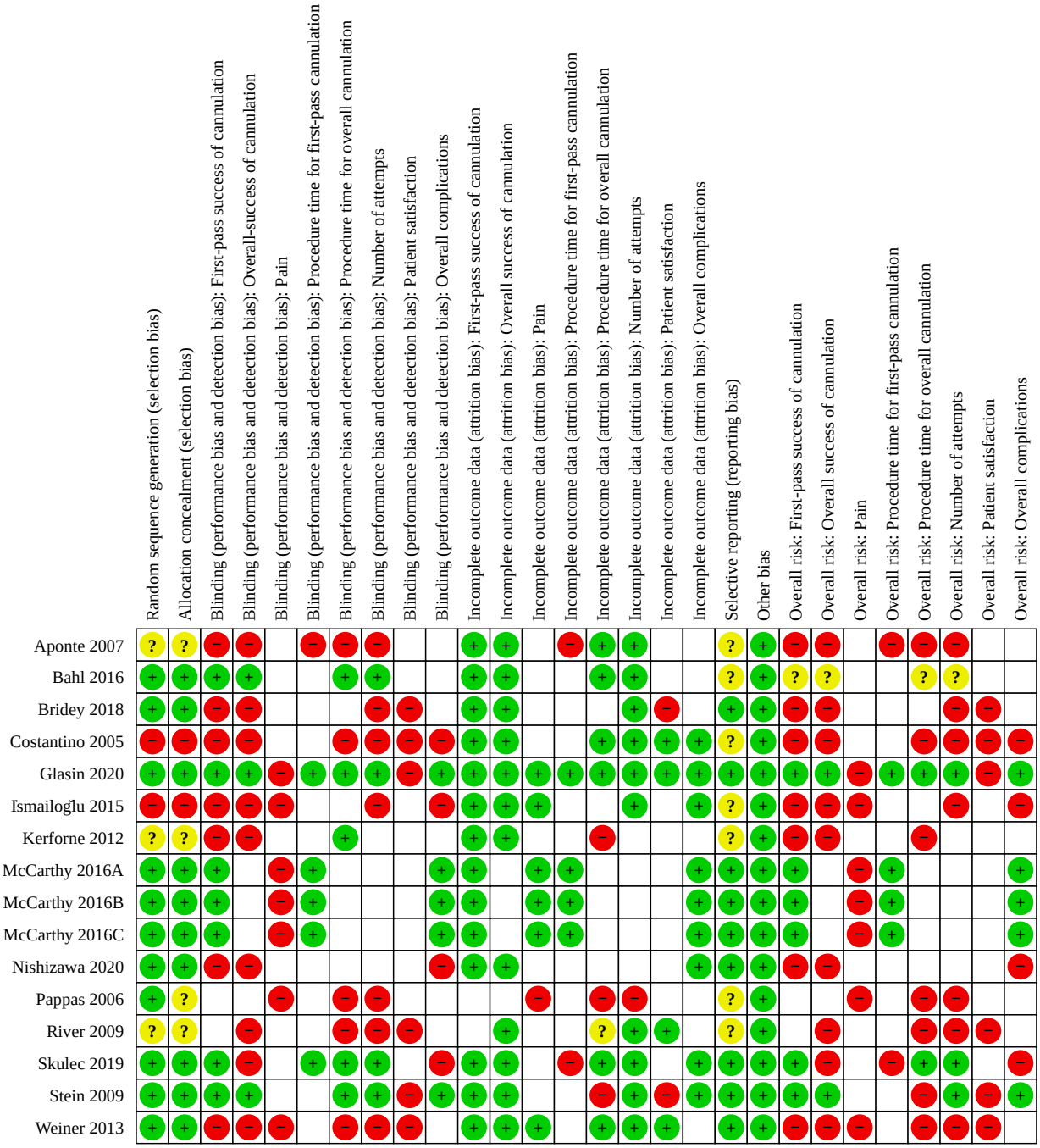


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study



Allocation

We assessed most of the studies (10/16) to be at low risk of selection bias (Bahl 2016; Bridey 2018; Glasin 2020; McCarthy 2016A; McCarthy 2016B; McCarthy 2016C; Nishizawa 2020; Skulec 2019; Stein 2009; Weiner 2013). One study allocated participants according to whether the emergency department visit was on an even or odd date (Costantino 2005). Another study allocated participants alternately to ultrasound guidance or the landmark method in the order in which they were seen (İsmailoğlu 2015). Therefore, we evaluated both random sequence generation and allocation concealment as high risk for both these studies. Four studies did not report the details on randomisation methods or allocation concealment, so we judged these to have an unclear risk

of selection bias (Aponte 2007; Kerforne 2012; Pappas 2006; River 2009).

Blinding

Due to the nature of the intervention, it was impossible to blind participants and operators, so the main source of bias was performance and detection bias. We assessed each outcome for bias. Amongst the blinding domain risk assessments, 39% were low risk, and 61% were high risk. In six studies, a third person acted as the outcome assessor for all outcomes; we evaluated these as low risk for objective outcomes (successful cannulation, procedure time, number of attempts, and complications), and as high risk for subjective outcomes (pain and satisfaction) (Bahl 2016; Glasin 2020; McCarthy 2016A; McCarthy 2016B; McCarthy 2016C; Stein 2009). In four studies, the outcome assessors were operators themselves for all outcomes (Aponte 2007; Bridey 2018; Costantino 2005; Pappas 2006), and investigators in three studies (İsmailoğlu 2015; Nishizawa 2020; Weiner 2013). Therefore, we evaluated these as high risk for all outcomes. One study did not report who assessed the outcomes, and we evaluated it as high risk for all outcomes (River 2009). In Kerforne 2012, the operators assessed successful cannulation (we evaluated as high risk), but a third person assessed procedure time (we evaluated as low risk) (Kerforne 2012). In Skulec 2019, operators assessed the overall success of cannulation and complications (we evaluated as high risk), but a third person assessed the other outcomes (we evaluated as low risk).

Incomplete outcome data

Eighty-seven per cent of the risk of bias assessments in this domain were low risk, and 13% were high risk. All studies that reported on first-pass success and overall success of cannulation were at low risk for attrition bias. One study reported results only for participants with successful cannulation in all its outcomes, and we evaluated all the outcomes of this study as high risk (Pappas 2006). The procedure time for first-pass cannulation in Aponte 2007 and Skulec 2019, and the procedure time for overall cannulation in Kerforne 2012, Pappas 2006, and Stein 2009 were reported only for participants with successful cannulation, and so we evaluated these as high risk. River 2009 did not specify whether the procedure time was reported for all participants or not, so we considered it at unclear risk. Bridey 2018 had 10 dropouts amongst 114 total participants (five in the ultrasound guidance group and five in the landmark method group; i.e. an 8.8% dropout rate), and Stein 2009 had seven dropouts amongst 59 participants (four in the ultrasound guidance group and three in the landmark method group; i.e. a 12% dropout rate) from the assessment of patient satisfaction. Although the numbers of dropouts were balanced between the two arms, the total numbers were substantial, and we considered these studies at high risk of attrition bias.

Selective reporting

Seven studies did not publish their protocols or register the studies (Aponte 2007; Bahl 2016; Costantino 2005; İsmailoğlu 2015; Kerforne 2012; Pappas 2006; River 2009). Thus, we could not exclude selective reporting and evaluated them as at unclear risk of bias. The remaining nine studies were at low risk of selective reporting (Bridey 2018; Glasin 2020; McCarthy 2016A; McCarthy 2016B; McCarthy 2016C; Nishizawa 2020; Skulec 2019; Stein 2009; Weiner 2013).

Other potential sources of bias

There were no other potential sources of bias in any included study.

Overall bias

The percentage of studies with low overall risk was 43% (6/14) for first-pass success of cannulation, 17% (2/12) for overall success of cannulation, zero (0/7) for pain, 67% (4/6) for procedure time for first-pass cannulation, 20% (2/10) for procedure time for overall cannulation, 27% (3/11) for number of attempts, zero (0/6) for patient satisfaction, and 56% (5/9) for complications.

The percentage of studies with unclear overall risk was 7% (1/14) for first-pass success of cannulation, 8% (1/12) for overall success of cannulation, zero (0/7) for pain, zero (0/6) for procedure time for first-pass cannulation, 10% (1/10) for procedure time for overall cannulation, 9% (1/11) for number of attempts, zero (0/6) for patient satisfaction, and zero (0/9) for complications.

The percentage of studies with high overall risk was 50% (7/14) for first-pass success of cannulation, 75% (9/12) for overall success of cannulation, 100% (7/7) for pain, 33% (2/6) for procedure time for first-pass cannulation, 70% (7/10) for procedure time for overall cannulation, 64% (7/11) for number of attempts, 100% (6/6) for patient satisfaction, and 44% (4/9) for complications.

Effects of interventions

See: **Summary of findings 1** Ultrasound guidance versus landmark method for peripheral venous cannulation in adults classed as difficult; **Summary of findings 2** Ultrasound guidance versus landmark method for peripheral venous cannulation in adults classed as moderately difficult; **Summary of findings 3** Ultrasound guidance versus landmark method for peripheral venous cannulation in adults classed as easy

We have reported the results of our meta-analyses subgrouped by level of difficulty as we expected the effect of ultrasound-guided peripheral venous cannulation to be largest in participants classed as ‘difficult’ and smaller in participants classed as ‘moderate’ and ‘easy’. We have presented results using the original studies' definition of difficulty and also when defined by success rate with the landmark method. We have presented the main findings by level of difficulty defined by the original studies in Summary of findings 1, Summary of findings 2, and Summary of findings 3. We have presented the main findings by level of difficulty defined by success rate with the landmark method in additional Summary of findings tables in Appendix 4, Appendix 5, and Appendix 6.

Primary outcomes

First-pass success of cannulation

All participants

Fourteen studies (2202 participants) evaluated first-pass success of cannulation (Aponte 2007; Bahl 2016; Bridey 2018; Costantino 2005; Glasin 2020; İsmailoğlu 2015; Kerforne 2012; McCarthy 2016A; McCarthy 2016B; McCarthy 2016C; Nishizawa 2020; Skulec 2019; Stein 2009; Weiner 2013). Ultrasound guidance increased the first-pass success of cannulation by 31% (RR 1.31, 95% CI 1.08 to 1.59; I^2 = 90%; low-certainty evidence; Analysis 1.1). The heterogeneity was considerable and the test for subgroup difference indicated a difference (P < 0.001). The effect sizes of ultrasound guidance varied: the effect size was the largest in difficult participants and

became smaller with decreasing difficulty according to the original studies' definitions. Meta-regression analysis for the effect of the difficulty level indicated a difference (P = 0.009). This difficulty-dependent trend of the effect sizes was similar when we defined the studies' difficulty by their success rate with the landmark method. Both the test for subgroup difference and the meta-regression analysis for the effect of the difficulty level also indicated a difference using the definition of success rate with the landmark method (P < 0.001) (Analysis 1.2).

Difficult participants

Ultrasound guidance improved the first-pass success of cannulation in difficult participants. According to the original studies' definitions, we classified ten studies (815 participants) as having difficult participants (Aponte 2007; Bahl 2016; Bridey 2018; Costantino 2005; İsmailoğlu 2015; Kerforne 2012; McCarthy 2016A; Nishizawa 2020; Stein 2009; Weiner 2013). Ultrasound guidance increased the first-pass success of cannulation by 50% (RR 1.50, 95% CI 1.15 to 1.95; I^2 = 62%; low-certainty evidence; Analysis 1.1). When we categorised studies based on their success rate with the landmark method, we classified nine studies (780 participants) as having difficult participants (Bahl 2016; Bridey 2018; Costantino 2005; İsmailoğlu 2015; Kerforne 2012; McCarthy 2016A; Nishizawa 2020; Stein 2009; Weiner 2013). With this definition, ultrasound guidance increased the first-pass success of cannulation by 62%, and the heterogeneity was lower than that defined by the original studies' definitions (RR 1.62, 95% CI 1.28 to 2.06; I^2 = 43%; moderate-certainty evidence; Analysis 1.2).

Moderate participants

Ultrasound guidance improved the first-pass success of cannulation in moderately difficult participants, but to a lesser extent than that in the difficult participants. According to the original studies' definitions, we classified one study (401 participants) as having moderately difficult participants (McCarthy 2016B). Ultrasound guidance increased the first-pass success of cannulation by 14% (RR 1.14, 95% CI 1.02 to 1.27; moderate-certainty evidence; Analysis 1.1). When we categorised studies based on their success rate with the landmark method, we classified three studies (791 participants) as having moderately difficult participants (Glasin 2020; McCarthy 2016B; Skulec 2019), and ultrasound guidance increased the first-pass success of cannulation by 17% (RR 1.17, 95% CI 1.09 to 1.26; I^2 = 0%; high-certainty evidence; Analysis 1.2).

Easy participants

Ultrasound guidance was less effective than the landmark method in easy participants. According to the original studies' definitions, we classified one study (596 participants) as having easy participants (McCarthy 2016C). Ultrasound guidance decreased the first-pass success of cannulation by 11% (RR 0.89, 95% CI 0.85 to 0.94; high-certainty evidence; Analysis 1.1). When we categorised studies based on their success rate with the landmark method, we classified two studies (631 participants) as having easy participants (Aponte 2007; McCarthy 2016C), and ultrasound guidance decreased the first-pass success of cannulation by 11% (RR 0.89, 95% CI 0.85 to 0.94; I^2 = 0%; moderate-certainty evidence; Analysis 1.2).

No restriction by intravenous access difficulty level

According to the original studies' definitions, there were no restrictions in terms of difficulty levels in two studies (390 participants) (Glasin 2020; Skulec 2019). Ultrasound guidance increased the first-pass success of cannulation by 20% (RR 1.20, 95% CI 1.09 to 1.33; I^2 = 0%; moderate-certainty evidence; Analysis 1.1).

Overall success of cannulation

All participants

Twelve studies (1059 participants) evaluated overall success of cannulation (Aponte 2007; Bahl 2016; Bridey 2018; Costantino 2005; Glasin 2020; İsmailoğlu 2015; Kerforne 2012; Nishizawa 2020; River 2009; Skulec 2019; Stein 2009; Weiner 2013). Ultrasound guidance increased the overall success of cannulation by 27% (RR 1.27, 95% CI 1.08 to 1.49; I^2 = 92%; very low-certainty evidence; Analysis 2.1). The majority of studies focused on difficult participants, there were no studies with moderate and easy participants, and two studies were classified as having no restrictions of difficulty with the original studies' definition. Heterogeneity was considerable and the test for subgroup difference indicated a difference (P = 0.04). The effect size of ultrasound guidance was larger in studies with difficult participants than in studies without restrictions of difficulty. When we categorised studies based on their success rate with the landmark method, we classified eight studies as having difficult participants and three studies as moderate and one as easy. The test for subgroup difference indicated a difference (P = 0.04). The effect of ultrasound guidance visually showed the difficulty-dependent trend, and the meta-regression analysis for the effect of the difficulty level indicated a difference (P = 0.032) (Analysis 2.2).

Difficult participants

Ultrasound guidance improved the overall success of cannulation in difficult participants. According to the original studies' definitions, we classified ten studies (670 participants) as having difficult participants (Aponte 2007; Bahl 2016; Bridey 2018; Costantino 2005; İsmailoğlu 2015; Kerforne 2012; Nishizawa 2020; River 2009; Stein 2009; Weiner 2013). Ultrasound guidance increased the overall success of cannulation by 40% (RR 1.40, 95% CI 1.10 to 1.77; I^2 = 88%; very low-certainty evidence; Analysis 2.1). When we categorised studies based on their success rate with the landmark method, we classified eight studies (588 participants) as having difficult participants (Bahl 2016; Bridey 2018; Costantino 2005; İsmailoğlu 2015; Kerforne 2012; Nishizawa 2020; Stein 2009; Weiner 2013). Ultrasound guidance increased the overall success of cannulation by 53% (RR 1.53, 95% CI 1.12 to 2.08; I^2 = 86%; very low-certainty evidence; Analysis 2.2).

Moderate participants

According to the original studies' definitions, none of the studies included participants with moderate difficulty. When we categorised studies based on their success rate with the landmark method, we classified three studies (436 participants) as having moderately difficult participants (Glasin 2020; River 2009; Skulec 2019). We found no clear difference between the ultrasound guidance and landmark method groups in the overall success of cannulation (RR 1.07, 95% CI 0.94 to 1.23; I^2 = 87%; very low-certainty evidence; Analysis 2.2).

Easy participants

According to the original studies' definitions, none of the studies included easy participants. When we categorised studies based on their success rate with the landmark method, we classified one study (35 participants) as having easy participants (Aponte 2007). We found no evidence of a difference in overall success in cannulation (RR 1.00, 95% CI 0.90 to 1.11; low-certainty evidence; Analysis 2.2).

No restriction by intravenous access difficulty level

According to the original studies' definitions, there were no restrictions in terms of difficulty levels in two studies (389 participants) (Glasin 2020; Skulec 2019). We found no clear difference in overall success in cannulation (RR 1.05, 95% CI 0.92 to 1.19; I^2 = 91%; very low-certainty evidence; Analysis 2.1). No studies remained in this subgroup when we categorised studies based on their success rate with the landmark method.

Pain

All participants

Seven studies (1410 participants) evaluated pain (Glasin 2020; İsmailoğlu 2015; McCarthy 2016A; McCarthy 2016B; McCarthy 2016C; Pappas 2006; Weiner 2013). All studies used a numerical rating scale (NRS), with scores ranging from 0 to 10, with 0 indicating no pain and 10 indicating maximum pain. We found no clear difference (MD 0.05, 95% CI -0.42 to 0.51; I^2 = 58%; very low-certainty evidence; Analysis 3.1). The effect of ultrasound guidance visually showed the difficulty-dependent trend with both definitions of the difficulty, but the tests for subgroup differences did not indicate a difference for both definitions of difficulty (P = 0.20 for the original studies' and P = 0.09 for the success rate definition) (Analysis 3.2).

Difficult participants

According to the original studies' definitions, we classified four studies (323 participants) as having difficult participants (Pappas 2006; McCarthy 2016A; Weiner 2013). We found no clear difference in pain (MD -0.20, 95% CI -1.13 to 0.72; I^2 = 62%; very low-certainty evidence; Analysis 3.1). When we categorised studies based on their success rate with the landmark method, we classified three studies (305 participants) as having difficult participants (İsmailoğlu 2015; McCarthy 2016A; Weiner 2013). We found no clear difference in pain (MD -0.49, 95% CI -1.48 to 0.49; I^2 = 60%; very low-certainty evidence; Analysis 3.2).

Moderate participants

According to the original studies' definitions, we classified one study (401 participants) as having moderately difficult participants (McCarthy 2016B), and we found no clear difference in pain (MD 0.10, 95% CI -0.47 to 0.67; low-certainty evidence; Analysis 3.1). When we categorised studies based on their success rate with the landmark method, we classified two studies (491 participants) as having moderately difficult participants (Glasin 2020; McCarthy 2016B). We found no clear difference in pain (MD 0.03, 95% CI -0.43 to 0.48; I^2 = 0%; low-certainty evidence; Analysis 3.2).

Easy participants

According to the original studies' definitions, we classified one study (596 participants) as having easy participants (McCarthy 2016C), and ultrasound guidance increased pain (MD 0.60, 95% CI 0.17 to 1.03; moderate-certainty evidence; Analysis 3.1). When we categorised studies based on their success rate with the landmark method, we found the same study and the same result (Analysis 3.2).

No restriction by intravenous access difficulty level

According to the original studies' definitions, there were no restrictions in terms of difficulty levels in one study (Glasin 2020). We found no clear difference in pain (MD -0.10, 95% CI -0.85 to 0.65; low-certainty evidence; Analysis 3.1). No studies remained in this subgroup when we categorised studies based on their success rate with the landmark method.

Secondary outcomes

Procedure time for first-pass cannulation

All participants

Six studies (1564 participants) evaluated procedure time for first-pass cannulation (Aponte 2007; Glasin 2020; McCarthy 2016A; McCarthy 2016B; McCarthy 2016C; Skulec 2019). Two studies reported the outcome only for participants in whom cannulation was successful (Aponte 2007; Skulec 2019). Ultrasound guidance increased the procedure time for first-pass cannulation by 61.4 seconds (MD 61.4, 95% CI 10.4 to 112.5; I^2 = 98%; low-certainty evidence; Analysis 4.1). Although the difficulty-dependent trend was visually unclear, the test for subgroup differences indicated a difference for both definitions of the difficulty due to two studies where ultrasound guidance did not have as much effect as that in other studies (P < 0.001 for the original studies' definition and P = 0.02 for the success rate definition) (Glasin 2020; Skulec 2019) (Analysis 4.2).

Difficult participants

Ultrasound guidance increased the procedure time for first-pass cannulation in difficult participants. According to the original studies' definitions, we classified two studies (219 participants) as having difficult participants (Aponte 2007; McCarthy 2016A). Ultrasound guidance increased the procedure time for first-pass cannulation by 119.9 seconds (MD 119.9, 95% CI 88.6 to 151.1; I^2 = 0%; low-certainty evidence; Analysis 4.1). When we categorised studies based on their success rate with the landmark method, we classified one study as having difficult participants (192 participants) (McCarthy 2016A), and ultrasound guidance increased the procedure time for first-pass cannulation by 120.6 seconds (MD 120.6, 95% CI 88.3 to 152.9; moderate-certainty evidence; Analysis 4.2).

Moderate participants

Ultrasound guidance increased the procedure time for first-pass cannulation in moderately difficult participants. According to the original studies' definitions, we classified one study (401 participants) as having moderately difficult participants (McCarthy 2016B). Ultrasound guidance increased the procedure time for first-pass cannulation by 95.2 seconds (MD 95.2, 95% CI 72.8 to 117.6; high-certainty evidence; Analysis 4.1). When we categorised studies based on their success rate with the landmark method, we classified three studies (749 participants) as having moderately difficult participants (Glasin 2020; McCarthy 2016B; Skulec 2019). Ultrasound guidance did not clearly increase the procedure time for

first-pass cannulation (MD 23.0, 95% CI -39.9 to 85.9; I^2 = 97%; very low-certainty evidence; Analysis 4.2).

Easy participants

Ultrasound guidance increased the procedure time for first-pass cannulation in easy participants. According to the original studies' definitions, we classified one study (596 participants) as having easy participants (McCarthy 2016C). Ultrasound guidance increased the procedure time for first-pass cannulation by 94.8 seconds (MD 94.8, 95% CI 81.2 to 108.5; high-certainty evidence; Analysis 4.1). When we categorised studies based on their success rate with the landmark method, we classified two studies (623 participants) as having easy participants (Aponte 2007; McCarthy 2016C). Ultrasound guidance increased the procedure time for first-pass cannulation by 95.0 seconds (MD 95.0, 95% CI 81.4 to 108.6; I^2 = 0%; moderate-certainty evidence; Analysis 4.2).

No restriction by intravenous access difficulty level

According to the original studies' definitions, there were no restrictions in terms of difficulty levels in two studies (348 participants) (Glasin 2020; Skulec 2019). We found no clear difference in procedure time for first-pass cannulation (MD -11.3, 95% CI -58.4 to 35.7; I^2 = 85%; low-certainty evidence; Analysis 4.1). No studies remained in this subgroup when we categorised studies based on their success rate with the landmark method.

Procedure time for overall cannulation

All participants

Ten studies (803 participants) evaluated the procedure time for overall cannulation (Aponte 2007; Bahl 2016; Costantino 2005; Glasin 2020; Kerforne 2012; Pappas 2006; River 2009; Skulec 2019; Stein 2009; Weiner 2013). Three studies reported the outcome only for participants in whom cannulation was successful (Kerforne 2012; Pappas 2006; Stein 2009). River 2009 was unclear for which participants they assessed the outcome; therefore, we assumed they assessed only participants with successful cannulation, as in a study by the same research team (Stein 2009). We found no clear difference in the procedure time for overall cannulation (MD -61.1 seconds, 95% CI -161.3 to 39.1; I^2 = 86%; very low-certainty evidence; Analysis 5.1). The tests for subgroup differences did not indicate a difference by either definition of the difficulty (P = 0.75 for the original studies' definition and P = 0.23 for the success rate definition) (Analysis 5.1; Analysis 5.2).

Difficult participants

According to the original studies' definitions, we classified eight studies (413 participants) as having difficult participants (Aponte 2007; Bahl 2016; Costantino 2005; Kerforne 2012; Pappas 2006; River 2009; Stein 2009; Weiner 2013). We found no clear difference in the procedure time for overall cannulation (MD -24.9 seconds, 95% CI -323.1 to 273.3; I^2 = 77%; very low-certainty evidence; Analysis 5.1). When we categorised studies based on their success rate with the landmark method, we classified five studies (322 participants) as having difficult participants (Bahl 2016; Costantino 2005; Kerforne 2012; Stein 2009; Weiner 2013). We found no clear difference in the procedure time for overall cannulation (MD -117.0 seconds, 95% CI -662.8 to 428.8; I^2 = 83%; very low-certainty evidence; Analysis 5.2).

Moderate participants

According to the original studies' definitions, none of the studies included moderately difficult participants. When we categorised studies based on their success rate with the landmark method, we classified three studies (428 participants) as having moderately difficult participants (Glasin 2020; River 2009; Skulec 2019). We found no clear difference in the procedure time for overall cannulation (MD -69.8 seconds, 95% CI -176.2 to 36.6; I^2 = 94%; very low-certainty evidence; Analysis 5.2).

Easy participants

According to the original studies' definitions, none of the studies included easy participants. When we categorised studies based on their success rate with the landmark method, we classified one study (35 participants) as having easy participants (Aponte 2007). Ultrasound guidance tended to increase the procedure time for overall cannulation, but there was no clear difference (MD 131.6 seconds, 95% CI -39.8 to 303.0; low-certainty evidence; Analysis 5.2).

No restriction by intravenous access difficulty level

According to the original studies' definitions, there were no restrictions in terms of difficulty levels in two studies (390 participants) (Glasin 2020; Skulec 2019). We found no clear difference in the procedure time for overall cannulation (MD -77.4, 95% CI -185.7 to 30.9; I^2 = 97%; very low-certainty evidence; Analysis 5.1).

No data on the success of cannulation

Pappas 2006 (18 participants) did not report data on the success rate of cannulation with either ultrasound guidance or the landmark method. Thus, we could not classify this study according to its success rate with the landmark method. We found no clear difference in the procedure time for overall cannulation (MD 156.0 seconds, 95% CI -450.1 to 762.1; low-certainty evidence; Analysis 5.2).

Number of cannulation attempts

All participants

Eleven studies (958 participants) evaluated the number of cannulation attempts (Aponte 2007; Bahl 2016; Bridey 2018; Costantino 2005; Glasin 2020; İsmailoğlu 2015; Pappas 2006; River 2009; Skulec 2019; Stein 2009; Weiner 2013). Ultrasound guidance may slightly decrease the number of cannulation attempts (MD -0.29, 95% CI -0.49 to -0.09; I^2 = 61%; very low-certainty evidence; Analysis 6.1). The tests for subgroup differences did not indicate a difference by either definition of the difficulty (P = 0.87 for the original studies' definition and P = 0.31 for the success rate definition) (Analysis 6.2).

Difficult participants

According to the original studies' definitions, we classified nine studies (568 participants) as having difficult participants (Aponte 2007; Bahl 2016; Bridey 2018; Costantino 2005; İsmailoğlu 2015; Pappas 2006; River 2009; Stein 2009; Weiner 2013). Ultrasound guidance may slightly decrease the number of cannulation attempts (MD -0.33, 95% CI -0.64 to -0.02; I^2 = 64%; very low-certainty evidence; Analysis 6.1). When we categorised studies based on their success rate with the landmark method,

we classified six studies (468 participants) as having difficult participants (Bahl 2016; Bridey 2018; Costantino 2005; İsmailoğlu 2015; Stein 2009; Weiner 2013). Ultrasound guidance tended to decrease the number of cannulation attempts, but there was no clear difference (MD -0.36, 95% CI -0.75 to 0.03; I^2 = 73%; very low-certainty evidence; Analysis 6.2).

Moderate participants

According to the original studies' definitions, none of the studies included moderately difficult participants. When we categorised studies based on their success rate with the landmark method, we classified three studies (437 participants) as having moderately difficult participants (Glasin 2020; River 2009; Skulec 2019). Ultrasound guidance probably decreased the number of cannulation attempts (MD -0.32, 95% CI -0.47 to -0.16; I^2 = 20%; moderate-certainty evidence; Analysis 6.2).

Easy participants

According to the original studies' definitions, none of the studies included easy participants. When we categorised studies based on their success rate with the landmark method, we classified one study (35 participants) as having easy participants (Aponte 2007). We found no clear difference in the number of cannulation attempts (MD 0.10, 95% CI -0.44 to 0.64; low-certainty evidence; Analysis 6.2).

No restriction by intravenous access difficulty level

According to the original studies' definitions, there were no restrictions in terms of difficulty levels in two studies (390 participants) (Glasin 2020; Skulec 2019). Ultrasound guidance probably decreased the number of cannulation attempts (MD -0.30, 95% CI -0.50 to -0.11; I^2 = 52%; moderate-certainty evidence; Analysis 6.1). No studies remained in this subgroup when we categorised studies based on their success rate with the landmark method.

No data on the success rate

Pappas 2006 (18 participants) did not report data on the success rate of cannulation with either ultrasound guidance or the landmark method. Thus, we could not classify this study according to its success rate with the landmark method. We found no clear difference in the number of cannulation attempts (MD -1.50, 95% CI -3.50 to 0.50; low-certainty evidence; Analysis 6.2).

Patient satisfaction

All participants

Six studies (423 participants) evaluated patient satisfaction using an NRS of 0 to 10 or a 4-step Likert scale. (Bridey 2018; Costantino 2005; Glasin 2020; River 2009; Stein 2009; Weiner 2013). Ultrasound guidance tended to increase patient satisfaction, but there was no clear difference (standardised mean difference (SMD) 0.37, 95% CI -0.03 to 0.77; I^2 = 75%; very low-certainty evidence; Analysis 7.1). Satisfaction was higher in studies including difficult participants than in studies with no restriction in terms of difficulty levels according to the original studies' definitions (test for subgroup differences: P = 0.02). We found no clear difference between studies including difficult participants and those including moderately difficult participants according to the definition of the success rate with the landmark method (P = 0.27).

Difficult participants

According to the original studies' definitions, we classified five studies (333 participants) as having difficult participants (Bridey 2018; Costantino 2005; River 2009; Stein 2009; Weiner 2013). Ultrasound guidance increased patient satisfaction (SMD 0.49, 95% CI 0.07 to 0.92; I^2 = 71%; very low-certainty evidence; Analysis 7.1). When we categorised studies based on their success rate with the landmark method, we classified four studies (286 participants) as having difficult participants (Bridey 2018; Costantino 2005; Stein 2009; Weiner 2013). Ultrasound guidance tended to increase patient satisfaction, but there was no clear difference (SMD 0.52, 95% CI -0.01 to 1.05; I^2 = 78%; very low-certainty evidence; Analysis 7.2).

Moderate participants

According to the original studies' definitions, none of the studies included moderately difficult participants. When we categorised studies based on their success rate with the landmark method, we classified two studies (137 participants) as having moderately difficult participants (Glasin 2020; River 2009). We found no clear difference in patient satisfaction (SMD 0.08, 95% CI -0.51 to 0.66; I^2 = 63%; very low-certainty evidence; Analysis 7.2).

No restriction by intravenous access difficulty level

According to the original studies' definitions, there were no restrictions in terms of difficulty levels in one study (90 participants) (Glasin 2020). We found no clear difference in patient satisfaction (SMD -0.19, 95% CI -0.60 to 0.23; low-certainty evidence; Analysis 7.1). No studies remained in this subgroup when we categorised studies based on their success rate with the landmark method.

Overall complications

All participants

Nine studies (1818 participants) evaluated overall complications (Costantino 2005; Glasin 2020; İsmailoğlu 2015; Nishizawa 2020; McCarthy 2016A; McCarthy 2016B; McCarthy 2016C; Skulec 2019; Stein 2009). The most frequent complication was swelling or haematoma. The details of the complications are given in Table 1. We found no clear difference in overall complications for all participants (RR 0.72, 95% CI 0.46 to 1.14; I^2 = 44%; low-certainty evidence; Analysis 8.1). Ultrasound guidance tended to have more complications in easy participants than in difficult and moderately difficult participants according to both definitions of difficulty. The test for subgroup differences did not indicate a difference amongst difficulty levels with the original studies' definitions (P = 0.06), but indicated a difference when we categorised studies based on their success rate with the landmark method (P = 0.04) (Analysis 8.2). This was due to a study of easy participants (McCarthy 2016C), and the subgroup difference disappeared when this study was excluded.

Difficult participants

According to the original studies' definitions, we classified five studies (431 participants) as having difficult participants (Costantino 2005; İsmailoğlu 2015; McCarthy 2016A; Nishizawa 2020; Stein 2009). Ultrasound guidance tended to decrease overall complications, but there was no clear difference (RR 0.64, 95% CI 0.37 to 1.10; I^2 = 0%; low-certainty evidence; Analysis 8.1). When we categorised studies based on their success rate with the landmark method, we got the same five studies and results (Analysis 8.2).

Moderate participants

According to the original studies' definitions, we classified one study as having moderately difficult participants (401 participants) (McCarthy 2016B). We found no clear difference in overall complications (RR 0.83, 95% CI 0.38 to 1.82; moderate-certainty evidence; Analysis 8.1). When we categorised studies based on their success rate with the landmark method, we classified three studies (791 participants) as having moderately difficult participants (Glasin 2020; McCarthy 2016B; Skulec 2019). Ultrasound guidance tended to decrease overall complications, but there was no clear difference (RR 0.58, 95% CI 0.33 to 1.02; I^2 = 40%; low-certainty evidence; Analysis 8.2).

Easy participants

According to the original studies' definitions, we classified one study (596 participants) as having easy participants (McCarthy 2016C). Ultrasound guidance tended to increase overall complications, but there was no clear difference (RR 2.48, 95% CI 0.90 to 6.87; moderate-certainty evidence; Analysis 8.1). When we categorised studies based on their success rate with the landmark method, we got the same study and result (Analysis 8.2).

No restriction by intravenous access difficulty level

According to the original studies' definitions, there were no restrictions in terms of difficulty levels in two studies (390 participants) (Glasin 2020; Skulec 2019). Ultrasound guidance decreased the overall complications (RR 0.48, 95% CI 0.24 to 0.96; I^2 = 34%; low-certainty evidence; Analysis 8.1). No studies remained in this subgroup when we categorised studies based on their success rate with the landmark method.

Additional subgroup analysis

We conducted additional subgroup analyses only for the three primary outcomes: first-pass success of cannulation; overall success of cannulation; and pain. Due to the small number of studies with moderate and easy participants, we conducted the subgroup analyses only for studies including difficult participants, except for the type of ultrasound guidance. Only two studies defined the difficulty at the discretion of operators, and we did not perform subgroup analyses with this definition of the difficulty. Because none of the studies used only long-axis ultrasound guidance, we did not conduct a subgroup analysis for short- and long-axis ultrasound guidance. See Appendix 2 and Appendix 3.

First-pass success of cannulation

Difficulty of obtaining access:

Difficult: operator could not see and palpate a target vein

When we defined a difficult case as "an operator could not see and palpate a target vein", we included five studies (486 participants) (Bridey 2018; İsmailoğlu 2015; Kerforne 2012; McCarthy 2016A; Nishizawa 2020). Ultrasound guidance increased the first-pass success of cannulation by 94% (RR 1.94, 95% CI 1.53 to 2.45; I^2 = 12%; low-certainty evidence; Analysis 1.3).

Difficult: participants had a history of difficult intravenous cannulation

When we defined a difficult case as "participants had a history of difficult intravenous cannulation", we included six studies (390 participants) (Aponte 2007; Bahl 2016; Costantino 2005; İsmailoğlu 2015; Nishizawa 2020; Weiner 2013). Ultrasound guidance tended to increase the first-pass success of cannulation, but there was no clear difference (RR 1.28, 95% CI 0.97 to 1.70; I^2 = 38%; very low-certainty evidence; Analysis 1.4).

Difficult: participants had multiple failed attempts

When we defined a difficult case as "participants had multiple failed attempts", we included four studies (232 participants) (Costantino 2005; Nishizawa 2020; Stein 2009; Weiner 2013). Ultrasound guidance increased the first-pass success of cannulation by 60% (RR 1.60, 95% CI 1.15 to 2.21; I^2 = 0%; low-certainty evidence; Analysis 1.5).

Operator's skill and study setting:

Operators finished any training programme for ultrasound guidance

When we divided the RCTs according to whether operators had finished any training programme for ultrasound guidance, nine studies had had any training programme (755 participants) (Aponte 2007; Bahl 2016; Bridey 2018; Costantino 2005; İsmailoğlu 2015; McCarthy 2016A; Nishizawa 2020; Stein 2009; Weiner 2013), and one study (60 participants) did not specify whether operators had finished a training programme (Kerforne 2012). Because all studies had had any training programme, we could not compare studies with and without any training programme (Analysis 1.6).

Operators had any clinical experience with ultrasound guidance

Operators had had any clinical experience with ultrasound guidance before study initiation in five studies (460 participants) (Aponte 2007; Bridey 2018; Costantino 2005; McCarthy 2016A; Stein 2009). Ultrasound guidance tended to increase the first-pass success of cannulation, but there was no clear difference (RR 1.44, 95% CI 0.91 to 2.27; I^2 = 78%; very low-certainty evidence; Analysis 1.7). Operators did not have any clinical experience with ultrasound guidance in three studies (235 participants) (Bahl 2016; Nishizawa 2020; Weiner 2013). Ultrasound guidance tended to increase the first-pass success of cannulation, but there was no clear difference (RR 1.33, 95% CI 0.99 to 1.79; I^2 = 19%; low-certainty evidence). Two studies did not specify whether operators had had any clinical experience (120 participants) (İsmailoğlu 2015; Kerforne 2012). The test for subgroup difference did not indicate a difference (P = 0.33), and it was similar even when we excluded the two studies without the specification.

Operators finished any kind of training programme for ultrasound guidance and had any clinical experience of ultrasound guidance

We had the same results as for the definition "operators had any clinical experience of ultrasound guidance" (Analysis 1.8).

Types of operators

Operators were nurses in seven studies (504 participants) (Aponte 2007; Bahl 2016; Bridey 2018; İsmailoğlu 2015; Kerforne 2012; Nishizawa 2020; Weiner 2013). Ultrasound guidance increased the first-pass success of cannulation by 32% (RR 1.32, 95% CI 1.03 to 1.71; I^2 = 40%; low-certainty evidence; Analysis 1.9). Operators were physicians in two studies (119 participants) (Costantino 2005; Stein 2009). Ultrasound guidance tended to increase the first-pass success of cannulation, but there was no clear difference (RR 1.47, 95% CI 0.86 to 2.50; I^2 = 0%; low-certainty evidence). Operators were technicians in one study (192 participants) (McCarthy 2016A). Ultrasound guidance increased the first-pass success of

cannulation by 133% (RR 2.33, 95% CI 1.74 to 3.11; moderate-certainty evidence). The test for subgroup difference indicated a difference (P = 0.01) and was considered to originate from McCarthy 2016A.

Study setting

Six studies were conducted in the emergency department (546 participants) (Bahl 2016; Costantino 2005; İsmailoğlu 2015; McCarthy 2016A; Stein 2009; Weiner 2013). Ultrasound guidance increased the first-pass success of cannulation by 60% (RR 1.60, 95% CI 1.12 to 2.28; I^2 = 59%; very low-certainty evidence, Analysis 1.10). Three studies were in the intensive care unit (ICU) (234 participants) (Bridey 2018; Kerforne 2012; Nishizawa 2020). Ultrasound guidance increased the first-pass success of cannulation by 64% (RR 1.64, 95% CI 1.20 to 2.23; I^2 = 0%; low-certainty evidence). One study was in the operating room (35 participants) (Aponte 2007). We found no clear difference in the first-pass success of cannulation (RR 0.91, 95% CI 0.63 to 1.30; low-certainty evidence). Although the test for subgroup difference indicated there was a difference (P = 0.03), it disappeared when Aponte 2007 was excluded.

Year of publication

Two studies were published between 1999 and 2008 in two studies (95 participants) (Aponte 2007; Costantino 2005). We found no clear difference in the first-pass success of cannulation (RR 1.24, 95% CI 0.51 to 3.02; I^2 = 75%; very low-certainty evidence; Analysis 1.11). Eight studies were published in 2009 or later (720 participants) (Bahl 2016; Bridey 2018; İsmailoğlu 2015; Kerforne 2012; McCarthy 2016A; Nishizawa 2020; Stein 2009; Weiner 2013). Ultrasound guidance increased the first-pass success of cannulation by 60% (RR 1.60, 95% CI 1.24 to 2.07; I^2 = 50%; low-certainty evidence). The test for subgroup differences did not indicate a difference (P = 0.59).

Type of ultrasound guidance

One study evaluated both dynamic and static ultrasound guidance (300 participants) (Skulec 2019). Dynamic ultrasound guidance did not clearly increase the first-pass success of cannulation (RR 1.16, 95% CI 0.98 to 1.37; moderate-certainty evidence; Analysis 1.12). Static ultrasound guidance increased the first-pass success of cannulation by 24% (RR 1.24, 95% CI 1.05 to 1.46; moderate-certainty evidence). The test for subgroup differences did not indicate a difference (P = 0.59).

Overall success of cannulation

Difficulty of obtaining access:

Difficult: operator could not see and palpate a target vein

When we defined a difficult case as "an operator could not see and palpate a target vein", we included four studies (294 participants) (Bridey 2018; İsmailoğlu 2015; Kerforne 2012; Nishizawa 2020). Ultrasound guidance tended to increase the overall success of cannulation, but there was no clear difference (RR 1.53, 95% CI 0.98 to 2.41; I^2 = 77%; very low-certainty evidence; Analysis 2.3).

Difficult: participants had a history of difficult intravenous cannulation

When we defined a difficult case as "participants had a history of difficult intravenous cannulation", we included six studies (390 participants) (Aponte 2007; Bahl 2016; Costantino 2005; İsmailoğlu 2015; Nishizawa 2020; Weiner 2013). Ultrasound guidance tended to increase the overall success of cannulation, but there was no clear difference (RR 1.66, 95% CI 0.97 to 2.86; I^2 = 94%; very low-certainty evidence; Analysis 2.4).

Difficult: participants had multiple failed attempts

When we defined a difficult case as "participants had multiple failed attempts", we included five studies (279 participants) (Costantino 2005; Nishizawa 2020; River 2009; Stein 2009; Weiner 2013). Ultrasound guidance tended to increase the overall success of cannulation, but there was no clear difference (RR 1.53, 95% CI 0.93 to 2.51; I^2 = 91%; very low-certainty evidence; Analysis 2.5).

Operator's skill and study setting:

Operators finished any training programme for ultrasound guidance

When we divided the RCTs according to whether operators had finished any training programme for ultrasound guidance, nine studies had had any training programme (610 participants) (Aponte 2007; Bahl 2016; Bridey 2018; Costantino 2005; İsmailoğlu 2015; Nishizawa 2020; River 2009; Stein 2009; Weiner 2013), and one study (60 participants) did not specify whether operators had finished a training programme (Kerforne 2012). Because all studies had had any training programme, we could not compare studies with and without any training programme (Analysis 2.6).

Operators had any clinical experience with ultrasound guidance

Operators had had any clinical experience with ultrasound guidance before study initiation in five studies (315 participants) (Aponte 2007; Bridey 2018; Costantino 2005; River 2009; Stein 2009). We found no clear difference (RR 1.15, 95% CI 0.91 to 1.44; I^2 = 85%; very low-certainty evidence; Analysis 2.7). Operators did not have any clinical experience with ultrasound guidance in three studies (235 participants) (Bahl 2016; Nishizawa 2020; Weiner 2013). Ultrasound guidance increased the overall success of cannulation by 46% (RR 1.46, 95% CI 1.18 to 1.79; I^2 = 0%; low-certainty evidence). Two studies (120 participants) did not specify whether operators had had any clinical experience (İsmailoğlu 2015; Kerforne 2012). Although the test for subgroup difference indicated a difference (P = 0.03), this was lost when we excluded the two studies without the specification.

Operators finished any kind of training programme for ultrasound guidance and had any clinical experience of ultrasound guidance

We had the same results as for the definition "operators had any clinical experience of ultrasound guidance" (Analysis 2.8).

Types of operators

Operators were nurses in eight studies (551 participants) (Aponte 2007; Bahl 2016; Bridey 2018; İsmailoğlu 2015; Kerforne 2012; Nishizawa 2020; River 2009; Weiner 2013). Ultrasound guidance increased the overall success of cannulation by 37% (RR 1.37, 95% CI 1.05 to 1.78; I^2 = 83%; very low-certainty evidence; Analysis 2.9). Operators were physicians in two studies (119 participants) (Costantino 2005; Stein 2009). Ultrasound guidance did not clearly increase the overall success of cannulation (RR 1.72, 95% CI 0.22 to 13.47; I^2 = 98%; very low-certainty evidence). The test for subgroup difference did not indicate a difference (P = 0.83).

Study setting

Six studies (401 participants) were conducted in the emergency department (Bahl 2016; Costantino 2005; İsmailoğlu 2015; River 2009; Stein 2009; Weiner 2013). Ultrasound guidance increased the overall success of cannulation by 57% (RR 1.57, 95% CI 1.05 to 2.36; I^2 = 90%; very low-certainty evidence). Three studies (234 participants) were in the ICU (Bridey 2018; Kerforne 2012; Nishizawa 2020). Ultrasound guidance did not clearly increase the overall success of cannulation (RR 1.36, 95% CI 0.86 to 2.15; I^2 = 75%; very low-certainty evidence). One study (35 participants) was in the operating room (Aponte 2007), and we found no evidence of a difference (RR 1.00, 95% CI 0.90 to 1.11; low-certainty evidence; Analysis 2.10). The test for subgroup difference did not indicate a difference between settings (P = 0.06).

Year of publication

Two studies (95 participants) were published between 1999 and 2008 (Aponte 2007; Costantino 2005). We found no clear difference (RR 1.70, 95% CI 0.10 to 29.24; I^2 = 99%; very low-certainty evidence; Analysis 2.11). Eight studies (575 participants) were published in 2009 or later (Bahl 2016; Bridey 2018; İsmailoğlu 2015; Kerforne 2012; Nishizawa 2020; River 2009; Stein 2009; Weiner 2013). Ultrasound guidance increased the overall success of cannulation by 36% (RR 1.36, 95% CI 1.08 to 1.71; I^2 = 78%; very low-certainty evidence). The test for subgroup difference did not indicate a difference (P = 0.88).

Type of ultrasound guidance

One study (300 participants) evaluated both dynamic and static ultrasound guidance (Skulec 2019). The overall success of cannulation for dynamic and static ultrasound guidance was the same; ultrasound guidance did not clearly increase the success of cannulation and the 95% CI included no effect (RR 1.10, 95% CI 1.00 to 1.21; low-certainty evidence; Analysis 2.12). The test for subgroup difference did not indicate a difference (P = 1.00).

