National Institute for Health and Care Excellence

FINAL

Antenatal care

[Q] Routine third trimester ultrasound for fetal growth

NICE guideline NG201

Evidence reviews underpinning recommendations 1.2.31 and 1.2.33 to 1.2.35

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Final

These evidence reviews were developed by the National Guideline Alliance, which is a part of the Royal College of Obstetricians and Gynaecologists

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Routine third trimester ultrasound for fetal growth

Review question

Is routine ultrasound in women from 28 weeks effective?

Introduction

In the UK, third trimester ultrasound in uncomplicated pregnancies is carried out when a clinical indication arises. Routine or universal ultrasound in uncomplicated pregnancies is not current practice. The aim of this review is to determine whether routine ultrasound is effective in the third trimester for women with uncomplicated pregnancies and could improve outcomes like admissions to neonatal units or stillbirths.

Summary of the protocol

See Table 1 for a summary of the Population, Intervention, Comparison and Outcome (PICO) characteristics of this review.

Table 1: Summary of the protocol (PICO table)

Population	All unselected or low risk pregnancies in late pregnancy (after 28 weeks gestational age)
Intervention	Any combination of • Routine ultrasound scan for assessing growth +/- Liquor volume +/- Umbilical artery Doppler
Comparison	• Indicated/selective ultrasound scan to assess fetal growth, concealed ultrasound scan, or no routine ultrasound scan

Outcome	**Critical**
	• Admission to neonatal unit
	• Perinatal mortality (stillbirth at or after 24+0 weeks gestation and neonatal death up to 6 weeks after birth)
	• Obstetric anal sphincter injury (OASIS)
	Important
	• Maternal anxiety
	• Length of neonatal stay in neonatal unit
	• Mode of birth
	  ○ Vaginal birth
	  - Spontaneous
	  - Assisted
	  ○ Caesarean section
	  - Elective
	  - Emergency
	• Shoulder dystocia

For further details see the review protocol in appendix A.

Methods and process

This evidence review was developed using the methods and process described in developing NICE guidelines: the manual 2014. Methods specific to this review question are described in the review protocol in appendix A.

Declarations of interest were recorded according to NICE's conflicts of interest policy.

Clinical evidence

Included studies

Sixteen articles reporting 15 randomised controlled trials (RCTs) and 1 cluster randomised trial were identified for this review.

The included studies are summarised in Table 2.

Eleven studies compared routine care with ultrasound in the third trimester to routine care (Ashimi 2018, Bakketeig 1984, Duff 1993, Eik-Nes 2000, Ewigman 1993, Hammad 2016, Henrichs 2019, McKenna 2003, Neilson 1984, Proud 1987, Skrastad 2013). Five studies compared routine care with Doppler scan in the third trimester to routine care (Davies 1992, Doppler French Study group 1997, Mason 1993, Newnham 1993, Whittle 1994).

One study was conducted in Australia (Newnham 1993); 1 study was conducted in France (Doppler French Study group 1997); 1 study was conducted in the Netherlands (Henrichs 2019); 1 study conducted in New Zealand (Duff 1993); 3 studies conducted in Norway (Bakketeig 1984, Eik-Nes 2000, Skrastad 2013); 6 studies conducted in the UK (Davies 1992, Mason 1993, McKenna 2003, Neilson 1984, Proud 1987, Whittle 1994); and 3 studies conducted in US (Ashimi 2018, Ewigman 1993, Hammad 2016).

See the literature search strategy in appendix B and study selection flow chart in appendix C.

Excluded studies

Studies not included in this review are listed, and reasons for their exclusion are provided in appendix K.

Summary of studies included in the evidence review

Summaries of the studies that were included in this review are presented in Table 2.

Table 2: Summary of included studies

Study	Population	Intervention	Comparison	Outcomes
Ashimi 2018 RCT US	N=205 pregnant women Mean maternal age: Not reported Mean gestational age: 29.1 weeks	Routine care (no details provided) + US every 4 weeks (at approximately 30, 34, and 38 weeks of gestation)	Routine care (no details provided)	• Admission to neonatal unit • Perinatal mortality • Mode of birth
Bakketeig 1984 RCT	N=1009 pregnant women Mean maternal age: Not reported	Routine care (US at 19 gestational weeks) + US at 32 gestational weeks	Routine care (US at 19 gestational weeks)	• Admission to neonatal unit • Perinatal mortality

Study	Population	Intervention	Comparison	Outcomes
Norway	Mean gestational age: Not reported <1% multiple pregnancies included in both arms			• Mode of birth
Davies 1992 RCT UK	N=2475 pregnant women Mean maternal age: 29.65 years Mean gestational age: Not reported <5% high-risk pregnancies included in both arms	Routine care (US at 19-22 weeks) + Doppler scan at 19-22 weeks + Doppler scan at 32 gestational weeks	Routine care (US at 19-22 weeks)	• Admission to neonatal unit • Perinatal mortality • Mode of birth
Doppler French Study Group 1997 RCT France	N=3839 pregnant women Mean maternal age: 27.85 years Mean gestational age: Not reported	Routine care (no details provided) + Doppler scan 28-34 gestational weeks	Routine care (no details provided)	• Admission to neonatal unit • Perinatal mortality • Mode of birth
Duff 1993 RCT New Zealand	N=1527 pregnant women Mean maternal age: Not reported Mean gestational age: Not reported 12.4% indigenous population included	Routine care (US at 16-24 weeks) + US at 32-36 gestational weeks	Routine care (US at 16-24 weeks)	• Admission to neonatal unit • Perinatal mortality
Eik-Nes 2000 RCT Norway	N=1628 pregnant women Mean maternal age: 26 years Mean gestational age: Not reported <2% multiple pregnancies included in both arms	Routine care (US at 18 weeks) + US at 32 gestational weeks (+ additional examination at 35 weeks' gestation if breech presentation)	Routine care (US at 18 weeks)	• Perinatal mortality • Mode of birth

Study	Population	Intervention	Comparison	Outcomes
Ewigman 1993 RCT US	N=15151 pregnant women Maternal age range: 20 to 35 years Mean gestational age: Not reported	Routine care (US at 15-22 gestational weeks) + US at 31 to 35 gestational weeks	Routine care (US at 15-22 gestational weeks)	• Perinatal mortality • Mode of birth
Hammad 2016 RCT US	N=145 pregnant women Mean maternal age: 26.06 years Mean gestational age: 28.1 years	Routine care (US at 26-29 weeks) + US at 30-32 gestational weeks + US at 36-37 gestational weeks	Routine care (US at 26-29 weeks)	• Admission to neonatal unit • Mode of birth
Henrichs 2019 Cluster randomised trial The Netherlands	Clusters: N=59 midwifery practices N=13046 pregnant women Mean maternal age: 31.0 years Mean gestational age: Not reported	Routine care (no details provided) + two US at 28-30 and 34-36 gestational weeks	Routine care (no details provided)	• Perinatal mortality • Obstetric anal sphincter injury (OASIS) • Mode of birth
Mason 1993 RCT UK	N=2025 pregnant women Mean maternal age: 25.17 years Mean gestational age: Not reported	Routine care (no details provided) + Doppler scan at 28 gestational weeks + Doppler scan at 34 gestational weeks	Routine care (no details provided)	• Admission to neonatal unit • Perinatal mortality • Mode of birth
McKenna 2003 RCT UK	N=1998 pregnant women Mean maternal age: 27.5 years Mean gestational age: Not reported	Routine care (US at 18-20 weeks) + US at 30-32 gestational weeks + US at 36-37 gestational weeks	Routine care (US at 18-20 weeks)	• Admission to neonatal unit • Perinatal mortality • Mode of birth
Neilson 1984 RCT UK	N=877 pregnant women Mean maternal age: 27.35 years	Routine care (US at <24 gestational weeks) + US at 34-36.5 gestational weeks	Routine care (US at <24 gestational weeks) + US at 34-36.5 gestational weeks (Concealed)	• Perinatal mortality • Mode of birth

Study	Population	Intervention	Comparison	Outcomes
	Mean gestational age: Not reported			
Newnham 1993 RCT Australia	N=2801 pregnant women Mean maternal age: 27.35 years Mean gestational age: Not reported	Routine care (US at 18 weeks) + Doppler scan at 24, 28, 34, and 38 gestational weeks	Routine care (US at 18 weeks)	• Perinatal mortality • Length of neonatal stay in neonatal unit • Mode of birth
Proud 1987 RCT UK	N=2000 pregnant women Mean maternal age: 25.55 years Mean gestational age: Not reported Multiple pregnancies included in both arms (unclear how many)	Routine care (US in early pregnancy) + US at 30-32 weeks + US at 34-36 weeks	Routine care (US in early pregnancy) + US at 30-32 weeks + US at 34-36 weeks (Concealed)	• Admission to neonatal unit • Perinatal mortality • Mode of birth
Skrastad 2013 RCT Norway	N=6399 pregnant women Mean maternal age: 27 years Mean gestational age: Not reported	Routine care (US at 18 gestational weeks) + US at 33 gestational weeks	Routine care (US at 18 gestational weeks)	• Admission to neonatal unit • Perinatal mortality • Mode of birth
Whittle 1994 RCT UK	N=2986 pregnant women Mean maternal age: 27.55 years Mean gestational age: Not reported	Routine care (no details provided) + Doppler scan at 26-30 gestational week + Doppler scan at 34-36 gestational weeks	Routine care (no details provided) + Doppler scan at 26-30 gestational week + Doppler scan at 34-36 gestational weeks (Concealed)	• Admission to neonatal unit • Perinatal mortality • Mode of birth

RCT: randomised controlled trial; US: ultrasound. Note: concealed = person not told of results

See the full evidence tables in appendix D and the forest plots in appendix E.

Quality assessment of studies included in the evidence review

See the evidence profiles in appendix F.

Economic evidence

Included studies

One economic study was identified which was relevant to this question (Wastlund 2019).

See the literature search strategy in appendix B and economic study selection flow chart in appendix G.

Excluded studies

Economic studies not included in this review are listed, and reasons for their exclusion are provided in appendix K.

Summary of studies included in the economic evidence review

See the economic evidence tables in appendix H and economic evidence profiles in appendix I.

Wastlund (2019) assessed the cost effectiveness of universal ultrasound scanning of late pregnancy screening for macrosomia (defined in study as equivalent to large for gestational age) in nulliparous women. The clinical inputs were informed from a cohort study conducted in Oxfordshire (Sovio 2018) on nulliparous women (N=3879). The comparator was selective ultrasound scanning which was also reported as current practice in the UK. The model structure separated diagnostic and clinical outcomes, with the latter used to compute the downstream costs and quality-adjusted life years (QALYs). Upon detection of a large for gestational age (LGA) fetus, the model assumes one of three management strategies that can be followed:

1. Planned caesarean section
2. Induction of labour
3. Expectant management

Where LGA is not detected, it was assumed that vaginal birth would be attempted, with the risk of an emergency caesarean section. 5 neonatal outcomes were possible; No complications, respiratory morbidity, shoulder dystocia, other acidosis and perinatal mortality.

Costing was undertaken using an NHS perspective, with all cost inputs either being extracted directly from the NHS Reference Costs database or costed using a ‘bottoms up’ approach from information of the included clinical studies, where an NHS unit cost code was unavailable. A discount rate of 3.5% was applied to all costs and QALYs that occur downstream, as in accordance with the NICE Reference case. Health-related quality of life, as measured by EQ-5D, pertained to both maternal and neonatal utility.

The incremental costs were mostly driven by the cost of the ultrasound scan, with universal ultrasound being a more expensive option for all treatment strategies. The model, assuming each of the treatment strategies are mutually exclusive, presented the results according to their rank dominance. In this instance, the results are ordered from the least expensive option, with the incremental cost effectiveness ratio (ICER) calculated beginning with the least expensive option, and comparing with the next most expensive, non-dominated option. Only the probabilistic results (n=100,000 simulations) were reported which showed that three strategies (selective ultrasound & planned caesarean, universal ultrasound & expectant management, and universal ultrasound & planned caesarean section) are dominated or extendedly dominated by other strategies. The most cost effective strategy was selective ultrasound & induction of labour where LGA is suspected. This represents current practice and was 70% likely to be the most cost effective option compared to the alternative strategies.

Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation.

Evidence statements

Clinical evidence statements

Comparison 1. Routine care plus third trimester ultrasound scan versus Routine care

Critical outcomes

Admission to neonatal unit

- Moderate quality evidence from 7 RCTs (N=13503) showed that there is no clinically important difference between routine care with a third trimester ultrasound scan and routine care on admission to neonatal unit in pregnant women with uncomplicated pregnancies: RR 1.03 (95% CI 0.92 to 1.16).

Perinatal mortality

- Very low quality evidence from 9 RCTs (N=30793) showed that there is no statistically significant difference between routine care with a third trimester ultrasound scan and routine care on perinatal mortality in pregnant women with uncomplicated pregnancies: POR 1.15 (95% CI 0.91 to 1.46) p=0.25.
- Very low quality evidence from 1 cluster randomised trial (N=13043) showed that there is no statistically significant difference between routine care with a third trimester ultrasound scan and routine care on perinatal mortality in pregnant women with uncomplicated pregnancies: OR 0.79 (95%CI 0.38 to 1.64) p=0.53.

Obstetric anal sphincter injury (OASIS)

- Moderate quality evidence from 1 cluster randomised trial (N=13044) showed that there is no clinically important difference between routine care with a third trimester ultrasound scan and routine care on OASIS in pregnant women with uncomplicated pregnancies: OR 1.18 (95%CI 0.94 to 1.48).

Important outcomes

Maternal anxiety

No evidence was identified to inform this outcome.

Length of neonatal stay in neonatal unit

No evidence was identified to inform this outcome.

Mode of birth

- Low quality evidence from 5 RCTs (N=5220) showed that there is no clinically important difference between routine care with a third trimester ultrasound scan and routine care on spontaneous vaginal birth in pregnant women with uncomplicated pregnancies: RR 0.98 (95% CI 0.95 to 1.02).
- Moderate quality evidence from 1 cluster randomised trial (N=12490) showed that there is no clinically important difference between routine care with a third trimester ultrasound scan and routine care on spontaneous vaginal birth in pregnant women with uncomplicated pregnancies: OR 0.97 (95% CI 0.90 to 1.50).