Pain

We conducted subgroup analyses only for the following four parameters for this outcome, and not for the other parameters owing to the small number of studies.

Operator's skill and study setting:

Operators finished any training programme for ultrasound guidance

When we divided the RCTs by whether operators had finished any training programme for ultrasound guidance, three studies (305 participants) had had any training programme (İsmailoğlu 2015; McCarthy 2016A; Weiner 2013). One study (18 participants) did not specify whether operators had finished a training programme (Pappas 2006). Because all studies had had any training programme, we could not compare studies with and without any training programme (Analysis 3.3).

Types of operators

Operators were nurses in three studies (131 participants) (İsmailoğlu 2015; Pappas 2006; Weiner 2013). We found no clear difference in pain between the ultrasound guidance and landmark method groups in these studies (MD -0.36, 95% CI -1.68 to 0.95; I^2 = 66%; very low-certainty evidence; Analysis 3.4). Operators were technicians in one study (192 participants) (McCarthy 2016A). We found no clear difference in pain between the two groups in this study (MD 0.20, 95% CI -0.61 to 1.01; low-certainty evidence). The test for subgroup difference did not indicate a difference (p = 0.48).

Study setting

Four studies (323 participants) were conducted in the emergency department (İsmailoğlu 2015; McCarthy 2016A; Pappas 2006; Weiner 2013). Because there were no studies in other settings, we could not compare them (Analysis 3.5).

Year of publication

One study (18 participants) was published between 1999 and 2008 (Pappas 2006). We found no clear difference in pain (MD 0.90, 95% CI -0.52 to 2.32; low-certainty evidence; Analysis 3.6). Three studies (305 participants) were published in 2009 or later (İsmailoğlu 2015; McCarthy 2016A; Weiner 2013). We found no clear difference (MD -0.49, 95% CI -1.48 to 0.49; I^2 = 60%; very low-certainty evidence). The test for subgroup difference did not indicate a difference (P = 0.11).

Sensitivity analysis

We limited the studies to RCTs only or studies with a low overall risk of bias (see Sensitivity analysis), and all the results were comparable to the original results and not qualitatively different (Analysis 9.1 to Analysis 9.8; Analysis 10.1 to Analysis 10.7; Table 2; Table 3; Table 4).

DISCUSSION

Summary of main results

We included 16 studies that compared ultrasound guidance with the landmark guidance method for peripheral venous cannulation in adults. The effect of ultrasound guidance on achieving peripheral venous cannulation depends on the difficulty level and the included studies used varying definitions of difficulty. We described the results by the difficulty levels used by the studies, and we also defined the difficulty by the success rate of the landmark method to evaluate consistency.

Difficult participants

Ultrasound guidance was probably helpful for difficult participants. Ultrasound guidance probably increased the primary outcome first-pass success of cannulation (low-certainty evidence) and may increase the overall success of cannulation (very low-certainty evidence), but not pain (very low-certainty evidence). The results were consistent across the two definitions of the difficulty, but the certainty of the evidence was moderate when we defined the difficulty levels based on the success rate with the landmark method. For secondary outcomes, ultrasound guidance may decrease the number of cannulation attempts (very low-certainty evidence) and may improve patient satisfaction (very low-certainty evidence) with the original studies' definitions. Ultrasound guidance did not show a clear benefit to the number of cannulation attempts or patient satisfaction using the definition based on the success rate with the landmark method. In contrast, ultrasound guidance probably increased the procedure time for first-pass cannulation with both definitions (low-certainty evidence), but the difference was less than three minutes, which is clinically small unless the patient has a very urgent condition. The certainty of the evidence was moderate when we defined

the difficulty levels based on the success rate with the landmark method. We found no clear difference in the procedure time for overall cannulation (very low-certainty evidence) and overall complications with both definitions (low-certainty evidence).

Moderate participants

Ultrasound guidance might be helpful for moderately difficult participants. Ultrasound guidance probably increased the first-pass success of cannulation to a lesser extent than in the difficult participants (moderate-certainty evidence), but not pain (low-certainty evidence). Results were consistent across both definitions of the difficulty, but the certainty of the evidence was high for first-pass success of cannulation when we defined the difficulty levels based on the success rate with the landmark method. For the overall success of cannulation, no relevant studies involved moderately difficult participants with the original definition, and there was no apparent effect of ultrasound guidance based on the definition of the success rate with the landmark method (very low-certainty evidence). For secondary outcomes, ultrasound guidance increased the procedure time for first-pass cannulation with the original studies' definitions (high-certainty evidence), but not with the definition based on the success rate (very low-certainty evidence). For the procedure time for overall cannulation, number of cannulation attempts, and patient satisfaction, no relevant studies involved moderately difficult participants with the original definition. Based on the definition of the success rate with the landmark method, ultrasound guidance decreased the number of cannulation attempts (moderate-certainty evidence), and there was no apparent effect of ultrasound guidance on the procedure time for overall cannulation (very low-certainty evidence), and patient satisfaction (very low-certainty evidence). Regardless of the definition used, we found no clear difference in overall complications (low- to moderate-certainty evidence).

Easy participants

Ultrasound guidance was likely not beneficial in easy participants. Ultrasound guidance probably decreased the first-pass success of cannulation (high-certainty evidence) and slightly increased pain (moderate-certainty evidence). The results were consistent across both definitions of the difficulty. For the overall success of cannulation, no relevant studies involved easy participants with the original definition, and there was no apparent effect of ultrasound guidance based on the definition of the success rate with the landmark method (low-certainty evidence). For secondary outcomes, ultrasound guidance increased the procedure time for first-pass cannulation with both definitions (moderate- to high-certainty evidence). For the procedure time for overall cannulation, and number of cannulation attempts, no relevant studies involved easy participants with the original definition. Based on the definition of the success rate with the landmark method, there was no apparent effect of ultrasound guidance on the procedure time for overall cannulation (low-certainty evidence), and number of cannulation attempts (low-certainty evidence). For patient satisfaction, there were no studies with easy participants for both definitions of the difficulty. Regardless of the definition used, we found no clear difference in overall complications (moderate-certainty evidence).

Subgroup analyses

In the subgroup analyses, the effect of ultrasound guidance was qualitatively similar for each original study's definition of difficulty, although the number of studies was very small to perform meta-analysis for some outcomes. There was no consistent definition of difficulty which showed low heterogeneity across the outcomes. Because all studies had had any training programme, we could not compare studies with and without any training programme. The clinical experience of operators, study settings, and year of publication did not affect the effects of ultrasound guidance. There were three types of operators, and the first-pass success of cannulation was higher for technicians than for nurses or physicians. We found no differences amongst types of operators in the overall success of cannulation or pain. Only one study compared dynamic and static ultrasound guidance, so we could not perform the meta-analysis. Static ultrasound guidance had a shorter procedure time for first-pass and overall cannulation and fewer overall complications for participants without restriction by difficulty level than dynamic ultrasound guidance. The other outcomes were similar for both types of guidance.

Overall completeness and applicability of evidence

We conducted a thorough search and contacted study authors directly to obtain unpublished data and studies, and also to confirm the details of the studies. Nine study authors provided us with unpublished data, making our meta-analysis the most comprehensive to date (Bahl 2016; Bridey 2018; Costantino 2005; Glasin 2020; Kerforne 2012; McCarthy 2016; Nishizawa 2020; Skulec 2019; Weiner 2013). The 16 included studies had various participant backgrounds, operators, and settings, and the effect of ultrasound guidance was similar amongst the various situations, except for the difficulty level. Therefore, we believe that ultrasound guidance is applicable in many situations, regardless of the operator's ultrasound experience if a training programme is available, and in settings including the emergency department, ICU, operating room, and prehospital setting. However, these results must be interpreted carefully in some respects.

As the effects of ultrasound guidance depend on the difficulty level with the landmark method, it is necessary to assess the difficulty when performing ultrasound guidance. However, as we expected, the definition of difficulty varied between studies. There were four types of original studies' definitions of difficulty, and we could not find any consistent difference across the outcomes amongst the four definitions. An accurate assessment was difficult because some outcomes were only evaluated in a few studies, and some studies combined multiple definitions of difficulty. Stratification by factors after randomisation should usually be avoided, but the landmark method is a widely used procedure, and the success rate of the landmark method would reflect the difficulty level (McCarthy 2016; Sebbane 2013; Van Loon 2016). The effect sizes and difficulty-dependent trends were similar for both definitions of difficulty, which made the results more certain. Clinically, each of the four definitions of difficulty seemed reasonable, but they might not be enough to stand alone, and there is also the issue of reproducibility. A promising way to assess the difficulty level is to use a prediction score. The modified Adult Difficult IntraVenous Access (A-DIVA) scale consists of five items, such as visibility or palpability of the target vein and a history of difficult intravenous access. The first-pass success of cannulation was 6% in the high-risk group, 63% in the moderate-risk group, and 96% in the low-risk group (Van Loon 2019). High-risk and probably moderate-risk patients are good candidates for ultrasound guidance on this scale. Another Enhanced Adult DIVA (EA-DIVA) score, consisting of eight items,

predicted patients who required four or more cannulation attempts with a positive predictive value of 56% and a negative predictive value of 97.5% (Civetta 2019). However, both prediction models have methodological limitations because univariate regression analysis was used to select predictors, and have not been validated externally to date.

Regarding the characteristics of operators, we could not compare the presence and absence of any training programme on ultrasound guidance, and previous experience with ultrasound guidance had no apparent benefit. However, from a clinical standpoint, proficiency in ultrasound guidance is essential, and an appropriate training programme and sufficient clinical experience are necessary. The first-pass success of ultrasound guidance cannulation varied widely amongst the included studies, ranging from approximately 20% to 80% (average 57%), and operators' proficiency was likely one major factor. İsmailoğlu 2015 had the lowest first-pass success of cannulation at 20% with ultrasound guidance, which according to the authors, was due to the low proficiency of the operators. In the three studies that showed high first-pass success of cannulation with ultrasound guidance (80% to 85%), the operators were technicians specialising in peripheral intravenous cannulation, with 39% of the operators performing five or more ultrasound guidance cases per day (McCarthy 2016A; McCarthy 2016B; McCarthy 2016C). Performing five ultrasound guidance cases per day was highly frequent, suggesting a high proficiency in these operators. In one study, a dedicated peripheral venous cannulation team of nurses was trained in ultrasound guidance and performed up to six ultrasound guidance cases per day, achieving a high first-pass success rate of 93% (Sou 2017). Therefore, increasing the frequency and proficiency of ultrasound guidance seems important, and having a dedicated team could be one way to achieve this. Monitoring operators' proficiency level, such as their success rates, would be preferable in the clinical application of ultrasound guidance. It would also allow an appropriate assessment by the operators of the difficulty levels of the patients eligible for ultrasound guidance. This is because, in studies classified as moderately difficult cases, the first-pass success of cannulation was as high as 80% or more, and the effectiveness of ultrasound guidance for moderately difficult cases can be expected in highly skilled operators (Glasin 2020; McCarthy 2016B; Skulec 2019). We did not aim to assess the content of training programmes or conduct a quantitative assessment of previous clinical ultrasound guidance experience in this review.

Complications varied widely, from 0% to 22% in the included studies and 1% to 60% in previous studies (Bauman 2009; Duran 2016; Oliveira 2016; Schoenfeld 2011). This large difference was probably due to operators' proficiency, patient characteristics, the definition of complications, and small sample sizes. İsmailoğlu 2015 had the most complications in the included studies; it also had the lowest successful cannulation rate. Low successful cannulation leads to more cannulation attempts and increased complications. Therefore, operators' proficiency may also be important in complications.

Three occupational groups were included in the subgroup analysis, with technicians having higher first-pass success of cannulation than nurses and physicians. However, this result was derived only from McCarthy 2016A, where technicians in this study performed a high frequency of ultrasound-guided cannulations and appeared to be more skilled. Previous studies have suggested that ultrasound guidance is similarly effective regardless of operator occupation (Duran-Gehring 2016; Oliveira 2016; Schoenfeld 2011). Therefore, we consider that proficiency is more likely to be a factor than occupational differences.

We could not find any consistent difference across the outcomes amongst the four settings—the emergency department, ICU, operating room, and prehospital setting. Only two studies were conducted in the operating room and the total number of participants was very small (53 combined). Only one study was conducted in a prehospital setting. Given the nature of the intervention, we believe that it is likely ultrasound guidance will be similarly effective irrespective of the setting.

Because quantitative evaluation was expected to be difficult and there are many models of ultrasound machines, we did not conduct an analysis of the effect of the quality of the ultrasound machines. Instead, we divided the studies by year of publication. Although we could not find any meaningful results, it is likely that the visibility of the needle could affect the effect of ultrasound guidance. Additional data in future updates may allow detection of differences due to the use of newer machines.

Another issue was whether the appropriate length of needle was used according to the depth of the vein. Because no studies reported the depth of the targeted vein, it was not possible to determine the extent of this effect. However, in two studies that used only short needles, the first-pass success of ultrasound guidance cannulation was low (40% to 50%), suggesting that the needles may have been too short (Bridey 2018; Costantino 2005).

This meta-analysis did not evaluate the longevity of functional catheters placed under ultrasound guidance and the landmark method. According to earlier studies, and as mentioned in the Methods section, it is crucial to use needles of the appropriate length according to the depth of the target vein (Avila 2019; Bahl 2019; Bahl 2020; Elia 2012; Pandurangadu 2018). We will consider including this issue in future updates.

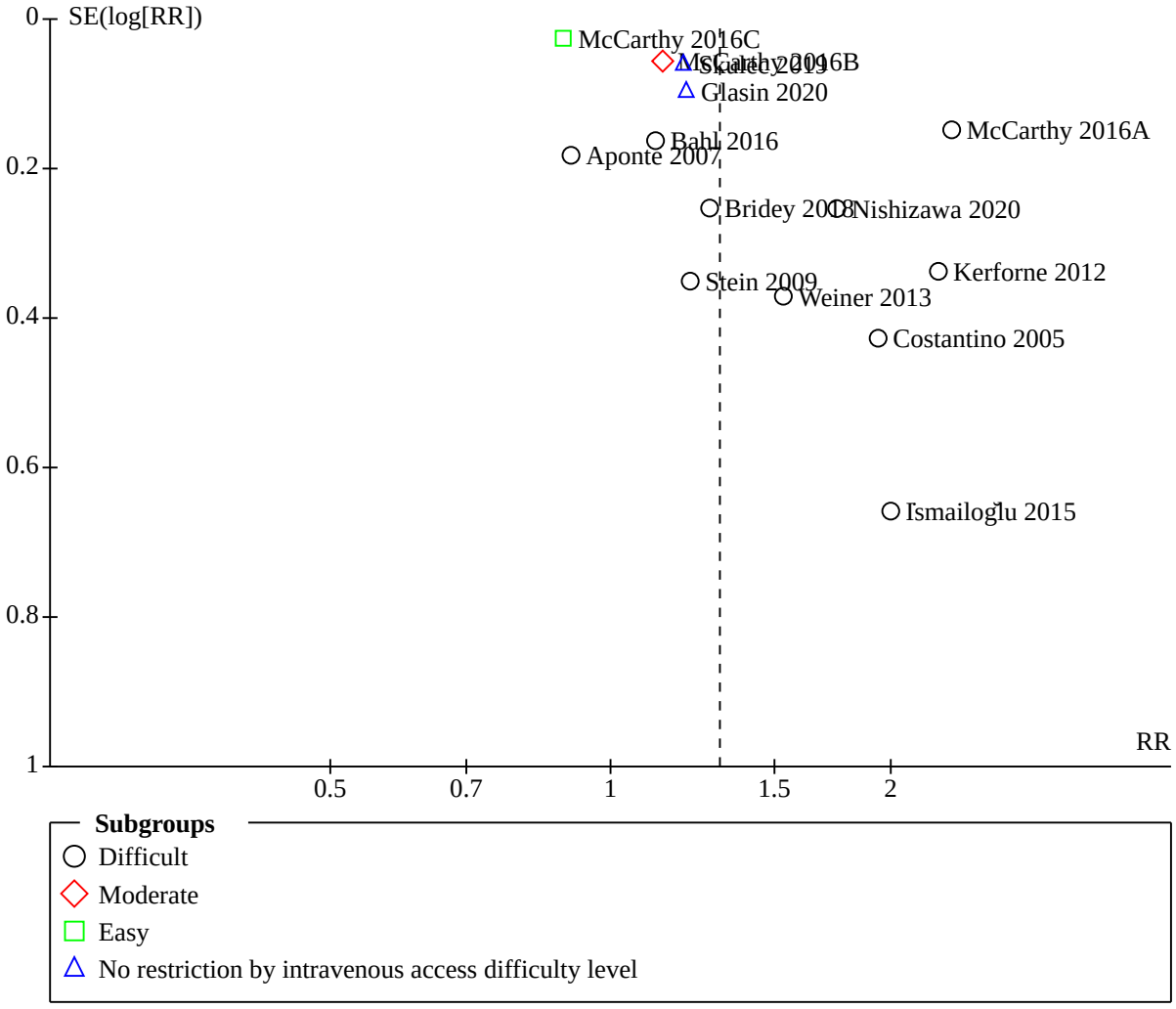
Certainty of the evidence

See Summary of findings 1; Summary of findings 2; Summary of findings 3; Appendix 4; Appendix 5; and Appendix 6.

First-pass success of cannulation

We downgraded to low-certainty evidence due to the serious risk of bias and heterogeneity in the difficult participants according to the original studies' definition. However, using the definition based on the success rate with the landmark method reduced heterogeneity, so we assessed it as moderate-certainty evidence. Although the risk of bias was high in seven of the 14 studies, the results of sensitivity analyses, which excluded quasi-RCTs or studies with high risk of bias, were similar to the overall results (Analysis 9.1; Analysis 10.1). We found no obvious publication bias (Figure 4).

Figure 4. Funnel plot of analysis 1.1: First-pass success of cannulation - difficulty levels defined by original studies



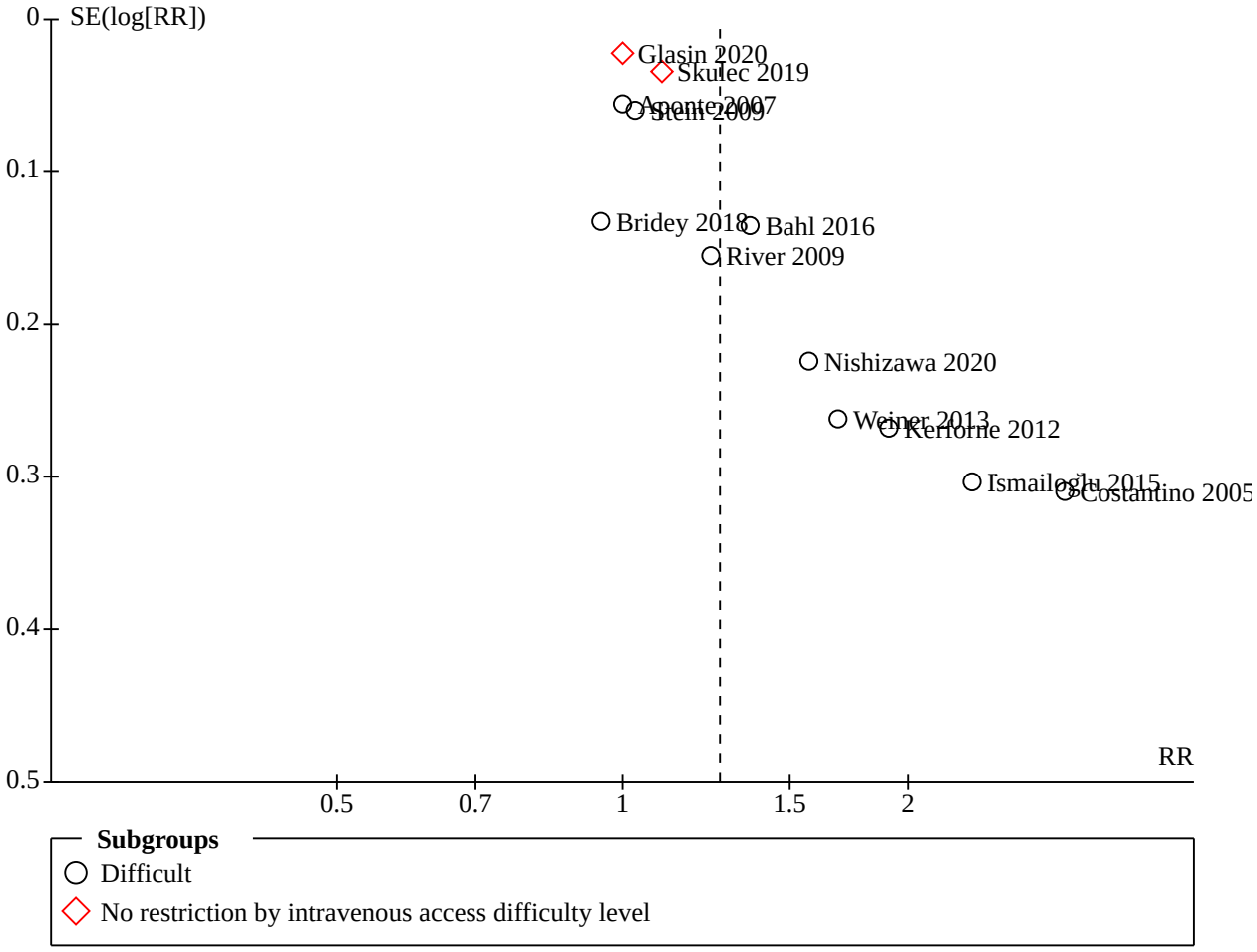
The certainty of the evidence for the moderately difficult participants was moderate, downgraded by one level for imprecision. When using the definition based on the success rate, the certainty of the evidence was high.

The certainty of the evidence for the easy participants was high according to the original studies' definitions, and it was moderate using the definition based on the success rate, downgraded for lack of blinding of the outcome assessors. The difficulty-dependent effect size was similar for both definitions of the difficulty.

Overall success of cannulation

The certainty of the evidence for the overall success of cannulation was very low for difficult participants. We downgraded by one level as the risk of bias was high in nine of 12 studies due to quasi-randomisation and non-blinding of the outcome assessors. We downgraded by two levels due to serious heterogeneity, mainly due to the lack of a standardised definition of failure. Two studies defined a failure as unsuccessful cannulation after three punctures (Bridey 2018; Costantino 2005), three studies defined failure as unsuccessful cannulation after two punctures (Bahl 2016; Kerforne 2012; Nishizawa 2020), and the remaining seven studies did not give a definition. Some participants in one study had as many as eight punctures, which would have been affected by the ceiling effect (Stein 2009). Furthermore, the threshold for judging failure could differ between the two arms. The funnel plot was asymmetric, but since this was due to two quasi-RCTs, we did not downgrade further due to publication bias (Figure 5).

Figure 5. Funnel plot of analysis 2.1: Overall success of cannulation - difficulty levels defined by original studies



Pain

We downgraded to very low-certainty evidence in the difficult participants, according to both definitions of the difficulty, because of the serious risk of bias mainly due to non-blinding, inconsistency, and imprecision. The certainty of the evidence for moderately difficult participants was low due to risk of bias concerns and imprecision. We downgraded the certainty of the evidence for easy participants to moderate due to risk of bias concerns.

Although we assessed the blinding domain as high risk in all studies because all participants were not blinded and this outcome is subjective, it seemed unlikely that participants would have had a strong preference for either of the intervention methods. The outcome assessors were not neutral third parties in three studies in difficult participants (İsmailoğlu 2015; Pappas 2006; Weiner 2013); excluding these three studies did not affect the results (data not shown). The outcome assessors were third parties in the studies including easy and moderately difficult participants (McCarthy 2016B; McCarthy 2016C).

To our knowledge, no studies have assessed the minimum clinically important difference (MCID) for pain in peripheral intravenous cannulation, but a meta-analysis examining the MCID for acute pain found it to be 1.7 for pain relief and 1.1 for worsening pain on an NRS of 0 to 10 (Olsen 2017). The mean differences and their upper limits of the 95% CI for all difficulty levels were less than the MCID in the overall analysis and all sensitivity analyses; hence, there was no clinically meaningful difference detected. However, the lower success of ultrasound guidance cannulation in easy participants can explain the increased pain, and therefore, it is reasonably certain that ultrasound guidance increased pain in easy participants. However, the upper limit of the 95% CI did not exceed the MCID, and the degree of increase in pain was considered small. Finally, excluding the quasi-RCT İsmailoğlu 2015 improved the heterogeneity to zero in difficult participants with both definitions, and the results were similar to the overall results.

Procedure time for first-pass cannulation

We downgraded to low certainty-evidence in difficult participants due to risk of bias concerns and imprecision. The certainty of the evidence for moderate and easy participants was high. There were important differences amongst the studies in the definitions of the outcome and study participants. First, the definitions of start and stop times were similar in all studies, except one (Aponte 2007), and included two steps: searching for a target vein and puncturing it. In Aponte 2007, the ultrasound guidance group started measuring time after the target vein was identified, but the

landmark method group started measuring when searching for the target vein. However, this study was small, and excluding it from the meta-analysis did not change the results. Second, ultrasound guidance increased the procedure time in all studies, except for two with different characteristics (Glasin 2020; Skulec 2019). In Skulec 2019, ultrasound guidance had a slightly longer procedure time than the landmark method (approximately 10 seconds), but to a lesser degree than in the other studies (90 to 120 seconds). The main reason is that the result was based only on successful cases. Another reason was that it was the only study that had a static ultrasound guidance arm in addition to dynamic ultrasound guidance, and the static ultrasound guidance was significantly faster than dynamic ultrasound guidance. Glasin 2020 was the only study to show a shorter procedure time in the ultrasound guidance arm. We believe that the reason for this was the difference in the time it took to search for a target vein. This study included only participants with obesity irrespective of the difficulty level. In participants with obesity, it is often more difficult to see and palpate veins (Sebbane 2013), and ultrasound guidance would help to find a target vein more quickly. However, puncturing with ultrasound guidance is more complicated than with the landmark method, and the puncture itself would take longer. Therefore, in cases where a target vein is easy to find with the landmark method, the procedure time as a whole will be longer with ultrasound guidance, especially dynamic ultrasound guidance. Of note, this outcome relies largely on a single article, McCarthy 2016. The three studies in it defined difficulty as an inability to see and palpate a target vein, but did not define how much to look for a vein. The difference in procedure time for first-pass cannulation with the landmark method between difficult and easy participants in the study was under one minute; in other words, even in difficult participants, the extra time to find a target vein was less than a minute. Therefore, the operators did not necessarily have difficulty finding a target vein in the difficult participants in this study. If ultrasound guidance is used in people in whom a target vein is more difficult to find, the benefit of the procedure time would probably increase.

Procedure time for overall cannulation

The certainty of the evidence for the procedure time for overall cannulation was very low in difficult participants. No participants were classed as moderate or easy for this outcome using the original studies' definitions. We downgraded by one level due to risk of bias concerns. One reason for this was incomplete outcome data, with three studies excluding failure cases from the analysis (Kerforne 2012; Pappas 2006; Stein 2009). We also downgraded by two levels for serious heterogeneity, because there was no standardised definition of failure, as with the overall success of cannulation outcome. In addition, another three studies included the time taken when the assigned intervention failed and a different method was used (Bahl 2016; Costantino 2005; Weiner 2013).

Number of cannulation attempts

The certainty of the evidence for the number of cannulation attempts was very low in difficult participants. No participants were classed as moderate or easy for this outcome using the original studies' definitions. We downgraded by one level due to risk of bias concerns. We downgraded one level each for considerable heterogeneity and inconsistency (lack of the same definition of failure or the outcome amongst studies). One study excluded failure cases from the analysis (Pappas 2006). Three studies included the number of cannulation attempts taken when the assigned intervention failed and a different method was used (Bahl 2016; Costantino 2005; Weiner 2013), six studies only analysed the allocated interventions (Aponte 2007; Bridey 2018; Glasin 2020; Pappas 2006; Skulec 2019; Stein 2009), and two studies did not specify details on this (İsmailoğlu 2015; River 2009). However, because ultrasound guidance tended to improve success rates, it is natural that the number of cannulation attempts also decreased. Although River 2009 did not specify a definition, Glasin 2020 and Skulec 2019 used the same definitions of the population and outcome in the moderately difficult participants using the definition of success rate, and ultrasound guidance reduced the number of cannulation attempts with moderate-certainty evidence (Analysis 6.2). Considering the difficulty-dependent effect, ultrasound guidance can potentially reduce the number of cannulation attempts even in difficult participants.

Patient satisfaction

The certainty of the evidence for patient satisfaction was very low for difficult participants. No participants were classed as moderate or easy for this outcome using the original studies' definitions. We downgraded by one level each for risk of bias concerns, inconsistency, and imprecision. The risk of bias was high in all the studies, and two studies only included successful cases, with weights accounting for a total of 35% of the results (Bridey 2018; Stein 2009). A quasi-RCT was the main source of heterogeneity, and when we excluded this study (Costantino 2005), the effect sizes decreased. The number of participants was small for all difficulty levels, and their CIs were wide.

Overall complications

The certainty of the evidence for overall complications was low for difficult participants, and we downgraded by one level each for risk of bias and imprecision. However, the risk of bias was low in five of the nine studies, and the results were similar when studies with a high risk of bias were excluded. The effect sizes in difficult and moderately difficult participants were reasonably consistent, except for Skulec 2019, in which ultrasound guidance reduced complications. The study included pain as a complication, and when we excluded pain, there was no apparent difference, consistent with other studies. The certainty of the evidence for moderately difficult and easy participants was moderate: we downgraded by one level due to imprecision.

Potential biases in the review process

We made every effort to identify and include all eligible studies and to assess them appropriately. The Cochrane Vascular Information Specialist conducted a thorough search to identify eligible studies for the review. Eight studies were potentially eligible, but their results had not been published at the time of the searches. We contacted the investigators and were able to obtain unpublished results owing to the courtesy of the investigators for Glasin 2020. Amongst the seven remaining studies, one was registered in 2014, and it is unclear if it was actually conducted (IRCT201408097751N4). The other six were registered between 2019 and 2021, and results may be available in the future (NCT03745209; NCT03841864; NCT04218643; NCT04853290; NCT04856826; NCT05119985). We will monitor the progress of these studies and include them, if possible, in an update of this review.

We contacted the investigators of the included studies and were able to obtain unpublished outcome results and design details from nine of the 14 articles. Therefore, we believe we managed to conduct comprehensive analyses and clarify the risk of bias assessments.

We analysed data for the number of cannulation attempts using mean values, because seven of the 11 included studies reported mean values, and only one reported median value (Costantino 2005). Following guidance in the *Cochrane Handbook for Systematic Reviews of Interventions*, we treated the median as the mean (Higgins 2021b). In the remaining three studies, we calculated means from tables and figures (Bridey 2018; Glasin 2020; Stein 2009). We used SMD as an outcome measure of satisfaction because two different measures were used, and four out of six studies reported an NRS of 0 to 10.

Agreements and disagreements with other studies or reviews

The results of this review differed from those of previous reviews in several ways (Egan 2013; Heinrichs 2013; Liu 2014; Stolz 2015; Van Loon 2018). First, the previous reviews included six to eight articles (involving 240 to 1660 participants), and our review included 14 articles (2267 participants). In addition, with the help of the investigators of the studies, we obtained some unpublished results and included them in this current review. Second, in the earlier reviews, three studies included children who were analysed together with adults (Egan 2013; Liu 2014; Stolz 2015). Children should be analysed separately because adults and children have different characteristics, such as the size and depth of a target vein, and adherence during the procedure.

The review by Van Loon 2018 included the largest trial (McCarthy 2016) and was the largest amongst previous meta-analyses. However, it did not distinguish the difficulty levels of the participants and analysed them together. It is necessary to analyse the effects of ultrasound guidance separately for each difficulty level because ultrasound guidance effects depend on the difficulty level. We separated the difficulty levels of participants in McCarthy 2016 and reported it as three different studies (McCarthy 2016A; McCarthy 2016B; McCarthy 2016C). This issue is important not only for the heterogeneity but also for the selection of appropriate patients for ultrasound guidance. Heinrichs 2013 included only adult difficult participants and the results were similar to those of this review. It included six studies with 242 participants. Each outcome included only one to three studies because Heinrichs and colleagues analysed settings, such as the emergency department, ICU, and operating room, separately. However, the differences in the settings did not have a substantial impact on the effect of ultrasound guidance, and separate analyses may have unnecessarily reduced the sample size.

AUTHORS' CONCLUSIONS

Implications for practice

There is very low- and low-certainty evidence that ultrasound guidance may benefit difficult participants compared to the landmark method because of increased first-pass success and overall cannulation with no difference detected in pain. With the exception of the procedure time for first-pass cannulation, all the primary and secondary outcomes favoured ultrasound guidance or showed no evidence of a difference, and the results were consistent with both definitions of the difficulty. We believe that the benefits of ultrasound guidance, especially the improvement in the first-pass success of cannulation, are clinically meaningful. In addition, ultrasound guidance did not clearly increase complications. The difference in the procedure time for first-pass cannulation was small, less than three minutes. This difference is unlikely to be clinically important unless the patient is in a very urgent condition. Therefore, we are certain that ultrasound guidance had some benefit but no apparent harm to difficult patients except in cases of urgency.

There is low- and moderate-certainty evidence that ultrasound guidance may benefit moderately difficult participants compared to the landmark method because of increased first-pass success of cannulation with no difference detected in pain. The results were consistent with both definitions of the difficulty. The direction of the effect of ultrasound guidance was similar to that of the difficult participants but to a lesser extent. As in the difficult participants, ultrasound guidance slightly increased the procedure time for first-pass cannulation, but this is of little clinical significance as discussed above. There were no clear differences in other outcomes, including complications. Therefore, in the absence of obvious harm, ultrasound guidance may be useful in moderately difficult patients.

There is moderate- and high-certainty evidence that ultrasound guidance does not benefit easy participants compared to the landmark method because ultrasound guidance decreased the first-pass success of cannulation and increased pain. All the outcomes, including the procedure time for first-pass cannulation and complications, consistently favoured the landmark method or showed no apparent difference with reasonable certainty with both definitions of the difficulty. Therefore, we believe ultrasound guidance should not be used in easy patients.

Although we were unable to demonstrate any apparent effect on training or previous experience in ultrasound guidance, both are clinically important. We consider attempts to maintain and monitor operators' proficiency essential in the clinical application of ultrasound guidance. Combined with a proper scale to assess the difficulty, ultrasound guidance could be used more appropriately.

Implications for research

The effectiveness of ultrasound guidance depended on the level of participants' difficulty, but the definition of difficulty varied, and this problem undermined the certainty of our results. A reproducible method of difficulty stratification will make the evidence more robust and allow for more appropriate selection of patients for ultrasound guidance.

Because the definition of failure and outcomes were not the same, the results of the overall success of cannulation, procedure time for overall cannulation, and number of cannulation attempts were uncertain. Future studies should use a common, standardised definition of failure for ultrasound guidance and the landmark method. Also, if an allocated intervention fails and another method is used, it is better to prioritise the results of only the allocated intervention. This is because the alternative methods are expected to vary and could be a source of further heterogeneity.

Because of the lack of detailed descriptions, the effect of operators' training and experience on ultrasound guidance was unclear. However, it is clearly a clinically important factor. We will include this issue in a future update if studies which randomise by training programmes or operators' occupation or experience levels are conducted.

Although not included in this review, devices such as midline catheters could be a new option. In a future update, we will evaluate these devices, especially for the duration of functional catheters and cost, if data are available. Differences in needle visibility due to features of ultrasound machines and their effects will also be an important issue to consider.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Aponte 2007

Study characteristics	
Methods	Randomised, open-label trial
Participants	Setting: operating room Number of participants: 35 (USG 19, LM 16) Age, mean (SD) years: USG 55.5 (15.7), LM 57.3 (18.9) Difficulty: difficult (participants reported past difficulties or anaesthesia providers identified them as having the potential for difficulty) Sites of peripheral veins: upper extremity
Interventions	**Technique** LM vs USG: Machine: Site-Rite 3 Ultrasound Unit (Bard Access Systems) with a 9.0 MHz probe Axis: not specified Guidance: dynamic **Operator** Profession: certified registered nurse anaesthetist Number of operators: two Experience of USG before the study: yes Length of experience with USG before the study: not specified A training programme of USG for the study: yes Number of clinical cases with USG required or experienced before the study intervention started: 5 **Needle** Length: not specified Gauge: 18 - 22

Aponte 2007 *(Continued)*

Outcomes	First-pass success of cannulation, overall success of cannulation, procedure time for first-pass cannulation, procedure time for overall cannulation, number of attempts **Definition of successful cannulation:** blood return from a catheter **Definition of start and end of time measurement** Start: • USG, a transducer was placed onto the skin, and a vein was identified on the ultrasound monitor • LM, a nurse started identifying potential target veins End: successful intravenous cannulation
Funding	Not specified
Declarations of interest	Not specified
Notes	We attempted to contact the authors to obtain additional information but were unable to reach them.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of randomisation process
Allocation concealment (selection bias)	Unclear risk	No description of allocation concealment process
Blinding (performance bias and detection bias) First-pass success of cannulation	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. Operators assessed the outcome themselves
Blinding (performance bias and detection bias) Overall-success of cannulation	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. Operators assessed the outcome themselves
Blinding (performance bias and detection bias) Procedure time for first-pass cannulation	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. Operators assessed the outcome themselves
Blinding (performance bias and detection bias) Procedure time for overall cannulation	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. Operators assessed the outcome themselves
Blinding (performance bias and detection bias) Number of attempts	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. Operators assessed the outcome themselves
Incomplete outcome data (attrition bias) First-pass success of cannulation	Low risk	The outcome was available for all participants

Aponte 2007 *(Continued)*

Incomplete outcome data (attrition bias) Overall success of cannulation	Low risk	The outcome was available for all participants
Incomplete outcome data (attrition bias) Procedure time for first-pass cannulation	High risk	The outcome was evaluated only for participants with successful cannulation
Incomplete outcome data (attrition bias) Procedure time for overall cannulation	Low risk	The outcome was available for all participants
Incomplete outcome data (attrition bias) Number of attempts	Low risk	The outcome was available for all participants
Selective reporting (reporting bias)	Unclear risk	No study register or protocol was available
Other bias	Low risk	No concerns about other sources of bias
Overall risk First-pass success of cannulation	High risk	At least one domain was at high risk
Overall risk Overall success of cannulation	High risk	At least one domain was at high risk
Overall risk Procedure time for first-pass cannulation	High risk	At least one domain was at high risk
Overall risk Procedure time for overall cannulation	High risk	At least one domain was at high risk
Overall risk Number of attempts	High risk	At least one domain was at high risk

Bahl 2016

Study characteristics	
Methods	Randomised, open-label trial
Participants	Setting: ED Number of participants: 122 (USG 63, LM 59) Age, mean (SD) years: USG 61 (not specified), LM 62 (not specified) Difficulty: difficult (participants reported past difficulties or experienced at least one previous episode where at least 2 attempts were required to obtain a peripheral IV) Sites of peripheral veins: upper extremity

Bahl 2016 *(Continued)*

Interventions	**Technique** LM vs USG: Machine: Sonosite M-turbo (Sonosite) with a high-frequency linear transducer Axis: not specified Guidance: not specified **Operator** Profession: ED registered nurses Number of operators: 20 Experience of USG before the study: no Length of experience with USG before the study: none A training programme of USG for the study: yes Number of clinical cases with USG required or experienced before the study intervention started: 10 **Needle** Length: not specified Gauge: not specified
Outcomes	First-pass success of cannulation, time for overall cannulation, number of attempts **Definition of successful cannulation:** blood return from a catheter, smooth normal saline flush, and no signs of extravasation **Definition of start and end of time measurement** Start: a study nurse placed a tourniquet on a participant End: functional intravenous cannulation was obtained and a tegaderm was positioned over the catheter
Funding	Blue Cross Blue Shield of Michigan Physician Investigator Award Number 2069
Declarations of interest	None declared
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The randomisation scheme was created by a biostatistician using a computer-generated program
Allocation concealment (selection bias)	Low risk	Randomisation with varying block sizes, sealed envelopes
Blinding (performance bias and detection bias) First-pass success of cannulation	Low risk	Although blinding of participants and operators is impossible due to the nature of the intervention, a third person assessed the outcome (this was not stated in the article, but obtained through the communication with an author (AB))
Blinding (performance bias and detection bias) Overall-success of cannulation	Low risk	Although blinding of participants and operators is impossible due to the nature of the intervention, a third person assessed the outcome (this was not stated in the article, but obtained through the communication with an author (AB))
Blinding (performance bias and detection bias) Procedure time for overall cannulation	Low risk	Although blinding of participants and operators is impossible due to the nature of the intervention, a third person assessed the outcome (this was not stated in the article, but obtained through the communication with an author (AB))

Bahl 2016 *(Continued)*

Blinding (performance bias and detection bias) Number of attempts	Low risk	Although blinding of participants and operators is impossible due to the nature of the intervention, a third person assessed the outcome (this was not stated in the article, but obtained through the communication with an author (AB))
Incomplete outcome data (attrition bias) First-pass success of cannulation	Low risk	The outcome was available for all participants
Incomplete outcome data (attrition bias) Overall success of cannulation	Low risk	The outcome was available for all participants
Incomplete outcome data (attrition bias) Procedure time for overall cannulation	Low risk	The outcome was available for all participants
Incomplete outcome data (attrition bias) Number of attempts	Low risk	The outcome was available for all participants
Selective reporting (reporting bias)	Unclear risk	No study register or protocol was available
Other bias	Low risk	No concerns about other sources of bias
Overall risk First-pass success of cannulation	Unclear risk	At least one domain was unclear
Overall risk Overall success of cannulation	Unclear risk	At least one domain was unclear
Overall risk Procedure time for overall cannulation	Unclear risk	At least one domain was unclear
Overall risk Number of attempts	Unclear risk	At least one domain was unclear

Bridey 2018

Study characteristics	
Methods	Randomised, open-label trial
Participants	Setting: ICU Number of participants: 114 (USG 57, LM 57) Age, mean (SD) years: USG 65.5 (17.6), LM 64 (17) Difficulty: difficult (could not see and palpate a vein) Sites of peripheral veins: upper extremity

Bridey 2018 *(Continued)*

Interventions	**Technique** LM vs USG: Machine: Sonosite M-turbo (Sonosite) with a high-frequency linear transducer Axis: not specified Guidance: not specified **Operator** Profession: ED registered nurse Number of operators: 20 Experience of USG before the study: 70% of the operators had previous experience Length of experience with USG before the study: not specified A training programme of USG for the study: yes Number of clinical cases with USG required or experienced before the study intervention started: 10 **Needle** Length: 29 mm Gauge: not specified
Outcomes	First-pass success of cannulation, overall success of cannulation, number of attempts, patient satisfaction **Definition of successful cannulation:** smooth normal saline flush, and no signs of extravasation
Funding	The French Intensive Care Society, 'Bourse Recherche Paramédicale 2016'
Declarations of interest	None declared
Notes	Although IV cannulation was attempted for four days in this study, we used results from day one to align with the conditions in other studies

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The randomisation list was computer-generated (this was not stated in the article, but obtained through communication with an author (AK))
Allocation concealment (selection bias)	Low risk	Randomisation with varying block sizes, sealed and opaque envelopes (this was not stated in the article, but obtained through communication with an author (AK))
Blinding (performance bias and detection bias) First-pass success of cannulation	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. Operators assessed the outcome themselves (this was not stated in the article, but obtained through communication with an author (AK))
Blinding (performance bias and detection bias) Overall-success of cannulation	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. Operators assessed the outcome themselves (this was not stated in the article, but obtained through communication with an author (AK))
Blinding (performance bias and detection bias) Number of attempts	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. Operators assessed the outcome themselves (this was not stated in the article, but obtained through communication with an author (AK))
Blinding (performance bias and detection bias) Patient satisfaction	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. Operators assessed the outcome themselves

Bridey 2018 *(Continued)*

Incomplete outcome data (attrition bias) First-pass success of cannulation	Low risk	There were only three dropouts (USG 1, LM 2), and the reasons were detailed
Incomplete outcome data (attrition bias) Overall success of cannulation	Low risk	There were only two dropouts (USG 1, LM 1), and the reasons were detailed
Incomplete outcome data (attrition bias) Number of attempts	Low risk	There were only three dropouts (USG 1, LM 2), and the reasons were detailed
Incomplete outcome data (attrition bias) Patient satisfaction	High risk	There were 10 dropouts from the assessment (USG 5, LM 5), and the reasons were not detailed
Selective reporting (reporting bias)	Low risk	The outcomes reported in the article were consistent with the trial registry (NCT02285712)
Other bias	Low risk	No concerns about other sources of bias
Overall risk First-pass success of cannulation	High risk	At least one domain was at high risk
Overall risk Overall success of cannulation	High risk	At least one domain was at high risk
Overall risk Number of attempts	High risk	At least one domain was at high risk
Overall risk Patient satisfaction	High risk	At least one domain was at high risk

Costantino 2005

Study characteristics	
Methods	Quasi-randomised (participants' presentation on an odd or even day), open-label trial
Participants	Setting: ED Number of participants: 60 (USG 39, LM 21) Age, mean (SD) years: not specified Difficulty: difficult (at least 3 failed attempts and a history of difficult IV cannulation) Sites of peripheral veins: upper extremity
Interventions	**Technique** LM vs USG: Machine: Versapro (Siemens) with a 7.5 MHz probe or Sonosite 180 plus (Sonosite) with an 8.0 MHz probe Axis: short Guidance: dynamic

Costantino 2005 *(Continued)*

	Operator Profession: emergency physicians (resident and attending) Number of operators: 20 Experience of USG before the study: yes Length of experience with USG before the study: not specified A training programme of USG for the study: yes Number of clinical cases with USG required or experienced before the study intervention started: not specified **Needle** Length: 32 mm Gauge: 18
Outcomes	First-pass success of cannulation, overall success of cannulation, procedure time for overall cannulation, number of attempts, patient satisfaction, complications **Definition of successful cannulation:** blood return from a catheter **Definition of start and end of time measurement** Start: first percutaneous puncture End: successful cannulation
Funding	None
Declarations of interest	Not specified
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Systematically allocated based on the day of presentation to the ED (odd day: USG, even day: LM)
Allocation concealment (selection bias)	High risk	Concealment is impossible due to method of allocation
Blinding (performance bias and detection bias) First-pass success of cannulation	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. Operators assessed the outcome themselves
Blinding (performance bias and detection bias) Overall-success of cannulation	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. Operators assessed the outcome themselves
Blinding (performance bias and detection bias) Procedure time for overall cannulation	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. Operators assessed the outcome themselves
Blinding (performance bias and detection bias) Number of attempts	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. Operators assessed the outcome themselves
Blinding (performance bias and detection bias)	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. Operators assessed the outcome themselves