- Very low quality evidence from 8 RCTs (N=28974) showed that there is no clinically important difference between routine care with a third trimester ultrasound scan and routine care on assisted vaginal birth in pregnant women with uncomplicated pregnancies: RR 0.86 (95% CI 0.71 to 1.04).
- Moderate quality evidence from 1 cluster randomised trial (N=13044) showed that there is no clinically important difference between routine care with a third trimester ultrasound scan and routine care on assisted vaginal birth in pregnant women with uncomplicated pregnancies: OR 0.89 (95% CI 0.79 to 1.00).
- Low quality evidence from 9 RCTs (N=29179) showed that there is no clinically important difference between routine care with a third trimester ultrasound scan and routine care on elective caesarean sections in pregnant women with uncomplicated pregnancies: RR 1.03 (95% CI 0.97 to 1.10).
- Low quality evidence from 6 RCTs (N=12475) showed that there is no clinically important difference between routine care with a third trimester ultrasound scan and routine care on emergency caesarean sections in pregnant women with uncomplicated pregnancies: RR 1.03 (95% CI 0.89 to 1.19).
- High quality evidence from 1 cluster randomised trial (N=13043) showed that there is no clinically important difference between routine care with a third trimester ultrasound scan and routine care on caesarean section (unspecified) in pregnant women with uncomplicated pregnancies: OR 1.01 (95% CI 0.91 to 1.12).

Shoulder dystocia

No evidence was identified to inform this outcome.

Comparison 2. Routine care plus third trimester Doppler scan versus Routine care

Critical outcomes

Admission to neonatal unit

- Low quality evidence from 4 RCTs (N=11375) showed that there is no clinically important difference between routine care with a third trimester Doppler scan and routine care on admission to neonatal unit in pregnant women with uncomplicated pregnancies: RR 1.06 (95% CI 0.94 to 1.21).

Perinatal mortality

- Very low evidence from 5 RCTs (N=14209) showed that there is no statistically significant difference between routine care with a third trimester Doppler scan and routine care on perinatal mortality in pregnant women with uncomplicated pregnancies: RR 0.75 (95% CI 0.28 to 2.03) p=0.57.

Obstetric anal sphincter injury (OASIS)

No evidence was identified to inform this outcome.

Important outcomes

Maternal anxiety

No evidence was identified to inform this outcome.

Length of neonatal stay in neonatal unit

- High quality evidence from 1 RCT (N=2834) showed that there is no statistically significant difference between routine care with a third trimester Doppler scan and routine care on length of neonatal stay in neonatal unit in pregnant women with uncomplicated pregnancies: difference between medians 0, p=0.26.

Mode of birth

- Moderate quality evidence from 3 RCTs (N=9207) showed that there is no clinically important difference between routine care with a third trimester Doppler scan over and routine care on spontaneous vaginal birth in pregnant women with uncomplicated pregnancies: RR 0.99 (95% CI 0.97 to 1.08).
- Moderate quality evidence from 5 RCTs (N=14 209) showed that there is no clinically important difference between routine care with a third trimester Doppler scan and routine care on assisted vaginal birth in pregnant women with uncomplicated pregnancies: RR 1.02 (95% CI 0.97 to 1.08).
- Moderate quality evidence from 4 RCTs (N=11 375) showed that there is no clinically important difference between routine care with a third trimester Doppler scan and routine care on elective caesarean section in pregnant women with uncomplicated pregnancies: RR 1.02 (95% CI 0.86 to 1.20).
- Low quality evidence from 2 RCTs (N=6373) showed that there is no clinically important difference between routine care with a third trimester Doppler scan and routine care on emergency caesarean section in pregnant women with uncomplicated pregnancies: RR 0.94 (95% CI 0.74 to 1.19).

Shoulder dystocia

No evidence was identified to inform this outcome.

Economic evidence statements

- One directly applicable cost utility analysis from the UK showed that selective ultrasound, current UK practice, was the most cost effective strategy. The likelihood of cost effectiveness was >70% at a threshold of £20,000 per QALY gained.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

The outcomes of admission to the neonatal unit, perinatal mortality, and obstetric anal sphincter injury were considered critical outcomes as these may be influenced by ultrasound in the third trimester. Labour maybe induced if the baby was considered small or large for gestational age and birth maybe deferred if the baby was of appropriate size for gestational age. The outcomes of maternal anxiety, length of stay in neonatal unit, mode of birth, and shoulder dystocia were considered important outcomes. Ultrasound in third trimester could lead to maternal anxiety. It may influence length of stay in the neonatal unit, mode of birth, OASI and shoulder dystocia as scan findings can alter management of the woman's pregnancy.

The quality of the evidence

The quality of the evidence for establishing whether routine diagnostic ultrasound at or after 28+0 weeks gestation is effective for monitoring fetal wellbeing ranged from very low to high, with most of the evidence being of a moderate or low quality.

This was predominately due to serious overall risk of bias in some outcomes (due to the randomisation process and selection of the reported result); imprecision around the effect estimate in a few outcomes; and the presence of serious heterogeneity in a few outcomes, which was unresolved by subgroup analysis.

No evidence was identified to inform the outcomes of maternal anxiety and shoulder dystocia. No evidence was identified for routine liquor volume assessment.

Benefits and harms

The evidence showed that there was no difference in effectiveness between routine care plus third trimester ultrasound versus routine care (selective use of ultrasound) only, on all maternal and neonatal outcomes (admission to neonatal care, perinatal mortality, OASI (only reported for ultrasound) mode of birth, and length of neonatal stay in neonatal unit) in women with uncomplicated pregnancies.

Theoretically routine ultrasound will have effects on some outcomes not documented in this review. Inherently more testing will lead to more diagnoses of abnormalities, some of these will be true positives (in other words an increased detection rate), some of these will be false positives, potentially leading to increased maternal anxiety and inappropriate interventions. This review found no evidence relating to maternal anxiety and found evidence suggesting that the increased detection and intervention rate did not lead to clinically important differences between groups.

Based on the evidence included in this review, the committee agreed that there is no additional benefit to routinely scanning all women compared with selective scanning. However, it is important to emphasise this assumes appropriate selective scanning is being carried out. Based on the committee's experience there is a benefit to selective scanning of women with high risk pregnancies, this efficacy is partially informed by the accuracy of ultrasound (see review O on monitoring fetal growth). The results of this review were interpreted alongside evidence review O where the accuracy of symphysis fundal height measurement and ultrasound for growth to detect small or large for gestational age babies. The conclusions of the review were roughly that neither are particularly accurate but ultrasound was more accurate, although evidence on symphysis fundal height measurement was based on very limited evidence (only one small study which looked at small for gestational age [SGA] but not LGA).

The committee were aware that there are some risk factors for fetal growth restriction and agreed that a risk assessment should be done in early pregnancy (at booking appointment) when all pre and early pregnancy risk factors could be considered and again in the second trimester, when other risk factors may have become apparent (for example gestational hypertension). The committee were aware of available risk assessment tools, such as those in the Saving Babies Lives Care Bundle version 2 (2019) and RCOG Green-Top guideline on investigation and management of small-for-gestational age fetus (2013).

The committee also made informal consensus based recommendations about the response to concerns about SFH measurement being either SGA or LGA. For babies possibly being SGA, the committee agreed an ultrasound was required as being SGA may be associated with critical adverse outcomes including stillbirth that could require intervention of some kind. The urgency of this ultrasound would be dictated by the overall clinical findings and whether or not there were other reasons to be concerned about the wellbeing of the baby (for example a reduction in fetal movements) or mother (for example raised blood pressure or proteinuria). If there were concerns about SFH being LGA, the committee made a weaker recommendation to consider an ultrasound (for example to check for volume of amniotic fluid), however, LGA is less commonly associated with critical adverse outcomes such as stillbirth and may not warrant further investigation or intervention (particularly if the baby has been consistently LGA as opposed to changing growth trajectories), although LGA increases the risk of for example shoulder dystocia.

The committee noted that some women may have concerns that without a routine ultrasound scan in the third trimester their care may be worse or they may be at risk of worse outcomes. Given the relative strength of the evidence in this review the committee agreed that routine scanning in the third trimester should not be done because current evidence does not show that routinely scanning all women with uncomplicated, singleton pregnancies conveys a benefit. Although the committee agreed that the evidence in this review was of sufficient strength to recommend not offering a scan routinely, they noted the absence of evidence on the impact of anxiety. The committee was disappointed with the lack of evidence on maternal anxiety and would like to see this being researched in the future. However, a research recommendation was not prioritised because there was good amount of evidence on other key outcomes.

Cost effectiveness and resource use

There is unlikely to be a substantial increase in costs resulting from this recommendation as they align with current practice.

One included cost utility analysis presented to the committee (Wastlund 2019b) showed that selective ultrasound, current UK practice, was cost effective when compared with routine ultrasound. As there was no evidence of clinical efficacy from the evidence review of routine ultrasound, the committee noted that the recommendation to offer routine ultrasound would not be a cost effective use of resources as the incremental cost of the extra scan alone would entail a significant resource impact when multiplied by all pregnant women. The committee also noted that some outcomes related to morbidity may entail significant lifetime costs downstream. However, such outcomes were not found in the accompanying systematic review.

The one included economic study (Wastlund 2019b) did include outcomes related to brachial plexus injury which does have a high lifetime cost, though as this is weighted by the probability of an event occurring in both interventions, it is likely that such an outcome would have little bearing on cost effectiveness interpretations were a de novo model to be conducted. In the Wastlund 2019 study, inclusion of brachial plexus injury did not alter the cost effectiveness result (that selective ultrasound is cost effective).

The committee also highlighted litigation costs related to morbidity as being excessive. However, the committee acknowledged that this should not be a deciding factor in interpreting cost effectiveness of interventions as it falls outside the NICE Reference Case. Regardless, the evidence ascertained from the clinical review did not demonstrate efficacy of routine ultrasound scanning over selective ultrasound. Therefore, any linkage between the two treatment strategies with avoided litigation costs would be negligible, even if the unit cost of such costs would be appear individually substantial.

It is pertinent to note that Waslund (2019b) was concerned with screening for LGA only whereas the clinical review looked at both LGA and SGA. Whilst there were no economic studies that looked at SGA, the interpretation of the evidence in the guideline clinical review does not lend itself to making a recommendation for routine ultrasound scanning.

References

Ashimi 2018

Ashimi Balogun, O., Sibai, B. M., Pedroza, C., Blackwell, S. C., Barrett, T. L., Chauhan, S. P., Serial Third-Trimester Ultrasonography Compared With Routine Care in Uncomplicated Pregnancies: a Randomized Controlled Trial, Obstetrics and Gynecology, 132, 1358-1367, 2018

Bakketeig 1984

Bakketeig,L.S., Eik-Nes,S.H., Jacobsen,G., Ulstein,M.K., Brodtkorb,C.J., Balstad,P., Eriksen,B.C., Jorgensen,N.P., Randomised controlled trial of ultrasonographic screening in pregnancy, Lancet, 2, 207-211, 1984

Davies 1992

Davies,J.A., Gallivan,S., Spencer,J.A., Randomised controlled trial of Doppler ultrasound screening of placental perfusion during pregnancy, Lancet, 340, 1299-1303, 1992

Duff 1993

Duff, G. B., A randomized controlled trial in a hospital population of ultrasound measurement screening for the small for dates baby, Australian & New Zealand Journal of Obstetrics & Gynaecology, 33, 374-8, 1993

Eik-Nes 2000

Eik-Nes, S. H., Salvesen, K. A., Okland, O., Vatten, L. J., Routine ultrasound fetal examination in pregnancy: the 'Alesund' randomized controlled trial, Ultrasound in Obstetrics & Gynecology, 15, 473-8, 2000

Ewigman 1993

Ewigman, B. G., Crane, J. P., Frigoletto, F. D., LeFevre, M. L., Bain, R. P., McNellis, D., Effect of prenatal ultrasound screening on perinatal outcome. RADIUS Study Group, N Engl J MedThe New England journal of medicine, 329, 821-7, 1993

French Doppler Group 1997

A randomised controlled trial of Doppler ultrasound velocimetry of the umbilical artery in low risk pregnancies. Doppler French Study Group, Br J Obstet GynaecolBritish journal of obstetrics and gynaecology, 104, 419-24, 1997

Hammad 2015

Hammad, I. A., Chauhan, S. P., Mlynarczyk, M., Rabie, N., Goodie, C., Chang, E., Magann, E. F., Abuhamad, A. Z., Uncomplicated Pregnancies and Ultrasounds for Fetal Growth Restriction: A Pilot Randomized Clinical Trial, AJP Reports, 6, e83-e90, 2015

Henrichs 2019

Henrichs, J., Verfaille, V., Jellema, P., Viester, L., Pajkrt, E., Wilschut, J., van der Horst, H. E., Franx, A., de Jonge, A., Iris study group, Effectiveness of routine third trimester ultrasonography to reduce adverse perinatal outcomes in low risk pregnancy (the IRIS study): nationwide, pragmatic, multicentre, stepped wedge cluster randomised trial, BMJ, 367, l5517, 2019

Mason 1993

Mason, G. C., Lilford, R. J., Porter, J., Nelson, E., Tyrell, S., Randomised comparison of routine versus highly selective use of Doppler ultrasound in low risk pregnancies, British Journal of Obstetrics and Gynaecology, 100, 130-133, 1993

McKenna 2003

McKenna,D., Tharmaratnam,S., Mahsud,S., Bailie,C., Harper,A., Dornan,J., A randomized trial using ultrasound to identify the high-risk fetus in a low-risk population, Obstetrics and Gynecology, 101, 626-632, 2003

Neilson 1984

Neilson, J. P., Munjanja, S. P., Whitfield, C. R., Screening for small for dates fetuses: A controlled trial, British Medical Journal, 289, 1179-1182, 1984

Newnham 1993

Newnham,J.P., Evans,S.F., Michael,C.A., Stanley,F.J., Landau,L.I., Effects of frequent ultrasound during pregnancy: a randomised controlled trial, Lancet, 342, 887-891, 1993

Proud 1987

Proud,J., Grant,A.M., Third trimester placental grading by ultrasonography as a test of fetal wellbeing, British Medical Journal Clinical Research Ed., 294, 1641-1644, 1987

Roma 2015

Roma, E., Arnau, A., Berdala, R., Bergos, C., Montesinos, J., Figueras, F., Ultrasound screening for fetal growth restriction at 36 vs 32 weeks' gestation: A randomized trial (ROUTE), Ultrasound in Obstetrics and Gynecology, 46, 391-397, 2015

Skrastad 2013

Skrastad,R.B., Eik-Nes,S.H., Sviggum,O., Johansen,O.J., Salvesen,K.A., Romundstad,P.R., Blaas,H.G., A randomized controlled trial of third-trimester routine ultrasound in a non-selected population, Acta Obstetricia et Gynecologica Scandinavica, 92, 1353-1360, 2013

Whittle 1994

Whittle,M.J., Hanretty,K.P., Primrose,M.H., Neilson,J.P., Screening for the compromised fetus: a randomized trial of umbilical artery velocimetry in unselected pregnancies, American Journal of Obstetrics and Gynecology, 170, 555-559, 1994

Appendices

Appendix A – Review protocol

Review protocol for review question: Is routine ultrasound in women from 28 weeks effective?