Costantino 2005 *(Continued)*

Patient satisfaction		
Blinding (performance bias and detection bias) Overall complications	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. Operators assessed the outcome themselves
Incomplete outcome data (attrition bias) First-pass success of cannulation	Low risk	The outcome was available for all participants
Incomplete outcome data (attrition bias) Overall success of cannulation	Low risk	The outcome was available for all participants
Incomplete outcome data (attrition bias) Procedure time for overall cannulation	Low risk	The outcome was available for all participants
Incomplete outcome data (attrition bias) Number of attempts	Low risk	The outcome was available for all participants
Incomplete outcome data (attrition bias) Patient satisfaction	Low risk	The outcome was available for all participants
Incomplete outcome data (attrition bias) Overall complications	Low risk	The outcome was available for all participants
Selective reporting (reporting bias)	Unclear risk	No study register or protocol was available
Other bias	Low risk	No concerns about other sources of bias
Overall risk First-pass success of cannulation	High risk	At least one domain was at high risk
Overall risk Overall success of cannulation	High risk	At least one domain was at high risk
Overall risk Procedure time for overall cannulation	High risk	At least one domain was at high risk
Overall risk Number of attempts	High risk	At least one domain was at high risk
Overall risk Patient satisfaction	High risk	At least one domain was at high risk
Overall risk Overall complications	High risk	At least one domain was at high risk

Glasin 2020

Study characteristics	
Methods	Randomised, open-label trial
Participants	Setting: ED Number of participants: 90 (USG 45, LM 45) Age, mean (SD) years: USG 61.7 (16), LM 60.8 (18.6) Difficulty: not restricted, but obese (BMI ≥ 25) Sites of peripheral veins: not specified
Interventions	**Technique** LM vs USG: Machine: x-Porte (Fujifilm Sonosite) with a high-frequency linear transducer Axis: short Guidance: dynamic **Operator** Profession: nurse Number of operators: 17 (16 nurses performed LM, 1 nurse performed USG) Experience of USG before the study: yes Length of experience with USG before the study: 1 year A training programme of USG for the study: yes Number of clinical cases with USG required or experienced before the study intervention started: 50 **Needle** Length: not specified Gauge: 12 - 18
Outcomes	First-pass success of cannulation, overall success of cannulation, pain, procedure time for first-pass cannulation, procedure time for overall cannulation, number of attempts, patient satisfaction, overall complications **Definition of successful cannulation:** smooth normal saline flush **Definition of start and end of time measurement** Start: applying stasis with either a tourniquet or a blood pressure cuff End: blood entered a catheter flashback chamber
Funding	DW obtained research funding, but the source was not specified
Declarations of interest	None declared
Notes	The study had not yet been published as of December 2020. We received an unpublished manuscript courtesy of the author

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	The randomisation list was computer-generated
Allocation concealment (selection bias)	Low risk	Used sequentially numbered, sealed and opaque envelopes (this was not stated in the article, but obtained through communication with an author (DW))
Blinding (performance bias and detection bias)	Low risk	Although blinding of participants and operators is impossible due to the nature of the intervention, a third person assessed the outcome

Glasin 2020 *(Continued)*

First-pass success of cannulation		
Blinding (performance bias and detection bias) Overall-success of cannulation	Low risk	Although blinding of participants and operators is impossible due to the nature of the intervention, a third person assessed the outcome
Blinding (performance bias and detection bias) Pain	High risk	Although a third person assessed the outcome, participants were not blinded and the outcome could be influenced by subjectivity
Blinding (performance bias and detection bias) Procedure time for first-pass cannulation	Low risk	Although blinding of participants and operators is impossible due to the nature of the intervention, a third person assessed the outcome
Blinding (performance bias and detection bias) Procedure time for overall cannulation	Low risk	Although blinding of participants and operators is impossible due to the nature of the intervention, a third person assessed the outcome
Blinding (performance bias and detection bias) Number of attempts	Low risk	Although blinding of participants and operators is impossible due to the nature of the intervention, a third person assessed the outcome
Blinding (performance bias and detection bias) Patient satisfaction	High risk	Although a third person assessed the outcome, participants were not blinded and the outcome could be influenced by subjectivity
Blinding (performance bias and detection bias) Overall complications	Low risk	Although blinding of participants and operators is impossible due to the nature of the intervention, a third person assessed the outcome
Incomplete outcome data (attrition bias) First-pass success of cannulation	Low risk	There was only one dropout (USG 1), and the reason was detailed
Incomplete outcome data (attrition bias) Overall success of cannulation	Low risk	There was only one dropout (USG 1), and the reason was detailed
Incomplete outcome data (attrition bias) Pain	Low risk	There was only one dropout (USG 1), and the reason was detailed
Incomplete outcome data (attrition bias) Procedure time for first-pass cannulation	Low risk	There was only one dropout (USG 1), and the reason was detailed
Incomplete outcome data (attrition bias) Procedure time for overall cannulation	Low risk	There was only one dropout (USG 1), and the reason was detailed

Glasin 2020 *(Continued)*

Incomplete outcome data (attrition bias) Number of attempts	Low risk	There was only one dropout (USG 1), and the reason was detailed
Incomplete outcome data (attrition bias) Patient satisfaction	Low risk	There was only one dropout (USG 1), and the reason was detailed
Incomplete outcome data (attrition bias) Overall complications	Low risk	There was only one dropout (USG 1), and the reason was detailed
Selective reporting (reporting bias)	Low risk	The outcomes reported in the article were consistent with the trial registry (NCT04412967)
Other bias	Low risk	No concerns about other sources of bias
Overall risk First-pass success of cannulation	Low risk	All domains were at low risk
Overall risk Overall success of cannulation	Low risk	All domains were at low risk
Overall risk Pain	High risk	At least one domain was at high risk
Overall risk Procedure time for first-pass cannulation	Low risk	All domains were at low risk
Overall risk Procedure time for overall cannulation	Low risk	All domains were at low risk
Overall risk Number of attempts	Low risk	All domains were at low risk
Overall risk Patient satisfaction	High risk	At least one domain was at high risk
Overall risk Overall complications	Low risk	All domains were at low risk

İsmailoğlu 2015

Study characteristics	
Methods	Quasi-randomised, open-label trial Participants were allocated to each group alternately, in the order in which they were seen
Participants	Setting: ED Number of participants: 60 (USG 30, LM 30) Age, mean (SD) years: not specified

İsmailoğlu 2015 *(Continued)*

	Difficulty: difficult (a history or suspicion of difficult cannulation, and could not see or palplate a target vein) Sites of peripheral veins: upper extremity
Interventions	**Technique** LM vs USG: Machine: Sonosite Micromaxx (Sonosite) with a high-frequency linear transducer Axis: not specified Guidance: dynamic **Operator** Profession: ED nurses Number of operators: not specified Experience of USG before the study: no Length of experience with USG before the study: not specified A training programme of USG for the study: yes Number of clinical cases with USG required or experienced before the study intervention started: not specified **Needle** Length: not specified Gauge: 20
Outcomes	First-pass success of cannulation, overall success of cannulation, number of attempts, pain, overall complications **Definition of successful cannulation:** blood return from a catheter, smooth normal saline flush, and no signs of extravasation
Funding	None
Declarations of interest	Not specified
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Participants were assigned alternately to USG and LM in the order in which they were seen. Not consecutive cases
Allocation concealment (selection bias)	High risk	This was a systematically allocated trial
Blinding (performance bias and detection bias) First-pass success of cannulation	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. One of the co-authors assessed the outcome
Blinding (performance bias and detection bias) Overall-success of cannulation	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. One of the co-authors assessed the outcome
Blinding (performance bias and detection bias) Pain	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. One of the co-authors assessed the outcome

İsmailoğlu 2015 *(Continued)*

Blinding (performance bias and detection bias) Number of attempts	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. One of the co-authors assessed the outcome
Blinding (performance bias and detection bias) Overall complications	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. One of the co-authors assessed the outcome
Incomplete outcome data (attrition bias) First-pass success of cannulation	Low risk	No dropouts from the analysis
Incomplete outcome data (attrition bias) Overall success of cannulation	Low risk	No dropouts from the analysis
Incomplete outcome data (attrition bias) Pain	Low risk	No dropouts from the analysis
Incomplete outcome data (attrition bias) Number of attempts	Low risk	No dropouts from the analysis
Incomplete outcome data (attrition bias) Overall complications	Low risk	No dropouts from the analysis
Selective reporting (reporting bias)	Unclear risk	No study register or protocol was available
Other bias	Low risk	No concerns about other sources of bias
Overall risk First-pass success of cannulation	High risk	At least one domain was at high risk
Overall risk Overall success of cannulation	High risk	At least one domain was at high risk
Overall risk Pain	High risk	At least one domain was at high risk
Overall risk Number of attempts	High risk	At least one domain was at high risk
Overall risk Overall complications	High risk	At least one domain was at high risk

Kerforne 2012

Study characteristics

Kerforne 2012 *(Continued)*

Methods	Randomised, open-label trial
Participants	Setting: ICU Number of participants: 60 (USG 30, LM 30) Age, mean (SD) years: USG 61 (17), LM 56 (15) Difficulty: difficult (an operator could not see and palpate the targeted vein) Sites of peripheral veins: upper extremity
Interventions	**Technique** LM vs USG: Machine: Vivid e (General Electric) with a 10 MHz probe Axis: not specified Guidance: dynamic **Operator** Profession: nurse Number of operators: not specified Experience of USG before the study: not specified Length of experience with USG before the study: not specified A training programme of USG for the study: not specified Number of clinical cases with USG required or experienced before the study intervention started: not specified **Needle** Length: not specified Gauge: not specified
Outcomes	First-pass success of cannulation, overall successful of cannulation, procedure time for overall cannulation **Definition of successful cannulation:** not specified **Definition of start and end of time measurement** • Start: an operator put on sterile gloves • End: a return of blood in tubing and the possibility of infusing a few millilitres of saline without pain or extravasation
Funding	University Hospital of Poitiers
Declarations of interest	None declared
Notes	Data for first-pass success of cannulation were unpublished and obtained through communication with an author (TK). We attempted to contact the authors to obtain additional information for the risk of bias (ROB) assessment but did not receive a response.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of randomisation process
Allocation concealment (selection bias)	Unclear risk	No description of allocation concealment
Blinding (performance bias and detection bias)	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. Operators assessed the outcome themselves (this was not stated in the article, but obtained through communication with an author (TK))

Kerforne 2012 *(Continued)*

First-pass success of cannulation		
Blinding (performance bias and detection bias) Overall-success of cannulation	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. Operators assessed the outcome themselves (this was not stated in the article, but obtained through communication with an author (TK))
Blinding (performance bias and detection bias) Procedure time for overall cannulation	Low risk	Although blinding of participants and operators is impossible due to the nature of the intervention, a third-person assessed the outcome (this was not stated in the article, but obtained through communication with an author (TK))
Incomplete outcome data (attrition bias) First-pass success of cannulation	Low risk	The outcome was available for all participants
Incomplete outcome data (attrition bias) Overall success of cannulation	Low risk	The outcome was available for all participants
Incomplete outcome data (attrition bias) Procedure time for overall cannulation	High risk	The outcome was evaluated only for participants with successful cannulation
Selective reporting (reporting bias)	Unclear risk	No study register or protocol was available
Other bias	Low risk	No concerns about other sources of bias
Overall risk First-pass success of cannulation	High risk	At least one domain was at high risk
Overall risk Overall success of cannulation	High risk	At least one domain was at high risk
Overall risk Procedure time for overall cannulation	High risk	At least one domain was at high risk

McCarthy 2016A

Study characteristics	
Methods	Randomised, open-label trial
Participants	Setting: ED Number of participants: 192 (USG 98, LM 94) Age, mean (SD) years: not specified Difficulty: difficult (could not see or palpate a vein) Sites of peripheral veins: upper extremity

McCarthy 2016A *(Continued)*

Interventions	**Technique** LM vs USG: Machine: Sonosite M-Turbo (Sonosite) or Zonare ultra (Zonare) Axis: not specified Guidance: dynamic **Operator** Profession: technician Number of operators: 33 Experience of USG before the study: yes Length of experience with USG before the study: 82% of the operators had more than one year of experience A training programme of USG for the study: yes Number of clinical cases with USG required or experienced before the study intervention started: not specified **Needle** Length: 32 or 48 mm Gauge: 18 - 22
Outcomes	First-pass success of cannulation, procedure time for first-pass cannulation, pain, complications **Definition of successful cannulation:** smooth normal saline flush, and no signs of extravasation **Definition of start and end of time measurement** • Start: tourniquet placement • End: saline solution flush through a peripheral intravenous line
Funding	Award K01HS017957 from the Agency for Healthcare Research and Quality
Declarations of interest	None declared
Notes	McCarthy 2016 randomised participants separately according to the difficulty of the LM (easy, moderate, and difficult), and we split them according to the difficulty level (McCarthy 2016A; McCarthy 2016B; McCarthy 2016C)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The randomisation scheme was created by SAS software (version 9.3; SAS Institute Inc, Cary, NC)
Allocation concealment (selection bias)	Low risk	Centrally randomised with REDCap (version 6.5.12; Nashville, TN)
Blinding (performance bias and detection bias) First-pass success of cannulation	Low risk	Although blinding of participants and operators is impossible due to the nature of the intervention, a third person assessed the outcome
Blinding (performance bias and detection bias) Pain	High risk	Although a third person assessed the outcome, participants were not blinded and the outcome could be influenced by subjectivity
Blinding (performance bias and detection bias)	Low risk	Although blinding of participants and operators is impossible due to the nature of the intervention, a third person assessed the outcome

McCarthy 2016A *(Continued)*

Procedure time for first-pass cannulation		
Blinding (performance bias and detection bias) Overall complications	Low risk	Although blinding of participants and operators is impossible due to the nature of the intervention, a third person assessed the outcome
Incomplete outcome data (attrition bias) First-pass success of cannulation	Low risk	There were only two dropouts (USG 1, LM 1)
Incomplete outcome data (attrition bias) Pain	Low risk	There were only 4 dropouts out of 1189 participants across the whole study
Incomplete outcome data (attrition bias) Procedure time for first-pass cannulation	Low risk	There were only 7 dropouts out of 1189 participants across the whole study
Incomplete outcome data (attrition bias) Overall complications	Low risk	The outcome was available for all participants
Selective reporting (reporting bias)	Low risk	The outcomes reported in the article were consistent with the trial registry (NCT01859559)
Other bias	Low risk	No concerns about other sources of bias
Overall risk First-pass success of cannulation	Low risk	All domains were at low risk
Overall risk Pain	High risk	At least one domain was at high risk
Overall risk Procedure time for first-pass cannulation	Low risk	All domains were at low risk
Overall risk Overall complications	Low risk	All domains were at low risk

McCarthy 2016B

Study characteristics	
Methods	Randomised, open-label trial
Participants	Setting: ED Number of participants: 401 (USG 202, LM 199) Age, mean (SD) years: not specified Difficulty: moderate (could see or palpate at least 1 vein but anticipated difficulty using LM) Sites of peripheral veins: upper extremity

McCarthy 2016B *(Continued)*

Interventions	**Technique** LM vs USG: Machine: Sonosite M-Turbo (Sonosite) or Zonare ultra (Zonare) Axis: not specified Guidance: dynamic **Operator** Profession: technician Number of operators: 33 Experience of USG before the study: yes Length of experience with USG before the study: 82% of the operators had more than one year of experience A training programme of USG for the study: yes Number of clinical cases with USG required or experienced before the study intervention started: not specified **Needle** Length: 32 or 48 mm Gauge: 18 - 22
Outcomes	First-pass success of cannulation, procedure time for first-pass cannulation, pain, complications **Definition of successful cannulation:** smooth normal saline flush, and no signs of extravasation **Definition of start and end of time measurement** • Start: tourniquet placement • End: saline solution flush through a peripheral intravenous line
Funding	Award K01HS017957 from the Agency for Healthcare Research and Quality
Declarations of interest	None declared
Notes	McCarthy 2016 randomised participants separately according to the difficulty of the LM (easy, moderate, and difficult), and we split them according to the difficulty level (McCarthy 2016A; McCarthy 2016B; McCarthy 2016C)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The randomisation scheme was created by SAS software (version 9.3; SAS Institute Inc., Cary, NC)
Allocation concealment (selection bias)	Low risk	Centrally randomised with REDCap (version 6.5.12; Nashville, TN)
Blinding (performance bias and detection bias) First-pass success of cannulation	Low risk	Although blinding of participants and operators is impossible due to the nature of the intervention, a third person assessed the outcome
Blinding (performance bias and detection bias) Pain	High risk	Although a third person assessed the outcome, patients were not blinded and the outcome could be influenced by subjectivity
Blinding (performance bias and detection bias)	Low risk	Although blinding of participants and operators is impossible due to the nature of the intervention, a third person assessed the outcome

McCarthy 2016B *(Continued)*

Procedure time for first-pass cannulation		
Blinding (performance bias and detection bias) Overall complications	Low risk	Although blinding of participants and operators is impossible due to the nature of the intervention, a third person assessed the outcome
Incomplete outcome data (attrition bias) First-pass success of cannulation	Low risk	The outcome was available for all participants
Incomplete outcome data (attrition bias) Pain	Low risk	There were only 4 dropouts out of 1189 participants across the whole study
Incomplete outcome data (attrition bias) Procedure time for first-pass cannulation	Low risk	There were only 7 dropouts out of 1189 participants across the whole study
Incomplete outcome data (attrition bias) Overall complications	Low risk	The outcome was available for all participants
Selective reporting (reporting bias)	Low risk	The outcomes reported in the article were consistent with the trial registry (NCT01859559)
Other bias	Low risk	No concerns about other sources of bias
Overall risk First-pass success of cannulation	Low risk	All domains were at low risk
Overall risk Pain	High risk	At least one domain was at high risk
Overall risk Procedure time for first-pass cannulation	Low risk	All domains were at low risk
Overall risk Overall complications	Low risk	All domains were at low risk

McCarthy 2016C

Study characteristics	
Methods	Randomised, open-label trial
Participants	Setting: ED Number of participants: 596 (USG 305, LM 291) Age, mean (SD) years: not specified Difficulty: easy (could see or palpate at least 1 vein and thought IV access would be easy with LM) Sites of peripheral veins: upper extremity

McCarthy 2016C *(Continued)*

Interventions	**Technique** LM vs USG: Machine: Sonosite M-Turbo (Sonosite) or Zonare ultra (Zonare) Axis: not specified Guidance: dynamic **Operator** Profession: technician Number of operators: 33 Experience of USG before the study: yes Length of experience with USG before the study: 82% of the operators had more than one year of experience A training programme of USG for the study: yes Number of clinical cases with USG required or experienced before the study intervention started: not specified **Needle** Length: 32 or 48 mm Gauge: 18 - 22
Outcomes	First-pass success of cannulation, procedure time for first-pass cannulation, pain, complications **Definition of successful cannulation:** smooth normal saline flush, and no signs of extravasation **Definition of start and end of time measurement** • Start: tourniquet placement • End: saline solution flush through a peripheral intravenous line
Funding	Award K01HS017957 from the Agency for Healthcare Research and Quality
Declarations of interest	None declared
Notes	McCarthy 2016 randomised participants separately according to the difficulty of the LM (easy, moderate, and difficult), and we split them according to the difficulty level (McCarthy 2016A; McCarthy 2016B; McCarthy 2016C)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The randomisation scheme was created by SAS software (version 9.3; SAS Institute Inc., Cary, NC)
Allocation concealment (selection bias)	Low risk	Centrally randomised with REDCap (version 6.5.12; Nashville, TN)
Blinding (performance bias and detection bias) First-pass success of cannulation	Low risk	Although blinding of participants and operators is impossible due to the nature of the intervention, a third person assessed the outcome
Blinding (performance bias and detection bias) Pain	High risk	Although a third person assessed the outcome, participants were not blinded and the outcome could be influenced by subjectivity
Blinding (performance bias and detection bias)	Low risk	Although blinding of participants and operators is impossible due to the nature of the intervention, a third person assessed the outcome

McCarthy 2016C *(Continued)*

Procedure time for first-pass cannulation		
Blinding (performance bias and detection bias) Overall complications	Low risk	Although blinding of participants and operators is impossible due to the nature of the intervention, a third person assessed the outcome
Incomplete outcome data (attrition bias) First-pass success of cannulation	Low risk	There were only 5 dropouts (USG 5) out of 305 participants
Incomplete outcome data (attrition bias) Pain	Low risk	There were only 4 dropouts out of 1189 participants across the whole study
Incomplete outcome data (attrition bias) Procedure time for first-pass cannulation	Low risk	There were only 7 dropouts out of 1189 participants across the whole study
Incomplete outcome data (attrition bias) Overall complications	Low risk	The outcome was available for all participants
Selective reporting (reporting bias)	Low risk	The outcomes reported in the article were consistent with the trial registry (NCT01859559)
Other bias	Low risk	No concerns about other sources of bias
Overall risk First-pass success of cannulation	Low risk	All domains were at low risk
Overall risk Pain	High risk	At least one domain was at high risk
Overall risk Procedure time for first-pass cannulation	Low risk	All domains were at low risk
Overall risk Overall complications	Low risk	All domains were at low risk

Nishizawa 2020

Study characteristics	
Methods	Randomised, open-label trial
Participants	Setting: ICU Number of participants: 60 (USG 30, LM 30) Age, mean (SD) years: USG 74.2 (14.7), LM 79.4 (10.8) Difficulty: difficult (at least 2 failed attempts with LM, or at least 2 experienced nurses anticipated difficulty with LM based on the absence of a palpable vein or a history of difficult IV cannulation) Sites of peripheral veins: upper extremity

Nishizawa 2020 *(Continued)*

Interventions	**Technique** LM vs USG: Machine: Noblus (Hitachi) with a 10-5 MHz probe Axis: short Guidance: dynamic **Operator** Profession: nurse Number of operators: 30 Experience of USG before the study: no Length of experience with USG before the study: none A training programme of USG for the study: yes Number of clinical cases with USG required or experienced before the study intervention started: 3 **Needle** Length: 31 or 51 mm Gauge: 20
Outcomes	First-pass success of cannulation, overall success of cannulation, complications **Definition of successful cannulation:** blood return from a catheter, saline flush without signs of extravasation
Funding	None
Declarations of interest	None declared
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random sequence was created by a computer
Allocation concealment (selection bias)	Low risk	Concealed using opaque, sealed envelopes
Blinding (performance bias and detection bias) First-pass success of cannulation	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. One of the co-authors assessed the outcome
Blinding (performance bias and detection bias) Overall-success of cannulation	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. One of the co-authors assessed the outcome
Blinding (performance bias and detection bias) Overall complications	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. One of the co-authors assessed the outcome
Incomplete outcome data (attrition bias) First-pass success of cannulation	Low risk	The outcome was available for all participants

Nishizawa 2020 *(Continued)*

Incomplete outcome data (attrition bias) Overall success of cannulation	Low risk	The outcome was available for all participants
Incomplete outcome data (attrition bias) Overall complications	Low risk	The outcome was available for all participants
Selective reporting (reporting bias)	Low risk	The outcomes reported in the article were consistent with the trial protocol (obtained through communication with an author (TN))
Other bias	Low risk	No concerns about other sources of bias
Overall risk First-pass success of cannulation	High risk	At least one domain was at high risk
Overall risk Overall success of cannulation	High risk	At least one domain was at high risk
Overall risk Overall complications	High risk	At least one domain was at high risk

Pappas 2006

Study characteristics	
Methods	Randomised, open-label trial
Participants	Setting: operating room Number of participants: 18 (USG 12, LM 6) Age, mean (SD) years: not specified Difficulty: at least 2 failed attempts with LM Sites of peripheral veins: upper extremity (forearm)
Interventions	**Technique** LM vs USG: Machine: Site-Rite3 Ultrasound Unit (Bard Access Systems) with a 9.0 MHz probe Axis: not specified Guidance: dynamic **Operator** Profession: anaesthesia provider Number of operators: 3 Experience of USG before the study: yes Length of experience with USG before the study: not specified A training programme of USG for the study: not specified Number of clinical cases with USG required or experienced before the study intervention started: 5 **Needle** Length: not specified Gauge: 18 or 20
Outcomes	Procedure time for overall cannulation, number of attempts, pain

Pappas 2006 *(Continued)*

Definition of successful cannulation: blood return from a catheter

Definition of start and end of time measurement:

- Start:
  - USG, a transducer was placed and a target vein was identified
  - LM, an anesthesia provider began detecting potential veins
- End: successful intravenous cannulation

Funding	None
Declarations of interest	Not specified
Notes	Although original sample size was 46, they actually randomised only 22 participants, and did not mention the reason. Of the 22 participants, 2 were excluded due to broken randomisation and another 2 were excluded due to unsuccessful cannulation. We attempted to contact the authors to obtain additional information but were unable to reach them.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Packets, including consent and data collection tool with operational definitions, were shuffled and then numbered consecutively
Allocation concealment (selection bias)	Unclear risk	No description of allocation concealment
Blinding (performance bias and detection bias) Pain	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. Operators assessed the outcome themselves
Blinding (performance bias and detection bias) Procedure time for overall cannulation	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. Operators assessed the outcome themselves
Blinding (performance bias and detection bias) Number of attempts	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. Operators assessed the outcome themselves
Incomplete outcome data (attrition bias) Pain	High risk	22 participants were initially randomised, but two participants were excluded due to broken randomisation, and another two participants were excluded from analysis due to unsuccessful cannulation
Incomplete outcome data (attrition bias) Procedure time for overall cannulation	High risk	22 participants were initially randomised, but two participants were excluded due to broken randomisation, and another two participants were excluded from analysis due to unsuccessful cannulation
Incomplete outcome data (attrition bias) Number of attempts	High risk	22 participants were initially randomised, but two participants were excluded due to broken randomisation, and another two participants were excluded from analysis due to unsuccessful cannulation
Selective reporting (reporting bias)	Unclear risk	No study register or protocol was available
Other bias	Low risk	No concerns about other sources of bias

Pappas 2006 *(Continued)*

Overall risk Pain	High risk	At least one domain was at high risk
Overall risk Procedure time for overall cannulation	High risk	At least one domain was at high risk
Overall risk Number of attempts	High risk	At least one domain was at high risk

River 2009

Study characteristics	
Methods	Randomised, open-label trial
Participants	Setting: ED Number of participants: 47 (USG 26, LM 21) Age, mean (SD) years: not specified Difficulty: difficult (2 prior unsuccessful attempts with LM) Sites of peripheral veins: not specified
Interventions	**Technique** LM vs USG: Machine: not specified Axis: not specified Guidance: not specified **Operator** Profession: nurse Number of operators: not specified Experience of USG before the study: yes Length of experience with USG before the study: several months A training programme of USG for the study: yes Number of clinical cases with USG required or experienced before the study intervention started: not specified **Needle** Length: not specified Gauge: not specified
Outcomes	Overall success of cannulation, procedure time for overall cannulation, number of attempts, patient satisfaction **Definition of successful cannulation:** not specified **Definition of start and end of time measurement:** not specified
Funding	Not specified
Declarations of interest	Not specified
Notes	We attempted to contact the authors to obtain additional information but were unable to reach them.
Risk of bias	

River 2009 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of randomisation process
Allocation concealment (selection bias)	Unclear risk	No description of randomisation process
Blinding (performance bias and detection bias) Overall-success of cannulation	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. Who assessed the outcome was not specified
Blinding (performance bias and detection bias) Procedure time for overall cannulation	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. Who assessed the outcome was not specified
Blinding (performance bias and detection bias) Number of attempts	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. Who assessed the outcome was not specified
Blinding (performance bias and detection bias) Patient satisfaction	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. Who assessed the outcome was not specified
Incomplete outcome data (attrition bias) Overall success of cannulation	Low risk	The outcome was available for all participants
Incomplete outcome data (attrition bias) Procedure time for overall cannulation	Unclear risk	No mention of which participants were assessed
Incomplete outcome data (attrition bias) Number of attempts	Low risk	The outcome was available for all participants
Incomplete outcome data (attrition bias) Patient satisfaction	Low risk	The outcome was available for all participants
Selective reporting (reporting bias)	Unclear risk	No study register or protocol was available
Other bias	Low risk	No concerns about other sources of bias
Overall risk Overall success of cannulation	High risk	At least one domain was at high risk
Overall risk Procedure time for overall cannulation	High risk	At least one domain was at high risk
Overall risk	High risk	At least one domain was at high risk

River 2009 *(Continued)*

Number of attempts		
Overall risk	High risk	At least one domain was at high risk
Patient satisfaction		

Skulec 2019

Study characteristics	
Methods	Randomised, open-label trial
Participants	Setting: prehospital Number of participants: 300 (dynamic USG 100, static USG 100, LM 100) Age, mean (SD) years: dynamic USG 66.6 (17.4), static USG 65.3 (21.2), LM 64.5 (18.8) Difficulty: not restricted (all participants irrespective of difficulty) Sites of peripheral veins: upper extremity
Interventions	**Technique** LM vs Dynamic USG vs Static USG Machine: Vscan dual probe (General Electric) Axis: short **Operator** Profession: paramedic, emergency physician Number of operators: 7 (5 paramedics, 2 emergency physicians) Experience of USG before the study: paramedics no; emergency physicians yes Length of experience with USG before the study: paramedics none, emergency physicians not specified A training programme of USG for the study: paramedics yes; emergency physicians no Number of clinical cases with USG required or experienced before the study intervention started: • paramedics: static 5, dynamic 5 • emergency physicians: static > 200, dynamic > 200 **Needle** Length: 32 or 45 mm Gauge: 20 or more
Outcomes	First-pass success of cannulation, overall success of cannulation, procedure time for first-pass cannulation, procedure time for overall cannulation, number of attempts, complications **Definition of successful cannulation:** blood return from a catheter, smooth normal saline flush, and no signs of extravasation **Definition of start and end of time measurement** • Start: all equipment was prepared, including the ultrasound device being turned on • End: successful cannulation or termination of the cannulation attempts
Funding	None
Declarations of interest	The author received a temporary loan of ultrasound machines from GE Medical Systems Ceska republika for study purposes, but no financial support
Notes	
Risk of bias	

Skulec 2019 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The randomisation scheme was created by computer (this was not stated in the article, but obtained through communication with an author (RS))
Allocation concealment (selection bias)	Low risk	Each random allocation was conducted by a person independent of the study, and used opaque, sealed envelopes (this was not stated in the article, but obtained through communication with an author (RS))
Blinding (performance bias and detection bias) First-pass success of cannulation	Low risk	Although blinding of participants and operators is impossible due to the nature of the intervention, a third-person assessed the outcome (this was not stated in the article, but obtained through communication with an author (RS))
Blinding (performance bias and detection bias) Overall-success of cannulation	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. Operators assessed the outcome themselves (this was not stated in the article, but obtained through communication with an author (RS))
Blinding (performance bias and detection bias) Procedure time for first-pass cannulation	Low risk	Although blinding of participants and operators is impossible due to the nature of the intervention, a third-person assessed the outcome (this was not stated in the article, but obtained through communication with an author (RS))
Blinding (performance bias and detection bias) Procedure time for overall cannulation	Low risk	Although blinding of participants and operators is impossible due to the nature of the intervention, a third-person assessed the outcome (this was not stated in the article, but obtained through communication with an author (RS))
Blinding (performance bias and detection bias) Number of attempts	Low risk	Although blinding of participants and operators is impossible due to the nature of the intervention, a third-person assessed the outcome (this was not stated in the article, but obtained through communication with an author (RS))
Blinding (performance bias and detection bias) Overall complications	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. Operators assessed the outcome themselves (this was not stated in the article, but obtained through the communication with an author (RS))
Incomplete outcome data (attrition bias) First-pass success of cannulation	Low risk	The outcome was available for all participants
Incomplete outcome data (attrition bias) Overall success of cannulation	Low risk	The outcome was available for all participants
Incomplete outcome data (attrition bias) Procedure time for first-pass cannulation	High risk	The outcome was evaluated only for participants with successful cannulation
Incomplete outcome data (attrition bias) Procedure time for overall cannulation	Low risk	The outcome was available for all participants

Skulec 2019 *(Continued)*

Incomplete outcome data (attrition bias) Number of attempts	Low risk	The outcome was available for all participants
Incomplete outcome data (attrition bias) Overall complications	Low risk	The outcome was available for all participants
Selective reporting (reporting bias)	Low risk	The outcomes reported in the article were consistent with the trial registry (NCT03709394)
Other bias	Low risk	No concerns about other sources of bias
Overall risk First-pass success of cannulation	Low risk	All domains were at low risk
Overall risk Overall success of cannulation	High risk	At least one domain was at high risk
Overall risk Procedure time for first-pass cannulation	High risk	At least one domain was at high risk
Overall risk Procedure time for overall cannulation	Low risk	All domains were at low risk
Overall risk Number of attempts	Low risk	All domains were at low risk
Overall risk Overall complications	High risk	At least one domain was at high risk

Stein 2009

Study characteristics	
Methods	Randomised, open-label trial
Participants	Setting: ED Number of participants: 59 (USG 28, LM 31) Age, mean (SD) years: USG 58.1 (15.6), LM 54.8 (17.8) Difficulty: difficult (at least 2 failed attempts with LM) Sites of peripheral veins: upper extremity and jugular vein
Interventions	**Technique** LM vs USG: Machine: Sonosite Titan (Sonosite) with a 10 MHz probe Axis: not specified Guidance: dynamic **Operator** Profession: emergency physician (attending: USG and LM, resident: LM) Number of operators: 20

Stein 2009 *(Continued)*

	Experience of USG before the study: yes Length of experience with USG before the study: more than 6 months A training programme of USG for the study: yes Number of clinical cases with USG required or experienced before the study intervention started: not specified **Needle** Length: not specified Gauge: not specified
Outcomes	First-pass success of cannulation, overall success of cannulation, procedure time for overall cannulation, number of attempts, patient satisfaction, complications **Definition of successful cannulation:** blood return from a catheter, smooth normal saline flush, and no signs of extravasation **Definition of start and end of time measurement:** • Start: participant enrollment • End: successful cannulation
Funding	None
Declarations of interest	None declared
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomised by a research computer
Allocation concealment (selection bias)	Low risk	Research staff randomised participants with a research computer
Blinding (performance bias and detection bias) First-pass success of cannulation	Low risk	Although blinding of participants and operators is impossible due to the nature of the intervention, a third-person assessed the outcome
Blinding (performance bias and detection bias) Overall-success of cannulation	Low risk	Although blinding of participants and operators is impossible due to the nature of the intervention, a third-person assessed the outcome
Blinding (performance bias and detection bias) Procedure time for overall cannulation	Low risk	Although blinding of participants and operators is impossible due to the nature of the intervention, a third-person assessed the outcome
Blinding (performance bias and detection bias) Number of attempts	Low risk	Although blinding of participants and operators is impossible due to the nature of the intervention, a third-person assessed the outcome
Blinding (performance bias and detection bias) Patient satisfaction	High risk	Blinding of participants and operators is impossible due to the nature of the intervention

Stein 2009 *(Continued)*

Blinding (performance bias and detection bias) Overall complications	Low risk	Although blinding of participants and operators is impossible due to the nature of the intervention, a third-person assessed the outcome
Incomplete outcome data (attrition bias) First-pass success of cannulation	Low risk	The outcome was available for all participants
Incomplete outcome data (attrition bias) Overall success of cannulation	Low risk	There were only 2 dropouts (USG 1, LM 1), and the reasons were detailed
Incomplete outcome data (attrition bias) Procedure time for overall cannulation	High risk	It seems likely that only participants with successful cannulation were analysed
Incomplete outcome data (attrition bias) Number of attempts	Low risk	There were only 2 dropouts (USG 1, LM 1), and the reasons were detailed
Incomplete outcome data (attrition bias) Patient satisfaction	High risk	There were 7 dropouts (USG 4, LM 3), and the reasons were not specified
Incomplete outcome data (attrition bias) Overall complications	Low risk	There were only 2 dropouts (USG 1, LM 1), and the reasons were detailed
Selective reporting (reporting bias)	Low risk	The outcomes reported in the article were consistent with the trial registry (NCT00692549)
Other bias	Low risk	No concerns about other sources of bias
Overall risk First-pass success of cannulation	Low risk	All domains were at low risk
Overall risk Overall success of cannulation	Low risk	All domains were at low risk
Overall risk Procedure time for overall cannulation	High risk	At least one domain was at high risk
Overall risk Number of attempts	Low risk	All domains were at low risk
Overall risk Patient satisfaction	High risk	At least one domain was at high risk
Overall risk Overall complications	Low risk	All domains were at low risk

Weiner 2013

Study characteristics	
Methods	Randomised, open-label trial
Participants	Setting: ED Number of participants: 53 (USG 30, LM 23) Age, mean (SD) years: USG 46.2 (14.6), LM 53 (14.2) Difficulty: difficult (had a history of difficult IV cannulation, or at least 2 failed attempts with LM) Sites of peripheral veins: upper extremity
Interventions	**Technique** LM vs USG: Machine: Zonare z.one ultra Convertible Ultrasound System (Zonare) with a 8-3 MHz probe, or Sonosite M-turbo (Sonosite) with a 13-6 MHz probe Axis: short Guidance: dynamic **Operator** Profession: nurse Number of operators: not specified Experience of USG before the study: no Length of experience with USG before the study: not specified A training programme of USG for the study: yes Number of clinical cases with USG required or experienced before the study intervention started: not specified **Needle** Length: up to operators' discretion Gauge: 18 - 20
Outcomes	First-pass success of cannulation, overall success of cannulation, procedure time for overall cannulation, number of attempts, pain, patient satisfaction **Definition of successful cannulation:** blood return from a catheter, and no signs of extravasation **Definition of start and end of time measurement:** • Start: a nurse was informed of the result of randomisation • End: intravenous access was achieved
Funding	Not specified
Declarations of interest	Not specified
Notes	Data for first-pass success of cannulation and patient satisfaction were unpublished and obtained through communication with an author (SW)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Initially a computerised coin-toss, later randomised by shuffling sealed envelopes
Allocation concealment (selection bias)	Low risk	Initially a computerised coin-toss, later randomised by shuffling sealed envelopes

Weiner 2013 *(Continued)*

Blinding (performance bias and detection bias) First-pass success of cannulation	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. One of the co-authors assessed the outcome
Blinding (performance bias and detection bias) Overall-success of cannulation	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. One of the co-authors assessed the outcome
Blinding (performance bias and detection bias) Pain	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. One of the co-authors assessed the outcome
Blinding (performance bias and detection bias) Procedure time for overall cannulation	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. One of the co-authors assessed the outcome
Blinding (performance bias and detection bias) Number of attempts	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. One of the co-authors assessed the outcome
Blinding (performance bias and detection bias) Patient satisfaction	High risk	Blinding of participants and operators is impossible due to the nature of the intervention. One of the co-authors assessed the outcome
Incomplete outcome data (attrition bias) First-pass success of cannulation	Low risk	There were only 3 dropouts (USG 1, LM 2)
Incomplete outcome data (attrition bias) Overall success of cannulation	Low risk	There were only 3 dropouts (USG 1, LM 2)
Incomplete outcome data (attrition bias) Pain	Low risk	There were only 3 dropouts (USG 1, LM 2)
Incomplete outcome data (attrition bias) Procedure time for overall cannulation	Low risk	There were only 3 dropouts (USG 1, LM 2)
Incomplete outcome data (attrition bias) Number of attempts	Low risk	There were only 3 dropouts (USG 1, LM 2)
Incomplete outcome data (attrition bias) Patient satisfaction	Low risk	There were only 3 dropouts (USG 1, LM 2)
Selective reporting (reporting bias)	Low risk	The outcomes reported in the article were consistent with the trial registry (NCT01439113)
Other bias	Low risk	No concerns about other sources of bias

Weiner 2013 *(Continued)*

Overall risk First-pass success of cannulation	High risk	At least one domain was at high risk
Overall risk Overall success of cannulation	High risk	At least one domain was at high risk
Overall risk Pain	High risk	At least one domain was at high risk
Overall risk Procedure time for overall cannulation	High risk	At least one domain was at high risk
Overall risk Number of attempts	High risk	At least one domain was at high risk
Overall risk Patient satisfaction	High risk	At least one domain was at high risk

BMI: body mass index
ED: emergency department
ICU: intensive care unit
IV: intravenous
LM: landmark method
SD: standard deviation
USG: ultrasound guidance

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Bauman 2009	Not a randomised controlled trial
Costantino 2010	This trial compared ultrasound guidance and external jugular vein
Curtis 2015	The participants in this study were children
DRKS00013797	Not a randomised controlled trial
Evans 2013	Not a randomised controlled trial
Galen 2018	Not a randomised controlled trial
Hill 2017	Not a comparison of USG peripheral intravenous cannulation and landmark method (long-axis vs short-axis USG)
NCT01602133	Not a randomised controlled trial
NCT02360163	This study was withdrawn (no enrolment was achieved)
NCT03440944	Not a comparison of ultrasound-guided peripheral intravenous cannulation and landmark method (midline vs USG)

Study	Reason for exclusion
NCT03457259	Not a comparison of ultrasound-guided peripheral intravenous cannulation and landmark method (midline vs peripheral, central, or peripherally inserted central lines)
NCT04234347	Not a comparison of ultrasound-guided peripheral intravenous cannulation and landmark method
Raio 2018	Not a randomised controlled trial
Troisi 2013	We contacted the author for further information but received no response

USG: ultrasound guidance

Characteristics of studies awaiting classification *[ordered by study ID]*

IRCT201408097751N4

Methods	Randomised, controlled, multicentre trial
Participants	ED patients with difficult intravenous cannulation
Interventions	USG vs LM
Outcomes	Duration of USG and LM procedures Reason for using USG
Notes	This trial was registered in 2015, but the results have not been published and its status is unknown.

ED: emergency department
LM: landmark method
USG: ultrasound guidance

Characteristics of ongoing studies *[ordered by study ID]*

NCT03745209

Study name	Ultrasound-guided peripheral IV vs standard technique in difficult vascular access patients by ICU nurses
Methods	Randomised, controlled, single-center trial
Participants	ICU patients with difficult cannulation
Interventions	USG vs LM
Outcomes	Overall success rate of IV cannulation Number of attempts 24 hours catheter survival Complications Subsequent need for PICC or central line
Starting date	21 January 2019

NCT03745209 *(Continued)*

Contact information	Kingston General Hospital, Kingston, Ontario, Canada, K7L 2V7 Contact: Mohammed R Alshamsi, MD, 17mras@queensu.ca Contact: Gordon Boyd, MD, boydj@kgh.kari.net
Notes	We asked about the status of this trial but received no response.

NCT03841864

Study name	Ultrasound guided peripheral IV insertion (USGPIV)
Methods	Randomised, controlled, single-center trial
Participants	Adult elective pre-operative patients Grade 1: visual vein classification grade described as excellent visualisation Grade 2a: veins that don't fit grade 1 or 2b classification Grade 2b: only faint vein shadow appearance described as poor visualisation Grade 3: no vein visualisation
Interventions	USG vs LM
Outcomes	IV insertion success rate
Starting date	21 January 2019
Contact information	Roya Yumul, MD, PhD, Roya.Yumul@cshs.org Ofelia Loani Elvir Lazo, MD, loanidoc@yahoo.com
Notes	We asked about the status of this trial but received no response.