Table 3: Review protocol

Field (based on PRISMA-P)	Content
Review question	Is routine ultrasound in women from 28 weeks effective?
Type of review question	Intervention review
Objective of the review	The aim of this review is to establish whether routine diagnostic ultrasound at or after 28+0 weeks gestation is effective for monitoring fetal wellbeing.
Eligibility criteria – population	All unselected or low-risk pregnant woman in late pregnancy (after 28 weeks gestational age)
Eligibility criteria – Intervention(s)	Any combination of Routine ultrasound scan for assessing growth +/- Liquor volume +/- Umbilical artery Doppler
Eligibility criteria – Comparator(s)	Indicated/selective ultrasound scan to assess fetal growth, concealed ultrasound scan, or no routine ultrasound scan Note: Data on all 3 eligible comparators will be pooled. Concealed = person not told of results

Outcomes and prioritisation	**Critical outcomes**
	• Admission to neonatal unit
	• Perinatal mortality (stillbirth at or after 24+0 weeks gestation and neonatal death up to 6 weeks after birth)
	• Obstetric anal sphincter injury (OASIS)
	
	Important outcomes
	• Maternal anxiety
	• Length of neonatal stay in neonatal unit
	• Mode of birth:
	  ○ Vaginal birth
	  - Spontaneous

Field (based on PRISMA-P)	Content
	- Assisted ○ Caesarean Section - Elective - Emergency • Shoulder dystocia
Eligibility criteria – study design	INCLUDE: • Systematic reviews of randomised controlled trials • Randomised or quasi-randomised controlled trials (individual or cluster) Note: For further details, see the algorithm in appendix H, Developing NICE guidelines: the manual.
Other inclusion exclusion criteria	Exclusion POPULATION: • Studies exclusively on multiple pregnancies • Pregnancy with known or pre-existing congenital anomalies STUDY DESIGN: • Cohort studies • Case control studies • Cross-sectional studies • Epidemiological reviews or reviews on associations • Non-comparative studies • Non-randomised controlled trials PUBLICATION STATUS: • Conference abstract LANGUAGE: • Non-English Inclusion COUNTRY: • High-income (as defined by the World Bank) countries only (see https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups for classification of countries).
Proposed sensitivity/sub-group analysis, or meta-regression	Statistical heterogeneity will be assessed by visually examining the forest plots and by calculating the I^2 inconsistency statistic (with an I^2 value ≥50% indicating serious heterogeneity, and ≥80% indicating very serious heterogeneity).

Field (based on PRISMA-P)	Content
Selection process – duplicate screening/selection/analysis	Studies included in the 2008 NICE guideline on antenatal care for uncomplicated pregnancies (CG62) that satisfy the review protocol will be included in this review. Review questions selected as high priorities for health economic analysis (and those selected as medium priorities and where health economic analysis could influence recommendations) will be subject to dual weeding and study selection; any discrepancies above 10% of the dual weeded resources will be resolved through discussion between the first and second reviewers or by reference to a third person. All data extraction will quality assured by a senior reviewer. Draft excluded studies and evidence tables will be circulated to the Topic Group for their comments. Resolution of disputes will be by discussion between the senior reviewer, Topic Advisor and Chair.
Data management (software)	NGA STAR software will be used to generate bibliographies/citations, and conduct sifting and data extraction. Pairwise meta-analyses, if possible, will be conducted using Cochrane Review Manager (RevMan5). For details please see supplement 1: methods. 'GRADEpro' will be used to assess the quality of evidence for each outcome.
Information sources – databases and dates	Sources to be searched: Medline, Medline In-Process, CCTR, CDSR, DARE, HTA, Embase. Limits (for example, date, study design): Date limit: 2014 (2008 NICE guideline on antenatal care for uncomplicated pregnancies (CG62) included original 2001 version of 2015 Cochrane update review and no other articles, so 2015 version will include all CG62 studies. Last date of Cochrane review search was August 2014) Apply standard animal/non-English language exclusion Limit to RCTs and systematic reviews in first instance but download all results.
Identify if an update	This guideline update will replace the 2008 NICE guideline on antenatal care for uncomplicated pregnancies (CG62). The following relevant recommendations in CG62 regarding fetal growth and well-being were made: 1.10.1 Symphysis–fundal height should be measured and recorded at each antenatal appointment from 24 weeks. [2008] 1.10.2 Ultrasound estimation of fetal size for suspected large-for-gestational-age unborn babies should not be undertaken in a low-risk population. [2008] 1.10.3 Routine Doppler ultrasound should not be used in low-risk pregnancies. [2008] 1.10.4 Fetal presentation should be assessed by abdominal palpation at 36 weeks or later, when presentation is likely to influence the plans for the birth. Routine assessment of presentation by abdominal palpation should not be offered before 36 weeks because it is not always accurate and may be uncomfortable. 1.10.5 Suspected fetal malpresentation should be confirmed by an ultrasound assessment. 1.10.6 Routine formal fetal-movement counting should not be offered. 1.10.7 Auscultation of the fetal heart may confirm that the fetus is alive but is unlikely to have any predictive value and routine listening is therefore not recommended. However, when requested by the mother, auscultation of the fetal heart may provide reassurance. 1.10.8 The evidence does not support the routine use of antenatal electronic fetal heart rate monitoring (cardiotocography) for fetal assessment in women with an uncomplicated pregnancy and therefore it should not be offered. 1.10.9 The evidence does not support the routine use of ultrasound scanning after 24 weeks of gestation and therefore it should not be offered.
Author contacts	Developer: National Guideline Alliance

Field (based on PRISMA-P)	Content
Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual.
Search strategy – for one database	For details please see appendix B.
Data collection process – forms/duplicate	A standardised evidence table format will be used, and published as appendix D (clinical evidence tables) or H (economic evidence tables).
Data items – define all variables to be collected	For details please see evidence tables in appendix D (clinical evidence tables) or H (economic evidence tables).
Methods for assessing bias at outcome/study level	Quality assessment of individual studies will be performed using the following checklists: • ROBIS tool for systematic reviews • Cochrane RoB tool, v.2, for RCTs For details please see section 6.2 of Developing NICE guidelines: the manual. The risk of bias across all available evidence will be evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group: http://www.gradeworkinggroup.org/
Criteria for quantitative synthesis (where suitable)	For details please see section 6.4 of Developing NICE guidelines: the manual.
Methods for analysis – combining studies and exploring (in)consistency	For details please see supplement 1: methods.
Meta-bias assessment – publication bias, selective reporting bias	For details please see supplement 1: methods and section 6.2 of Developing NICE guidelines: the manual. If sufficient relevant RCT evidence is available, publication bias will be explored using RevMan software to examine funnel plots. Trial registries will be examined to identify missing evidence: Clinical trials.gov, NIHR Clinical Trials Gateway.
Assessment of confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual.
Rationale/context – Current management	For details please see the introduction to the evidence review.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the guideline. The committee was convened by the National Guideline Alliance and chaired by Kate Harding in line with section 3 of Developing NICE guidelines: the manual. Staff from the National Guideline Alliance undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the guideline in collaboration with the committee. For details please see supplement 1: methods.
Sources of funding/support	The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists.
Name of sponsor	The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists.

Field (based on PRISMA-P)	Content
Roles of sponsor	NICE funds the National Guideline Alliance to develop guidelines for those working in the NHS, public health, and social care in England.
PROSPERO registration number	This protocol is not registered with PROSPERO.

CCTR: Cochrane Controlled Trials Register; CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; DARE: Database of Abstracts of Reviews of Effects; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HTA: Health Technology Assessment; NGA: National Guideline Alliance; NICE: National Institute for Health and Care Excellence; NIHR: National Institute for Health Research; RCT(s): randomised controlled trial(s); RoB: risk of bias; ROBIS: Risk Of Bias In Systematic reviews tool; ROBINS-I: Risk Of Bias In Non-randomized studies – of Interventions tool; US: ultrasound

Appendix B – Literature search strategies

Literature search strategies for review question: Is routine ultrasound in women from 28 weeks effective?

Database(s): Medline & Embase (Multifile)
Last searched on **Embase Classic+Embase** 1947 to 2020 September 08, **Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily** 1946 to September 08, 2020
Date of last search: 8th September 2020
Multifile database codes: emczd = Embase Classic+Embase; ppez= MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily

#	Searches
1	Pregnancy Trimester, Third/ or *Prenatal Care/
2	third trimester pregnancy/ or *prenatal care/
3	pregnan$.tw,kw.
4	((antenatal$ or ante-natal$ or ante natal$ or prenatal$ or pre-natal$ or pre natal$) adj care).tw,kw.
5	(1 or 3 or 4) use ppez
6	(2 or 3 or 4) use emczd
7	5 or 6
8	Ultrasonography, Prenatal/ use ppez
9	fetus echography/ use emczd
10	Ultrasonography/ use ppez
11	Fetus/ or Fetal Monitoring/ or Fetal Growth Retardation/ or Fetal Development/ or Pregnancy Outcome/
12	11 use ppez
13	10 and 12
14	echography/ or real-time echography/ or ultrasound/
15	14 use emczd
16	fetus/ or fetus monitoring/ or intrauterine growth retardation/ or fetal development/ or pregnancy outcome/
17	16 use emczd
18	15 and 17
19	(routine adj3 (ultrasound$ or ultrasonograph$ or doppler$)).tw,kw.
20	((ultrasound$ or ultrasonograph$ or ultrasonic$ or doppler$) adj screening).tw,kw.
21	8 or 9 or 13 or 18 or 19 or 20
22	7 and 21
23	Pregnancy/
24	8 or 9 or 10 or 15
25	Birth Weight/ or Fetal Weight/
26	25 use ppez
27	birth weight/ or fetus weight/ or fetus size/
28	27 use emczd
29	26 or 28
30	23 and 24 and 29
31	((fetal or foetal or fetus or foetus) adj1 (well-being or wellbeing or well being)).tw,kw.
32	23 and 24 and 31
33	22 or 30 or 32
34	(controlled clinical trial or pragmatic clinical trial or randomized controlled trial).pt. or drug therapy.fs. or (groups or placebo or randomi#ed or randomly or trial).ab.
35	crossover procedure/ or double blind procedure/ or randomized controlled trial/ or single blind procedure/ or (assign* or allocat* or crossover* or cross over* or ((doubl* or singl*) adj blind*) or factorial* or placebo* or random* or volunteer*).ti,ab.
36	meta-analysis/
37	meta-analysis as topic/
38	systematic review/
39	meta-analysis/
40	(meta analy* or metanaly* or metaanaly*).ti,ab.
41	((systematic or evidence) adj2 (review* or overview*)).ti,ab.
42	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
43	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
44	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
45	(search* adj4 literature).ab.
46	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
47	cochrane.jw.

#	Searches
48	((pool* or combined) adj2 (data or trials or studies or results)).ab.
49	letter/
50	editorial/
51	news/
52	exp historical article/
53	Anecdotes as Topic/
54	comment/
55	case report/
56	(letter or comment*).ti.
57	49 or 50 or 51 or 52 or 53 or 54 or 55 or 56
58	randomized controlled trial/ or random*.ti,ab.
59	57 not 58
60	animals/ not humans/
61	exp Animals, Laboratory/
62	exp Animal Experimentation/
63	exp Models, Animal/
64	exp Rodentia/
65	(rat or rats or mouse or mice).ti.
66	59 or 60 or 61 or 62 or 63 or 64 or 65
67	letter.pt. or letter/
68	note.pt.
69	editorial.pt.
70	case report/ or case study/
71	(letter or comment*).ti.
72	67 or 68 or 69 or 70 or 71
73	randomized controlled trial/ or random*.ti,ab.
74	72 not 73
75	animal/ not human/
76	nonhuman/
77	exp Animal Experiment/
78	exp Experimental Animal/
79	animal model/
80	exp Rodent/
81	(rat or rats or mouse or mice).ti.
82	74 or 75 or 76 or 77 or 78 or 79 or 80 or 81
83	66 use ppez
84	82 use emczd
85	83 or 84
86	34 use ppez
87	35 use emczd
88	86 or 87
89	(or/36-37,40,42-47) use ppez
90	(or/38-41,43-48) use emczd
91	89 or 90
92	33 and 85
93	33 not 92
94	88 or 91
95	93 and 94
96	limit 95 to english language
97	limit 96 to yr="2014 -Current"

Database(s): Cochrane Library
Last searched on **Cochrane Database of Systematic Reviews**, Issue 9 of 12, September 2020, **Cochrane Central Register of Controlled Trials**, Issue 9 of 12, September 2020
Date of last search: 8th September 2020

#	Searches
#1	MeSH descriptor: [Pregnancy Trimester, Third] this term only
#2	MeSH descriptor: [Prenatal Care] this term only
#3	(pregnan*):ti,ab,kw
#4	(((antenatal* or ante-natal* or ante natal* or prenatal* or pre-natal* or pre natal*) NEXT care)):ti,ab,kw
#5	#1 OR #2 OR #3 OR #4
#6	MeSH descriptor: [Ultrasonography, Prenatal] this term only
#7	MeSH descriptor: [Ultrasonography] this term only
#8	MeSH descriptor: [Fetus] this term only
#9	MeSH descriptor: [Fetal Monitoring] this term only
#10	MeSH descriptor: [Fetal Growth Retardation] this term only
#11	MeSH descriptor: [Fetal Development] this term only

#	Searches
#12	MeSH descriptor: [Pregnancy Outcome] this term only
#13	#8 OR #9 OR #10 OR #11 OR #12
#14	#7 AND #13
#15	((routine NEAR/3 (ultrasound* or ultrasonograph* or doppler*))):ti,ab,kw
#16	(((ultrasound* or ultrasonography* or ultrasonic* or doppler*) NEXT screening)):ti,ab,kw
#17	#6 OR #14 OR #15 OR #16
#18	#5 AND #17
#19	MeSH descriptor: [Pregnancy] this term only
#20	MeSH descriptor: [Birth Weight] this term only
#21	MeSH descriptor: [Fetal Weight] this term only
#22	(((fetal or foetal or fetus or foetus) NEAR/1 (well-being or wellbeing or well being))):ti,ab,kw
#23	#20 OR #21 OR #22
#24	#6 OR #7
#25	#19 AND #23 AND #24
#26	#18 OR #25 Publication Year from 2014 to current