NCT04218643

Study name	Ultrasound-guided peripheral intravenous catheter insertion technique (PIVC)
Methods	Randomised, controlled trial
Participants	Adult patients requiring a peripheral intravenous catheter
Interventions	USG vs LM
Outcomes	Post insertion failure rates Overall dwell time of the catheter Post removal complication rates Catheter to vein ratio
Starting date	11 February 2020

NCT04218643 *(Continued)*

Contact information	Principal Investigator: Scott Leroux, BS NRP Reading Hospital
Notes	

NCT04853290

Study name	Patient experience in peripheral venipuncture with and without ultrasound (PERCEPT)
Methods	Randomised, controlled trial
Participants	Patients admitted to clinical inpatient units
Interventions	USG vs LM
Outcomes	Pain Patient satisfaction Overall success rate of IV cannulation Sleep quality Functional life of the catheter Complications
Starting date	23 June 2021
Contact information	Universidade Federal do Rio Grande do Sul - Post Graduated Program Porto Alegre, Rio Grande Do Sul, Brazil Principal Investigator: Eneida R Rabelo da Silva, RN, ScD, eneidarabelo@gmail.com
Notes	

NCT04856826

Study name	Placement of peripheral venous catheters under echo guidance in a post-emergency medical service (KatECHO)
Methods	Randomised, controlled trial
Participants	Patients hospitalised in a post-emergency unit
Interventions	USG vs LM
Outcomes	First-pass success rate of IV placement Pain Patients satisfaction Number of attempts Overall success of cannulation Location of the final placement site

NCT04856826 *(Continued)*

	Calibre of the catheter placed Infectious or thromboembolic events Duration of catheter placement Functional life of the catheter Satisfaction of nursing staff
Starting date	5 March 2021
Contact information	CHU Grenoble Alpes La Tronche, France, 38700 Contact: Julie Duhoo, jduhoo@chu-grenoble.fr
Notes	

NCT05119985

Study name	Ultrasound guided peripheral venous cannulation in patient undergoing elective surgery under general anesthesia
Methods	Randomised, controlled trial
Participants	Patients undergoing elective surgery under general anesthesia
Interventions	USG vs LM
Outcomes	First-pass success of cannulation Number of attempts Complications Procedure time
Starting date	1 October 2021
Contact information	Masarykova Nemocnice v Ústí nad Labem, Krajská Zdravotní a.s. Ústí Nad Labem, Ústí Nad Labem Region, Czechia, 40001 Contact: Michal Kalina, michal.kalina@kzcr.eu
Notes	

ICU: intensive care unit
IV: intravenous
LM: landmark method
PICC: peripheral intravenous central catheter
USG: ultrasound guidance
vs: versus

DATA AND ANALYSES

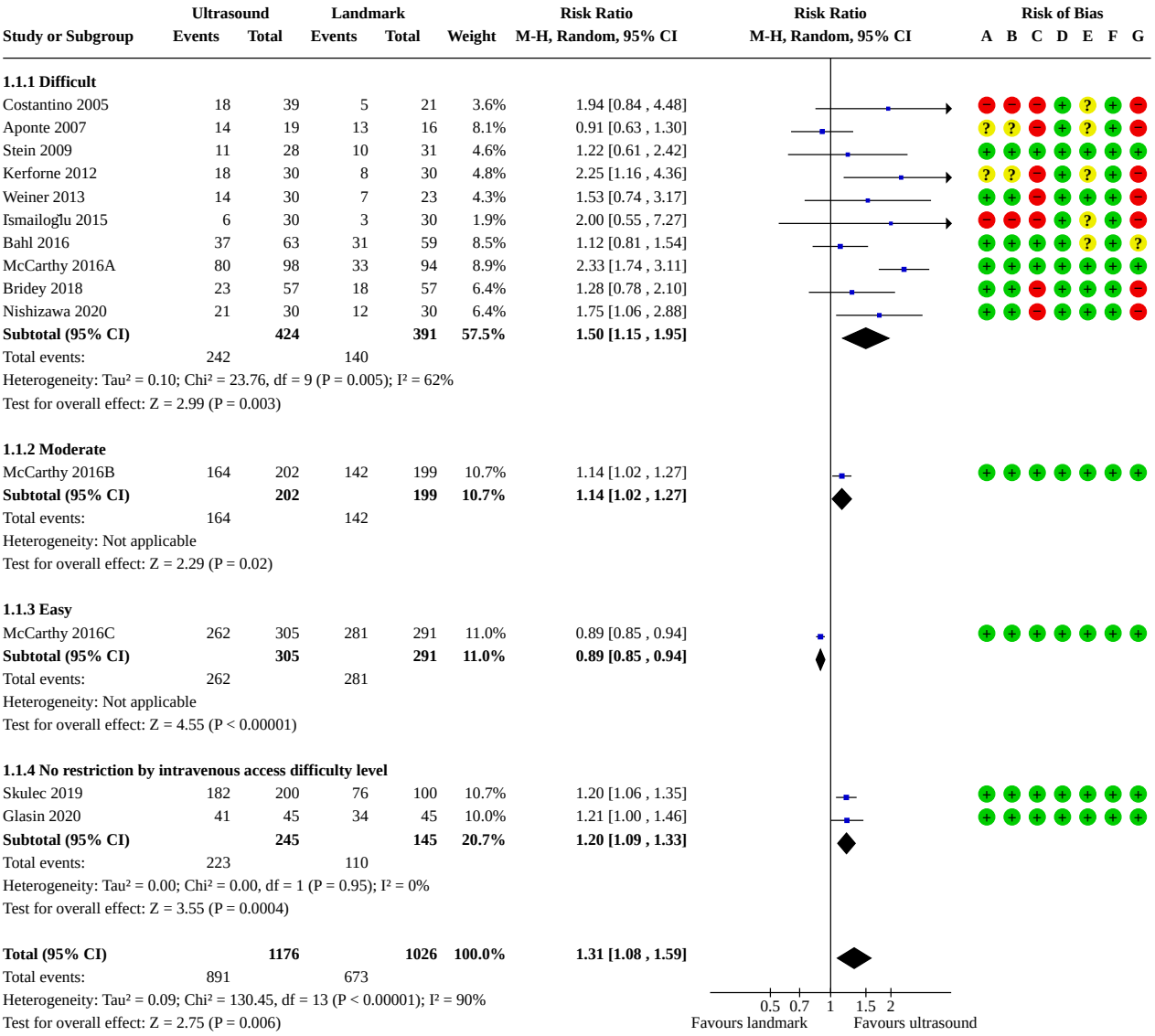
Comparison 1. First-pass success of cannulation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Difficulty levels defined by original studies	14	2202	Risk Ratio (M-H, Random, 95% CI)	1.31 [1.08, 1.59]
1.1.1 Difficult	10	815	Risk Ratio (M-H, Random, 95% CI)	1.50 [1.15, 1.95]
1.1.2 Moderate	1	401	Risk Ratio (M-H, Random, 95% CI)	1.14 [1.02, 1.27]
1.1.3 Easy	1	596	Risk Ratio (M-H, Random, 95% CI)	0.89 [0.85, 0.94]
1.1.4 No restriction by intravenous access difficulty level	2	390	Risk Ratio (M-H, Random, 95% CI)	1.20 [1.09, 1.33]
1.2 Difficulty levels defined by the success rate with landmark method	14	2202	Risk Ratio (M-H, Random, 95% CI)	1.31 [1.08, 1.59]
1.2.1 Difficult	9	780	Risk Ratio (M-H, Random, 95% CI)	1.62 [1.28, 2.06]
1.2.2 Moderate	3	791	Risk Ratio (M-H, Random, 95% CI)	1.17 [1.09, 1.26]
1.2.3 Easy	2	631	Risk Ratio (M-H, Random, 95% CI)	0.89 [0.85, 0.94]
1.3 Operators could not see and palpate a target vein	5	486	Risk Ratio (M-H, Random, 95% CI)	1.94 [1.53, 2.45]
1.4 Participants had a history of difficult intravenous access	6	390	Risk Ratio (M-H, Random, 95% CI)	1.28 [0.97, 1.70]
1.5 Participants had multiple failed attempts	4	232	Risk Ratio (M-H, Random, 95% CI)	1.60 [1.15, 2.21]
1.6 Operators finished any training program for ultrasound-guided peripheral venous cannulation	10	815	Risk Ratio (M-H, Random, 95% CI)	1.50 [1.15, 1.95]
1.6.1 Finished	9	755	Risk Ratio (M-H, Random, 95% CI)	1.44 [1.09, 1.91]
1.6.2 Not specified	1	60	Risk Ratio (M-H, Random, 95% CI)	2.25 [1.16, 4.36]
1.7 Operators had any clinical experience with ultrasound-guided peripheral intravenous cannulation	10	815	Risk Ratio (M-H, Random, 95% CI)	1.50 [1.15, 1.95]
1.7.1 Had any clinical experience	5	460	Risk Ratio (M-H, Random, 95% CI)	1.44 [0.91, 2.27]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.7.2 Did not have any clinical experience	3	235	Risk Ratio (M-H, Random, 95% CI)	1.33 [0.99, 1.79]
1.7.3 Not specified	2	120	Risk Ratio (M-H, Random, 95% CI)	2.20 [1.22, 3.96]
1.8 Operators finished any training program for ultrasound-guided peripheral venous cannulation plus any clinical experience	10	815	Risk Ratio (M-H, Random, 95% CI)	1.50 [1.15, 1.95]
1.8.1 Finished any training program for ultrasound-guided peripheral venous cannulation plus any clinical experience	5	460	Risk Ratio (M-H, Random, 95% CI)	1.44 [0.91, 2.27]
1.8.2 Not finished any training program for ultrasound-guided peripheral venous cannulation or no clinical experience	3	235	Risk Ratio (M-H, Random, 95% CI)	1.33 [0.99, 1.79]
1.8.3 Not specified	2	120	Risk Ratio (M-H, Random, 95% CI)	2.20 [1.22, 3.96]
1.9 Types of operators	10	815	Risk Ratio (M-H, Random, 95% CI)	1.50 [1.15, 1.95]
1.9.1 Nurses	7	504	Risk Ratio (M-H, Random, 95% CI)	1.32 [1.03, 1.71]
1.9.2 Physicians	2	119	Risk Ratio (M-H, Random, 95% CI)	1.47 [0.86, 2.50]
1.9.3 Technicians	1	192	Risk Ratio (M-H, Random, 95% CI)	2.33 [1.74, 3.11]
1.10 Setting	10	815	Risk Ratio (M-H, Random, 95% CI)	1.50 [1.15, 1.95]
1.10.1 Emergency department	6	546	Risk Ratio (M-H, Random, 95% CI)	1.60 [1.12, 2.28]
1.10.2 ICU	3	234	Risk Ratio (M-H, Random, 95% CI)	1.64 [1.20, 2.23]
1.10.3 Operating room	1	35	Risk Ratio (M-H, Random, 95% CI)	0.91 [0.63, 1.30]
1.11 Year of publication	10	815	Risk Ratio (M-H, Random, 95% CI)	1.50 [1.15, 1.95]
1.11.1 Publication year: 1999 ~ 2008	2	95	Risk Ratio (M-H, Random, 95% CI)	1.24 [0.51, 3.02]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.11.2 Publication year: 2009 ~	8	720	Risk Ratio (M-H, Random, 95% CI)	1.60 [1.24, 2.07]
1.12 Dynamic guidance or static guidance	1	300	Risk Ratio (M-H, Random, 95% CI)	1.20 [1.06, 1.35]
1.12.1 Dynamic	1	150	Risk Ratio (M-H, Random, 95% CI)	1.16 [0.98, 1.37]
1.12.2 Static	1	150	Risk Ratio (M-H, Random, 95% CI)	1.24 [1.05, 1.46]

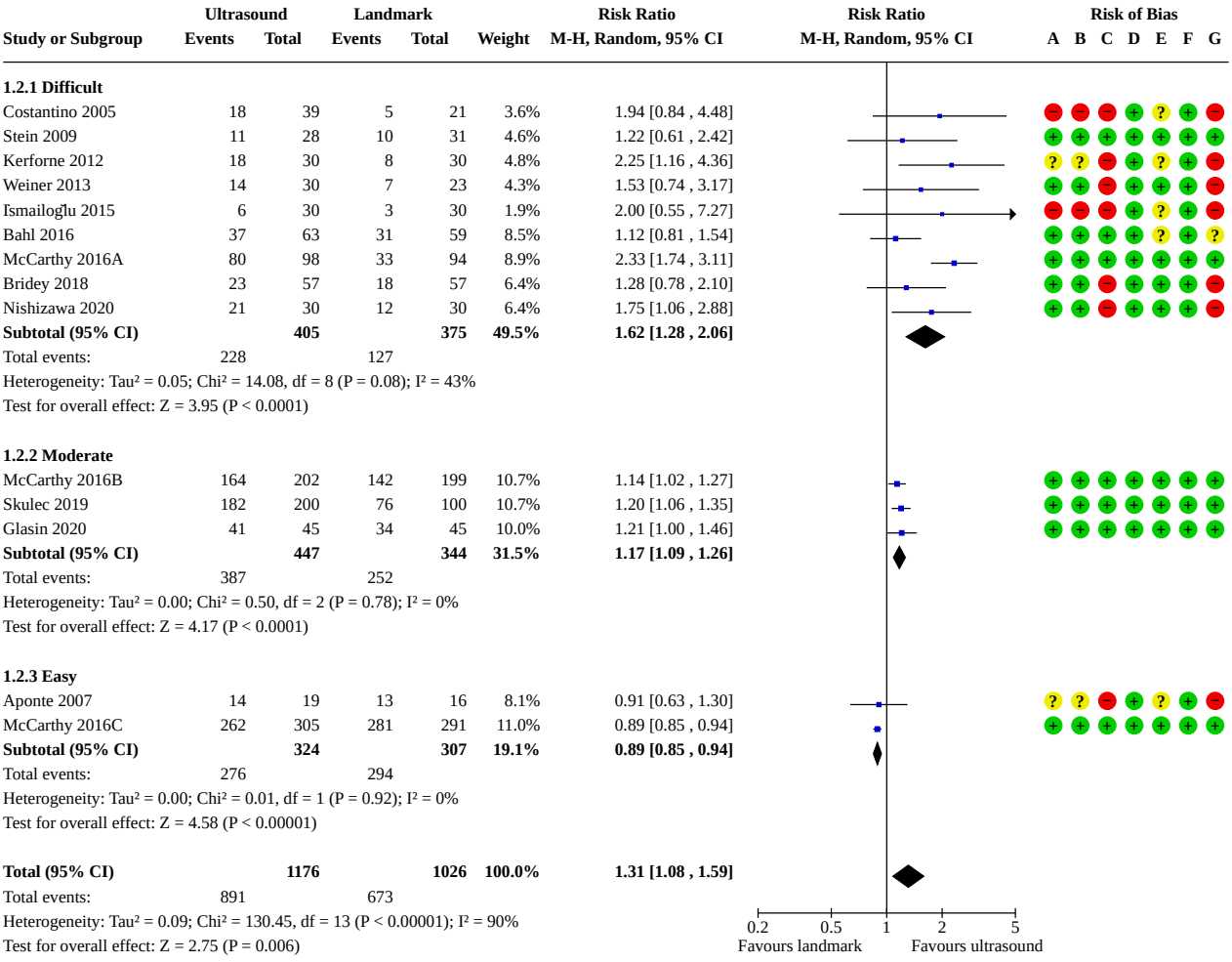
Analysis 1.1. Comparison 1: First-pass success of cannulation, Outcome 1: Difficulty levels defined by original studies



Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): First-pass success of cannulation
(D) Incomplete outcome data (attrition bias): First-pass success of cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: First-pass success of cannulation

Analysis 1.2. Comparison 1: First-pass success of cannulation, Outcome 2: Difficulty levels defined by the success rate with landmark method



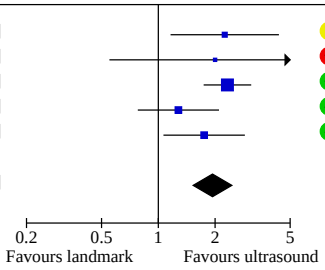
Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): First-pass success of cannulation
(D) Incomplete outcome data (attrition bias): First-pass success of cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: First-pass success of cannulation

Analysis 1.3. Comparison 1: First-pass success of cannulation, Outcome 3: Operators could not see and palpate a target vein

Study or Subgroup	Ultrasound Events	Ultrasound Total	Landmark Events	Landmark Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk of Bias A	B	C	D	E	F	G
Kerforne 2012	18	30	8	30	11.7%	2.25 [1.16 , 4.36]	?	?	−	+	?	+	−
Ismailoglu 2015	6	30	3	30	3.3%	2.00 [0.55 , 7.27]	−	−	−	+	?	+	−
McCarthy 2016A	80	98	33	94	45.8%	2.33 [1.74 , 3.11]	+	+	+	+	+	+	+
Bridey 2018	23	57	18	57	19.7%	1.28 [0.78 , 2.10]	+	+	−	+	+	+	−
Nishizawa 2020	21	30	12	30	19.6%	1.75 [1.06 , 2.88]	+	+	−	+	+	+	−
Total (95% CI)		**245**		**241**	**100.0%**	**1.94 [1.53 , 2.45]**							
Total events:	148		74										

Heterogeneity: Tau² = 0.01; Chi² = 4.56, df = 4 (P = 0.34); I² = 12%
Test for overall effect: Z = 5.50 (P < 0.00001)
Test for subgroup differences: Not applicable

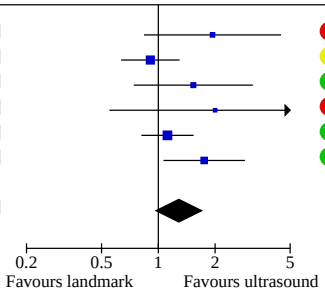


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): First-pass success of cannulation
(D) Incomplete outcome data (attrition bias): First-pass success of cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: First-pass success of cannulation

Analysis 1.4. Comparison 1: First-pass success of cannulation, Outcome 4: Participants had a history of difficult intravenous access

Study or Subgroup	Ultrasound Events	Ultrasound Total	Landmark Events	Landmark Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk of Bias A	B	C	D	E	F	G
Costantino 2005	18	39	5	21	9.0%	1.94 [0.84 , 4.48]	−	−	−	+	?	+	−
Aponte 2007	14	19	13	16	26.9%	0.91 [0.63 , 1.30]	?	?	−	+	?	+	−
Weiner 2013	14	30	7	23	11.3%	1.53 [0.74 , 3.17]	+	+	−	+	+	+	−
Ismailoglu 2015	6	30	3	30	4.3%	2.00 [0.55 , 7.27]	−	−	−	+	?	+	−
Bahl 2016	37	63	31	59	29.5%	1.12 [0.81 , 1.54]	+	+	+	+	?	+	?
Nishizawa 2020	21	30	12	30	19.0%	1.75 [1.06 , 2.88]	+	+	−	+	+	+	−
Total (95% CI)		**211**		**179**	**100.0%**	**1.28 [0.97 , 1.70]**							
Total events:	110		71										

Heterogeneity: Tau² = 0.04; Chi² = 8.01, df = 5 (P = 0.16); I² = 38%
Test for overall effect: Z = 1.76 (P = 0.08)
Test for subgroup differences: Not applicable

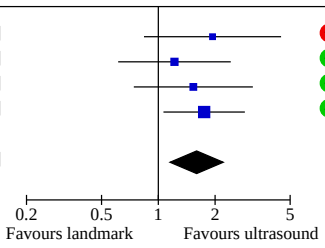


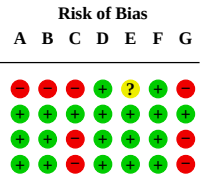
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): First-pass success of cannulation
(D) Incomplete outcome data (attrition bias): First-pass success of cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: First-pass success of cannulation

Analysis 1.5. Comparison 1: First-pass success of cannulation, Outcome 5: Participants had multiple failed attempts

Study or Subgroup	Ultrasound Events	Ultrasound Total	Landmark Events	Landmark Total	Weight	Risk Ratio M-H, Random, 95% CI
Costantino 2005	18	39	5	21	15.0%	1.94 [0.84 , 4.48]
Stein 2009	11	28	10	31	22.3%	1.22 [0.61 , 2.42]
Weiner 2013	14	30	7	23	20.0%	1.53 [0.74 , 3.17]
Nishizawa 2020	21	30	12	30	42.7%	1.75 [1.06 , 2.88]
Total (95% CI)		**127**		**105**	**100.0%**	**1.60 [1.15 , 2.21]**
Total events:	64		34			

Heterogeneity: Tau² = 0.00; Chi² = 0.95, df = 3 (P = 0.81); I² = 0%
Test for overall effect: Z = 2.82 (P = 0.005)
Test for subgroup differences: Not applicable





Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): First-pass success of cannulation
(D) Incomplete outcome data (attrition bias): First-pass success of cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: First-pass success of cannulation

Analysis 1.6. Comparison 1: First-pass success of cannulation, Outcome 6: Operators finished any training program for ultrasound-guided peripheral venous cannulation

Study or Subgroup	Ultrasound Events	Ultrasound Total	Landmark Events	Landmark Total	Weight	Risk Ratio M-H, Random, 95% CI
1.6.1 Finished						
Costantino 2005	18	39	5	21	6.5%	1.94 [0.84 , 4.48]
Aponte 2007	14	19	13	16	13.8%	0.91 [0.63 , 1.30]
Stein 2009	11	28	10	31	8.2%	1.22 [0.61 , 2.42]
Weiner 2013	14	30	7	23	7.7%	1.53 [0.74 , 3.17]
Ismailoglu 2015	6	30	3	30	3.4%	2.00 [0.55 , 7.27]
Bahl 2016	37	63	31	59	14.5%	1.12 [0.81 , 1.54]
McCarthy 2016A	80	98	33	94	15.0%	2.33 [1.74 , 3.11]
Bridey 2018	23	57	18	57	11.2%	1.28 [0.78 , 2.10]
Nishizawa 2020	21	30	12	30	11.2%	1.75 [1.06 , 2.88]
Subtotal (95% CI)		**394**		**361**	**91.4%**	**1.44 [1.09 , 1.91]**
Total events:	224		132			

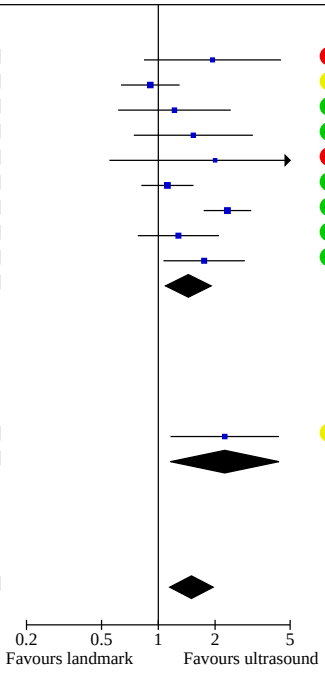
Heterogeneity: Tau² = 0.10; Chi² = 22.03, df = 8 (P = 0.005); I² = 64%
Test for overall effect: Z = 2.58 (P = 0.01)

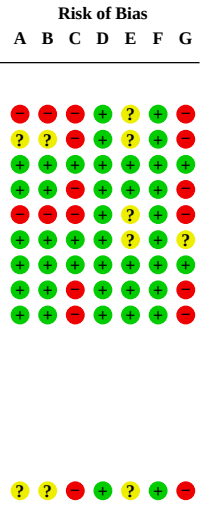
1.6.2 Not specified						
Kerforne 2012	18	30	8	30	8.6%	2.25 [1.16 , 4.36]
Subtotal (95% CI)		**30**		**30**	**8.6%**	**2.25 [1.16 , 4.36]**
Total events:	18		8			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.40 (P = 0.02)

Total (95% CI)		**424**		**391**	**100.0%**	**1.50 [1.15 , 1.95]**
Total events:	242		140			

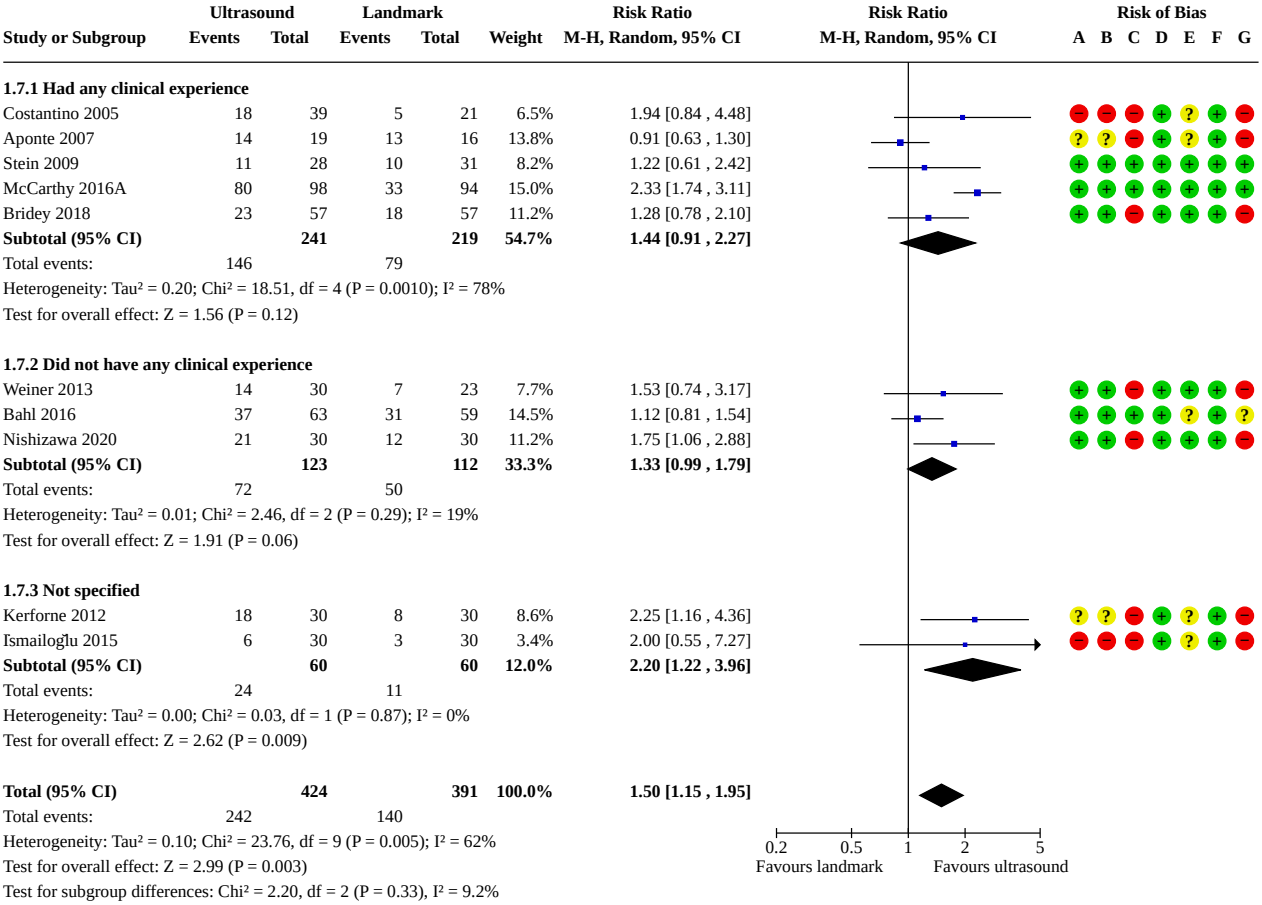
Heterogeneity: Tau² = 0.10; Chi² = 23.76, df = 9 (P = 0.005); I² = 62%
Test for overall effect: Z = 2.99 (P = 0.003)
Test for subgroup differences: Chi² = 1.47, df = 1 (P = 0.23), I² = 32.0%





Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): First-pass success of cannulation
(D) Incomplete outcome data (attrition bias): First-pass success of cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: First-pass success of cannulation

Analysis 1.7. Comparison 1: First-pass success of cannulation, Outcome 7: Operators had any clinical experience with ultrasound-guided peripheral intravenous cannulation

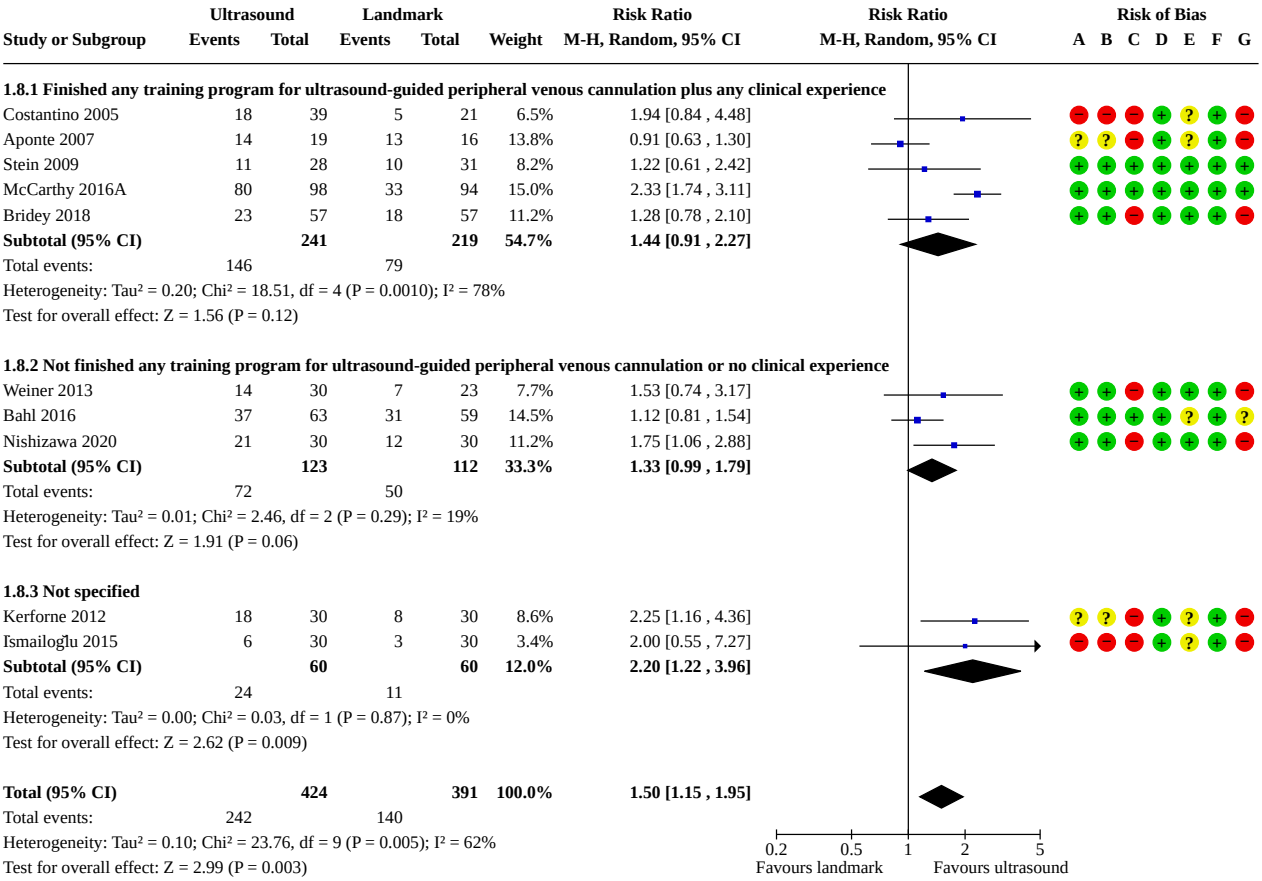


Study or Subgroup	Ultrasound Events	Ultrasound Total	Landmark Events	Landmark Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk of Bias A B C D E F G
1.7.1 Had any clinical experience							
Costantino 2005	18	39	5	21	6.5%	1.94 [0.84 , 4.48]	
Aponte 2007	14	19	13	16	13.8%	0.91 [0.63 , 1.30]	
Stein 2009	11	28	10	31	8.2%	1.22 [0.61 , 2.42]	
McCarthy 2016A	80	98	33	94	15.0%	2.33 [1.74 , 3.11]	
Bridey 2018	23	57	18	57	11.2%	1.28 [0.78 , 2.10]	
Subtotal (95% CI)		**241**		**219**	**54.7%**	**1.44 [0.91 , 2.27]**	
Total events:	146		79				
Heterogeneity: Tau² = 0.20; Chi² = 18.51, df = 4 (P = 0.0010); I² = 78%							
Test for overall effect: Z = 1.56 (P = 0.12)							
1.7.2 Did not have any clinical experience							
Weiner 2013	14	30	7	23	7.7%	1.53 [0.74 , 3.17]	
Bahl 2016	37	63	31	59	14.5%	1.12 [0.81 , 1.54]	
Nishizawa 2020	21	30	12	30	11.2%	1.75 [1.06 , 2.88]	
Subtotal (95% CI)		**123**		**112**	**33.3%**	**1.33 [0.99 , 1.79]**	
Total events:	72		50				
Heterogeneity: Tau² = 0.01; Chi² = 2.46, df = 2 (P = 0.29); I² = 19%							
Test for overall effect: Z = 1.91 (P = 0.06)							
1.7.3 Not specified							
Kerforne 2012	18	30	8	30	8.6%	2.25 [1.16 , 4.36]	
Ismailoglu 2015	6	30	3	30	3.4%	2.00 [0.55 , 7.27]	
Subtotal (95% CI)		**60**		**60**	**12.0%**	**2.20 [1.22 , 3.96]**	
Total events:	24		11				
Heterogeneity: Tau² = 0.00; Chi² = 0.03, df = 1 (P = 0.87); I² = 0%							
Test for overall effect: Z = 2.62 (P = 0.009)							
Total (95% CI)		**424**		**391**	**100.0%**	**1.50 [1.15 , 1.95]**	
Total events:	242		140				
Heterogeneity: Tau² = 0.10; Chi² = 23.76, df = 9 (P = 0.005); I² = 62%							
Test for overall effect: Z = 2.99 (P = 0.003)							
Test for subgroup differences: Chi² = 2.20, df = 2 (P = 0.33), I² = 9.2%							

Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): First-pass success of cannulation
(D) Incomplete outcome data (attrition bias): First-pass success of cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: First-pass success of cannulation

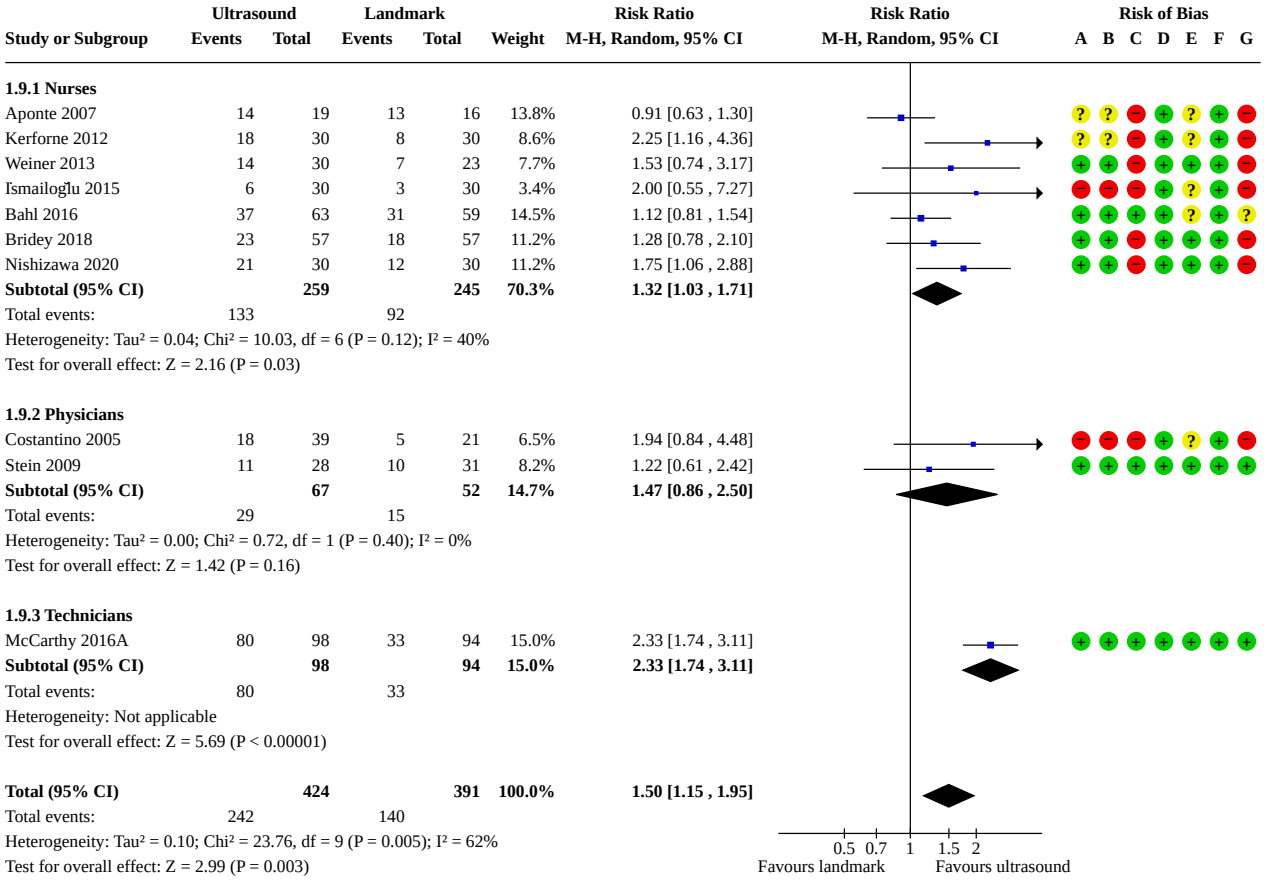
Analysis 1.8. Comparison 1: First-pass success of cannulation, Outcome 8: Operators finished any training program for ultrasound-guided peripheral venous cannulation plus any clinical experience



Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): First-pass success of cannulation
(D) Incomplete outcome data (attrition bias): First-pass success of cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: First-pass success of cannulation

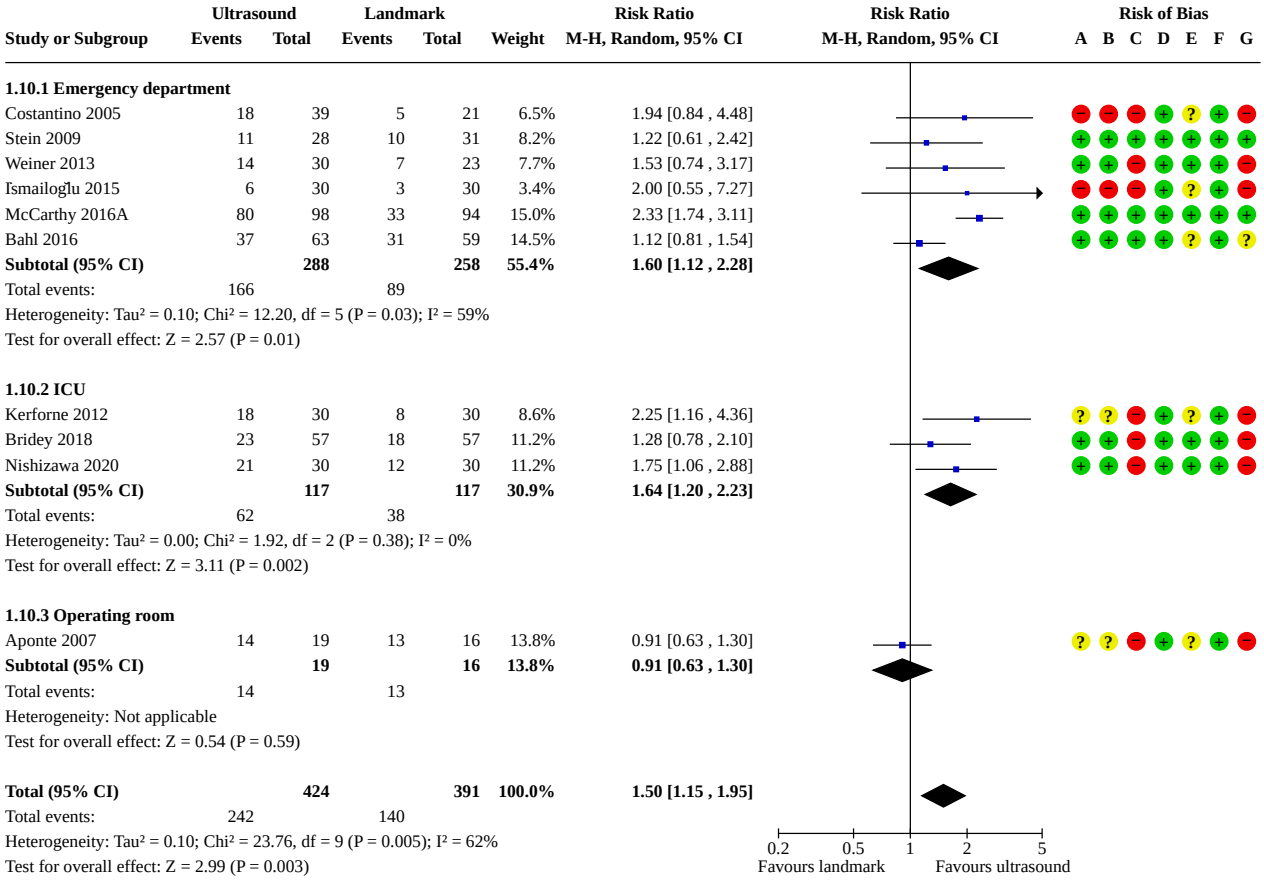
Analysis 1.9. Comparison 1: First-pass success of cannulation, Outcome 9: Types of operators



Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): First-pass success of cannulation
(D) Incomplete outcome data (attrition bias): First-pass success of cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: First-pass success of cannulation

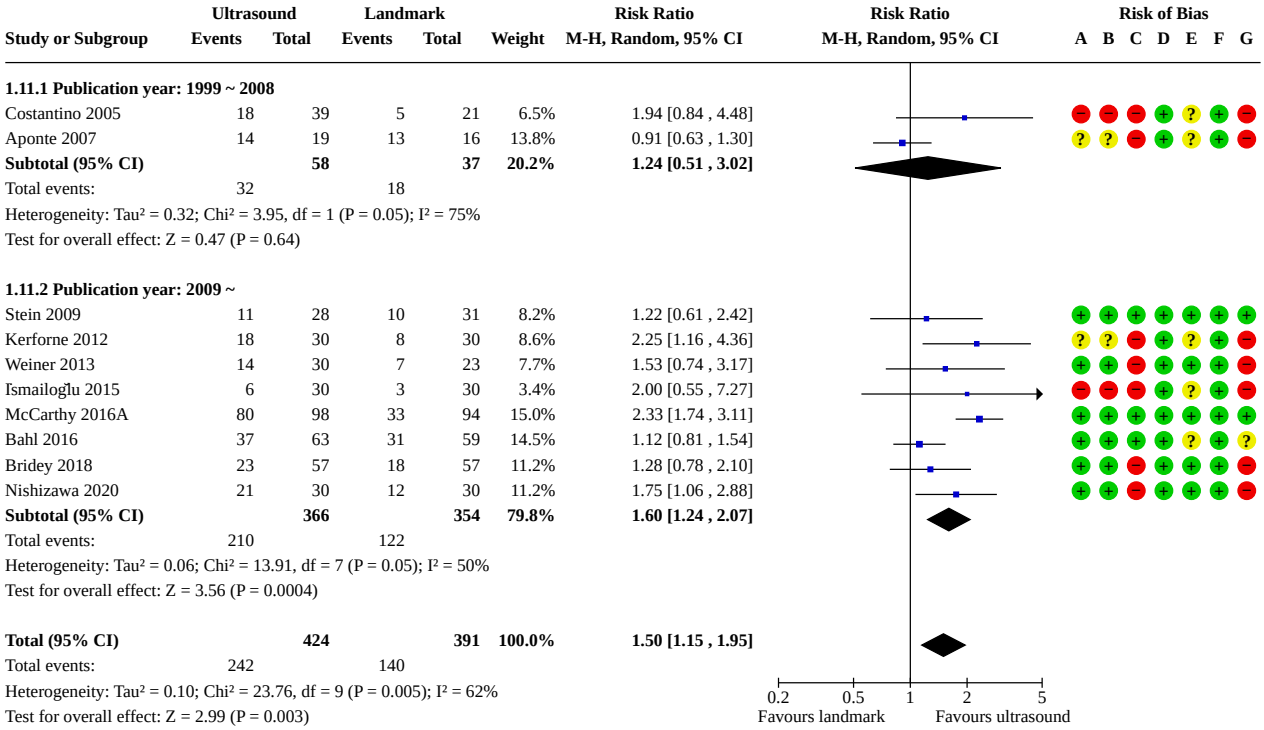
Analysis 1.10. Comparison 1: First-pass success of cannulation, Outcome 10: Setting



Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): First-pass success of cannulation
(D) Incomplete outcome data (attrition bias): First-pass success of cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: First-pass success of cannulation

Analysis 1.11. Comparison 1: First-pass success of cannulation, Outcome 11: Year of publication

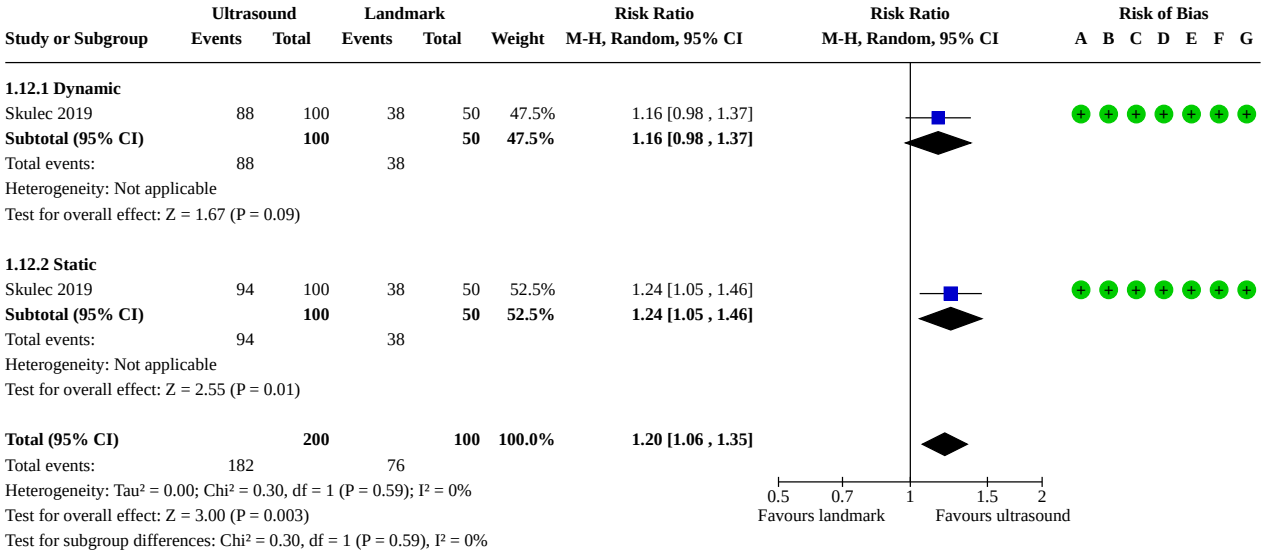


Study or Subgroup	Ultrasound Events	Ultrasound Total	Landmark Events	Landmark Total	Weight	Risk Ratio M-H, Random, 95% CI
1.11.1 Publication year: 1999 ~ 2008						
Costantino 2005	18	39	5	21	6.5%	1.94 [0.84 , 4.48]
Aponte 2007	14	19	13	16	13.8%	0.91 [0.63 , 1.30]
Subtotal (95% CI)		**58**		**37**	**20.2%**	**1.24 [0.51 , 3.02]**
Total events:	32		18			
Heterogeneity: Tau² = 0.32; Chi² = 3.95, df = 1 (P = 0.05); I² = 75%						
Test for overall effect: Z = 0.47 (P = 0.64)						
1.11.2 Publication year: 2009 ~						
Stein 2009	11	28	10	31	8.2%	1.22 [0.61 , 2.42]
Kerforne 2012	18	30	8	30	8.6%	2.25 [1.16 , 4.36]
Weiner 2013	14	30	7	23	7.7%	1.53 [0.74 , 3.17]
Ismailoglu 2015	6	30	3	30	3.4%	2.00 [0.55 , 7.27]
McCarthy 2016A	80	98	33	94	15.0%	2.33 [1.74 , 3.11]
Bahl 2016	37	63	31	59	14.5%	1.12 [0.81 , 1.54]
Bridey 2018	23	57	18	57	11.2%	1.28 [0.78 , 2.10]
Nishizawa 2020	21	30	12	30	11.2%	1.75 [1.06 , 2.88]
Subtotal (95% CI)		**366**		**354**	**79.8%**	**1.60 [1.24 , 2.07]**
Total events:	210		122			
Heterogeneity: Tau² = 0.06; Chi² = 13.91, df = 7 (P = 0.05); I² = 50%						
Test for overall effect: Z = 3.56 (P = 0.0004)						
Total (95% CI)		**424**		**391**	**100.0%**	**1.50 [1.15 , 1.95]**
Total events:	242		140			
Heterogeneity: Tau² = 0.10; Chi² = 23.76, df = 9 (P = 0.005); I² = 62%						
Test for overall effect: Z = 2.99 (P = 0.003)						
Test for subgroup differences: Chi² = 0.29, df = 1 (P = 0.59), I² = 0%						

Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): First-pass success of cannulation
(D) Incomplete outcome data (attrition bias): First-pass success of cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: First-pass success of cannulation

Analysis 1.12. Comparison 1: First-pass success of cannulation, Outcome 12: Dynamic guidance or static guidance



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): First-pass success of cannulation
(D) Incomplete outcome data (attrition bias): First-pass success of cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: First-pass success of cannulation