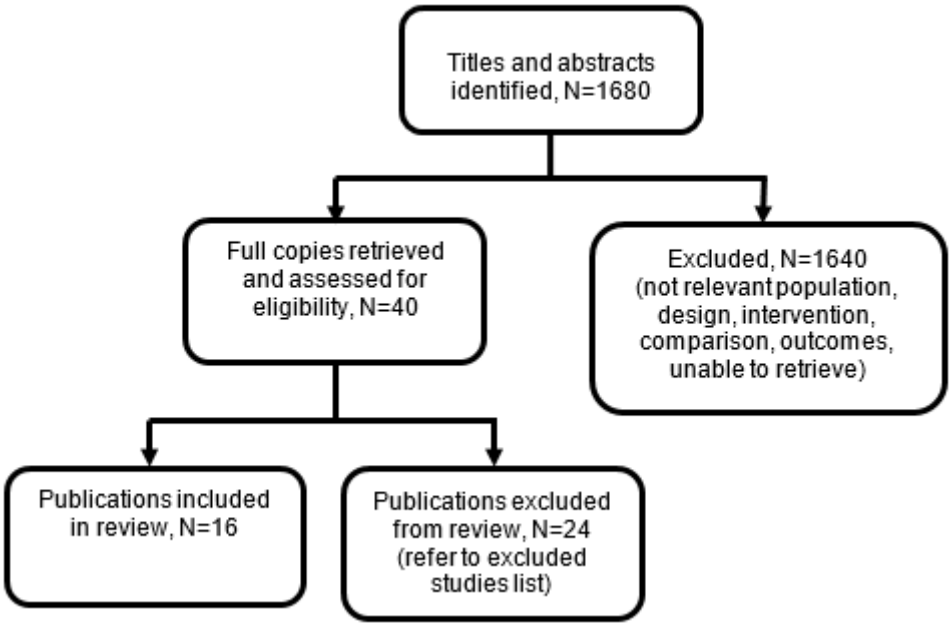
Database(s): CRD: Database of Abstracts of Reviews of Effects (DARE), HTA Database
Date of last search: 8th September 2020

#	Searches
1	MeSH DESCRIPTOR Pregnancy Trimester, Third IN DARE,HTA
2	MeSH DESCRIPTOR Prenatal care IN DARE,HTA
3	(pregnan*) IN DARE, HTA
4	(((antenatal* or ante-natal* or ante natal* or prenatal* or pre-natal* or pre natal*) NEXT care)) IN DARE, HTA
5	#1 OR #2 OR #3 OR #4
6	MeSH DESCRIPTOR Ultrasonography, Prenatal IN DARE,HTA
7	MeSH DESCRIPTOR Ultrasonography IN DARE,HTA
8	MeSH DESCRIPTOR Fetus IN DARE,HTA
9	MeSH DESCRIPTOR Fetal Monitoring IN DARE,HTA
10	MeSH DESCRIPTOR Fetal Growth Retardation IN DARE,HTA
11	MeSH DESCRIPTOR Fetal Development IN DARE,HTA
12	MeSH DESCRIPTOR Pregnancy Outcome IN DARE,HTA
13	#8 OR #9 OR #10 OR #11 OR #12
14	#7 AND #13
15	((routine NEAR3 (ultrasound* or ultrasonograph* or doppler*))) IN DARE, HTA
16	(((ultrasound* or ultrasonograph* or ultrasonic* or doppler*) NEXT screening)) IN DARE, HTA
17	#6 OR #14 OR #15 OR #16
18	#5 AND #17
19	MeSH DESCRIPTOR Pregnancy IN DARE,HTA
20	MeSH DESCRIPTOR Birth weight IN DARE,HTA
21	MeSH DESCRIPTOR Fetal weight IN DARE,HTA
22	(((fetal or foetal or fetus or foetus) NEAR1 (well-being or wellbeing or well being))) IN DARE, HTA
23	#20 OR #21 OR #22
24	#6 OR #7
25	#19 AND #23 AND #24
26	#18 OR #25 Publication Year from 2014 to current

Appendix C – Clinical evidence study selection

Study selection for: Is routine ultrasound in women from 28 weeks effective?

Figure 1: Study selection flow chart



Appendix D – Clinical evidence tables

Evidence tables for review question: Is routine ultrasound in women from 28 weeks effective?

Table 4: Evidence tables

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Ashimi Balogun, O., Sibai, B. M., Pedroza, C., Blackwell, S. C., Barrett, T. L., Chauhan, S. P., Serial Third-Trimester Ultrasonography Compared With Routine Care in Uncomplicated Pregnancies: a Randomized Controlled Trial, Obstetrics and Gynecology, 132, 1358-1367, 2018 **Ref Id** 1030665 **Country/ies where the study was carried out** USA **Study type** Randomised controlled trial **Aim of the study** To evaluate whether serial ultrasound examinations in the third trimester increase	**Sample size** N=206 (N=205 analysed) Intervention: n=104 Control: n=102 (n=101 analysed since n=1 gave birth elsewhere so data unavailable for analysis) **Characteristics** Maternal age- 18-19 (years)- Number Intervention: 10/104 Control: 5/102 Maternal age- 35 or older (years)- Number Intervention: 10/104 Control: 12/102 Gestational age at randomisation- Weeks Intervention: 29.0±1.1 Control: 29.2±1.0 Race-ethnicity- Black- Number Intervention: 34/104 Control: 32/102 Race-ethnicity- White- Number Intervention: 25/104 Control: 23/102	**Interventions** Intervention: ultrasound examination every 4 weeks (at approximately 30, 34, and 38 weeks of gestation) Control: routine care (serial fundal height measurements at each clinical appointment prompting an ultrasound examination if a discrepancy was present)	**Details** **Power analysis** A total of 194 women needed to be randomized for an alpha of 5% and a power of 80%. An estimated 5% of women were predicted to be lost to follow-up based on a previous pilot study. **Statistical analyses** Descriptive statistics were used to summarise all study variables. Categorical variables were reported as frequencies and percentages. Fisher exact, χ^2 tests, or two-sample t tests were used to assess group differences (routine vs serial ultrasound examinations) in patient outcomes. Subgroup analysis was performed using similar methods. Relative risk (RR) and 95% CI were calculated as was number needed to identify the primary composite outcome. All analyses were	**Results** **Critical outcomes** **Admission to neonatal unit** Admission to ICU- Number Intervention: 0/104 Control: 0/101 **Perinatal mortality** Stillbirth and neonatal death within 28 days- Number Intervention: 0/104 Control: 1/101 **Important outcomes** **Mode of birth** Vaginal birth-Spontaneous- Number Intervention: 81/104 Control: 73/101 Caesarean section-Elective- Number Intervention: 22/104 Control: 28/101 Caesarean section-Emergency (Caesarean delivery in labour)- Number Intervention: 5/104 Control: 6/101	**Limitations** **Cochrane risk of bias tool V2:** Randomisation process: Low risk. (Block randomisation from computer randomisation. Allocation concealment by randomisation module) Deviations from intended interventions (assignment): Low risk. (It was not feasible to blind participants due to study design). Missing outcome data: Low risk. (0.5% participants lost to follow-up in control arm). Measurement of the outcome: Low risk. (Outcomes reported were objective). Selection of the reported result: Low risk. (Study trial protocol reported). Other bias: Low risk. (No other biases detected). Overall risk: Low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
identification of a composite of growth or amniotic fluid abnormalities when compared with routine care among pregnancies that are uncomplicated between 24 0/7 and 30 6/7 weeks of gestation. **Study dates** 11th July 2016 to 24th May 2017 **Source of funding** No report of any funding that may cause potential conflicts of interest.	Race-ethnicity- Hispanic-Number Intervention: 22/104 Control: 20/102 Race-ethnicity- Other-Number Intervention: 23/104 Control: 27/102 Nulliparity- Number Intervention: 39/104 Control: 43/102 **Inclusion criteria** • Women who were at least 18 years old; • Women who had a singleton pregnancy with no major prenatally diagnosed fetal anomalies; • Women who had an estimated due date based on IVF or ultrasound examination before 22 0/7 weeks. **Exclusion criteria** • First ultrasound examination after 22 weeks of gestation;		conducted using Stata 13.0. **Intention-to-treat analysis** All randomsied women were included in the intent-to-treat analysis.		