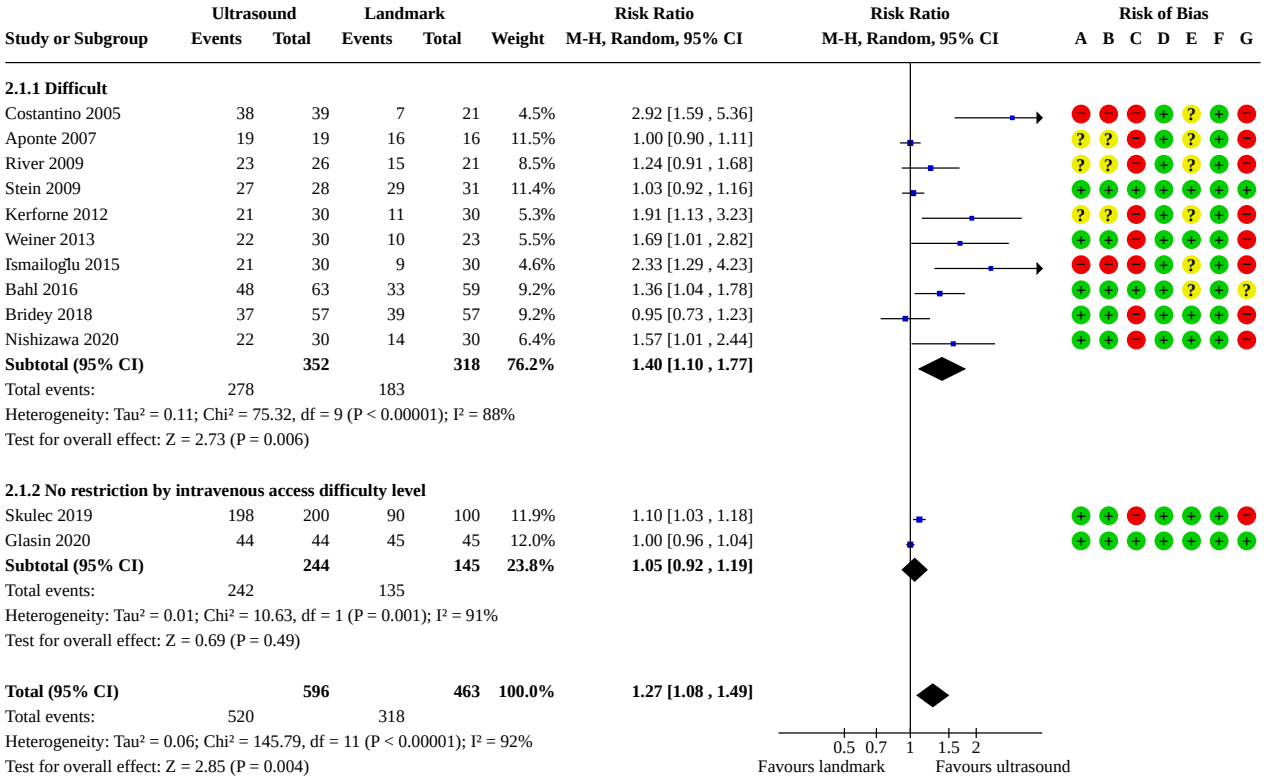
Comparison 2. Overall success of cannulation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 Difficulty levels defined by original studies	12	1059	Risk Ratio (M-H, Random, 95% CI)	1.27 [1.08, 1.49]
2.1.1 Difficult	10	670	Risk Ratio (M-H, Random, 95% CI)	1.40 [1.10, 1.77]
2.1.2 No restriction by intravenous access difficulty level	2	389	Risk Ratio (M-H, Random, 95% CI)	1.05 [0.92, 1.19]
2.2 Difficulty levels defined by the success rate with landmark method	12	1059	Risk Ratio (M-H, Random, 95% CI)	1.27 [1.08, 1.49]
2.2.1 Difficult	8	588	Risk Ratio (M-H, Random, 95% CI)	1.53 [1.12, 2.08]
2.2.2 Moderate	3	436	Risk Ratio (M-H, Random, 95% CI)	1.07 [0.94, 1.23]
2.2.3 Easy	1	35	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.90, 1.11]
2.3 Operators could not see and palpate a target vein	4	294	Risk Ratio (M-H, Random, 95% CI)	1.53 [0.98, 2.41]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.4 Participants had a history of difficult intravenous access	6	390	Risk Ratio (M-H, Random, 95% CI)	1.66 [0.97, 2.86]
2.5 Participants had multiple failed attempts	5	279	Risk Ratio (M-H, Random, 95% CI)	1.53 [0.93, 2.51]
2.6 Operators finished any training program for ultrasound-guided peripheral venous cannulation	10	670	Risk Ratio (M-H, Random, 95% CI)	1.40 [1.10, 1.77]
2.6.1 Finished	9	610	Risk Ratio (M-H, Random, 95% CI)	1.35 [1.06, 1.71]
2.6.2 Not specified	1	60	Risk Ratio (M-H, Random, 95% CI)	1.91 [1.13, 3.23]
2.7 Operators had any clinical experience with ultrasound-guided peripheral intravenous cannulation	10	670	Risk Ratio (M-H, Random, 95% CI)	1.40 [1.10, 1.77]
2.7.1 Had any clinical experience	5	315	Risk Ratio (M-H, Random, 95% CI)	1.15 [0.91, 1.44]
2.7.2 Did not have any clinical experience	3	235	Risk Ratio (M-H, Random, 95% CI)	1.46 [1.18, 1.79]
2.7.3 Not specified	2	120	Risk Ratio (M-H, Random, 95% CI)	2.08 [1.41, 3.09]
2.8 Operators finished any training program for ultrasound-guided peripheral venous cannulation and had any clinical experience	10	670	Risk Ratio (M-H, Random, 95% CI)	1.40 [1.10, 1.77]
2.8.1 Finished any training program for ultrasound-guided peripheral venous cannulation and had any clinical experience	5	315	Risk Ratio (M-H, Random, 95% CI)	1.15 [0.91, 1.44]
2.8.2 Not finished any training program for ultrasound-guided peripheral venous cannulation or no clinical experience	3	235	Risk Ratio (M-H, Random, 95% CI)	1.46 [1.18, 1.79]
2.8.3 Not specified	2	120	Risk Ratio (M-H, Random, 95% CI)	2.08 [1.41, 3.09]
2.9 Types of operators	10	670	Risk Ratio (M-H, Random, 95% CI)	1.40 [1.10, 1.77]
2.9.1 Nurses	8	551	Risk Ratio (M-H, Random, 95% CI)	1.37 [1.05, 1.78]
2.9.2 Physicians	2	119	Risk Ratio (M-H, Random, 95% CI)	1.72 [0.22, 13.47]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.10 Setting	10	670	Risk Ratio (M-H, Random, 95% CI)	1.40 [1.10, 1.77]
2.10.1 Emergency department	6	401	Risk Ratio (M-H, Random, 95% CI)	1.57 [1.05, 2.36]
2.10.2 ICU	3	234	Risk Ratio (M-H, Random, 95% CI)	1.36 [0.86, 2.15]
2.10.3 Operating room	1	35	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.90, 1.11]
2.11 Year of publication	10	670	Risk Ratio (M-H, Random, 95% CI)	1.40 [1.10, 1.77]
2.11.1 Publication year: 1999 ~ 2008	2	95	Risk Ratio (M-H, Random, 95% CI)	1.70 [0.10, 29.24]
2.11.2 Publication year: 2009 ~	8	575	Risk Ratio (M-H, Random, 95% CI)	1.36 [1.08, 1.71]
2.12 Dynamic guidance or static guidance	1	300	Risk Ratio (M-H, Random, 95% CI)	1.10 [1.03, 1.18]
2.12.1 Dynamic	1	150	Risk Ratio (M-H, Random, 95% CI)	1.10 [1.00, 1.21]
2.12.2 Static	1	150	Risk Ratio (M-H, Random, 95% CI)	1.10 [1.00, 1.21]

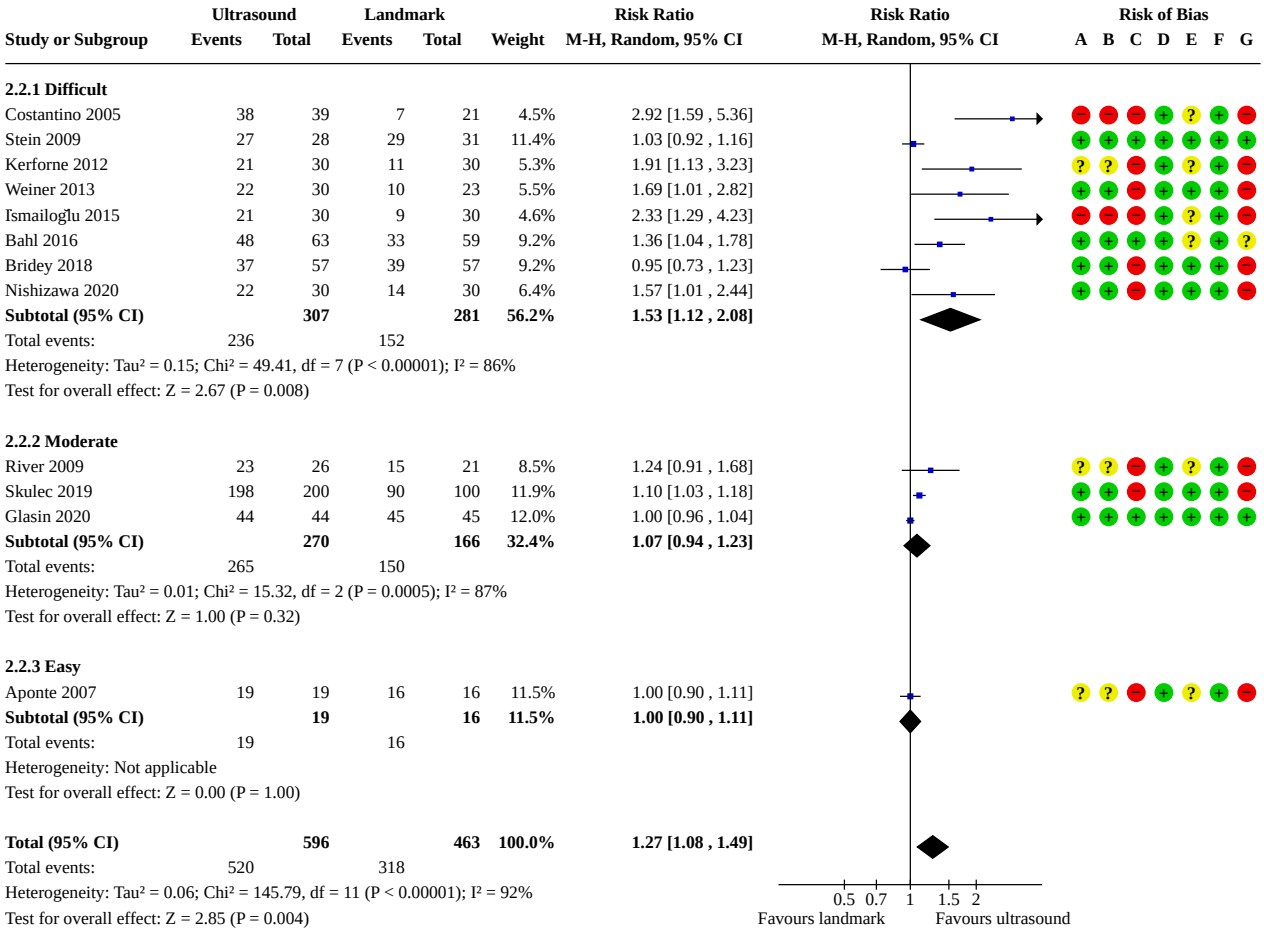
Analysis 2.1. Comparison 2: Overall success of cannulation, Outcome 1: Difficulty levels defined by original studies



Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Overall-success of cannulation
(D) Incomplete outcome data (attrition bias): Overall success of cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Overall success of cannulation

Analysis 2.2. Comparison 2: Overall success of cannulation, Outcome 2: Difficulty levels defined by the success rate with landmark method



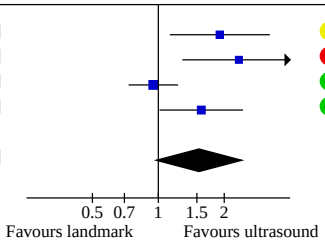
Risk of bias legend

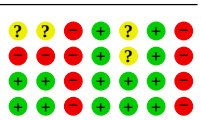
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Overall-success of cannulation
(D) Incomplete outcome data (attrition bias): Overall success of cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Overall success of cannulation

Analysis 2.3. Comparison 2: Overall success of cannulation, Outcome 3: Operators could not see and palpate a target vein

Study or Subgroup	Ultrasound Events	Ultrasound Total	Landmark Events	Landmark Total	Weight	Risk Ratio M-H, Random, 95% CI
Kerforne 2012	21	30	11	30	23.1%	1.91 [1.13 , 3.23]
Ismailoğlu 2015	21	30	9	30	21.2%	2.33 [1.29 , 4.23]
Bridey 2018	37	57	39	57	30.3%	0.95 [0.73 , 1.23]
Nishizawa 2020	22	30	14	30	25.5%	1.57 [1.01 , 2.44]
Total (95% CI)		**147**		**147**	**100.0%**	**1.53 [0.98 , 2.41]**
Total events:	101		73			

Heterogeneity: Tau² = 0.16; Chi² = 12.83, df = 3 (P = 0.005); I² = 77%
Test for overall effect: Z = 1.86 (P = 0.06)
Test for subgroup differences: Not applicable



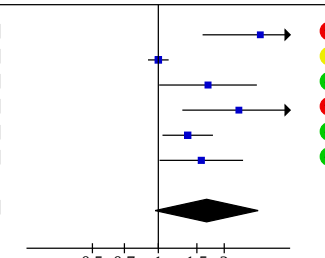


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Overall-success of cannulation
(D) Incomplete outcome data (attrition bias): Overall success of cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Overall success of cannulation

Analysis 2.4. Comparison 2: Overall success of cannulation, Outcome 4: Participants had a history of difficult intravenous access

Study or Subgroup	Ultrasound Events	Ultrasound Total	Landmark Events	Landmark Total	Weight	Risk Ratio M-H, Random, 95% CI
Costantino 2005	38	39	7	21	15.2%	2.92 [1.59 , 5.36]
Aponte 2007	19	19	16	16	18.7%	1.00 [0.90 , 1.11]
Weiner 2013	22	30	10	23	16.1%	1.69 [1.01 , 2.82]
Ismailoğlu 2015	21	30	9	30	15.3%	2.33 [1.29 , 4.23]
Bahl 2016	48	63	33	59	18.0%	1.36 [1.04 , 1.78]
Nishizawa 2020	22	30	14	30	16.7%	1.57 [1.01 , 2.44]
Total (95% CI)		**211**		**179**	**100.0%**	**1.66 [0.97 , 2.86]**
Total events:	170		89			

Heterogeneity: Tau² = 0.41; Chi² = 79.70, df = 5 (P < 0.00001); I² = 94%
Test for overall effect: Z = 1.84 (P = 0.07)
Test for subgroup differences: Not applicable

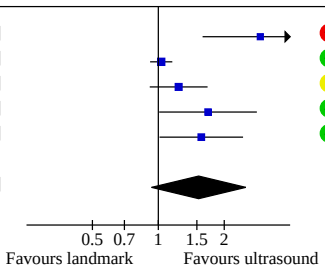


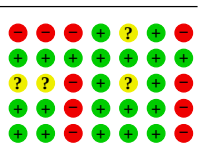
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Overall-success of cannulation
(D) Incomplete outcome data (attrition bias): Overall success of cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Overall success of cannulation

Analysis 2.5. Comparison 2: Overall success of cannulation, Outcome 5: Participants had multiple failed attempts

Study or Subgroup	Ultrasound Events	Ultrasound Total	Landmark Events	Landmark Total	Weight	Risk Ratio M-H, Random, 95% CI
Costantino 2005	38	39	7	21	17.3%	2.92 [1.59 , 5.36]
Stein 2009	27	28	29	31	23.0%	1.03 [0.92 , 1.16]
River 2009	23	26	15	21	21.4%	1.24 [0.91 , 1.68]
Weiner 2013	22	30	10	23	18.6%	1.69 [1.01 , 2.82]
Nishizawa 2020	22	30	14	30	19.7%	1.57 [1.01 , 2.44]
Total (95% CI)		**153**		**126**	**100.0%**	**1.53 [0.93 , 2.51]**
Total events:	132		75			

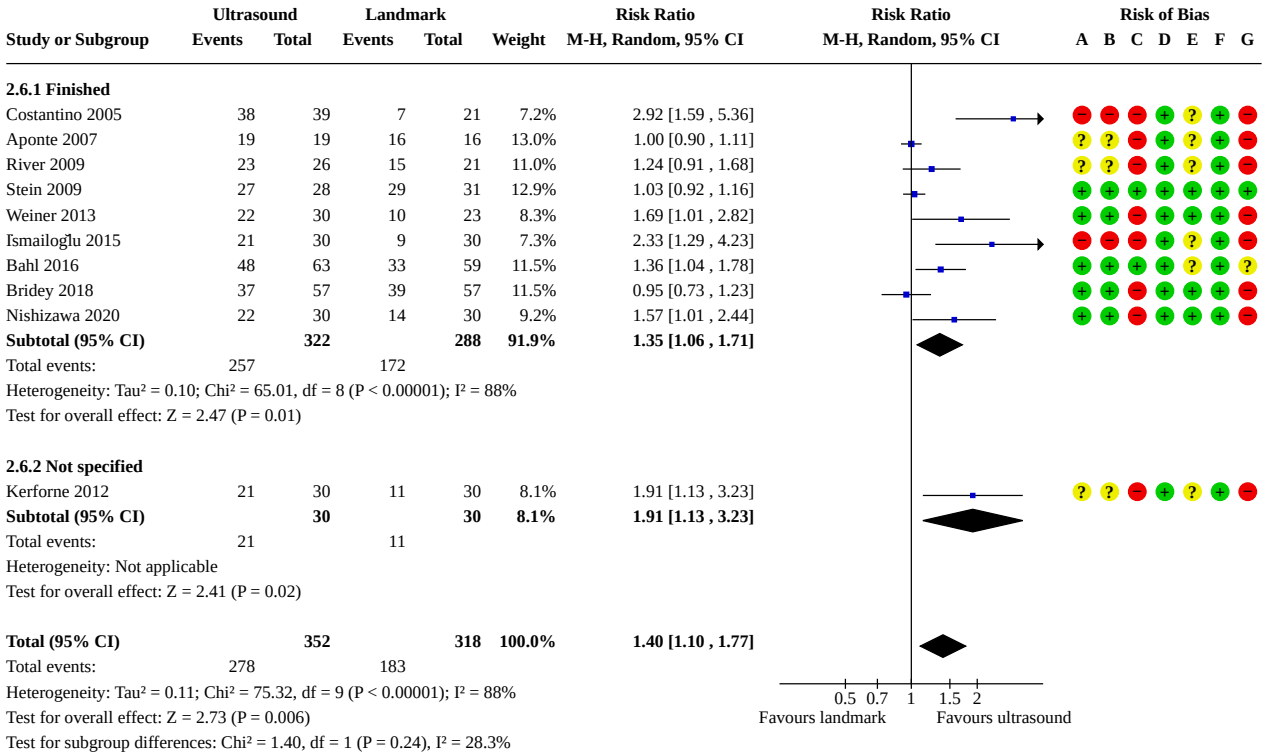
Heterogeneity: Tau² = 0.27; Chi² = 44.00, df = 4 (P < 0.00001); I² = 91%
Test for overall effect: Z = 1.68 (P = 0.09)
Test for subgroup differences: Not applicable





Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Overall-success of cannulation
(D) Incomplete outcome data (attrition bias): Overall success of cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Overall success of cannulation

Analysis 2.6. Comparison 2: Overall success of cannulation, Outcome 6: Operators finished any training program for ultrasound-guided peripheral venous cannulation

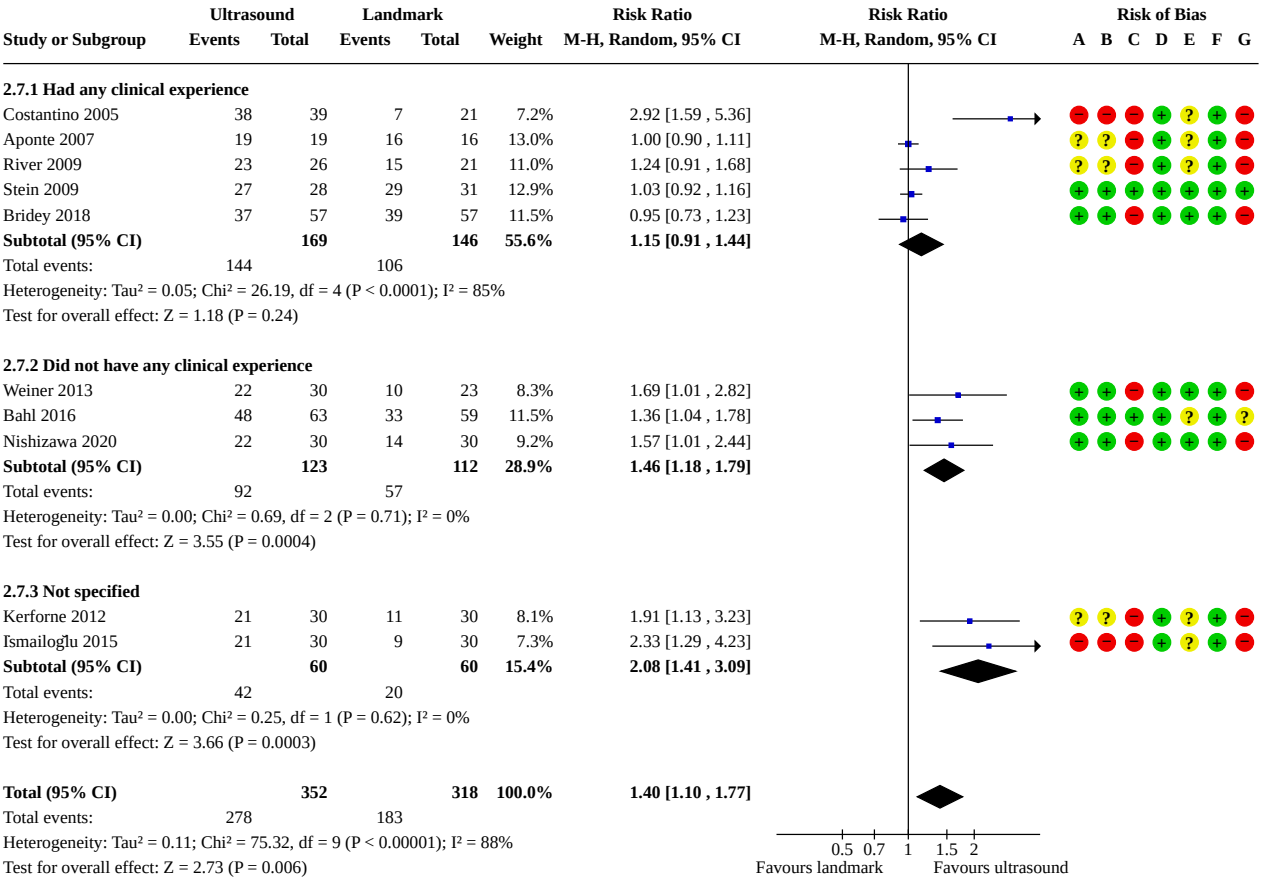


Study or Subgroup	Ultrasound Events	Ultrasound Total	Landmark Events	Landmark Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk of Bias A B C D E F G
2.6.1 Finished							
Costantino 2005	38	39	7	21	7.2%	2.92 [1.59 , 5.36]	− − − + ? + −
Aponte 2007	19	19	16	16	13.0%	1.00 [0.90 , 1.11]	? ? − + ? + −
River 2009	23	26	15	21	11.0%	1.24 [0.91 , 1.68]	? ? − + ? + −
Stein 2009	27	28	29	31	12.9%	1.03 [0.92 , 1.16]	+ + + + + + +
Weiner 2013	22	30	10	23	8.3%	1.69 [1.01 , 2.82]	+ + − + + + −
Ismailoğlu 2015	21	30	9	30	7.3%	2.33 [1.29 , 4.23]	− − − + ? + −
Bahl 2016	48	63	33	59	11.5%	1.36 [1.04 , 1.78]	+ + + + ? + ?
Bridey 2018	37	57	39	57	11.5%	0.95 [0.73 , 1.23]	+ + − + + + −
Nishizawa 2020	22	30	14	30	9.2%	1.57 [1.01 , 2.44]	+ + − + + + −
Subtotal (95% CI)		**322**		**288**	**91.9%**	**1.35 [1.06 , 1.71]**	
Total events:	257		172				
Heterogeneity: Tau² = 0.10; Chi² = 65.01, df = 8 (P < 0.00001); I² = 88%							
Test for overall effect: Z = 2.47 (P = 0.01)							
2.6.2 Not specified							
Kerforne 2012	21	30	11	30	8.1%	1.91 [1.13 , 3.23]	? ? − + ? + −
Subtotal (95% CI)		**30**		**30**	**8.1%**	**1.91 [1.13 , 3.23]**	
Total events:	21		11				
Heterogeneity: Not applicable							
Test for overall effect: Z = 2.41 (P = 0.02)							
Total (95% CI)		**352**		**318**	**100.0%**	**1.40 [1.10 , 1.77]**	
Total events:	278		183				
Heterogeneity: Tau² = 0.11; Chi² = 75.32, df = 9 (P < 0.00001); I² = 88%							
Test for overall effect: Z = 2.73 (P = 0.006)							
Test for subgroup differences: Chi² = 1.40, df = 1 (P = 0.24), I² = 28.3%							

Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Overall-success of cannulation
(D) Incomplete outcome data (attrition bias): Overall success of cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Overall success of cannulation

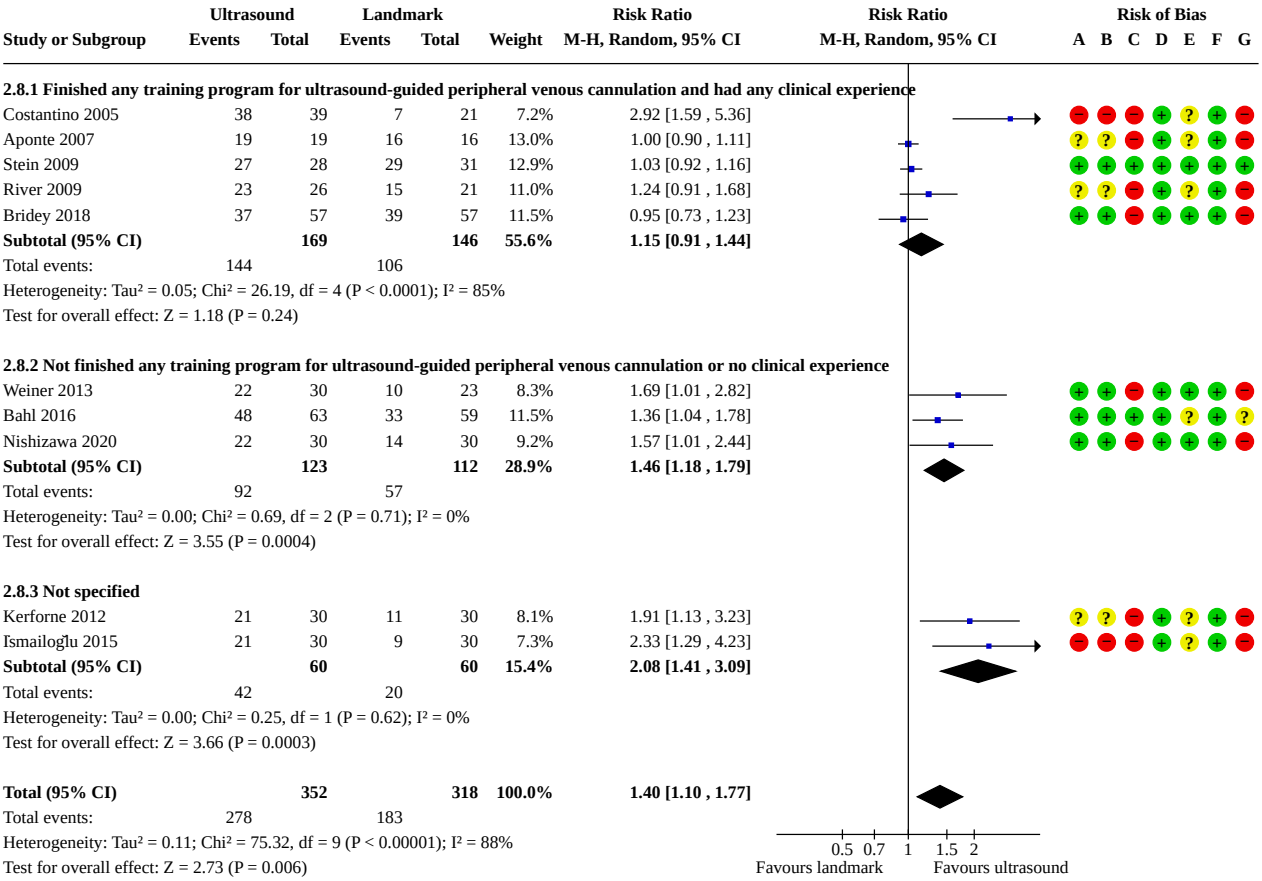
Analysis 2.7. Comparison 2: Overall success of cannulation, Outcome 7: Operators had any clinical experience with ultrasound-guided peripheral intravenous cannulation



Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Overall-success of cannulation
(D) Incomplete outcome data (attrition bias): Overall success of cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Overall success of cannulation

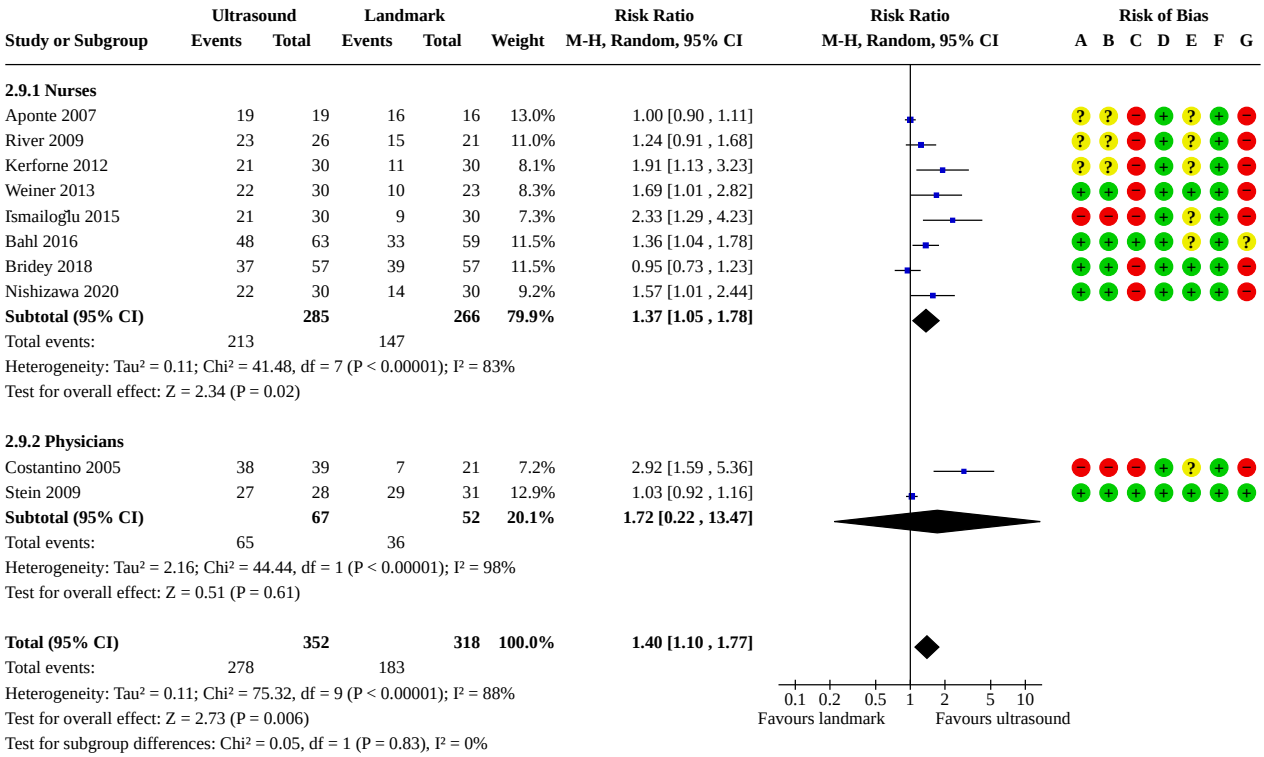
Analysis 2.8. Comparison 2: Overall success of cannulation, Outcome 8: Operators finished any training program for ultrasound-guided peripheral venous cannulation and had any clinical experience



Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Overall-success of cannulation
(D) Incomplete outcome data (attrition bias): Overall success of cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Overall success of cannulation

Analysis 2.9. Comparison 2: Overall success of cannulation, Outcome 9: Types of operators



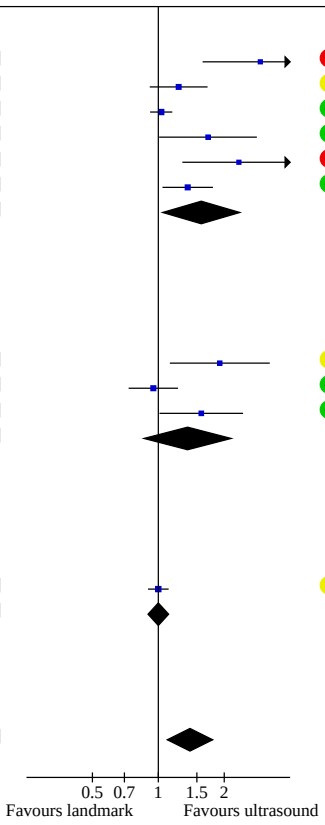
Study or Subgroup	Ultrasound Events	Ultrasound Total	Landmark Events	Landmark Total	Weight	Risk Ratio M-H, Random, 95% CI	Risk of Bias A B C D E F G
2.9.1 Nurses							
Aponte 2007	19	19	16	16	13.0%	1.00 [0.90 , 1.11]	? ? − + ? + −
River 2009	23	26	15	21	11.0%	1.24 [0.91 , 1.68]	? ? − + ? + −
Kerforne 2012	21	30	11	30	8.1%	1.91 [1.13 , 3.23]	? ? − + ? + −
Weiner 2013	22	30	10	23	8.3%	1.69 [1.01 , 2.82]	+ + − + + + −
Ismailoglu 2015	21	30	9	30	7.3%	2.33 [1.29 , 4.23]	− − − + ? + −
Bahl 2016	48	63	33	59	11.5%	1.36 [1.04 , 1.78]	+ + + + ? + ?
Bridey 2018	37	57	39	57	11.5%	0.95 [0.73 , 1.23]	+ + − + + + −
Nishizawa 2020	22	30	14	30	9.2%	1.57 [1.01 , 2.44]	+ + − + + + −
Subtotal (95% CI)		**285**		**266**	**79.9%**	**1.37 [1.05 , 1.78]**	
Total events:	213		147				
Heterogeneity: Tau² = 0.11; Chi² = 41.48, df = 7 (P < 0.00001); I² = 83%							
Test for overall effect: Z = 2.34 (P = 0.02)							
2.9.2 Physicians							
Costantino 2005	38	39	7	21	7.2%	2.92 [1.59 , 5.36]	− − − + ? + −
Stein 2009	27	28	29	31	12.9%	1.03 [0.92 , 1.16]	+ + + + + + +
Subtotal (95% CI)		**67**		**52**	**20.1%**	**1.72 [0.22 , 13.47]**	
Total events:	65		36				
Heterogeneity: Tau² = 2.16; Chi² = 44.44, df = 1 (P < 0.00001); I² = 98%							
Test for overall effect: Z = 0.51 (P = 0.61)							
Total (95% CI)		**352**		**318**	**100.0%**	**1.40 [1.10 , 1.77]**	
Total events:	278		183				
Heterogeneity: Tau² = 0.11; Chi² = 75.32, df = 9 (P < 0.00001); I² = 88%							
Test for overall effect: Z = 2.73 (P = 0.006)							
Test for subgroup differences: Chi² = 0.05, df = 1 (P = 0.83), I² = 0%							

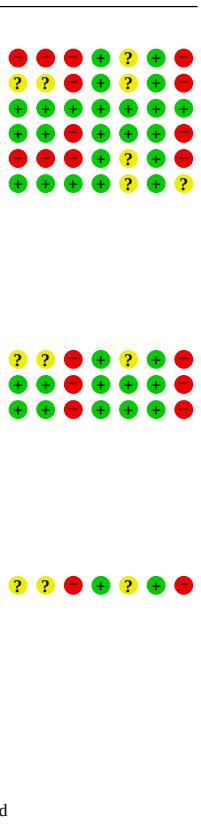
Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Overall-success of cannulation
(D) Incomplete outcome data (attrition bias): Overall success of cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Overall success of cannulation

Analysis 2.10. Comparison 2: Overall success of cannulation, Outcome 10: Setting

Study or Subgroup	Ultrasound Events	Ultrasound Total	Landmark Events	Landmark Total	Weight	Risk Ratio M-H, Random, 95% CI
2.10.1 Emergency department						
Costantino 2005	38	39	7	21	7.2%	2.92 [1.59 , 5.36]
River 2009	23	26	15	21	11.0%	1.24 [0.91 , 1.68]
Stein 2009	27	28	29	31	12.9%	1.03 [0.92 , 1.16]
Weiner 2013	22	30	10	23	8.3%	1.69 [1.01 , 2.82]
Ismailoglu 2015	21	30	9	30	7.3%	2.33 [1.29 , 4.23]
Bahl 2016	48	63	33	59	11.5%	1.36 [1.04 , 1.78]
Subtotal (95% CI)		**216**		**185**	**58.1%**	**1.57 [1.05 , 2.36]**
Total events:	179		103			
Heterogeneity: Tau² = 0.21; Chi² = 49.47, df = 5 (P < 0.00001); I² = 90%						
Test for overall effect: Z = 2.18 (P = 0.03)						
2.10.2 ICU						
Kerforne 2012	21	30	11	30	8.1%	1.91 [1.13 , 3.23]
Bridey 2018	37	57	39	57	11.5%	0.95 [0.73 , 1.23]
Nishizawa 2020	22	30	14	30	9.2%	1.57 [1.01 , 2.44]
Subtotal (95% CI)		**117**		**117**	**28.9%**	**1.36 [0.86 , 2.15]**
Total events:	80		64			
Heterogeneity: Tau² = 0.12; Chi² = 7.86, df = 2 (P = 0.02); I² = 75%						
Test for overall effect: Z = 1.31 (P = 0.19)						
2.10.3 Operating room						
Aponte 2007	19	19	16	16	13.0%	1.00 [0.90 , 1.11]
Subtotal (95% CI)		**19**		**16**	**13.0%**	**1.00 [0.90 , 1.11]**
Total events:	19		16			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.00 (P = 1.00)						
Total (95% CI)		**352**		**318**	**100.0%**	**1.40 [1.10 , 1.77]**
Total events:	278		183			
Heterogeneity: Tau² = 0.11; Chi² = 75.32, df = 9 (P < 0.00001); I² = 88%						
Test for overall effect: Z = 2.73 (P = 0.006)						
Test for subgroup differences: Chi² = 5.76, df = 2 (P = 0.06), I² = 65.3%						



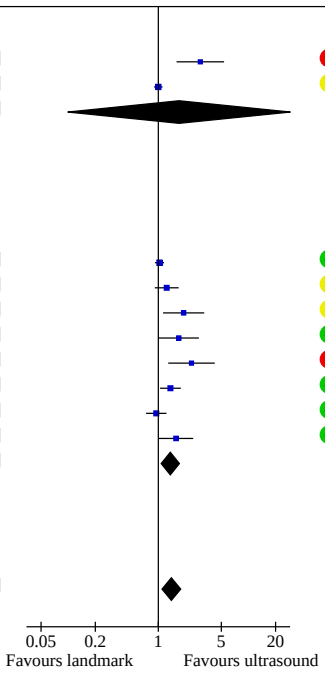


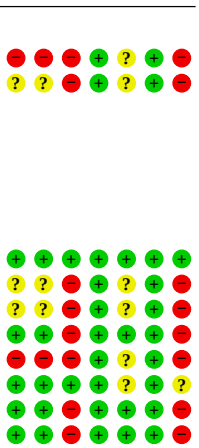
Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Overall-success of cannulation
(D) Incomplete outcome data (attrition bias): Overall success of cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Overall success of cannulation

Analysis 2.11. Comparison 2: Overall success of cannulation, Outcome 11: Year of publication

Study or Subgroup	Ultrasound Events	Ultrasound Total	Landmark Events	Landmark Total	Weight	Risk Ratio M-H, Random, 95% CI
2.11.1 Publication year: 1999 ~ 2008						
Costantino 2005	38	39	7	21	7.2%	2.92 [1.59 , 5.36]
Aponte 2007	19	19	16	16	13.0%	1.00 [0.90 , 1.11]
Subtotal (95% CI)		**58**		**37**	**20.2%**	**1.70 [0.10 , 29.24]**
Total events:	57		23			
Heterogeneity: Tau² = 4.17; Chi² = 85.17, df = 1 (P < 0.00001); I² = 99%						
Test for overall effect: Z = 0.37 (P = 0.71)						
2.11.2 Publication year: 2009 ~						
Stein 2009	27	28	29	31	12.9%	1.03 [0.92 , 1.16]
River 2009	23	26	15	21	11.0%	1.24 [0.91 , 1.68]
Kerforne 2012	21	30	11	30	8.1%	1.91 [1.13 , 3.23]
Weiner 2013	22	30	10	23	8.3%	1.69 [1.01 , 2.82]
Ismailoğlu 2015	21	30	9	30	7.3%	2.33 [1.29 , 4.23]
Bahl 2016	48	63	33	59	11.5%	1.36 [1.04 , 1.78]
Bridey 2018	37	57	39	57	11.5%	0.95 [0.73 , 1.23]
Nishizawa 2020	22	30	14	30	9.2%	1.57 [1.01 , 2.44]
Subtotal (95% CI)		**294**		**281**	**79.8%**	**1.36 [1.08 , 1.71]**
Total events:	221		160			
Heterogeneity: Tau² = 0.08; Chi² = 31.18, df = 7 (P < 0.0001); I² = 78%						
Test for overall effect: Z = 2.58 (P = 0.010)						
Total (95% CI)		**352**		**318**	**100.0%**	**1.40 [1.10 , 1.77]**
Total events:	278		183			
Heterogeneity: Tau² = 0.11; Chi² = 75.32, df = 9 (P < 0.00001); I² = 88%						
Test for overall effect: Z = 2.73 (P = 0.006)						
Test for subgroup differences: Chi² = 0.02, df = 1 (P = 0.88), I² = 0%						

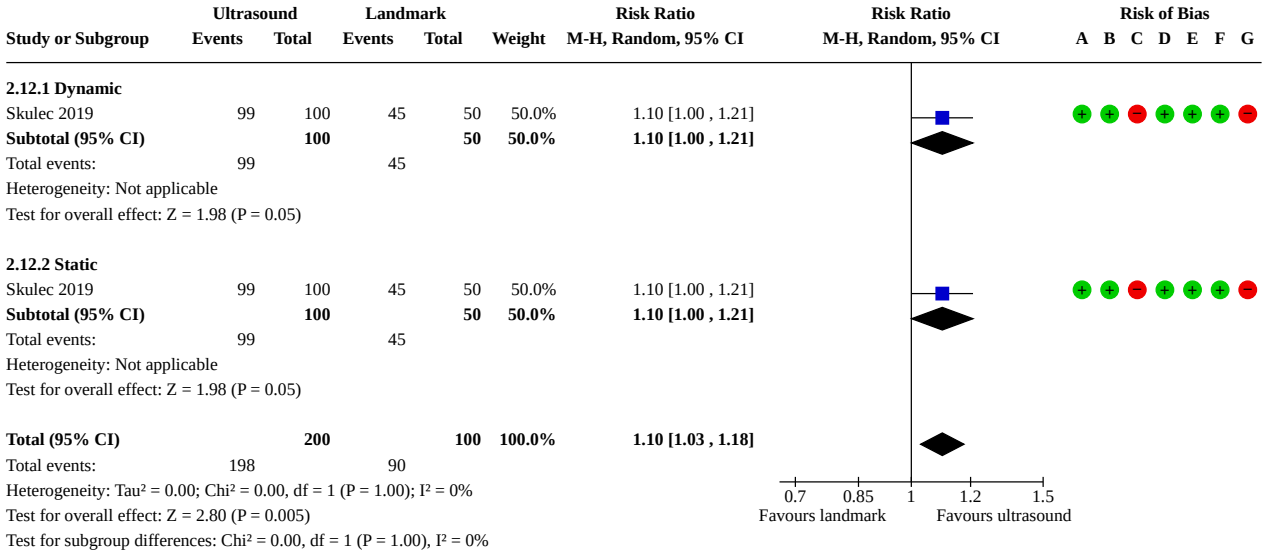




Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Overall-success of cannulation
(D) Incomplete outcome data (attrition bias): Overall success of cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Overall success of cannulation

Analysis 2.12. Comparison 2: Overall success of cannulation, Outcome 12: Dynamic guidance or static guidance



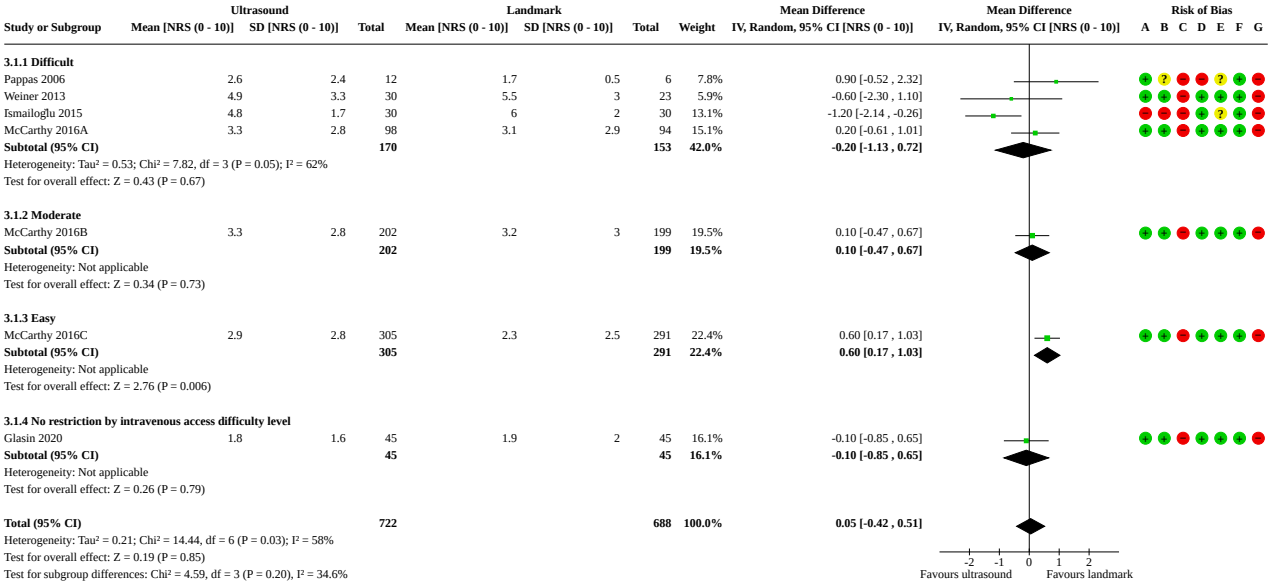
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Overall-success of cannulation
(D) Incomplete outcome data (attrition bias): Overall success of cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Overall success of cannulation

Comparison 3. Pain

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.1 Difficulty levels defined by original studies	7	1410	Mean Difference (IV, Random, 95% CI)	0.05 [-0.42, 0.51]
3.1.1 Difficult	4	323	Mean Difference (IV, Random, 95% CI)	-0.20 [-1.13, 0.72]
3.1.2 Moderate	1	401	Mean Difference (IV, Random, 95% CI)	0.10 [-0.47, 0.67]
3.1.3 Easy	1	596	Mean Difference (IV, Random, 95% CI)	0.60 [0.17, 1.03]
3.1.4 No restriction by intravenous access difficulty level	1	90	Mean Difference (IV, Random, 95% CI)	-0.10 [-0.85, 0.65]
3.2 Difficulty levels defined by the success rate with landmark method	7	1410	Mean Difference (IV, Random, 95% CI)	0.05 [-0.42, 0.51]
3.2.1 Difficult	3	305	Mean Difference (IV, Random, 95% CI)	-0.49 [-1.48, 0.49]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.2.2 Moderate	2	491	Mean Difference (IV, Random, 95% CI)	0.03 [-0.43, 0.48]
3.2.3 Easy	1	596	Mean Difference (IV, Random, 95% CI)	0.60 [0.17, 1.03]
3.2.4 No results on both first-pass and overall success of cannulation	1	18	Mean Difference (IV, Random, 95% CI)	0.90 [-0.52, 2.32]
3.3 Operators finished any training program for ultrasound-guided peripheral venous cannulation	4	323	Mean Difference (IV, Random, 95% CI)	-0.20 [-1.13, 0.72]
3.3.1 Finished	3	305	Mean Difference (IV, Random, 95% CI)	-0.49 [-1.48, 0.49]
3.3.2 Not specified	1	18	Mean Difference (IV, Random, 95% CI)	0.90 [-0.52, 2.32]
3.4 Types of operators	4	323	Mean Difference (IV, Random, 95% CI)	-0.20 [-1.13, 0.72]
3.4.1 Nurses	3	131	Mean Difference (IV, Random, 95% CI)	-0.36 [-1.68, 0.95]
3.4.2 Technicians	1	192	Mean Difference (IV, Random, 95% CI)	0.20 [-0.61, 1.01]
3.5 Setting	4	323	Mean Difference (IV, Random, 95% CI)	-0.20 [-1.13, 0.72]
3.5.1 Emergency department	4	323	Mean Difference (IV, Random, 95% CI)	-0.20 [-1.13, 0.72]
3.6 Year of publication	4	323	Mean Difference (IV, Random, 95% CI)	-0.20 [-1.13, 0.72]
3.6.1 Publication year: 1999 ~ 2008	1	18	Mean Difference (IV, Random, 95% CI)	0.90 [-0.52, 2.32]
3.6.2 Publication year: 2009 ~	3	305	Mean Difference (IV, Random, 95% CI)	-0.49 [-1.48, 0.49]

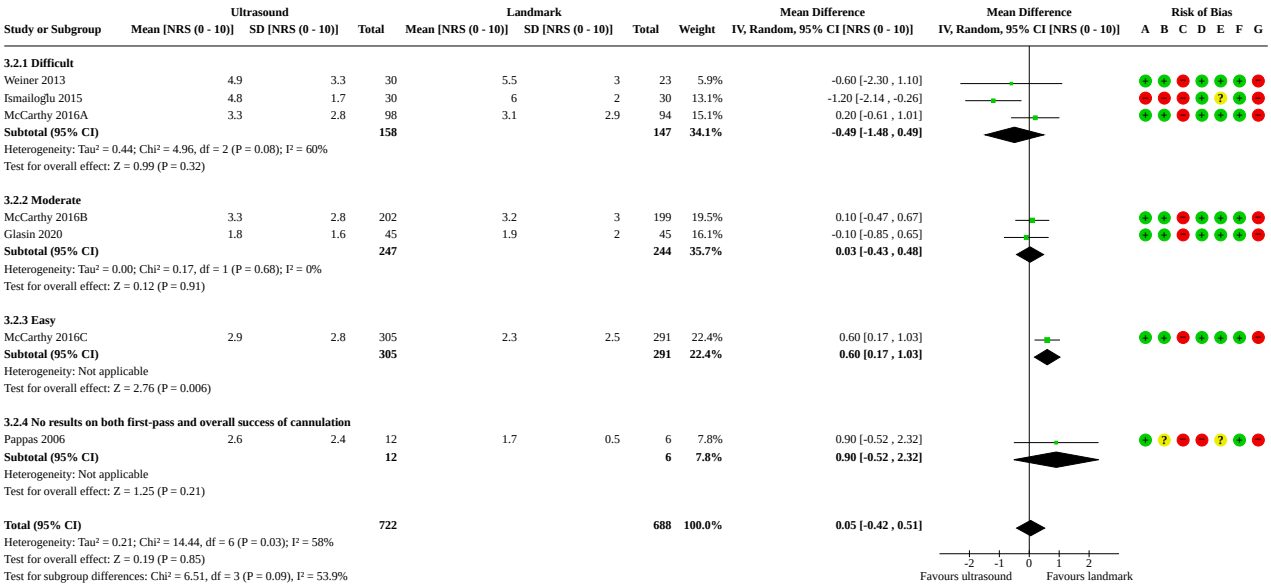
Analysis 3.1. Comparison 3: Pain, Outcome 1: Difficulty levels defined by original studies



Study or Subgroup	Ultrasound Mean [NRS (0 - 10)]	Ultrasound SD [NRS (0 - 10)]	Ultrasound Total	Landmark Mean [NRS (0 - 10)]	Landmark SD [NRS (0 - 10)]	Landmark Total	Weight	Mean Difference IV, Random, 95% CI [NRS (0 - 10)]	Risk of Bias A B C D E F G
3.1.1 Difficult									
Pappas 2006	2.6	2.4	12	1.7	0.5	6	7.8%	0.90 [-0.52 , 2.32]	+ ? - - ? + -
Weiner 2013	4.9	3.3	30	5.5	3	23	5.9%	-0.60 [-2.30 , 1.10]	+ + - + + + -
Ismailoğlu 2015	4.8	1.7	30	6	2	30	13.1%	-1.20 [-2.14 , -0.26]	- - - + ? + -
McCarthy 2016A	3.3	2.8	98	3.1	2.9	94	15.1%	0.20 [-0.61 , 1.01]	+ + - + + + -
Subtotal (95% CI)			**170**			**153**	**42.0%**	**-0.20 [-1.13 , 0.72]**	
Heterogeneity: Tau² = 0.53; Chi² = 7.82, df = 3 (P = 0.05); I² = 62%									
Test for overall effect: Z = 0.43 (P = 0.67)									
3.1.2 Moderate									
McCarthy 2016B	3.3	2.8	202	3.2	3	199	19.5%	0.10 [-0.47 , 0.67]	+ + - + + + -
Subtotal (95% CI)			**202**			**199**	**19.5%**	**0.10 [-0.47 , 0.67]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 0.34 (P = 0.73)									
3.1.3 Easy									
McCarthy 2016C	2.9	2.8	305	2.3	2.5	291	22.4%	0.60 [0.17 , 1.03]	+ + - + + + -
Subtotal (95% CI)			**305**			**291**	**22.4%**	**0.60 [0.17 , 1.03]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 2.76 (P = 0.006)									
3.1.4 No restriction by intravenous access difficulty level									
Glasin 2020	1.8	1.6	45	1.9	2	45	16.1%	-0.10 [-0.85 , 0.65]	+ + - + + + -
Subtotal (95% CI)			**45**			**45**	**16.1%**	**-0.10 [-0.85 , 0.65]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 0.26 (P = 0.79)									
Total (95% CI)			**722**			**688**	**100.0%**	**0.05 [-0.42 , 0.51]**	
Heterogeneity: Tau² = 0.21; Chi² = 14.44, df = 6 (P = 0.03); I² = 58%									
Test for overall effect: Z = 0.19 (P = 0.85)									
Test for subgroup differences: Chi² = 4.59, df = 3 (P = 0.20), I² = 34.6%									

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Pain
(D) Incomplete outcome data (attrition bias): Pain
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Pain

Analysis 3.2. Comparison 3: Pain, Outcome 2: Difficulty levels defined by the success rate with landmark method

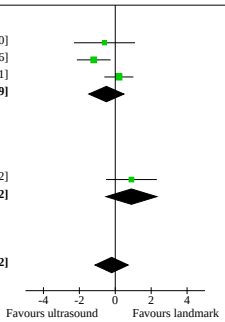


Study or Subgroup	Ultrasound Mean [NRS (0 - 10)]	Ultrasound SD [NRS (0 - 10)]	Ultrasound Total	Landmark Mean [NRS (0 - 10)]	Landmark SD [NRS (0 - 10)]	Landmark Total	Weight	Mean Difference IV, Random, 95% CI [NRS (0 - 10)]	Risk of Bias A B C D E F G
3.2.1 Difficult									
Weiner 2013	4.9	3.3	30	5.5	3	23	5.9%	-0.60 [-2.30 , 1.10]	+ + - + + + -
Ismailoğlu 2015	4.8	1.7	30	6	2	30	13.1%	-1.20 [-2.14 , -0.26]	- - - + ? + -
McCarthy 2016A	3.3	2.8	98	3.1	2.9	94	15.1%	0.20 [-0.61 , 1.01]	+ + - + + + -
Subtotal (95% CI)			**158**			**147**	**34.1%**	**-0.49 [-1.48 , 0.49]**	
Heterogeneity: Tau² = 0.44; Chi² = 4.96, df = 2 (P = 0.08); I² = 60%									
Test for overall effect: Z = 0.99 (P = 0.32)									
3.2.2 Moderate									
McCarthy 2016B	3.3	2.8	202	3.2	3	199	19.5%	0.10 [-0.47 , 0.67]	+ + - + + + -
Glasin 2020	1.8	1.6	45	1.9	2	45	16.1%	-0.10 [-0.85 , 0.65]	+ + - + + + -
Subtotal (95% CI)			**247**			**244**	**35.7%**	**0.03 [-0.43 , 0.48]**	
Heterogeneity: Tau² = 0.00; Chi² = 0.17, df = 1 (P = 0.68); I² = 0%									
Test for overall effect: Z = 0.12 (P = 0.91)									
3.2.3 Easy									
McCarthy 2016C	2.9	2.8	305	2.3	2.5	291	22.4%	0.60 [0.17 , 1.03]	+ + - + + + -
Subtotal (95% CI)			**305**			**291**	**22.4%**	**0.60 [0.17 , 1.03]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 2.76 (P = 0.006)									
3.2.4 No results on both first-pass and overall success of cannulation									
Pappas 2006	2.6	2.4	12	1.7	0.5	6	7.8%	0.90 [-0.52 , 2.32]	+ ? - - ? + -
Subtotal (95% CI)			**12**			**6**	**7.8%**	**0.90 [-0.52 , 2.32]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 1.25 (P = 0.21)									
Total (95% CI)			**722**			**688**	**100.0%**	**0.05 [-0.42 , 0.51]**	
Heterogeneity: Tau² = 0.21; Chi² = 14.44, df = 6 (P = 0.03); I² = 58%									
Test for overall effect: Z = 0.19 (P = 0.85)									
Test for subgroup differences: Chi² = 6.51, df = 3 (P = 0.09), I² = 53.9%									

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Pain
(D) Incomplete outcome data (attrition bias): Pain
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Pain

Analysis 3.3. Comparison 3: Pain, Outcome 3: Operators finished any training program for ultrasound-guided peripheral venous cannulation

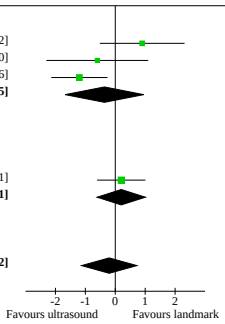
Study or Subgroup	Ultrasound Mean [NRS (1 - 10)]	Ultrasound SD [NRS (1 - 10)]	Ultrasound Total	Landmark Mean [NRS (1 - 10)]	Landmark SD [NRS (1 - 10)]	Landmark Total	Weight	Mean Difference IV, Random, 95% CI [NRS (1 - 10)]	Risk of Bias A B C D E F G
3.3.1 Finished									
Weiner 2013	4.9	3.3	30	5.5	3	23	17.4%	-0.60 [-2.30 , 1.10]	+ + - + + + -
Ismailoglu 2015	4.8	1.7	30	6	2	30	29.4%	-1.20 [-2.14 , -0.26]	- - - + ? + -
McCarthy 2016A	3.3	2.8	98	3.1	2.9	94	32.0%	0.20 [-0.61 , 1.01]	+ + - + + + -
Subtotal (95% CI)			**158**			**147**	**78.8%**	**-0.49 [-1.48 , 0.49]**	
Heterogeneity: Tau² = 0.44; Chi² = 4.96, df = 2 (P = 0.08); I² = 60%									
Test for overall effect: Z = 0.99 (P = 0.32)									
3.3.2 Not specified									
Pappas 2006	2.6	2.4	12	1.7	0.5	6	21.2%	0.90 [-0.52 , 2.32]	+ ? - - ? + -
Subtotal (95% CI)			**12**			**6**	**21.2%**	**0.90 [-0.52 , 2.32]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 1.25 (P = 0.21)									
Total (95% CI)			**170**			**153**	**100.0%**	**-0.20 [-1.13 , 0.72]**	
Heterogeneity: Tau² = 0.53; Chi² = 7.82, df = 3 (P = 0.05); I² = 62%									
Test for overall effect: Z = 0.43 (P = 0.67)									
Test for subgroup differences: Chi² = 2.52, df = 1 (P = 0.11), I² = 60.3%									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Pain
(D) Incomplete outcome data (attrition bias): Pain
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Pain

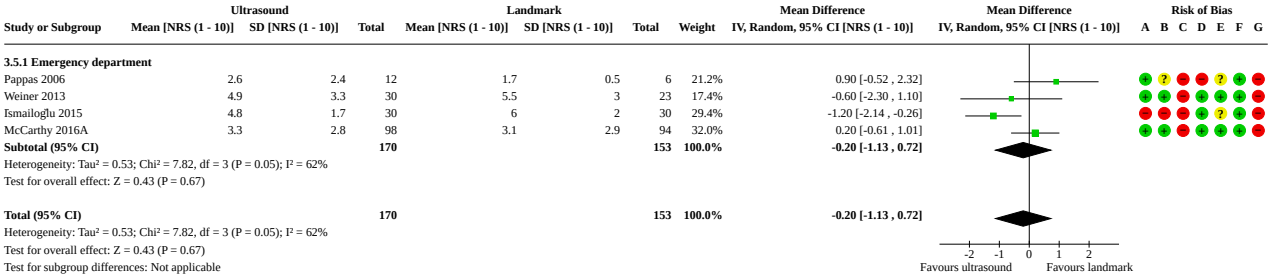
Analysis 3.4. Comparison 3: Pain, Outcome 4: Types of operators

Study or Subgroup	Ultrasound Mean [NRS (0 - 10)]	Ultrasound SD [NRS (0 - 10)]	Ultrasound Total	Landmark Mean [NRS (0 - 10)]	Landmark SD [NRS (0 - 10)]	Landmark Total	Weight	Mean Difference IV, Random, 95% CI [NRS (0 - 10)]	Risk of Bias A B C D E F G
3.4.1 Nurses									
Pappas 2006	2.6	2.4	12	1.7	0.5	6	21.2%	0.90 [-0.52 , 2.32]	+ ? - - ? + -
Weiner 2013	4.9	3.3	30	5.5	3	23	17.4%	-0.60 [-2.30 , 1.10]	+ + - + + + -
Ismailoglu 2015	4.8	1.7	30	6	2	30	29.4%	-1.20 [-2.14 , -0.26]	- - - + ? + -
Subtotal (95% CI)			**72**			**59**	**68.0%**	**-0.36 [-1.68 , 0.95]**	
Heterogeneity: Tau² = 0.88; Chi² = 5.87, df = 2 (P = 0.05); I² = 66%									
Test for overall effect: Z = 0.54 (P = 0.59)									
3.4.2 Technicians									
McCarthy 2016A	3.3	2.8	98	3.1	2.9	94	32.0%	0.20 [-0.61 , 1.01]	+ + - + + + -
Subtotal (95% CI)			**98**			**94**	**32.0%**	**0.20 [-0.61 , 1.01]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 0.49 (P = 0.63)									
Total (95% CI)			**170**			**153**	**100.0%**	**-0.20 [-1.13 , 0.72]**	
Heterogeneity: Tau² = 0.53; Chi² = 7.82, df = 3 (P = 0.05); I² = 62%									
Test for overall effect: Z = 0.43 (P = 0.67)									
Test for subgroup differences: Chi² = 0.51, df = 1 (P = 0.48), I² = 0%									



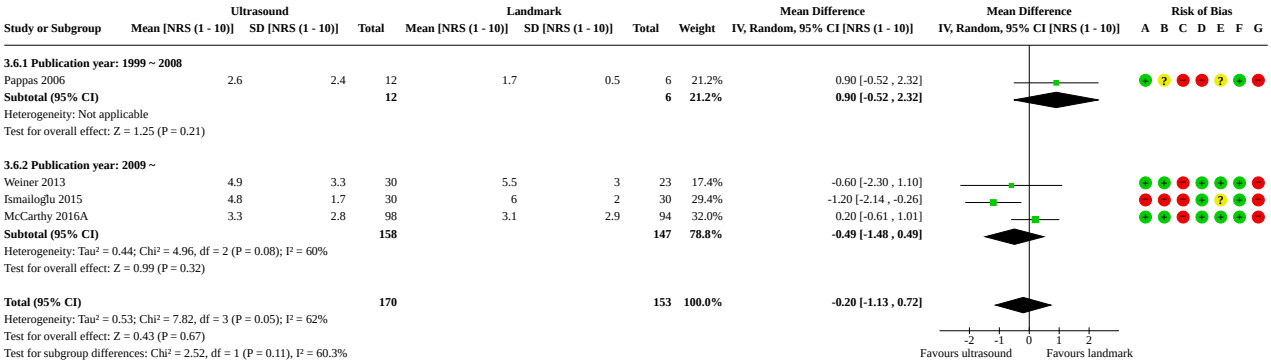
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Pain
(D) Incomplete outcome data (attrition bias): Pain
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Pain

Analysis 3.5. Comparison 3: Pain, Outcome 5: Setting



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Pain
(D) Incomplete outcome data (attrition bias): Pain
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Pain

Analysis 3.6. Comparison 3: Pain, Outcome 6: Year of publication



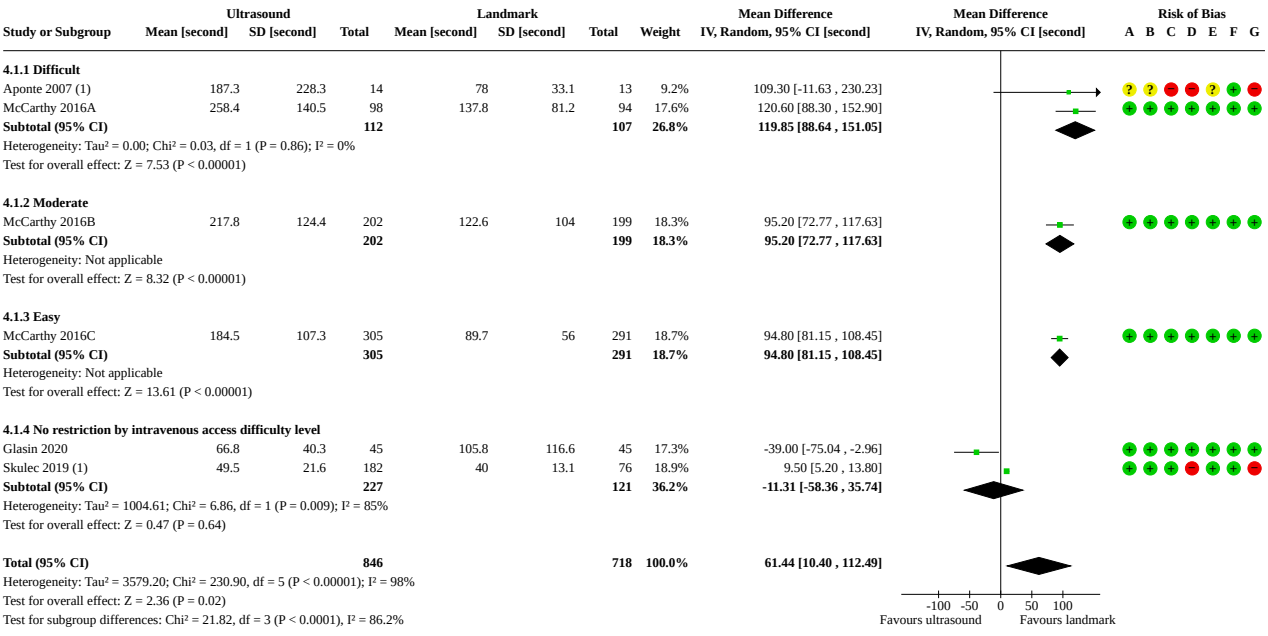
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Pain
(D) Incomplete outcome data (attrition bias): Pain
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Pain

Comparison 4. Procedure time for first-pass cannulation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.1 Difficulty levels defined by original studies	6	1564	Mean Difference (IV, Random, 95% CI)	61.44 [10.40, 112.49]
4.1.1 Difficult	2	219	Mean Difference (IV, Random, 95% CI)	119.85 [88.64, 151.05]
4.1.2 Moderate	1	401	Mean Difference (IV, Random, 95% CI)	95.20 [72.77, 117.63]
4.1.3 Easy	1	596	Mean Difference (IV, Random, 95% CI)	94.80 [81.15, 108.45]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.1.4 No restriction by intravenous access difficulty level	2	348	Mean Difference (IV, Random, 95% CI)	-11.31 [-58.36, 35.74]
4.2 Difficulty levels defined by the success rate with the landmark method	6	1564	Mean Difference (IV, Random, 95% CI)	61.44 [10.40, 112.49]
4.2.1 Difficult	1	192	Mean Difference (IV, Random, 95% CI)	120.60 [88.30, 152.90]
4.2.2 Moderate	3	749	Mean Difference (IV, Random, 95% CI)	23.01 [-39.89, 85.92]
4.2.3 Easy	2	623	Mean Difference (IV, Random, 95% CI)	94.98 [81.42, 108.55]

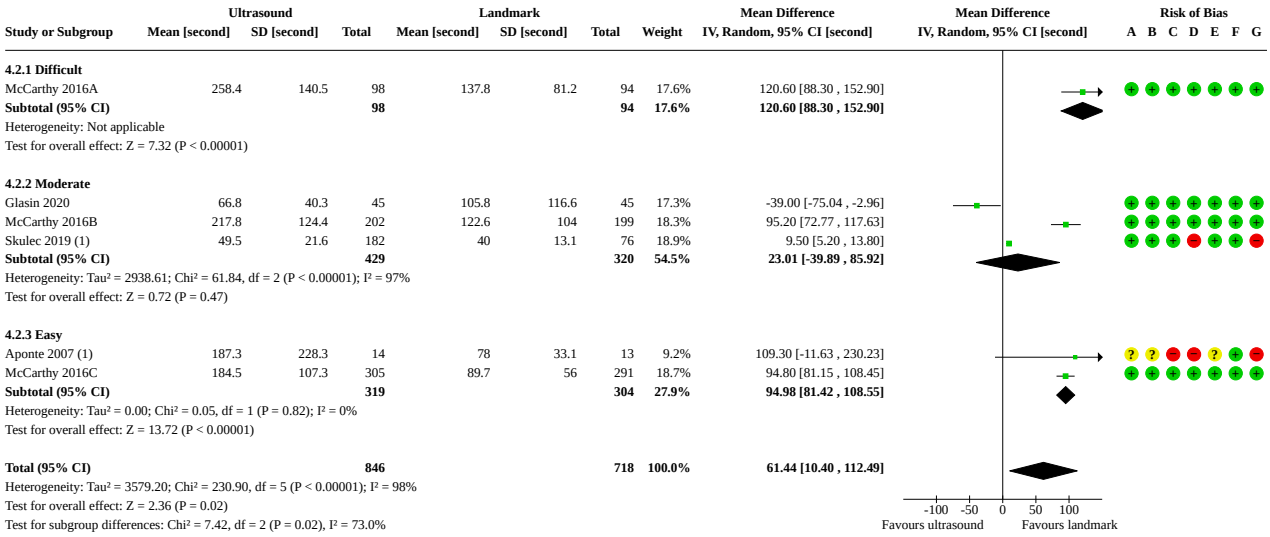
Analysis 4.1. Comparison 4: Procedure time for first-pass cannulation, Outcome 1: Difficulty levels defined by original studies



Footnotes
(1) Only for participants with successful cannulation

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Procedure time for first-pass cannulation
(D) Incomplete outcome data (attrition bias): Procedure time for first-pass cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Procedure time for first-pass cannulation

Analysis 4.2. Comparison 4: Procedure time for first-pass cannulation, Outcome 2: Difficulty levels defined by the success rate with the landmark method



Footnotes
(1) Only for participants with successful cannulation

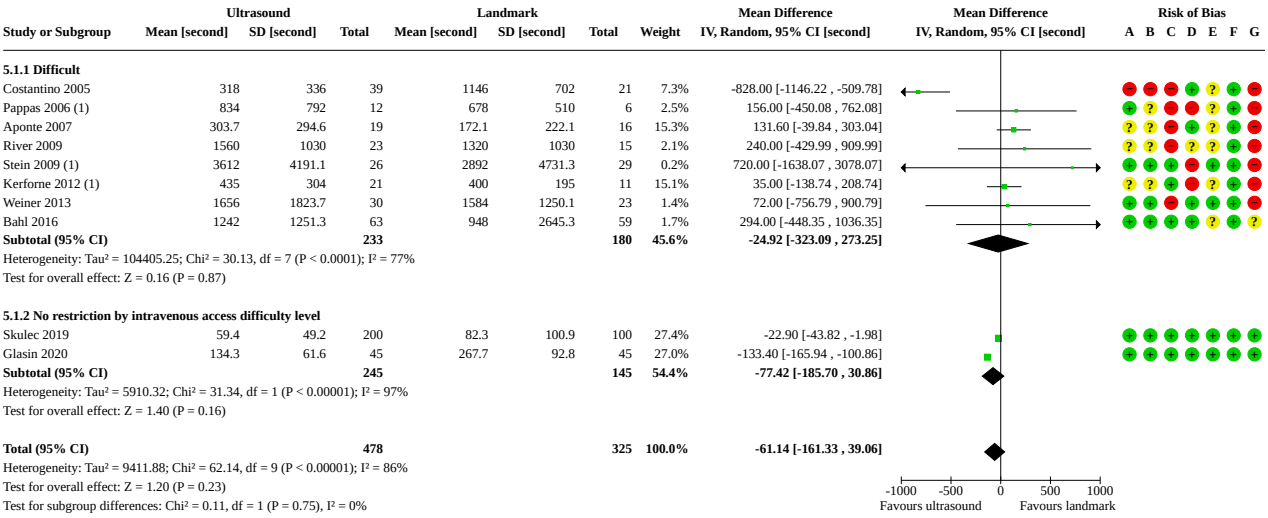
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Procedure time for first-pass cannulation
(D) Incomplete outcome data (attrition bias): Procedure time for first-pass cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Procedure time for first-pass cannulation

Comparison 5. Procedure time for overall cannulation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.1 Difficulty levels defined by original studies	10	803	Mean Difference (IV, Random, 95% CI)	-61.14 [-161.33, 39.06]
5.1.1 Difficult	8	413	Mean Difference (IV, Random, 95% CI)	-24.92 [-323.09, 273.25]
5.1.2 No restriction by intravenous access difficulty level	2	390	Mean Difference (IV, Random, 95% CI)	-77.42 [-185.70, 30.86]
5.2 Difficulty levels defined by the success rate with the landmark method	10	803	Mean Difference (IV, Random, 95% CI)	-61.14 [-161.33, 39.06]
5.2.1 Difficult	5	322	Mean Difference (IV, Random, 95% CI)	-116.99 [-662.82, 428.83]
5.2.2 Moderate	3	428	Mean Difference (IV, Random, 95% CI)	-69.79 [-176.18, 36.61]
5.2.3 Easy	1	35	Mean Difference (IV, Random, 95% CI)	131.60 [-39.84, 303.04]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.2.4 No data of the success rate	1	18	Mean Difference (IV, Random, 95% CI)	156.00 [-450.08, 762.08]

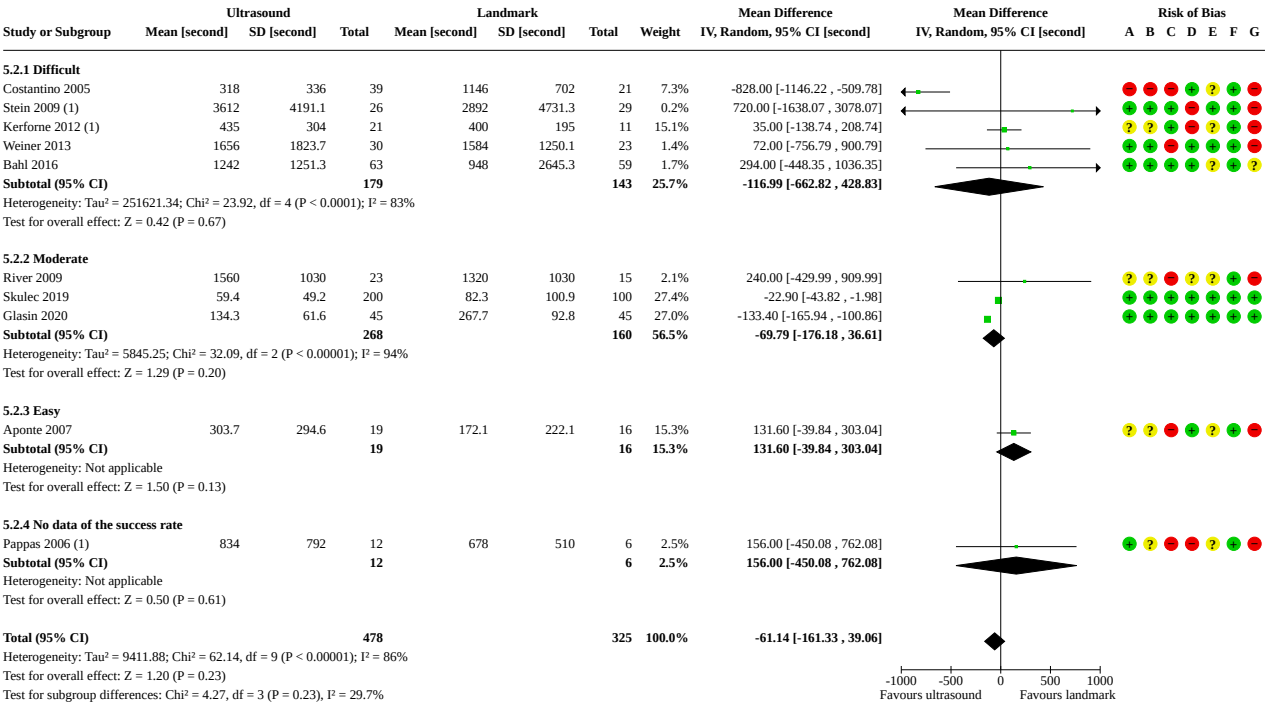
Analysis 5.1. Comparison 5: Procedure time for overall cannulation, Outcome 1: Difficulty levels defined by original studies



Footnotes
(1) Only for participants with successful cannulation

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Procedure time for overall cannulation
(D) Incomplete outcome data (attrition bias): Procedure time for overall cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Procedure time for overall cannulation

Analysis 5.2. Comparison 5: Procedure time for overall cannulation, Outcome 2: Difficulty levels defined by the success rate with the landmark method



Footnotes
(1) Only for participants with successful cannulation

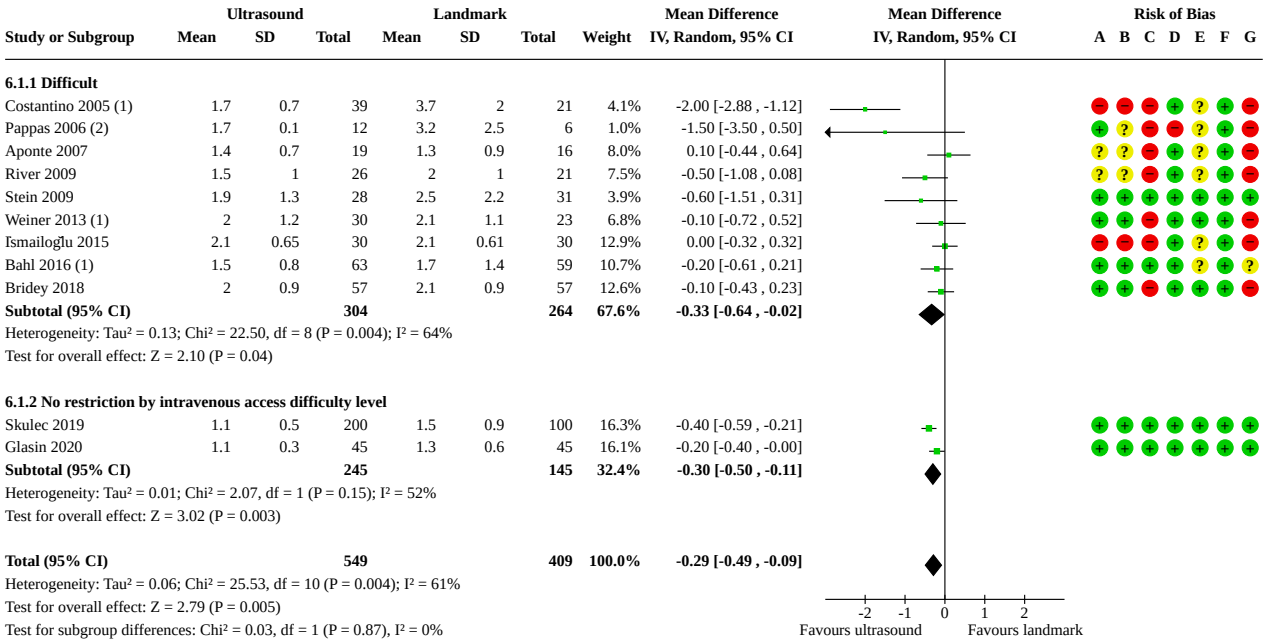
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Procedure time for overall cannulation
(D) Incomplete outcome data (attrition bias): Procedure time for overall cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Procedure time for overall cannulation

Comparison 6. Number of cannulation attempts

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6.1 Difficulty levels defined by original studies	11	958	Mean Difference (IV, Random, 95% CI)	-0.29 [-0.49, -0.09]
6.1.1 Difficult	9	568	Mean Difference (IV, Random, 95% CI)	-0.33 [-0.64, -0.02]
6.1.2 No restriction by intravenous access difficulty level	2	390	Mean Difference (IV, Random, 95% CI)	-0.30 [-0.50, -0.11]
6.2 Difficulty levels defined by the success rate with the landmark method	11	958	Mean Difference (IV, Random, 95% CI)	-0.29 [-0.49, -0.09]
6.2.1 Difficult	6	468	Mean Difference (IV, Random, 95% CI)	-0.36 [-0.75, 0.03]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6.2.2 Moderate	3	437	Mean Difference (IV, Random, 95% CI)	-0.32 [-0.47, -0.16]
6.2.3 Easy	1	35	Mean Difference (IV, Random, 95% CI)	0.10 [-0.44, 0.64]
6.2.4 No data of the success rate	1	18	Mean Difference (IV, Random, 95% CI)	-1.50 [-3.50, 0.50]

Analysis 6.1. Comparison 6: Number of cannulation attempts, Outcome 1: Difficulty levels defined by original studies



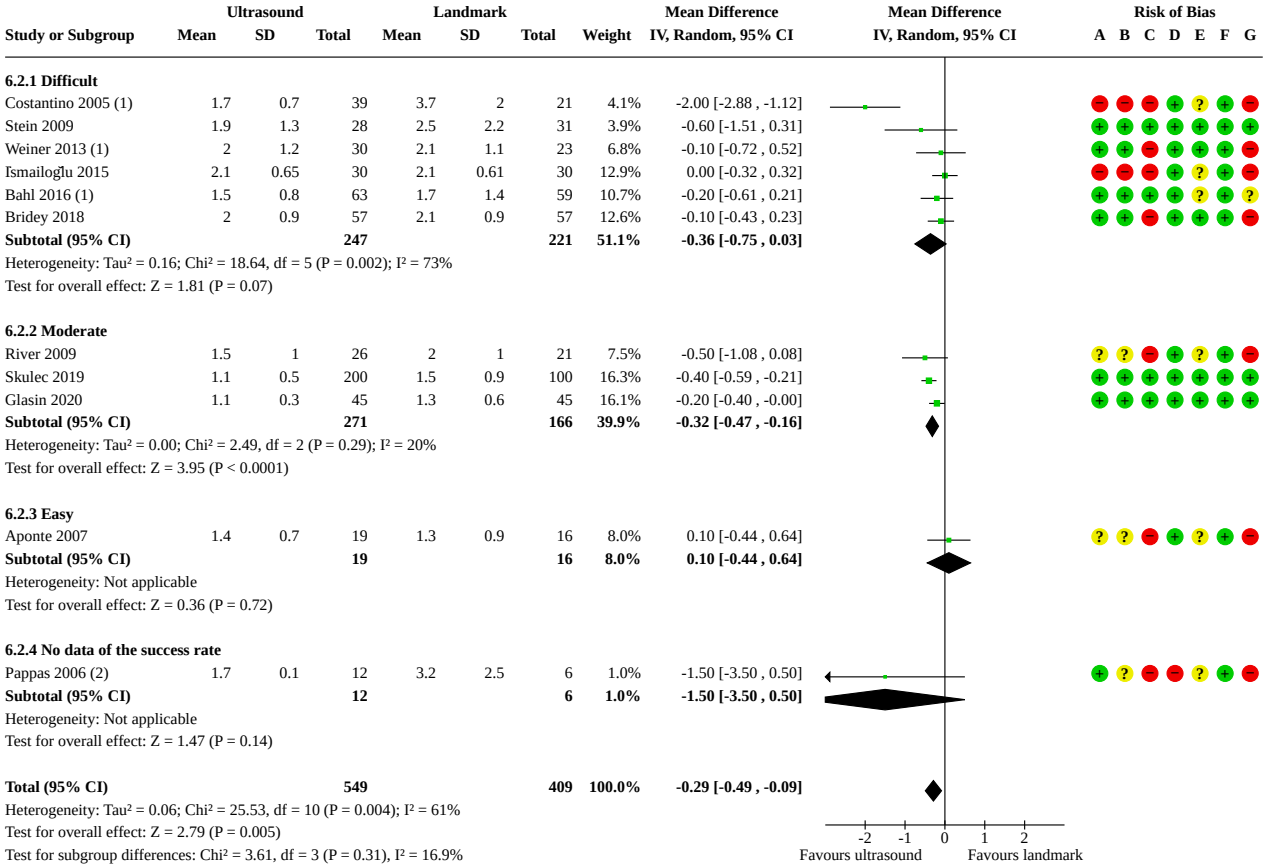
Footnotes

(1) Included the number of attempts taken when the assigned intervention failed and a different method was used
(2) Only for participants with successful cannulation

Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Number of attempts
(D) Incomplete outcome data (attrition bias): Number of attempts
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Number of attempts

Analysis 6.2. Comparison 6: Number of cannulation attempts, Outcome 2: Difficulty levels defined by the success rate with the landmark method



Footnotes

(1) Included the number of attempts taken when the assigned intervention failed and a different method was used
(2) Only for participants with successful cannulation

Risk of bias legend

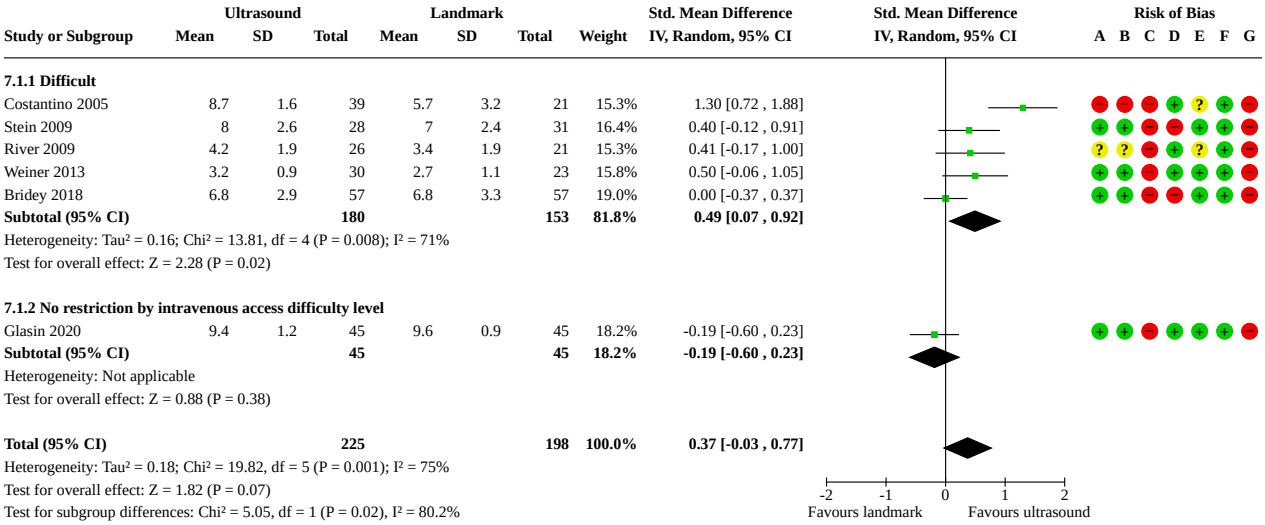
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Number of attempts
(D) Incomplete outcome data (attrition bias): Number of attempts
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Number of attempts

Comparison 7. Patient satisfaction

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.1 Difficulty levels defined by original studies	6	423	Std. Mean Difference (IV, Random, 95% CI)	0.37 [-0.03, 0.77]
7.1.1 Difficult	5	333	Std. Mean Difference (IV, Random, 95% CI)	0.49 [0.07, 0.92]
7.1.2 No restriction by intravenous access difficulty level	1	90	Std. Mean Difference (IV, Random, 95% CI)	-0.19 [-0.60, 0.23]

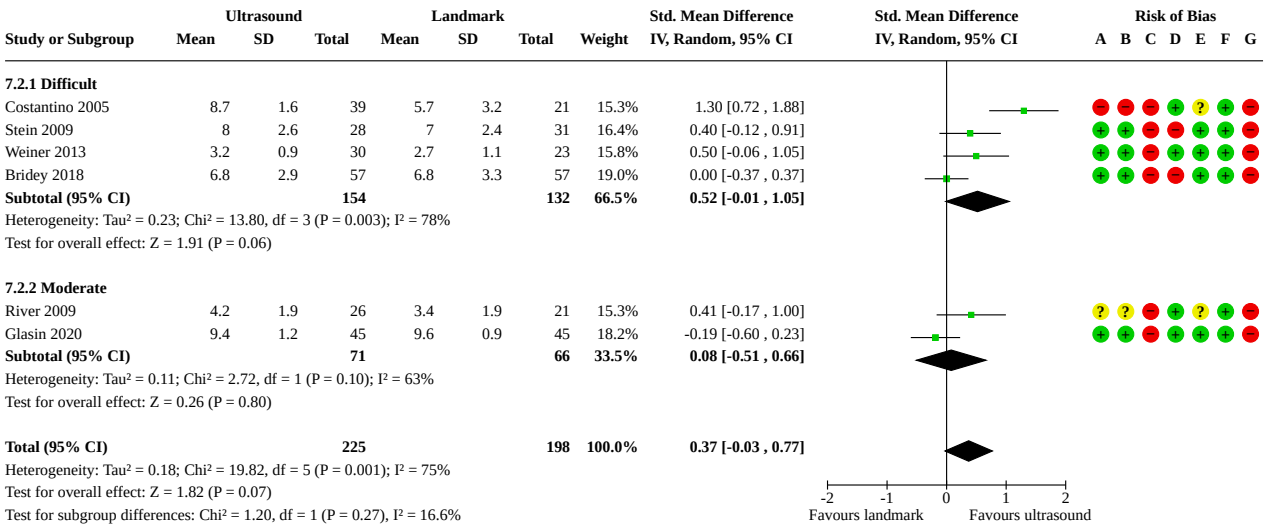
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.2 Difficulty levels defined by the success rate with the landmark method	6	423	Std. Mean Difference (IV, Random, 95% CI)	0.37 [-0.03, 0.77]
7.2.1 Difficult	4	286	Std. Mean Difference (IV, Random, 95% CI)	0.52 [-0.01, 1.05]
7.2.2 Moderate	2	137	Std. Mean Difference (IV, Random, 95% CI)	0.08 [-0.51, 0.66]

Analysis 7.1. Comparison 7: Patient satisfaction, Outcome 1: Difficulty levels defined by original studies



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Patient satisfaction
(D) Incomplete outcome data (attrition bias): Patient satisfaction
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Patient satisfaction

Analysis 7.2. Comparison 7: Patient satisfaction, Outcome 2: Difficulty levels defined by the success rate with the landmark method

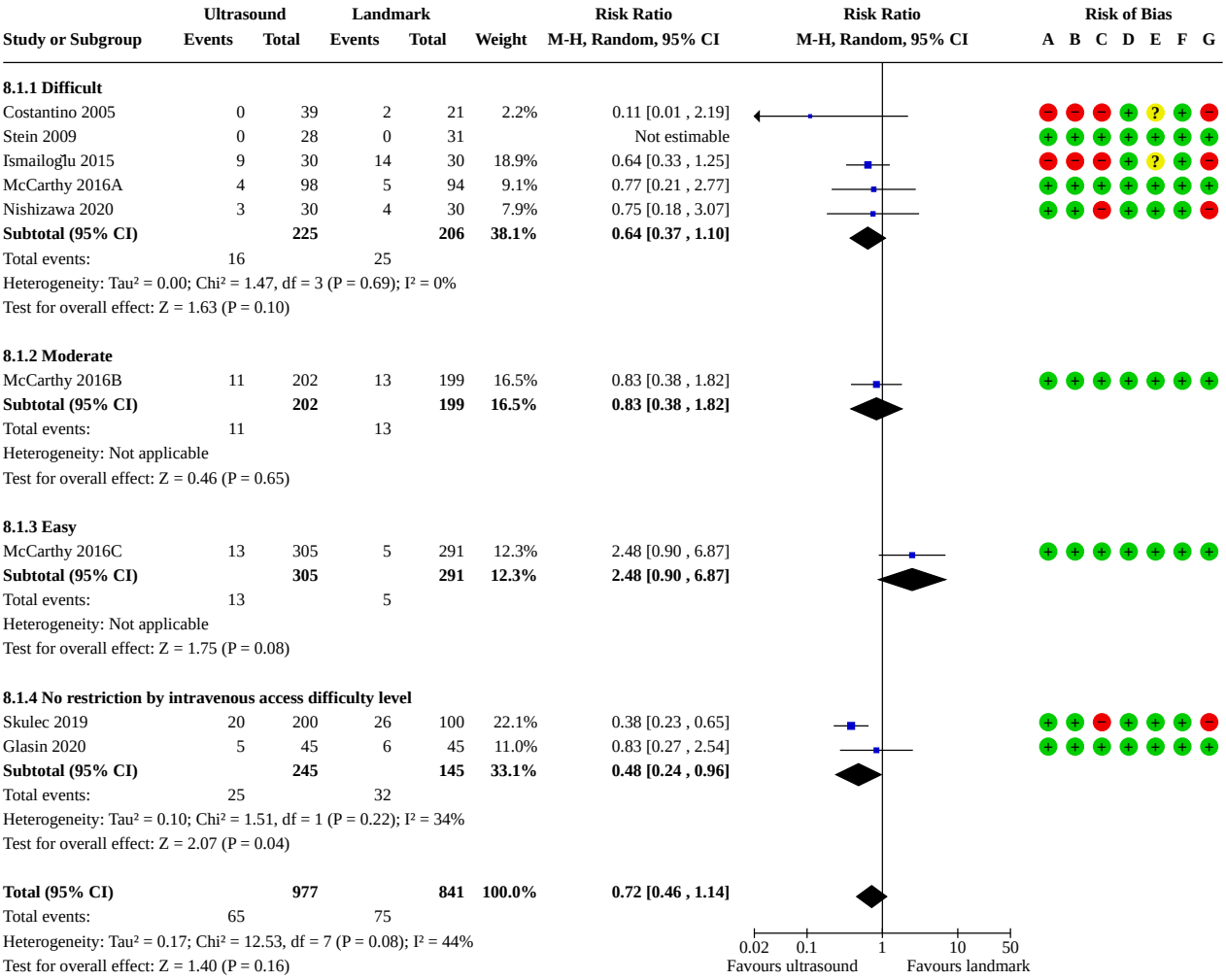


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Patient satisfaction
(D) Incomplete outcome data (attrition bias): Patient satisfaction
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Patient satisfaction

Comparison 8. Overall complications

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.1 Difficulty levels defined by original studies	9	1818	Risk Ratio (M-H, Random, 95% CI)	0.72 [0.46, 1.14]
8.1.1 Difficult	5	431	Risk Ratio (M-H, Random, 95% CI)	0.64 [0.37, 1.10]
8.1.2 Moderate	1	401	Risk Ratio (M-H, Random, 95% CI)	0.83 [0.38, 1.82]
8.1.3 Easy	1	596	Risk Ratio (M-H, Random, 95% CI)	2.48 [0.90, 6.87]
8.1.4 No restriction by intravenous access difficulty level	2	390	Risk Ratio (M-H, Random, 95% CI)	0.48 [0.24, 0.96]
8.2 Difficulty levels defined by the success rate with the landmark method	9	1818	Risk Ratio (M-H, Random, 95% CI)	0.72 [0.46, 1.14]
8.2.1 Difficult	5	431	Risk Ratio (M-H, Random, 95% CI)	0.64 [0.37, 1.10]
8.2.2 Moderate	3	791	Risk Ratio (M-H, Random, 95% CI)	0.58 [0.33, 1.02]
8.2.3 Easy	1	596	Risk Ratio (M-H, Random, 95% CI)	2.48 [0.90, 6.87]

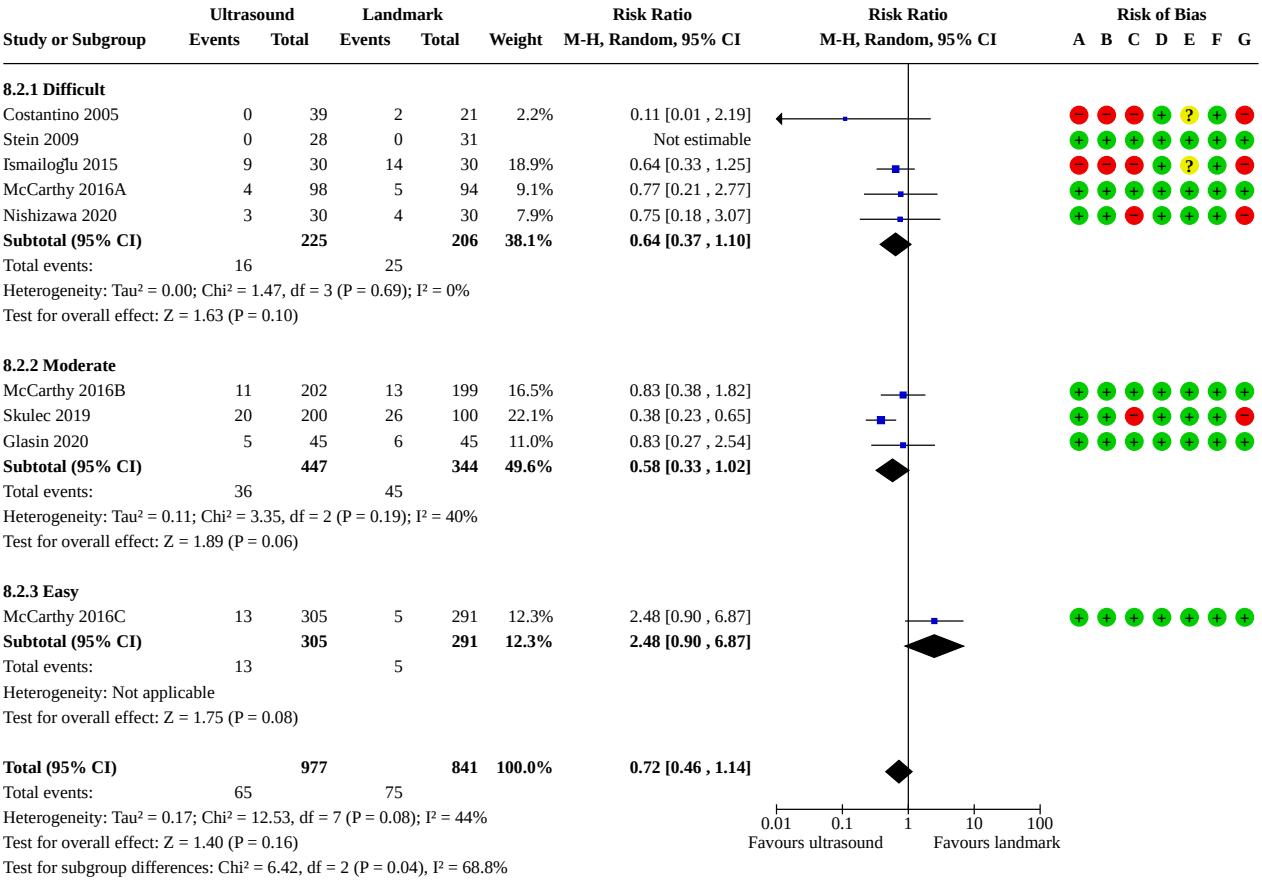
Analysis 8.1. Comparison 8: Overall complications, Outcome 1: Difficulty levels defined by original studies



Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Overall complications
(D) Incomplete outcome data (attrition bias): Overall complications
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Overall complications

Analysis 8.2. Comparison 8: Overall complications, Outcome 2: Difficulty levels defined by the success rate with the landmark method



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Overall complications
(D) Incomplete outcome data (attrition bias): Overall complications
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Overall complications

Comparison 9. Sensitivity analyses 1 (RCTs only)

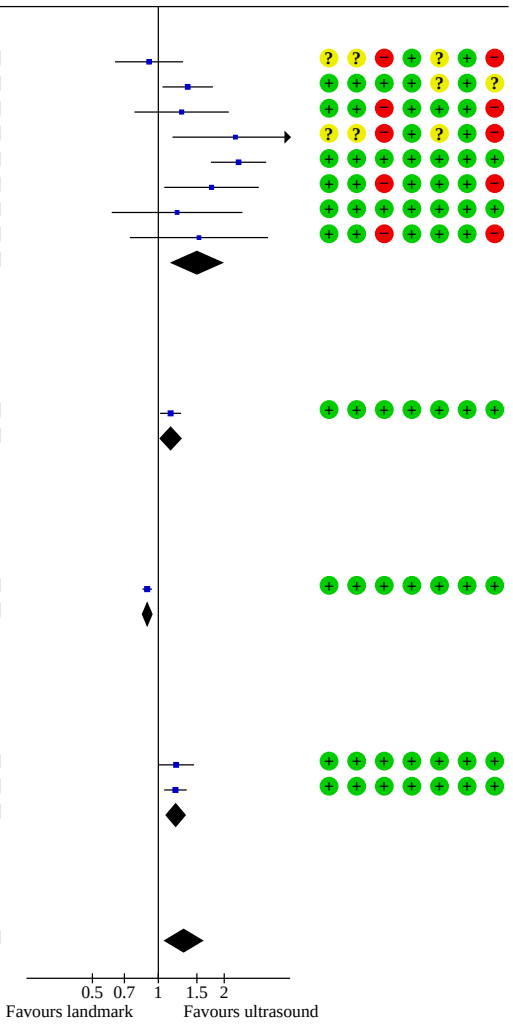
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
9.1 First-pass success of cannulation	12	2082	Risk Ratio (M-H, Random, 95% CI)	1.30 [1.07, 1.59]
9.1.1 Difficult	8	695	Risk Ratio (M-H, Random, 95% CI)	1.50 [1.15, 1.96]
9.1.2 Moderate	1	401	Risk Ratio (M-H, Random, 95% CI)	1.14 [1.02, 1.27]
9.1.3 Easy	1	596	Risk Ratio (M-H, Random, 95% CI)	0.89 [0.85, 0.94]
9.1.4 No restriction by intravenous access difficulty level	2	390	Risk Ratio (M-H, Random, 95% CI)	1.20 [1.09, 1.33]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
9.2 Overall success of cannulation	8	728	Risk Ratio (M-H, Random, 95% CI)	1.13 [1.00, 1.27]
9.2.1 Difficult	7	428	Risk Ratio (M-H, Random, 95% CI)	1.19 [0.98, 1.45]
9.2.2 No restriction by intravenous access difficulty level	1	300	Risk Ratio (M-H, Random, 95% CI)	1.10 [1.03, 1.18]
9.3 Pain	5	1260	Mean Difference (IV, Random, 95% CI)	0.38 [0.08, 0.68]
9.3.1 Difficult	3	263	Mean Difference (IV, Random, 95% CI)	0.23 [-0.42, 0.88]
9.3.2 Moderate	1	401	Mean Difference (IV, Random, 95% CI)	0.10 [-0.47, 0.67]
9.3.3 Easy	1	596	Mean Difference (IV, Random, 95% CI)	0.60 [0.17, 1.03]
9.4 Procedure time for first-pass cannulation	6	1564	Mean Difference (IV, Random, 95% CI)	61.44 [10.40, 112.49]
9.4.1 Difficult	2	219	Mean Difference (IV, Random, 95% CI)	119.85 [88.64, 151.05]
9.4.2 Moderate	1	401	Mean Difference (IV, Random, 95% CI)	95.20 [72.77, 117.63]
9.4.3 Easy	1	596	Mean Difference (IV, Random, 95% CI)	94.80 [81.15, 108.45]
9.4.4 No restriction by intravenous access difficulty level	2	348	Mean Difference (IV, Random, 95% CI)	-11.31 [-58.36, 35.74]
9.5 Procedure time for overall cannulation	9	743	Mean Difference (IV, Random, 95% CI)	-14.82 [-100.35, 70.72]
9.5.1 Difficult	7	353	Mean Difference (IV, Random, 95% CI)	97.47 [-17.58, 212.52]
9.5.2 No restriction by intravenous access difficulty level	2	390	Mean Difference (IV, Random, 95% CI)	-77.42 [-185.70, 30.86]
9.6 Number of cannulation attempts	8	748	Mean Difference (IV, Random, 95% CI)	-0.29 [-0.43, -0.15]
9.6.1 Difficult	7	448	Mean Difference (IV, Random, 95% CI)	-0.17 [-0.36, 0.03]
9.6.2 No restriction by intravenous access difficulty level	1	300	Mean Difference (IV, Random, 95% CI)	-0.40 [-0.59, -0.21]
9.7 Patient satisfaction	5	363	Std. Mean Difference (IV, Random, 95% CI)	0.17 [-0.10, 0.44]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
9.7.1 Difficult	4	273	Std. Mean Difference (IV, Random, 95% CI)	0.25 [0.01, 0.50]
9.7.2 No restriction by intravenous access difficulty level	1	90	Std. Mean Difference (IV, Random, 95% CI)	-0.19 [-0.60, 0.23]
9.8 Overall complications	7	1698	Risk Ratio (M-H, Random, 95% CI)	0.80 [0.45, 1.43]
9.8.1 Difficult	3	311	Risk Ratio (M-H, Random, 95% CI)	0.76 [0.29, 1.96]
9.8.2 Moderate	1	401	Risk Ratio (M-H, Random, 95% CI)	0.83 [0.38, 1.82]
9.8.3 Easy	1	596	Risk Ratio (M-H, Random, 95% CI)	2.48 [0.90, 6.87]
9.8.4 No restriction by intravenous access difficulty level	2	390	Risk Ratio (M-H, Random, 95% CI)	0.48 [0.24, 0.96]

Analysis 9.1. Comparison 9: Sensitivity analyses 1 (RCTs only), Outcome 1: First-pass success of cannulation

Study or Subgroup	Ultrasound Events	Ultrasound Total	Landmark Events	Landmark Total	Weight	Risk Ratio M-H, Random, 95% CI
9.1.1 Difficult						
Aponte 2007	14	19	13	16	8.5%	0.91 [0.63 , 1.30]
Bahl 2016	48	63	33	59	9.7%	1.36 [1.04 , 1.78]
Bridey 2018	23	57	18	57	6.7%	1.28 [0.78 , 2.10]
Kerforne 2012	18	30	8	30	5.1%	2.25 [1.16 , 4.36]
McCarthy 2016A	80	98	33	94	9.3%	2.33 [1.74 , 3.11]
Nishizawa 2020	21	30	12	30	6.7%	1.75 [1.06 , 2.88]
Stein 2009	11	28	10	31	4.9%	1.22 [0.61 , 2.42]
Weiner 2013	14	30	7	23	4.5%	1.53 [0.74 , 3.17]
Subtotal (95% CI)		**355**		**340**	**55.4%**	**1.50 [1.15 , 1.96]**
Total events:	229		134			
Heterogeneity: Tau² = 0.09; Chi² = 20.43, df = 7 (P = 0.005); I² = 66%						
Test for overall effect: Z = 2.96 (P = 0.003)						
9.1.2 Moderate						
McCarthy 2016B	164	202	142	199	11.3%	1.14 [1.02 , 1.27]
Subtotal (95% CI)		**202**		**199**	**11.3%**	**1.14 [1.02 , 1.27]**
Total events:	164		142			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.29 (P = 0.02)						
9.1.3 Easy						
McCarthy 2016C	262	305	281	291	11.6%	0.89 [0.85 , 0.94]
Subtotal (95% CI)		**305**		**291**	**11.6%**	**0.89 [0.85 , 0.94]**
Total events:	262		281			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.55 (P < 0.00001)						
9.1.4 No restriction by intravenous access difficulty level						
Glasin 2020	41	45	34	45	10.5%	1.21 [1.00 , 1.46]
Skulec 2019	182	200	76	100	11.2%	1.20 [1.06 , 1.35]
Subtotal (95% CI)		**245**		**145**	**21.7%**	**1.20 [1.09 , 1.33]**
Total events:	223		110			
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.95); I² = 0%						
Test for overall effect: Z = 3.55 (P = 0.0004)						
Total (95% CI)		**1107**		**975**	**100.0%**	**1.30 [1.07 , 1.59]**
Total events:	878		667			
Heterogeneity: Tau² = 0.09; Chi² = 130.28, df = 11 (P < 0.00001); I² = 92%						
Test for overall effect: Z = 2.63 (P = 0.009)						
Test for subgroup differences: Chi² = 46.49, df = 3 (P < 0.00001), I² = 93.5%						

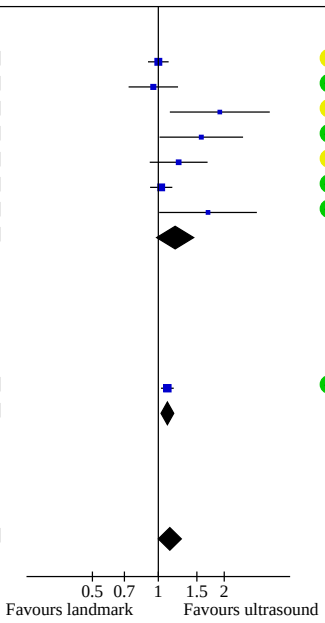


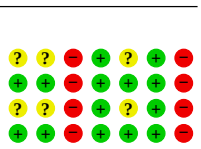
Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): First-pass success of cannulation
(D) Incomplete outcome data (attrition bias): First-pass success of cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: First-pass success of cannulation

Analysis 9.2. Comparison 9: Sensitivity analyses 1 (RCTs only), Outcome 2: Overall success of cannulation

Study or Subgroup	Ultrasound Events	Ultrasound Total	Landmark Events	Landmark Total	Weight	Risk Ratio M-H, Random, 95% CI
9.2.1 Difficult						
Aponte 2007	19	19	16	16	20.7%	1.00 [0.90 , 1.11]
Bridey 2018	37	57	39	57	11.6%	0.95 [0.73 , 1.23]
Kerforne 2012	21	30	11	30	4.4%	1.91 [1.13 , 3.23]
Nishizawa 2020	22	30	14	30	5.8%	1.57 [1.01 , 2.44]
River 2009	23	26	15	21	9.7%	1.24 [0.91 , 1.68]
Stein 2009	27	28	29	31	20.2%	1.03 [0.92 , 1.16]
Weiner 2013	22	30	10	23	4.5%	1.69 [1.01 , 2.82]
Subtotal (95% CI)		**220**		**208**	**76.9%**	**1.19 [0.98 , 1.45]**
Total events:	171		134			
Heterogeneity: Tau² = 0.04; Chi² = 28.04, df = 6 (P < 0.0001); I² = 79%						
Test for overall effect: Z = 1.78 (P = 0.07)						
9.2.2 No restriction by intravenous access difficulty level						
Skulec 2019	198	200	90	100	23.1%	1.10 [1.03 , 1.18]
Subtotal (95% CI)		**200**		**100**	**23.1%**	**1.10 [1.03 , 1.18]**
Total events:	198		90			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.80 (P = 0.005)						
Total (95% CI)		**420**		**308**	**100.0%**	**1.13 [1.00 , 1.27]**
Total events:	369		224			
Heterogeneity: Tau² = 0.02; Chi² = 22.90, df = 7 (P = 0.002); I² = 69%						
Test for overall effect: Z = 1.96 (P = 0.05)						
Test for subgroup differences: Chi² = 0.61, df = 1 (P = 0.44), I² = 0%						



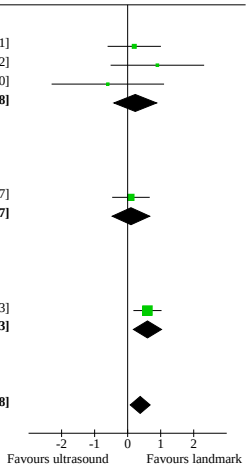


Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Overall-success of cannulation
(D) Incomplete outcome data (attrition bias): Overall success of cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Overall success of cannulation

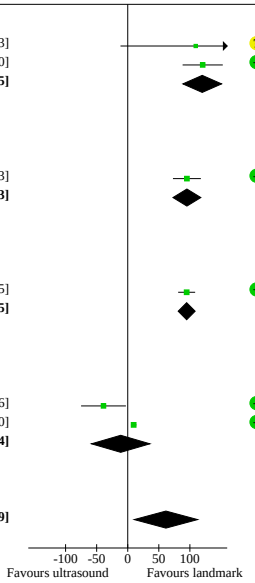
Analysis 9.3. Comparison 9: Sensitivity analyses 1 (RCTs only), Outcome 3: Pain

Study or Subgroup	Ultrasound Mean [NRS (0 - 10)]	Ultrasound SD [NRS (0 - 10)]	Ultrasound Total	Landmark Mean [NRS (0 - 10)]	Landmark SD [NRS (0 - 10)]	Landmark Total	Weight	Mean Difference IV, Random, 95% CI [NRS (0 - 10)]
9.3.1 Difficult								
McCarthy 2016A	3.3	2.8	98	3.1	2.9	94	14.0%	0.20 [-0.61 , 1.01]
Pappas 2006	2.6	2.4	12	1.7	0.5	6	4.5%	0.90 [-0.52 , 2.32]
Weiner 2013	4.9	3.3	30	5.5	3	23	3.1%	-0.60 [-2.30 , 1.10]
Subtotal (95% CI)			**140**			**123**	**21.6%**	**0.23 [-0.42 , 0.88]**
Heterogeneity: Tau² = 0.00; Chi² = 1.78, df = 2 (P = 0.41); I² = 0%								
Test for overall effect: Z = 0.70 (P = 0.49)								
9.3.2 Moderate								
McCarthy 2016B	3.3	2.8	202	3.2	3	199	28.2%	0.10 [-0.47 , 0.67]
Subtotal (95% CI)			**202**			**199**	**28.2%**	**0.10 [-0.47 , 0.67]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.34 (P = 0.73)								
9.3.3 Easy								
McCarthy 2016C	2.9	2.8	305	2.3	2.5	291	50.2%	0.60 [0.17 , 1.03]
Subtotal (95% CI)			**305**			**291**	**50.2%**	**0.60 [0.17 , 1.03]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.76 (P = 0.006)								
Total (95% CI)			**647**			**613**	**100.0%**	**0.38 [0.08 , 0.68]**
Heterogeneity: Tau² = 0.00; Chi² = 3.94, df = 4 (P = 0.41); I² = 0%								
Test for overall effect: Z = 2.46 (P = 0.01)								
Test for subgroup differences: Chi² = 2.16, df = 2 (P = 0.34), I² = 7.5%								



Analysis 9.4. Comparison 9: Sensitivity analyses 1 (RCTs only), Outcome 4: Procedure time for first-pass cannulation

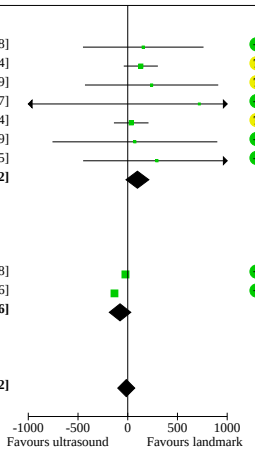
Study or Subgroup	Ultrasound Mean [second]	Ultrasound SD [second]	Ultrasound Total	Landmark Mean [second]	Landmark SD [second]	Landmark Total	Weight	Mean Difference IV, Random, 95% CI [second]
9.4.1 Difficult								
Aponte 2007	187.3	228.3	14	78	33.1	13	9.2%	109.30 [-11.63 , 230.23]
McCarthy 2016A	258.4	140.5	98	137.8	81.2	94	17.6%	120.60 [88.30 , 152.90]
Subtotal (95% CI)			**112**			**107**	**26.8%**	**119.85 [88.64 , 151.05]**
Heterogeneity: Tau² = 0.00; Chi² = 0.03, df = 1 (P = 0.86); I² = 0%								
Test for overall effect: Z = 7.53 (P < 0.00001)								
9.4.2 Moderate								
McCarthy 2016B	217.8	124.4	202	122.6	104	199	18.3%	95.20 [72.77 , 117.63]
Subtotal (95% CI)			**202**			**199**	**18.3%**	**95.20 [72.77 , 117.63]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 8.32 (P < 0.00001)								
9.4.3 Easy								
McCarthy 2016C	184.5	107.3	305	89.7	56	291	18.7%	94.80 [81.15 , 108.45]
Subtotal (95% CI)			**305**			**291**	**18.7%**	**94.80 [81.15 , 108.45]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 13.61 (P < 0.00001)								
9.4.4 No restriction by intravenous access difficulty level								
Glasin 2020	66.8	40.3	45	105.8	116.6	45	17.3%	-39.00 [-75.04 , -2.96]
Skulec 2019	49.5	21.6	182	40	13.1	76	18.9%	9.50 [5.20 , 13.80]
Subtotal (95% CI)			**227**			**121**	**36.2%**	**-11.31 [-58.36 , 35.74]**
Heterogeneity: Tau² = 1004.61; Chi² = 6.86, df = 1 (P = 0.009); I² = 85%								
Test for overall effect: Z = 0.47 (P = 0.64)								
Total (95% CI)			**846**			**718**	**100.0%**	**61.44 [10.40 , 112.49]**
Heterogeneity: Tau² = 3579.20; Chi² = 230.90, df = 5 (P < 0.00001); I² = 98%								
Test for overall effect: Z = 2.36 (P = 0.02)								
Test for subgroup differences: Chi² = 21.82, df = 3 (P < 0.0001), I² = 86.2%								

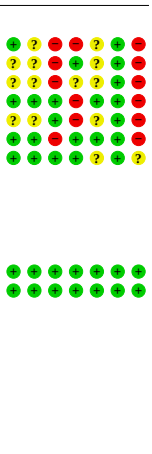


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Procedure time for first-pass cannulation
(D) Incomplete outcome data (attrition bias): Procedure time for first-pass cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Procedure time for first-pass cannulation

Analysis 9.5. Comparison 9: Sensitivity analyses 1 (RCTs only), Outcome 5: Procedure time for overall cannulation

Study or Subgroup	Ultrasound Mean [second]	Ultrasound SD [second]	Ultrasound Total	Landmark Mean [second]	Landmark SD [second]	Landmark Total	Weight	Mean Difference IV, Random, 95% CI [second]
9.5.1 Difficult								
Pappas 2006	834	792	12	678	510	6	1.9%	156.00 [-450.08 , 762.08]
Aponte 2007	303.7	294.6	19	172.1	222.1	16	14.4%	131.60 [-39.84 , 303.04]
River 2009	1560	1030	23	1320	1030	15	1.6%	240.00 [-429.99 , 909.99]
Stein 2009	3612	4191.1	26	2892	4731.3	29	0.1%	720.00 [-1638.07 , 3078.07]
Kerforne 2012	435	304	21	400	195	11	14.1%	35.00 [-138.74 , 208.74]
Weiner 2013	1656	1823.7	30	1584	1250.1	23	1.0%	72.00 [-756.79 , 900.79]
Bahl 2016	1242	1251.3	63	948	2645.3	59	1.3%	294.00 [-448.35 , 1036.35]
Subtotal (95% CI)			**194**			**159**	**34.4%**	**97.47 [-17.58 , 212.52]**
Heterogeneity: Tau² = 0.00; Chi² = 1.40, df = 6 (P = 0.97); I² = 0%								
Test for overall effect: Z = 1.66 (P = 0.10)								
9.5.2 No restriction by intravenous access difficulty level								
Skulec 2019	59.4	49.2	200	82.3	100.9	100	33.3%	-22.90 [-43.82 , -1.98]
Glasin 2020	134.3	61.6	45	267.7	92.8	45	32.4%	-133.40 [-165.94 , -100.86]
Subtotal (95% CI)			**245**			**145**	**65.6%**	**-77.42 [-185.70 , 30.86]**
Heterogeneity: Tau² = 5910.32; Chi² = 31.34, df = 1 (P < 0.00001); I² = 97%								
Test for overall effect: Z = 1.40 (P = 0.16)								
Total (95% CI)			**439**			**304**	**100.0%**	**-14.82 [-100.35 , 70.72]**
Heterogeneity: Tau² = 5611.01; Chi² = 39.35, df = 8 (P < 0.00001); I² = 80%								
Test for overall effect: Z = 0.34 (P = 0.73)								
Test for subgroup differences: Chi² = 4.71, df = 1 (P = 0.03), I² = 78.8%								

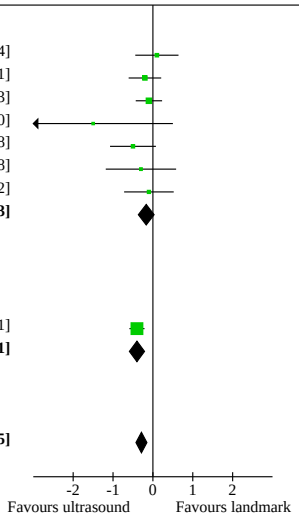




Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Procedure time for overall cannulation
(D) Incomplete outcome data (attrition bias): Procedure time for overall cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Procedure time for overall cannulation

Analysis 9.6. Comparison 9: Sensitivity analyses 1 (RCTs only), Outcome 6: Number of cannulation attempts

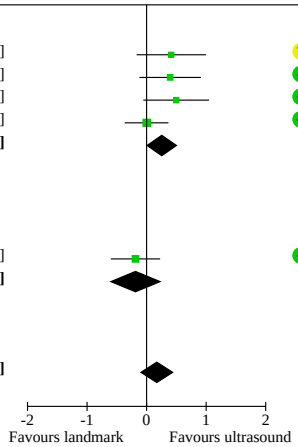
Study or Subgroup	Ultrasound Mean	Ultrasound SD	Ultrasound Total	Landmark Mean	Landmark SD	Landmark Total	Weight	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
9.6.1 Difficult									
Aponte 2007	1.4	0.7	19	1.3	0.9	16	6.4%	0.10 [-0.44 , 0.64]	? ? − + ? + −
Bahl 2016	1.5	0.8	63	1.7	1.4	59	11.3%	-0.20 [-0.61 , 0.21]	+ + + + ? + ?
Bridey 2018	2	0.9	57	2.1	0.9	57	17.2%	-0.10 [-0.43 , 0.23]	+ + − + + + −
Pappas 2006	1.7	0.1	12	3.2	2.5	6	0.5%	-1.50 [-3.50 , 0.50]	+ ? − − ? + −
River 2009	1.5	1	26	2	1	21	5.7%	-0.50 [-1.08 , 0.08]	? ? − + ? + −
Stein 2009	2.1	1.3	28	2.4	2.1	31	2.4%	-0.30 [-1.18 , 0.58]	+ + + + + + +
Weiner 2013	2	1.2	30	2.1	1.1	23	4.9%	-0.10 [-0.72 , 0.52]	+ + − + + + −
Subtotal (95% CI)			**235**			**213**	**48.3%**	**-0.17 [-0.36 , 0.03]**	
Heterogeneity: Tau² = 0.00; Chi² = 4.24, df = 6 (P = 0.64); I² = 0%									
Test for overall effect: Z = 1.66 (P = 0.10)									
9.6.2 No restriction by intravenous access difficulty level									
Skulec 2019	1.1	0.5	200	1.5	0.9	100	51.7%	-0.40 [-0.59 , -0.21]	+ + + + + + +
Subtotal (95% CI)			**200**			**100**	**51.7%**	**-0.40 [-0.59 , -0.21]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 4.14 (P < 0.0001)									
Total (95% CI)			**435**			**313**	**100.0%**	**-0.29 [-0.43 , -0.15]**	
Heterogeneity: Tau² = 0.00; Chi² = 7.02, df = 7 (P = 0.43); I² = 0%									
Test for overall effect: Z = 4.11 (P < 0.0001)									
Test for subgroup differences: Chi² = 2.78, df = 1 (P = 0.10), I² = 64.0%									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Number of attempts
(D) Incomplete outcome data (attrition bias): Number of attempts
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Number of attempts

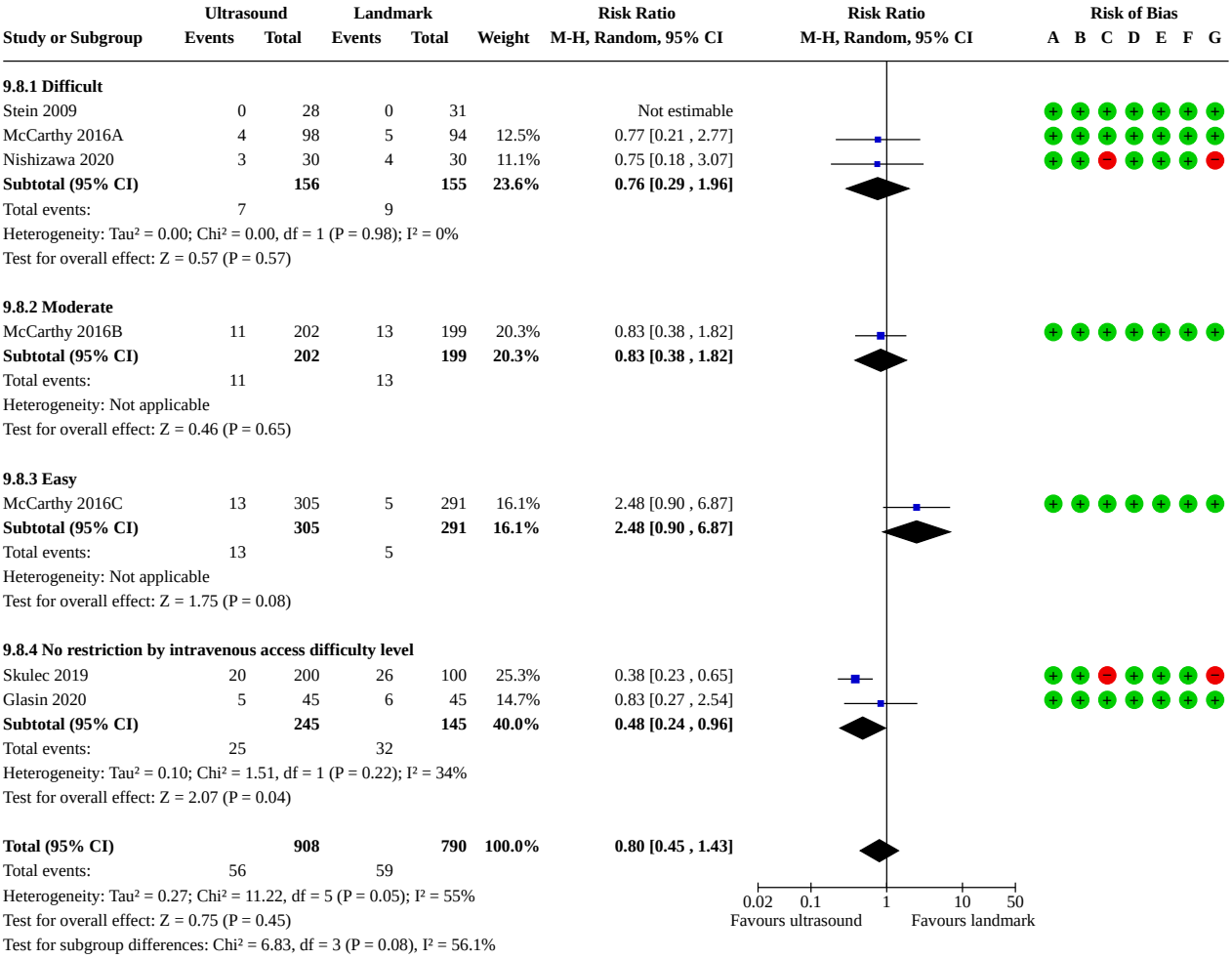
Analysis 9.7. Comparison 9: Sensitivity analyses 1 (RCTs only), Outcome 7: Patient satisfaction

Study or Subgroup	Ultrasound Mean	Ultrasound SD	Ultrasound Total	Landmark Mean	Landmark SD	Landmark Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
9.7.1 Difficult									
River 2009	4.2	1.9	26	3.4	1.9	21	15.2%	0.41 [-0.17 , 1.00]	? ? − + ? + −
Stein 2009	8	2.6	28	7	2.4	31	18.0%	0.40 [-0.12 , 0.91]	+ + − − + + −
Weiner 2013	3.2	0.9	30	2.7	1.1	23	16.4%	0.50 [-0.06 , 1.05]	+ + − + + + −
Bridey 2018	6.8	2.9	57	6.8	3.3	57	26.9%	0.00 [-0.37 , 0.37]	+ + − − + + −
Subtotal (95% CI)			**141**			**132**	**76.4%**	**0.25 [0.01 , 0.50]**	
Heterogeneity: Tau² = 0.00; Chi² = 3.16, df = 3 (P = 0.37); I² = 5%									
Test for overall effect: Z = 2.02 (P = 0.04)									
9.7.2 No restriction by intravenous access difficulty level									
Glasin 2020	9.4	1.2	45	9.6	0.9	45	23.6%	-0.19 [-0.60 , 0.23]	+ + − + + + −
Subtotal (95% CI)			**45**			**45**	**23.6%**	**-0.19 [-0.60 , 0.23]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 0.88 (P = 0.38)									
Total (95% CI)			**186**			**177**	**100.0%**	**0.17 [-0.10 , 0.44]**	
Heterogeneity: Tau² = 0.03; Chi² = 6.35, df = 4 (P = 0.17); I² = 37%									
Test for overall effect: Z = 1.26 (P = 0.21)									
Test for subgroup differences: Chi² = 3.22, df = 1 (P = 0.07), I² = 68.9%									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Patient satisfaction
(D) Incomplete outcome data (attrition bias): Patient satisfaction
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Patient satisfaction

Analysis 9.8. Comparison 9: Sensitivity analyses 1 (RCTs only), Outcome 8: Overall complications



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Overall complications
(D) Incomplete outcome data (attrition bias): Overall complications
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Overall complications

Comparison 10. Sensitivity analysis 2 (low risk of bias studies only)

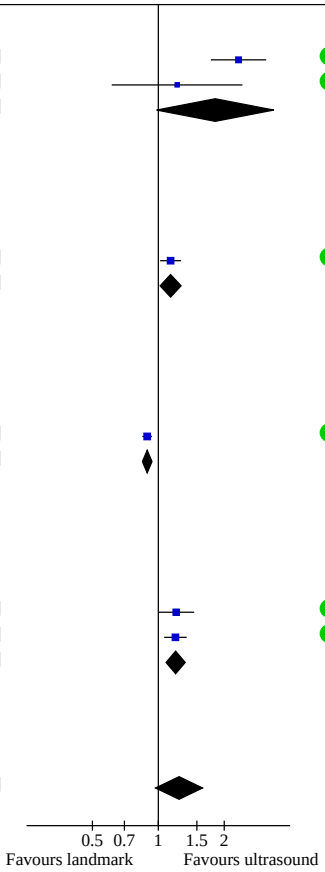
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10.1 First-pass success of cannulation	6	1638	Risk Ratio (M-H, Random, 95% CI)	1.24 [0.97, 1.59]
10.1.1 Difficult	2	251	Risk Ratio (M-H, Random, 95% CI)	1.82 [0.98, 3.37]
10.1.2 Moderate	1	401	Risk Ratio (M-H, Random, 95% CI)	1.14 [1.02, 1.27]
10.1.3 Easy	1	596	Risk Ratio (M-H, Random, 95% CI)	0.89 [0.85, 0.94]

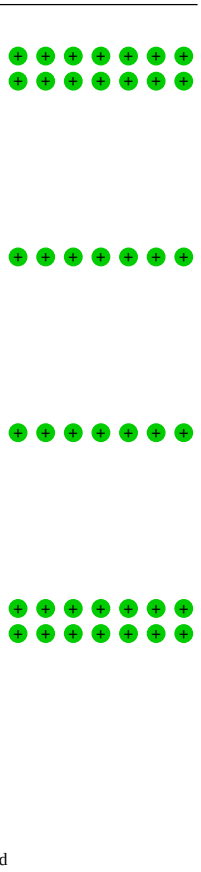
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10.1.4 No restriction by intravenous access difficulty level	2	390	Risk Ratio (M-H, Random, 95% CI)	1.20 [1.09, 1.33]
10.2 Overall success of cannulation	2	148	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.96, 1.05]
10.2.1 Difficult	1	59	Risk Ratio (M-H, Random, 95% CI)	1.03 [0.92, 1.16]
10.2.2 No restriction by intravenous access difficulty level	1	89	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.96, 1.04]
10.3 Pain	4	1279	Mean Difference (IV, Random, 95% CI)	0.29 [-0.03, 0.61]
10.3.1 Difficult	1	192	Mean Difference (IV, Random, 95% CI)	0.20 [-0.61, 1.01]
10.3.2 Moderate	1	401	Mean Difference (IV, Random, 95% CI)	0.10 [-0.47, 0.67]
10.3.3 Easy	1	596	Mean Difference (IV, Random, 95% CI)	0.60 [0.17, 1.03]
10.3.4 No restriction by intravenous access difficulty level	1	90	Mean Difference (IV, Random, 95% CI)	-0.10 [-0.85, 0.65]
10.4 Procedure time for first-pass cannulation	4	1279	Mean Difference (IV, Random, 95% CI)	69.47 [19.15, 119.78]
10.4.1 Difficult	1	192	Mean Difference (IV, Random, 95% CI)	120.60 [88.30, 152.90]
10.4.2 Moderate	1	401	Mean Difference (IV, Random, 95% CI)	95.20 [72.77, 117.63]
10.4.3 Easy	1	596	Mean Difference (IV, Random, 95% CI)	94.80 [81.15, 108.45]
10.4.4 No restriction by intravenous access difficulty level	1	90	Mean Difference (IV, Random, 95% CI)	-39.00 [-75.04, -2.96]
10.5 Procedure time for overall cannulation	2	390	Mean Difference (IV, Random, 95% CI)	-77.42 [-185.70, 30.86]
10.5.1 No restriction by intravenous access difficulty level	2	390	Mean Difference (IV, Random, 95% CI)	-77.42 [-185.70, 30.86]
10.6 Number of cannulation attempts	3	449	Mean Difference (IV, Random, 95% CI)	-0.31 [-0.47, -0.15]
10.6.1 Difficult	1	59	Mean Difference (IV, Random, 95% CI)	-0.60 [-1.51, 0.31]
10.6.2 No restriction by intravenous access difficulty level	2	390	Mean Difference (IV, Random, 95% CI)	-0.30 [-0.50, -0.11]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10.7 Overall complications	5	1338	Risk Ratio (M-H, Random, 95% CI)	1.07 [0.62, 1.85]
10.7.1 Difficult	2	251	Risk Ratio (M-H, Random, 95% CI)	0.77 [0.21, 2.77]
10.7.2 Moderate	1	401	Risk Ratio (M-H, Random, 95% CI)	0.83 [0.38, 1.82]
10.7.3 Easy	1	596	Risk Ratio (M-H, Random, 95% CI)	2.48 [0.90, 6.87]
10.7.4 No restriction by intravenous access difficulty level	1	90	Risk Ratio (M-H, Random, 95% CI)	0.83 [0.27, 2.54]

Analysis 10.1. Comparison 10: Sensitivity analysis 2 (low risk of bias studies only), Outcome 1: First-pass success of cannulation

Study or Subgroup	Ultrasound Events	Ultrasound Total	Landmark Events	Landmark Total	Weight	Risk Ratio M-H, Random, 95% CI
10.1.1 Difficult						
McCarthy 2016A	80	98	33	94	15.7%	2.33 [1.74 , 3.11]
Stein 2009	11	28	10	31	7.9%	1.22 [0.61 , 2.42]
Subtotal (95% CI)		**126**		**125**	**23.6%**	**1.82 [0.98 , 3.37]**
Total events:	91		43			
Heterogeneity: Tau² = 0.14; Chi² = 2.90, df = 1 (P = 0.09); I² = 65%						
Test for overall effect: Z = 1.90 (P = 0.06)						
10.1.2 Moderate						
McCarthy 2016B	164	202	142	199	19.3%	1.14 [1.02 , 1.27]
Subtotal (95% CI)		**202**		**199**	**19.3%**	**1.14 [1.02 , 1.27]**
Total events:	164		142			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.29 (P = 0.02)						
10.1.3 Easy						
McCarthy 2016C	262	305	281	291	19.9%	0.89 [0.85 , 0.94]
Subtotal (95% CI)		**305**		**291**	**19.9%**	**0.89 [0.85 , 0.94]**
Total events:	262		281			
Heterogeneity: Not applicable						
Test for overall effect: Z = 4.55 (P < 0.00001)						
10.1.4 No restriction by intravenous access difficulty level						
Glasin 2020	41	45	34	45	18.0%	1.21 [1.00 , 1.46]
Skulec 2019	182	200	76	100	19.2%	1.20 [1.06 , 1.35]
Subtotal (95% CI)		**245**		**145**	**37.2%**	**1.20 [1.09 , 1.33]**
Total events:	223		110			
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.95); I² = 0%						
Test for overall effect: Z = 3.55 (P = 0.0004)						
Total (95% CI)		**878**		**760**	**100.0%**	**1.24 [0.97 , 1.59]**
Total events:	740		576			
Heterogeneity: Tau² = 0.08; Chi² = 97.63, df = 5 (P < 0.00001); I² = 95%						
Test for overall effect: Z = 1.73 (P = 0.08)						
Test for subgroup differences: Chi² = 40.57, df = 3 (P < 0.00001), I² = 92.6%						



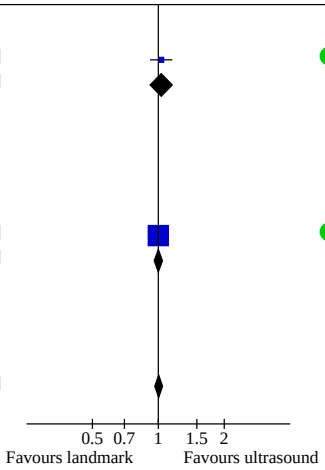


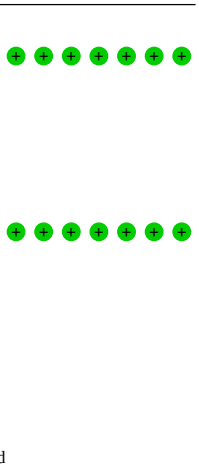
Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): First-pass success of cannulation
(D) Incomplete outcome data (attrition bias): First-pass success of cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: First-pass success of cannulation

Analysis 10.2. Comparison 10: Sensitivity analysis 2 (low risk of bias studies only), Outcome 2: Overall success of cannulation

Study or Subgroup	Ultrasound Events	Ultrasound Total	Landmark Events	Landmark Total	Weight	Risk Ratio M-H, Random, 95% CI
10.2.1 Difficult						
Stein 2009	27	28	29	31	12.1%	1.03 [0.92 , 1.16]
Subtotal (95% CI)		**28**		**31**	**12.1%**	**1.03 [0.92 , 1.16]**
Total events:	27		29			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.51 (P = 0.61)						
10.2.2 No restriction by intravenous access difficulty level						
Glasin 2020	44	44	45	45	87.9%	1.00 [0.96 , 1.04]
Subtotal (95% CI)		**44**		**45**	**87.9%**	**1.00 [0.96 , 1.04]**
Total events:	44		45			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.00 (P = 1.00)						
Total (95% CI)		**72**		**76**	**100.0%**	**1.00 [0.96 , 1.05]**
Total events:	71		74			
Heterogeneity: Tau² = 0.00; Chi² = 0.37, df = 1 (P = 0.54); I² = 0%						
Test for overall effect: Z = 0.18 (P = 0.86)						
Test for subgroup differences: Chi² = 0.23, df = 1 (P = 0.63), I² = 0%						

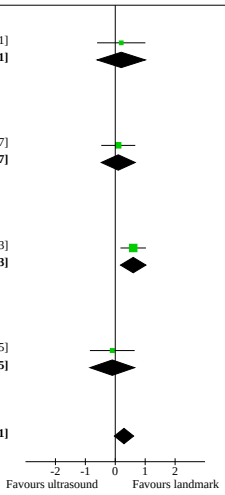


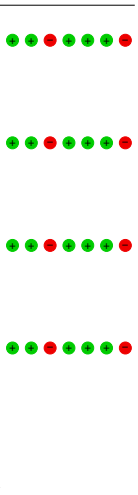


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Overall-success of cannulation
(D) Incomplete outcome data (attrition bias): Overall success of cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Overall success of cannulation

Analysis 10.3. Comparison 10: Sensitivity analysis 2 (low risk of bias studies only), Outcome 3: Pain

Study or Subgroup	Ultrasound Mean [NRS (0 - 10)]	Ultrasound SD [NRS (0 - 10)]	Ultrasound Total	Landmark Mean [NRS (0 - 10)]	Landmark SD [NRS (0 - 10)]	Landmark Total	Weight	Mean Difference IV, Random, 95% CI [NRS (0 - 10)]
10.3.1 Difficult								
McCarthy 2016A	3.3	2.8	98	3.1	2.9	94	14.5%	0.20 [-0.61 , 1.01]
Subtotal (95% CI)			**98**			**94**	**14.5%**	**0.20 [-0.61 , 1.01]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.49 (P = 0.63)								
10.3.2 Moderate								
McCarthy 2016B	3.3	2.8	202	3.2	3	199	26.8%	0.10 [-0.47 , 0.67]
Subtotal (95% CI)			**202**			**199**	**26.8%**	**0.10 [-0.47 , 0.67]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.34 (P = 0.73)								
10.3.3 Easy								
McCarthy 2016C	2.9	2.8	305	2.3	2.5	291	42.1%	0.60 [0.17 , 1.03]
Subtotal (95% CI)			**305**			**291**	**42.1%**	**0.60 [0.17 , 1.03]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.76 (P = 0.006)								
10.3.4 No restriction by intravenous access difficulty level								
Glasin 2020	1.8	1.6	45	1.9	2	45	16.6%	-0.10 [-0.85 , 0.65]
Subtotal (95% CI)			**45**			**45**	**16.6%**	**-0.10 [-0.85 , 0.65]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.26 (P = 0.79)								
Total (95% CI)			**650**			**629**	**100.0%**	**0.29 [-0.03 , 0.61]**
Heterogeneity: Tau² = 0.02; Chi² = 3.53, df = 3 (P = 0.32); I² = 15%								
Test for overall effect: Z = 1.77 (P = 0.08)								
Test for subgroup differences: Chi² = 3.53, df = 3 (P = 0.32), I² = 15.0%								

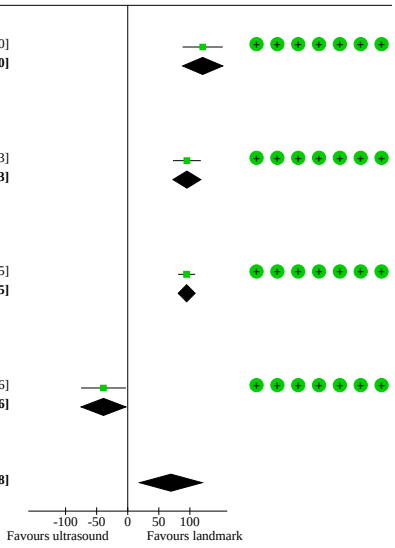




Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Pain
(D) Incomplete outcome data (attrition bias): Pain
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Pain

Analysis 10.4. Comparison 10: Sensitivity analysis 2 (low risk of bias studies only), Outcome 4: Procedure time for first-pass cannulation

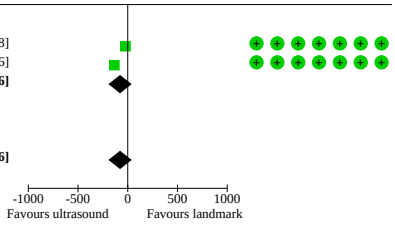
Study or Subgroup	Ultrasound Mean [second]	Ultrasound SD [second]	Ultrasound Total	Landmark Mean [second]	Landmark SD [second]	Landmark Total	Weight	Mean Difference IV, Random, 95% CI [second]	Risk of Bias A B C D E F G
10.4.1 Difficult									
McCarthy 2016A	258.4	140.5	98	137.8	81.2	94	24.3%	120.60 [88.30 , 152.90]	+ + + + + + +
Subtotal (95% CI)			**98**			**94**	**24.3%**	**120.60 [88.30 , 152.90]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 7.32 (P < 0.00001)									
10.4.2 Moderate									
McCarthy 2016B	217.8	124.4	202	122.6	104	199	25.6%	95.20 [72.77 , 117.63]	+ + + + + + +
Subtotal (95% CI)			**202**			**199**	**25.6%**	**95.20 [72.77 , 117.63]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 8.32 (P < 0.00001)									
10.4.3 Easy									
McCarthy 2016C	184.5	107.3	305	89.7	56	291	26.4%	94.80 [81.15 , 108.45]	+ + + + + + +
Subtotal (95% CI)			**305**			**291**	**26.4%**	**94.80 [81.15 , 108.45]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 13.61 (P < 0.00001)									
10.4.4 No restriction by intravenous access difficulty level									
Glasin 2020	66.8	40.3	45	105.8	116.6	45	23.7%	-39.00 [-75.04 , -2.96]	+ + + + + + +
Subtotal (95% CI)			**45**			**45**	**23.7%**	**-39.00 [-75.04 , -2.96]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 2.12 (P = 0.03)									
Total (95% CI)			**650**			**629**	**100.0%**	**69.47 [19.15 , 119.78]**	
Heterogeneity: Tau² = 2443.79; Chi² = 52.85, df = 3 (P < 0.00001); I² = 94%									
Test for overall effect: Z = 2.71 (P = 0.007)									
Test for subgroup differences: Chi² = 52.85, df = 3 (P < 0.00001), I² = 94.3%									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Procedure time for first-pass cannulation
(D) Incomplete outcome data (attrition bias): Procedure time for first-pass cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Procedure time for first-pass cannulation

Analysis 10.5. Comparison 10: Sensitivity analysis 2 (low risk of bias studies only), Outcome 5: Procedure time for overall cannulation

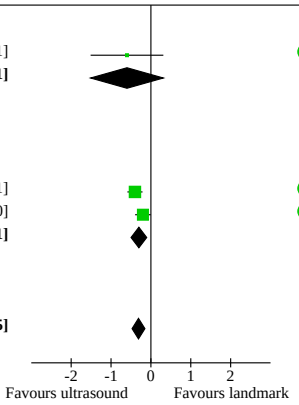
Study or Subgroup	Ultrasound Mean [second]	Ultrasound SD [second]	Ultrasound Total	Landmark Mean [second]	Landmark SD [second]	Landmark Total	Weight	Mean Difference IV, Random, 95% CI [second]	Risk of Bias A B C D E F G
10.5.1 No restriction by intravenous access difficulty level									
Skulec 2019	59.4	49.2	200	82.3	100.9	100	50.7%	-22.90 [-43.82 , -1.98]	+ + + + + + +
Glasin 2020	134.3	61.6	45	267.7	92.8	45	49.3%	-133.40 [-165.94 , -100.86]	+ + + + + + +
Subtotal (95% CI)			**245**			**145**	**100.0%**	**-77.42 [-185.70 , 30.86]**	
Heterogeneity: Tau² = 5910.32; Chi² = 31.34, df = 1 (P < 0.00001); I² = 97%									
Test for overall effect: Z = 1.40 (P = 0.16)									
Total (95% CI)			**245**			**145**	**100.0%**	**-77.42 [-185.70 , 30.86]**	
Heterogeneity: Tau² = 5910.32; Chi² = 31.34, df = 1 (P < 0.00001); I² = 97%									
Test for overall effect: Z = 1.40 (P = 0.16)									
Test for subgroup differences: Not applicable									



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Procedure time for overall cannulation
(D) Incomplete outcome data (attrition bias): Procedure time for overall cannulation
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Procedure time for overall cannulation

Analysis 10.6. Comparison 10: Sensitivity analysis 2 (low risk of bias studies only), Outcome 6: Number of cannulation attempts

Study or Subgroup	Ultrasound Mean	Ultrasound SD	Ultrasound Total	Landmark Mean	Landmark SD	Landmark Total	Weight	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F G
10.6.1 Difficult									
Stein 2009	1.9	1.3	28	2.5	2.2	31	3.1%	-0.60 [-1.51 , 0.31]	+ + + + + + +
Subtotal (95% CI)			**28**			**31**	**3.1%**	**-0.60 [-1.51 , 0.31]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 1.29 (P = 0.20)									
10.6.2 No restriction by intravenous access difficulty level									
Skulec 2019	1.1	0.5	200	1.5	0.9	100	49.6%	-0.40 [-0.59 , -0.21]	+ + + + + + +
Glasin 2020	1.1	0.3	45	1.3	0.6	45	47.3%	-0.20 [-0.40 , -0.00]	+ + + + + + +
Subtotal (95% CI)			**245**			**145**	**96.9%**	**-0.30 [-0.50 , -0.11]**	
Heterogeneity: Tau² = 0.01; Chi² = 2.07, df = 1 (P = 0.15); I² = 52%									
Test for overall effect: Z = 3.02 (P = 0.003)									
Total (95% CI)			**273**			**176**	**100.0%**	**-0.31 [-0.47 , -0.15]**	
Heterogeneity: Tau² = 0.00; Chi² = 2.46, df = 2 (P = 0.29); I² = 19%									
Test for overall effect: Z = 3.80 (P = 0.0001)									
Test for subgroup differences: Chi² = 0.39, df = 1 (P = 0.53), I² = 0%									

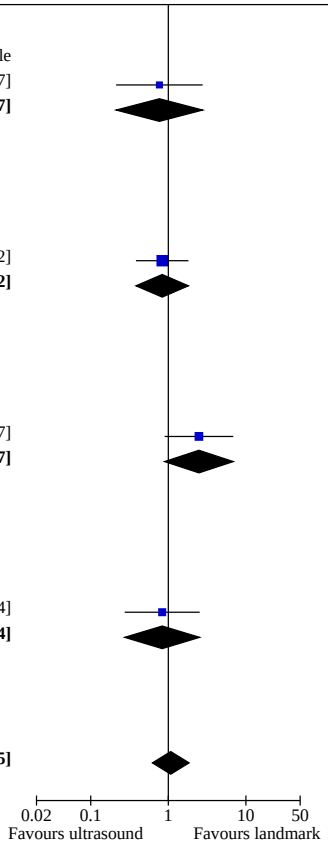


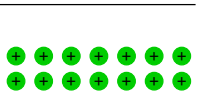
Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Number of attempts
(D) Incomplete outcome data (attrition bias): Number of attempts
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Number of attempts

Analysis 10.7. Comparison 10: Sensitivity analysis 2 (low risk of bias studies only), Outcome 7: Overall complications

Study or Subgroup	Ultrasound Events	Ultrasound Total	Landmark Events	Landmark Total	Weight	Risk Ratio M-H, Random, 95% CI
10.7.1 Difficult						
Stein 2009	0	28	0	31		Not estimable
McCarthy 2016A	4	98	5	94	16.3%	0.77 [0.21 , 2.77]
Subtotal (95% CI)		**126**		**125**	**16.3%**	**0.77 [0.21 , 2.77]**
Total events:	4		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.40 (P = 0.69)						
10.7.2 Moderate						
McCarthy 2016B	11	202	13	199	38.2%	0.83 [0.38 , 1.82]
Subtotal (95% CI)		**202**		**199**	**38.2%**	**0.83 [0.38 , 1.82]**
Total events:	11		13			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.46 (P = 0.65)						
10.7.3 Easy						
McCarthy 2016C	13	305	5	291	24.5%	2.48 [0.90 , 6.87]
Subtotal (95% CI)		**305**		**291**	**24.5%**	**2.48 [0.90 , 6.87]**
Total events:	13		5			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.75 (P = 0.08)						
10.7.4 No restriction by intravenous access difficulty level						
Glasin 2020	5	45	6	45	21.0%	0.83 [0.27 , 2.54]
Subtotal (95% CI)		**45**		**45**	**21.0%**	**0.83 [0.27 , 2.54]**
Total events:	5		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.32 (P = 0.75)						
Total (95% CI)		**678**		**660**	**100.0%**	**1.07 [0.62 , 1.85]**
Total events:	33		29			
Heterogeneity: Tau² = 0.04; Chi² = 3.48, df = 3 (P = 0.32); I² = 14%						
Test for overall effect: Z = 0.26 (P = 0.80)						
Test for subgroup differences: Chi² = 3.46, df = 3 (P = 0.33), I² = 13.4%						





Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding (performance bias and detection bias): Overall complications
(D) Incomplete outcome data (attrition bias): Overall complications
(E) Selective reporting (reporting bias)
(F) Other bias
(G) Overall risk: Overall complications

ADDITIONAL TABLES

Table 1. Complications

Level	Number of participants		Overall complications		Swelling or haematoma		Pain		Nerve injury		Arterial puncture		Catheter dislocation	
	USG	LM	USG	LM	USG	LM	USG	LM	USG	LM	USG	LM	USG	LM
Difficult														
Costantino 2005	39	21	0	2 (9.5)	0	2 (9.5)	NS	NS	NS	NS	NS	NS	NS	NS
Stein 2009	28	31	0	0	0	0	NS	NS	0	0	0	0	NS	NS
İsmailoğlu 2015	30	30	9 (30.0)	14 (46.7)	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
McCarthy 2016A	98	94	4 (4.1)	5 (5.3)	2 (2.0)	3 (3.2)	NS	NS	1 (1.0)	1 (1.1)	1 (1.0)	1 (1.1)	NS	NS
Nishizawa 2020	30	30	3 (10.0)	4 (13.3)	3 (10.0)	4 (13.3)	NS	NS	NS	NS	NS	NS	NS	NS
Moderate														
McCarthy 2016B	202	199	11 (5.4)	13* (6.5)	8 (4.0)	13 (6.5)	NS	NS	2 (1.0)	2 (1.0)	1 (0.5)	0	NS	NS
Easy														
McCarthy 2016C	305	291	13 (4.3)	5 (1.7)	12 (3.9)	5 (1.7)	NS	NS	1 (0.3)	0	0	0	NS	NS
No restriction of difficulty														
Glasin 2020	45	45	5 (11.1)	6† (13.3)	0	1 (2.2)	5 (11.1)	6 (13.3)	NS	NS	NS	NS	NS	NS
Skulec 2019	D 100 S 100	100	D 13 (13.0) S 7 (7.0)	26 (26.0)	D 8 (8.0) S 3 (3.0)	10 (10.0)	D 4 (4.0) S 3 (3.0)	16 (16.0)	D NS S NS	NS	D 0 S 1 (1.0)	0	D 1 (1.0) S 0	0
Total														

Table 1. Complications *(Continued)*

	977		841	65		75	36		38	12		22	4		3	3		1	1		0

Values are n (%)
USG: ultrasound guidance, **LM:** landmark method, **NS:** not specified, **D:** dynamic guidance, **S:** static guidance
*Two participants had complications of both swelling and nerve injury.
†One participant had complications of both swelling and pain.

Table 2. Sensitivity analysis for difficult participants

Outcomes		Original results	RCTs only	Low ROB studies only
First-pass success of cannulation	ES	1.50 (1.15, 1.95)	1.50 (1.15, 1.96)	1.82 (0.98, 3.37)
	I^2	62%	66%	65%
Overall success of cannulation	ES	1.40 (1.10, 1.77)	1.19 (0.98, 1.45)	1.03 (0.92, 1.16)
	I^2	88%	79%	NA *1
Pain	ES	-0.20 (-1.13, 0.72)	0.23 (-0.42, 0.88)	0.20 (-0.61, 1.01)
	I^2	62%	0%	NA *1
Procedure time for first-pass cannulation	ES	119.9 (88.6, 151.1)	119.9 (88.6, 151.1)	120.6 (88.3, 152.9)
	I^2	0%	0%	NA *1
Procedure time for overall cannulation	ES	-24.9 (-323.1, 273.3)	97.5 (-17.6, 212.5)	NA *2
	I^2	77%	0%	NA *2
Number of cannulation attempts	ES	-0.33 (-0.64, -0.02)	-0.17 (-0.36, 0.03)	-0.60 (-1.51, 0.31)
	I^2	64%	0%	NA *1
Patient satisfaction	ES	0.49 (0.07, 0.92)	0.25 (0.01, 0.50)	NA *2
	I^2	71%	5%	NA *2
Overall complications	ES	0.64 (0.37, 1.10)	0.76 (0.29, 1.96)	0.77 (0.21, 2.77)
	I^2	0%	0%	NA

Dichotomous outcomes shown as RR (95% CI), continuous outcomes as MD or SMD (95% CI)
ES: effect size; **MD:** mean difference; **NA:** not applicable; **RCT:** randomised controlled trial; **ROB:** risk of bias; **RR:** risk ratio; **SMD:** standardised mean difference
*1: only one study; *2: no study

Table 3. Sensitivity analysis for moderate participants

Outcomes		Original results	RCTs only	Low ROB studies only
First-pass success of cannulation	ES	1.14 (1.02, 1.27)	1.14 (1.02, 1.27)	1.14 (1.02, 1.27)
	I^2	NA *1	NA*1	NA*1
Overall success of cannulation	ES	NA *2	NA *2	NA *2
	I^2	NA *2	NA *2	NA *2
Pain	ES	0.10 (-0.47, 0.67)	0.10 (-0.47, 0.67)	0.10 (-0.47, 0.67)

Table 3. Sensitivity analysis for moderate participants *(Continued)*

	I^2	NA *1	NA *1	NA *1
Procedure time for first-pass cannulation	ES	95.2 (72.8, 117.6)	95.2 (72.8, 117.6)	95.2 (72.8, 117.6)
	I^2	NA *1	NA *1	NA *1
Procedure time for overall cannulation	ES	NA *2	NA *2	NA *2
	I^2	NA *2	NA *2	NA *2
Number of cannulation attempts	ES	NA *2	NA *2	NA *2
	I^2	NA *2	NA *2	NA *2
Patient satisfaction	ES	NA *2	NA *2	NA *2
	I^2	NA *2	NA *2	NA *2
Overall complications	ES	0.83 (0.38, 1.82)	0.83 (0.38, 1.82)	0.83 (0.38, 1.82)
	I^2	NA *1	NA *1	NA *1

Dichotomous outcomes shown as RR (95% CI), continuous outcomes as MD or SMD (95% CI)
ES: effect size; **MD:** mean difference; **NA:** not applicable; **RCT:** randomised controlled trial; **ROB:** risk of bias; **RR:** risk ratio; **SMD:** standardised mean difference
*1: only one study; *2: no study

Table 4. Sensitivity analysis for easy participants

Outcomes		Original results	RCTs only	Low ROB studies only
First-pass success of cannulation	ES	0.89 (0.85, 0.94)	0.89 (0.85, 0.94)	0.89 (0.85, 0.94)
	I^2	NA *1	NA*1	NA*1
Overall success of cannulation	ES	NA *2	NA *2	NA *2
	I^2	NA *2	NA *2	NA *2
Pain	ES	0.60 (0.17, 1.03)	0.60 (0.17, 1.03)	0.60 (0.17, 1.03)
	I^2	NA *1	NA *1	NA *1
Procedure time for first-pass cannulation	ES	94.8 (81.2, 108.5)	94.8 (81.2, 108.5)	94.8 (81.2, 108.5)
	I^2	NA *1	NA *1	NA *1
Procedure time for overall cannulation	ES	NA *2	NA *2	NA *2
	I^2	NA *2	NA *2	NA *2
Number of cannulation attempts	ES	NA *2	NA *2	NA *2

Table 4. Sensitivity analysis for easy participants *(Continued)*

	I^2	NA *2	NA *2	NA *2
Patient satisfaction	ES	NA *2	NA *2	NA *2
	I^2	NA *2	NA *2	NA *2
Overall complications	ES	2.48 (0.90, 6.87)	2.48 (0.90, 6.87)	2.48 (0.90, 6.87)
	I^2	NA *1	NA *1	NA *1

Dichotomous outcomes shown as RR (95% CI), continuous outcomes as MD or SMD (95% CI)
ES: effect size; **MD:** mean difference; **NA:** not applicable; **RCT:** randomised controlled trial; **ROB:** risk of bias; **RR:** risk ratio; **SMD:** standardised mean difference
*1: only one study; *2: no study

APPENDICES

Appendix 1. Sources searched and search strategies

Source	Search strategy	Hits retrieved
1. VASCULAR REGISTER IN CRSW (Date of most recent search: 29 November 2021)	#1 Catheterization, Peripheral OR peripheral vein OR peripheral venous OR peripheral intravenous AND INREGISTER #2 ULTRASONOGRAPHY OR Ultrasound AND INREGISTER #3 #1 AND #2	Oct 2019: 81 NOV 2020: 33 Nov 2021: 5
2. CENTRAL via CRSO (Date of most recent search: 29 November 2021)	#1 MESH DESCRIPTOR Catheterization, Peripheral EXPLODE ALL TREES #2 Cathlon:TI,AB,KY #3 (intravenous cannul*):TI,AB,KY #4 (peripheral intravenous):TI,AB,KY #5 (peripheral vein*):TI,AB,KY #6 (peripheral venous):TI,AB,KY #7 Venflon:TI,AB,KY #8 ((Catheter* or cannula* or puncture* or line or access) near3 (peripher* or intravenous)):TI,AB,KY #9 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 #10 MESH DESCRIPTOR ULTRASONOGRAPHY, INTERVENTIONAL EXPLODE ALL TREES #11 ultrasonograph*:TI,AB,KY #12 Ultrasound*:TI,AB,KY #13 #10 OR #11 OR #12	Oct 2019: 323 NOV 2020: 77 Nov 2021: 43

(Continued)

	#14 #9 AND #13	
3. Clinicaltrials.gov (Date of most recent search: 29 November 2021)	Catheterization, Peripheral OR peripheral vein OR peripheral venous OR peripheral intravenous | ULTRASONOGRAPHY OR Ultrasound	Oct 2019: 198 NOV 2020: 43 Nov 2021: 16
4. ICTRP Search Portal (Date of most recent search: 29 November 2021)	Catheterization, Peripheral OR peripheral vein OR peripheral venous OR peripheral intravenous | ULTRASONOGRAPHY OR Ultrasound	Oct 2019: 17 NOV 2020: 0 Nov 2021: 2
5. MEDLINE (Ovid MEDLINE Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE Daily and Ovid MEDLINE) 1946 to present Date of most recent search: 29 November 2021)	1 Catheterization, Peripheral/ 2 Cathlon.ti,ab. 3 "intravenous cannul*".ti,ab. 4 "peripheral intravenous".ti,ab. 5 "peripheral vein*".ti,ab. 6 "peripheral venous".ti,ab. 7 Venflon.ti,ab. 8 ((Catheter* or cannula* or puncture* or line or access) adj3 (peripher* or intravenous)).ti,ab. 9 or/1-8 10 exp ULTRASONOGRAPHY, INTERVENTIONAL/ 11 ultrasonograph*.ti,ab. 12 Ultrasound*.ti,ab. 13 or/10-12 14 9 and 13 15 randomized controlled trial.pt. 16 controlled clinical trial.pt. 17 randomized.ab. 18 placebo.ab. 19 drug therapy.fs. 20 randomly.ab. 21 trial.ab. 22 groups.ab. 23 or/15-22 24 exp animals/ not humans.sh. 25 23 not 24	Oct 2019: 432 NOV 2020: 90 Nov 2021: 96

(Continued)

	26 14 and 25	
6. Embase via OVID (Date of most recent search: 29 November 2021)	1 exp catheterization/ 2 Cathlon.ti,ab. 3 "intravenous cannul*".ti,ab. 4 "peripheral intravenous".ti,ab. 5 "peripheral vein*".ti,ab. 6 "peripheral venous".ti,ab. 7 Venflon.ti,ab. 8 ((Catheter* or cannula* or puncture* or line or access) adj3 (peripher* or intravenous)).ti,ab. 9 or/1-8 10 exp interventional ultrasonography/ 11 ultrasonograph*.ti,ab. 12 Ultrasound*.ti,ab. 13 or/10-12 14 9 and 13 15 randomized controlled trial/ 16 controlled clinical trial/ 17 random$.ti,ab. 18 randomization/ 19 intermethod comparison/ 20 placebo.ti,ab. 21 (compare or compared or comparison).ti. 22 ((evaluated or evaluate or evaluating or assessed or assess) and (compare or compared or comparing or comparison)).ab. 23 (open adj label).ti,ab. 24 ((double or single or doubly or singly) adj (blind or blinded or blindly)).ti,ab. 25 double blind procedure/ 26 parallel group$1.ti,ab. 27 (crossover or cross over).ti,ab. 28 ((assign$ or match or matched or allocation) adj5 (alternate or group$1 or intervention$1 or patient$1 or subject$1 or participant$1)).ti,ab. 29 (assigned or allocated).ti,ab. 30 (controlled adj7 (study or design or trial)).ti,ab. 31 (volunteer or volunteers).ti,ab.	Oct 2019: 2371 NOV 2020: 406 Nov 2021: 398

(Continued)

	32 trial.ti. 33 or/15-32 34 14 and 33 35 from 34 keep 2001-2371	
7. CINAHL via EBSCO (Date of most recent search: 29 November 2021)	S30 S14 AND S29 S29 S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 S28 MH "Random Assignment" S27 MH "Triple-Blind Studies" S26 MH "Double-Blind Studies" S25 MH "Single-Blind Studies" S24 MH "Crossover Design" S23 MH "Factorial Design" S22 MH "Placebos" S21 MH "Clinical Trials" S20 TX "multi-centre study" OR "multi-center study" OR "multicentre study" OR "multicenter study" OR "multi-site study" S19 TX crossover OR "cross-over" S18 AB placebo* S17 TX random* S16 TX trial* S15 TX "latin square" S14 S9 AND S13 S13 S10 OR S11 OR S12 S12 TX Ultrasound* S11 TX ultrasonograph* S10 (MH "Ultrasonography+") S9 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 S8 TX (Catheter* or cannula* or puncture* or line or access) N3 (peripher* or intravenous) S7 TX Venflon S6 TX peripheral venous S5 TX peripheral vein* S4 TX peripheral intravenous S3 TX intravenous cannul*	Oct 2019: 163 NOV 2020: 48 Nov 2021: 42

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	S2 TX Cathlon S1 (MH "Catheterization, Peripheral+")	
8. LILACS (Date of most recent search: 29 November 2021)	Catheterization, Peripheral OR peripheral vein OR peripheral venous OR peripheral intravenous OR Cateterización [Palavras] and ULTRASONOGRAPHY OR Ultrasound or Sonografía OR Ultrasonido [Palavras]	Oct 2019: 53 NOV 2020: 5 Nov 2021: 1
TOTAL before de-duplication		Oct 2019: 3638 Nov 2020: 702 Nov 2021: 603
TOTAL after de-duplication		Oct 2019: 2966 Nov 2020: 571 Nov 2021: 501

Appendix 2. Ultrasound guidance versus landmark method for peripheral venous cannulation in adults classed as difficult – subgrouped by operators' experience

Patient or population: adults undergoing peripheral venous cannulation classed as difficult[a]

Settings: emergency department, ICU, operating room

Intervention: USG

Comparison: LM

Outcomes	Subgroups	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)	Comments
		Risk with LM	Risk with USG				
First-pass success of cannulation Follow-up: immediately after the procedure	**Operators had any clinical experience**	**361 per 1000**	**519 per 1000** (328 to 819)	**RR 1.44** (0.91 to 2.27)	460 (5 RCTs)	⊕⊖⊖⊖ **Very low[b]**	
	Operators did not have any clinical experience	**446 per 1000**	**594 per 1000** (442 to 799)	**RR 1.33** (0.99 to 1.79)	235 (3 RCTs)	⊕⊕⊖⊖ **Low[c]**	
	Operators experience was not specified	**183 per 1000**	**403 per 1000** (224 to 726)	**RR 2.20** (1.22 to 3.96)	120 (2 RCTs)	⊕⊕⊖⊖ **Low[d]**	
Overall success of cannulation Follow-up: immediately after the procedure	**Operators had any clinical experience**	**726 per 1000**	**835 per 1000** (661 to 1000)	**RR 1.15** (0.91 to 1.44)	315 (5 RCTs)	⊕⊖⊖⊖ **Very low[e]**	
	Operators did not have any clinical experience	**509 per 1000**	**743 per 1000** (601 to 911)	**RR 1.46** (1.18 to 1.79)	235 (3 RCTs)	⊕⊖⊖⊖ **Very low[f]**	
	Operators experience was not specified	**333 per 1000**	**693 per 1000** (470 to 1000)	**RR 2.08** (1.41 to 3.09)	120 (2 RCTs)	⊕⊖⊖⊖ **Very low[g]**	
Pain NRS: from 0, no pain to 10, maximum pain	**Operators had any clinical experience**						Not performed due to insufficient number of studies

(Continued)

Follow-up: immediately after the procedure	**Operators did not have any clinical experience**		Not performed due to insufficient number of studies
	Operators experience was not specified		Not performed due to insufficient number of studies

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **ICU:** intensive care unit; **LM:** landmark method; **MD:** mean difference; **NRS:** numerical rating scale; **RCTs:** randomised controlled trials; **RR:** risk ratio; **USG:** ultrasound guidance

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]Participants were classified according to the original study's definition.
[b]We downgraded by a total of three levels to very low certainty due to risk of bias concerns (a quasi-randomised trial, lack of blinding of the outcome assessors), considerable inconsistency, and imprecision.
[c]We downgraded by a total of two levels to low certainty due to risk of bias concerns (lack of blinding of the outcome assessors), and imprecision.
[d]We downgraded by a total of two levels to low certainty due to risk of bias concerns (a quasi-randomised trial, lack of blinding of the outcome assessors), and imprecision.
[e]We downgraded by a total of three levels to very low certainty due to risk of bias concerns (a quasi-randomised trial, lack of blinding of the outcome assessors), considerable inconsistency, and imprecision.
[f]We downgraded by a total of three levels to very low certainty due to risk of bias concerns (lack of blinding of the outcome assessors), considerable inconsistency, and imprecision.
[g]We downgraded by a total of three levels to very low certainty due to risk of bias concerns (a quasi-randomised trial, lack of blinding of the outcome assessors), considerable inconsistency, and imprecision.

Appendix 3. Ultrasound guidance versus landmark method for peripheral venous cannulation in adults classed as difficult – subgrouped by settings

Patient or population: adults undergoing peripheral venous cannulation classed as difficult[a]

Settings: emergency department, ICU, operating room

Intervention: USG

Comparison: LM

Outcomes	Subgroups	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)	Comments
		Risk with LM	Risk with USG				
First-pass success of cannulation Follow-up: immediately after the procedure	Emergency department	**345 per 1000**	**552 per 1000** (386 to 787)	**RR 1.60** (1.12 to 2.28)	546 (6 RCTs)	⊕⊖⊖⊖ **Very low**[b]	
	ICU	**325 per 1000**	**533 per 1000** (390 to 724)	**RR 1.64** (1.20 to 2.23)	234 (3 RCTs)	⊕⊕⊖⊖ **Low**[c]	
	Operating room	**813 per 1000**	**739 per 1000** (512 to 1000)	**RR 0.91** (0.63 to 1.30)	35 (1 RCT)	⊕⊕⊖⊖ **Low**[c]	
Overall success of cannulation Follow-up: immediately after the procedure	Emergency department	**557 per 1000**	**874 per 1000** (585 to 1000)	**RR 1.57** (1.05 to 2.36)	401 (6 RCTs)	⊕⊖⊖⊖ **Very low**[d]	
	ICU	**547 per 1000**	**744 per 1000** (470 to 1000)	**RR 1.36** (0.86 to 2.15)	234 (3 RCTs)	⊕⊖⊖⊖ **Very low**[e]	
	Operating room	**1000 per 1000**	**1000 per 1000** (900 to 1000)	**RR 1.00** (0.90 to 1.11)	35 (1 RCT)	⊕⊕⊖⊖ **Low**[c]	
Pain NRS: from 0, no pain to 10, maximum pain Follow-up: immediately after the procedure	Emergency department	The mean pain score was **4.0**	**MD 0.2 lower** (1.13 lower to 0.72 higher)	-	323 (4 RCTs)	⊕⊖⊖⊖ **Very low**[f]	
	ICU						No eligible studies

(Continued)

	Operating room			No eligible studies

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **ICU:** intensive care unit; **LM:** landmark method; **MD:** mean difference; **NRS**: numerical rating scale; **RCTs:** randomised controlled trials; **RR:** risk ratio; **USG:** ultrasound guidance

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]Participants were classified according to the original study's definition.
[b]We downgraded by a total of three levels to very low certainty due to risk of bias concerns (a quasi-randomised trial, lack of blinding of the outcome assessors), substantial inconsistency, and imprecision.
[c]We downgraded by a total of two levels to low certainty due to risk of bias concerns (lack of blinding of the outcome assessors), and imprecision.
[d]We downgraded by a total of three levels to very low certainty due to risk of bias concerns (a quasi-randomised trial, lack of blinding of the outcome assessors), serious inconsistency, and imprecision.
[e]We downgraded by a total of three levels to very low certainty due to risk of bias concerns (lack of blinding of the outcome assessors), serious inconsistency, and imprecision.
[f]We downgraded by a total of three levels to very low certainty due to risk of bias concerns (a quasi-randomised trial, lack of blinding of the outcome assessors, incomplete outcome data), substantial inconsistency, and imprecision.

Appendix 4. Ultrasound guidance versus landmark method for peripheral venous cannulation in adults classed as difficult – classified according to the success rate with landmark method

Patient or population: adults undergoing peripheral venous cannulation classed as difficult[a]

Settings: emergency department, ICU

Intervention: USG

Comparison: LM

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with LM	Risk with USG				
First-pass success of cannulation Follow-up: immediately after the procedure	**339 per 1000**	**549 per 1000** (433 to 698)	**RR 1.62** (1.28 to 2.06)	780 (9 RCTs)	⊕⊕⊕⊖ **Moderate[b]**	
Overall success of cannulation Follow-up: immediately after the procedure	**541 per 1000**	**828 per 1000** (606 to 1000)	**RR 1.53** (1.12 to 2.08)	588 (8 RCTs)	⊕⊖⊖⊖ **Very low[c]**	
Pain NRS: from 0, no pain to 10, maximum pain Follow-up: immediately after the procedure	The mean pain score was **4.07**	**MD 0.49 lower** (1.48 lower to 0.49 higher)	-	305 (3 RCTs)	⊕⊖⊖⊖ **Very low[d]**	
Procedure time for first-pass cannulation (seconds) Follow-up: immediately after the procedure	The mean procedure time for first-pass cannulation was **137.8 seconds**	**MD 120.6 seconds longer** (88.3 longer to 152.9 longer)	-	192 (1 RCT)	⊕⊕⊕⊖ **Moderate[e]**	

(Continued)

Number of cannulation attempts Follow-up: immediately after the procedure	The mean number of cannulation attempts was **2.20**	**MD 0.36 lower** (0.75 lower to 0.03 higher)	-	468 (6 RCTs)	⊕⊖⊖⊖ **Very low**[f]
Patient satisfaction NRS from 0 to 10 or 4-step Likert scale The higher the score, the higher the level of satisfaction Follow-up: immediately after the procedure	The mean patient satisfaction score was **5.96**	**SMD 0.52 higher** (0.01 lower to 1.05 higher)	-	286 (4 RCTs)	⊕⊖⊖⊖ **Very low**[g]
Overall complications Follow-up: immediately after the procedure	**121 per 1000**	**78 per 1000** (45 to 133)	**RR 0.64** (0.37 to 1.10)	431 (5 RCTs)	⊕⊕⊖⊖ **Low**[h]

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **ICU:** intensive care unit; **LM:** landmark method; **MD:** mean difference; **NRS:** numeric rating scale; **RCTs:** randomised controlled trials; **RR:** risk ratio; **SMD:** standardised mean difference; **USG:** ultrasound guidance

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]Participants were classified according to the success rate with LM.
[b]We downgraded one level to moderate certainty due to risk of bias concerns (quasi-randomised trials, lack of blinding of the outcome assessors).
[c]We downgraded by a total of three levels to very low certainty due to risk of bias concerns (quasi-randomised trials, lack of blinding of the outcome assessors), serious inconsistency due to the lack of standardised definition of failure, and imprecision.
[d]We downgraded by a total of three levels to very low certainty due to risk of bias concerns (quasi-randomised trials, lack of blinding of the outcome assessors), inconsistency, and imprecision.
[e]We downgraded one level to moderate certainty due to imprecision.
[f]We downgraded by a total of three levels to very low certainty due to risk of bias concerns (quasi-randomised trials, lack of blinding of the outcome assessors), serious inconsistency due to the lack of standardised definition of failure, and imprecision.
[g]We downgraded by a total of three levels to very low certainty due to risk of bias concerns (quasi-randomised trials, lack of blinding of the outcome assessors, incomplete outcome data), inconsistency, and imprecision.
[h]We downgraded by a total of two levels to low certainty due to risk of bias concerns (quasi-randomised trials, lack of blinding of the outcome assessors), and imprecision.

Appendix 5. Ultrasound guidance versus landmark method for peripheral venous cannulation in adults classed as moderately difficult – classified according to the success rate with landmark method

Patient or population: adults undergoing peripheral venous cannulation classed as moderately difficult[a]

Settings: emergency department, prehospital setting

Intervention: USG

Comparison: LM

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with LM	Risk with USG				
First-pass success of cannulation Follow-up: immediately after the procedure	**733 per 1000**	**857 per 1000** (798 to 923)	**RR 1.17** (1.09 to 1.26)	791 (3 RCTs)	⊕⊕⊕⊕ **High**	
Overall success of cannulation Follow-up: immediately after the procedure	**904 per 1000**	**967 per 1000** (849 to 1000)	**RR 1.07** (0.94 to 1.23)	436 (3 RCTs)	⊕⊖⊖⊖ **Very low[b]**	
Pain NRS: from 0, no pain, to 10, maximum pain Follow-up: immediately after the procedure	The mean pain score was **2.96**	**MD 0.03 higher** (0.43 lower to 0.48 higher)	-	491 (2 RCTs)	⊕⊕⊖⊖ **Low[c]**	
Procedure time for first-pass cannulation (seconds) Follow-up: immediately after the procedure	The mean procedure time for first-pass cannulation was **100.6 seconds**	**MD 23.0 seconds longer** (39.9 shorter to 85.9 longer)	-	749 (3 RCTs)	⊕⊖⊖⊖ **Very low[d]**	
Number of cannulation attempts Follow-up: immediately after the procedure	The mean number of cannulation attempts was **1.51**	**MD 0.32 lower** (0.47 lower to 0.16 lower)	-	437 (3 RCTs)	⊕⊕⊕⊖ **Moderate[e]**	
Patient satisfaction NRS from 0 to 10 or 4-step Likert scale The higher the score the higher the level of satisfaction Follow-up: immediately after the procedure	The mean patient satisfaction score was **7.63**	**SMD 0.08 higher** (0.51 lower to 0.66 higher)	-	137 (2 RCTs)	⊕⊖⊖⊖ **Very low[f]**	

(Continued)

Overall complications Follow-up: immediately after the procedure	**131 per 1000**	**76 per 1000** (43 to 133)	**RR 0.58** (0.33 to 1.02)	791 (3 RCTs)	⊕⊕⊖⊖ **Low**[g]

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **LM:** landmark method; **MD:** mean difference; **NRS:** numeric rating scale; **RCTs:** randomised controlled trials; **RR:** risk ratio; **USG:** ultrasound guidance

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]Participants were classified according to the success rate with LM.
[b]We downgraded by a total of three levels to very low certainty due to risk of bias concerns (lack of blinding of the outcome assessors), serious inconsistency due to the lack of standardised definition of failure, and imprecision.
[c]We downgraded by a total of two levels to low certainty due to risk of bias concerns (lack of blinding of the outcome assessors), and imprecision.
[d]We downgraded by a total of three levels to very low certainty due to risk of bias concerns (incomplete outcome data), inconsistency, and imprecision.
[e]We downgraded one level to moderate certainty due to risk of bias concerns (lack of blinding of the outcome assessors).
[f]We downgraded by a total of three levels to very low certainty due to risk of bias concerns (lack of blinding of the outcome assessors), inconsistency, and imprecision.
[g]We downgraded by a total of two levels to low certainty due to risk of bias concerns (lack of blinding of the outcome assessors), and imprecision.

Appendix 6. Ultrasound guidance versus landmark method for peripheral venous cannulation in adults classed as easy – classified according to the success rate with landmark method

Patient or population: adults undergoing peripheral venous cannulation classed as easy[a]

Settings: emergency department, operating room

Intervention: USG

Comparison: LM

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with LM	Risk with USG				
First-pass success of cannulation Follow-up: immediately after the procedure	**958 per 1000**	**852 per 1000** (814 to 900)	**RR 0.89** (0.85 to 0.94)	631 (2 RCTs)	⊕⊕⊕⊖ **Moderate**[b]	

(Continued)

Overall success of cannulation Follow-up: immediately after the procedure	**1000 per 1000**	**1000 per 1000** (900 to 1000)	**RR 1.00** (0.90 to 1.11)	35 (1 RCT)	⊕⊕⊖⊖ **Low**[c]	
Pain NRS: from 0, no pain, to 10, maximum pain Follow-up: immediately after the procedure	The mean pain score was **2.30**	**MD 0.60 higher** (0.17 higher to 1.03 higher)	-	596 (1 RCT)	⊕⊕⊕⊖ **Moderate**[d]	
Procedure time for first-pass cannulation (seconds) Follow-up: immediately after the procedure	The mean procedure time for first-pass cannulation was **89.2 seconds**	**MD 95.0 seconds longer** (**81.4** longer to **108.6** longer)	-	623 (2 RCTs)	⊕⊕⊕⊖ **Moderate**[e]	
Number of cannulation attempts Follow-up: immediately after the procedure	The mean number of cannulation attempts was **1.30**	**MD 0.10 higher** (0.44 lower to 0.64 higher)	-	35 (1 RCT)	⊕⊕⊖⊖ **Low**[f]	
Patient satisfaction NRS from 0 to 10 or 4-step Likert scale The higher the score, the higher the level of satisfaction Follow-up: immediately after the procedure	See comment	-	-	-	-	None of the studies included easy participants
Overall complications Follow-up: immediately after the procedure	**17 per 1000**	**43 per 1000** (15 to 118)	**RR 2.48** (0.90 to 6.87)	596 (1 RCT)	⊕⊕⊕⊖ **Moderate**[g]	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **LM:** landmark method; **NRS:** numeric rating scale; **RCTs:** randomised controlled trials; **RR:** risk ratio; **USG:** ultrasound guidance

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

(Continued)

Very low certainty: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]Participants were classified according to the success rate with LM.
[b]We downgraded one level to moderate certainty due to risk of bias concerns (lack of blinding of the outcome assessors).
[c]We downgraded by a total of two levels to low certainty due to risk of bias concerns (lack of blinding of the outcome assessors), and imprecision.
[d]We downgraded one level to moderate certainty due to risk of bias concerns (lack of blinding of the outcome assessors).
[e]We downgraded by a total of one level to moderate certainty due to risk of bias concerns (lack of blinding of the outcome assessors, incomplete outcome data).
[f]We downgraded by a total of two levels to low certainty due to risk of bias concerns (lack of blinding of the outcome assessors), and imprecision.
[g]We downgraded one level to moderate certainty due to imprecision.

HISTORY

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CONTRIBUTIONS OF AUTHORS

MT: clinical expertise, study selection, data extraction and bias assessment, conception and writing of the manuscript
NY: clinical expertise, study selection, data extraction and bias assessment, and writing of the manuscript
TM: clinical expertise, study selection, data extraction and bias assessment, conception and writing of the manuscript
CT: clinical expertise, study selection, data extraction and bias assessment, and writing of the manuscript
TF: methodological expertise and advice, critical revising for important intellectual content, final approval of the manuscript
NW: methodological expertise and advice, conception and writing of the manuscript

DECLARATIONS OF INTEREST

MT: declared that his institute received research grants from Nakatani Foundation (ongoing multicentre prospective cohort study for myocardial infarction in the emergency department) and Radiometer America, Inc. (ongoing multicentre prospective cohort study of myocardial infarction in the emergency department). MT declared that he has received royalties from Japan Medical Journal as he co-authored a textbook about ultrasound-guided peripheral intravenous cannulation in emergency medicine. The textbook is about the technical issues of the review intervention. It explains the review intervention as one of various options and is not intended to promote the review intervention. Japan Medical Journal has no role in this Cochrane Review and meta-analysis.
NY: none known
TM: none known
CT: none known
TF: has received financial payment for speaker's fees (Mitsubishi Tanabe Pharma Corporation), clinical trial consultancy (Mitsubishi Tanabe Pharma Corporation, Sony Electronics), scientific advisory board (Kyoto University Original), grant (Shionogi) and declares intellectual properties and patent-pending (2020-548587) for smartphone CBT apps (Mitsubishi Tanabe Pharma Corporation).
NW: his institution has received research funds from the Japanese Ministry of Health Labor and Welfare and the Japanese Ministry of Education, Science, and Technology. He has also received royalties from Sogensha and Akatsuki for writing a book and developing software about interventions for insomnia. This review is completely independent from the intention of these grants.

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We initially intended to report the procedure time for peripheral venous cannulation. Due to different clinical significance, we reported two outcomes in the final review - first-pass and overall cannulation procedure times. For clarity, the secondary outcome 'number of attempts' was rephrased as 'number of cannulation atempts'.

We initially planned to evaluate performance bias and detection bias separately, but due to the nature of the intervention, we combined these. We assessed the blinding domain, incomplete outcome domain, and overall risk separately for each outcome.

We removed "difficult versus not difficult" and "experience of ultrasound-guided cannulation: training versus clinical experience versus training plus clinical experience" from the Subgroup analysis and investigation of heterogeneity section because they were unnecessary.

We have rephrased the planned subgroup analysis relating to the operators' skills and setting to clarify our intentions in the Subgroup analysis and investigation of heterogeneity section.

We changed some subgroup analyses to match the difficulty with the landmark method and added explanations about the post hoc analysis in the Subgroup analysis and investigation of heterogeneity section.

We performed a meta-regression analysis to assess the effect of difficulty levels in the primary outcomes and added an explanation for it.

Because the analysis showed clear heterogeneity between the difficulty levels, we regarded the results for all participants considered together to be less meaningful and only reported the results separately according to the difficulty levels in the abstract and summary of findings tables.

We added subgroup analyses on types of operators.

NOTES

Parts of the Methods section of this review are based on a standard template produced by Cochrane Vascular.

INDEX TERMS

Medical Subject Headings (MeSH)

*Catheterization, Central Venous [methods]; *Catheterization, Peripheral [adverse effects]; Pain; Randomized Controlled Trials as Topic

MeSH check words

Adult; Humans