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	• Women with any medical complication or co-morbidity at the time of randomisation; • Women who were unable to sign a consent in the English language; • Institutionalised individuals (prisoners).				
Full citation Bakketeig,L.S., Eik-Nes,S.H., Jacobsen,G., Ulstein,M.K., Brodtkorb,C.J., Balstad,P., Eriksen,B.C., Jorgensen,N.P., Randomised controlled trial of ultrasonographic screening in pregnancy, Lancet, 2, 207-211, 1984 **Ref Id** 193453 **Country/ies where the study was carried out** Norway **Study type** Randomised controlled trial	**Sample size** N=1009 (N=974 analysed) Intervention: n=510 (n=496 analysed of which 490 singletons) Control: n=499 (n=478 analsyed of which 478 singletons) *Data extracted for singleton pregnancies only. **Characteristics** There were no significant differences between two groups. **Inclusion criteria**	**Interventions** Intervention: routine care (scan at 19 weeks gestation) + scan at 32 weeks gestation Control: routine care (scan at 19 weeks gestation) only	**Details** **Power analysis** The sample size was based on an expected 50% reduction in post-term induced labours (α=0.05, β=0.10). **Statistical analyses** Results in the two study groups were compared by the χ^2 statistic and Student's *t* test. **Intention-to-treat analysis** Not mentioned.	**Results** **Critical outcomes** **Admission to neonatal unit** Transfer to neonatal intensive-care unit- Number (%) Intervention: 17/490 (3.5) Control: 22/474 (4.6) **Perinatal mortality** Perinatal death- Number (%) Intervention: 5/490 (1.0) Control: 3/474 (0.6) **Important outcomes** **Mode of birth** Vaginal birth- Induced labour- Number (%)* Intervention: 32/496 (6.5) Control: 38/478 (7.9) Vaginal birth- Assisted (forceps)- Number (%)* Intervention: 16/496 (3.2) Control: 14/478 (2.9)	**Limitations** **Cochrane risk of bias tool V2:** Randomisation process: Some concerns. (No details given on random sequence generation. Allocation concealment by sealed-envelope method). Deviations from intended interventions (assignment): Low risk. (It was not feasible to blind participants due to study design). Missing outcome data: Low risk. (2.75% lost in intervention arm and 4.21% lost in control arm to follow-up). Measurement of the outcome: Low risk. (Those who assessed outcomes did not know which group the women were in).

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Aim of the study Not mentioned. **Study dates** May 1979 to September 1980 **Source of funding** The county public health office of Sor-Trondelag County	• Women attending their first antenatal care visit; • Women before 18 gestational weeks. **Exclusion criteria** Not mentioned			Vaginal birth- Assisted (vacuum)- Number (%)* Intervention: 14/496 (2.8) Control: 8/478 (1.7) Vaginal birth- Assisted breech- Number (%)* Intervention: 13/496 (2.6) Control: 10/478 (2.1) Caesarean section- Elective- Number (%)* Intervention: 8/496 (1.6) Control: 5/478 (1.0) Caesarean section- Emergency- Number (%)* Intervention: 21/496 (4.2) Control: 12/478 (2.5) *Includes both singleton and multiple pregnancies. Data extracted for births available for analysis.	Selection of the reported result: Some concerns. (No trial protocol reported). Other bias: Low risk. (No other bias apparent). Overall risk: Some concerns
Full citation Davies,J.A., Gallivan,S., Spencer,J.A., Randomised controlled trial of Doppler ultrasound screening of placental perfusion during pregnancy, Lancet, 340, 1299-1303, 1992 **Ref Id** 169164 **Country/ies where the study was carried out** United Kingdom	**Sample size** N=2600 (n=2475 analysed) Intervention: n=1246 Control: n=1229 **Characteristics** Mean age (years)- Mean (±SD) Intervention: 29.6 (5.2) Control: 29.7 (5.1) Nulliparous- Number (%) Intervention: 652 (52.3) Control: 627 (51) Number of high risk pregnancies- Number (%) Intervention: 192 (15.4)	**Interventions** Intervention: routine care + doppler at 19-22 weeks + doppler at 32 weeks (low risk pregnancies) Control: routine care only	**Details** **Power analysis** The sample size was chosen to have an 80% chance at the 5% level of significance of demonstrating a 20% reduction in antenatal admissions during pregnancy in the doppler group. **Statistical analyses** Data were analysed with SPSS/PC+ statistical software. Analysis was done by Student's t test, chi-squared, or Fisher's	**Results** **Critical outcomes** **Admission to neonatal unit** Admission to the neonatal intensive care unit- Number Intervention: 44/1246 Control: 43/1229 **Perinatal mortality** Stillbirths- Number Intervention: 11/1246 Control: 4/1229 Fetal deaths- Number Intervention: 11/1246 Control: 4/1229	**Limitations** **Cochrane risk of bias tool V2:** Randomisation process: Low risk. (Participants randomised by block randomisation. Allocation concealment by sealed opaque envelopes). Deviations from intended interventions (assignment): Low risk. (Blinding of participants and personnel was not feasible for this study). Missing outcome data:

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study type Randomised controlled trial **Aim of the study** To test the value of routine doppler ultrasonography in general obstetric population. **Study dates** 1989 **Source of funding** Institute Trust Fund and Queen Charlotte's and Hammersmith Special Health Authority (grant RC/110)	Control: 189 (15.4) **Inclusion criteria** • First (booking) visit to antenatal clinic at Queen Charlotte's and Chelsea Hospital before 20 weeks' gestation **Exclusion criteria** Not mentioned		exact tests, depending on the variable. **Intention-to-treat analysis** Not mentioned.	Early neonatal deaths- Number Intervention: 4/1246 Control: 0/1229 Perinatal deaths- Number Intervention: 33/1246 Control: 11/1229 **Important outcomes** **Mode of birth** Vaginal birth- Spontaneous- Number (%) Intervention: 877/1246 (70.4) Control: 863/1229 (70.2) Vaginal birth- Assisted- Number (%) Intervention: 278/1246 (22.3) Control: 274/1229 (22.3) Caesarean section- Elective- Number (%) Intervention: 78/1246 (7.8) Control: 81/1229 (6.6) Caesarean section- Emergency- Number (%) Intervention: 13/1246 (1.0) Control: 11/1229 (0.9)	Low risk. (4.81% lost to follow-up overall. Unclear which arms participants lost from). Measurement of the outcome: Low risk. (Outcomes reported were objective). Selection of the reported result: Some concerns. (No trial protocol reported). Other bias: Some concerns. (No details provided for participant baseline characteristics). Overall risk: Some concerns
Full citation A randomised controlled trial of Doppler ultrasound velocimetry of the umbilical artery in low risk pregnancies. Doppler French Study Group, British journal of obstetrics and gynaecology, 104, 419-24, 1997	**Sample size** N= 4072 (3839 analysed) Intervention: n=2041 (1950 analysed) Control: 2031 (1948 analysed) **Characteristics** Maternal age (years)- Mean (±SD)	**Interventions** Intervention: routine care + doppler at 28-34 weeks Control: routine care only	**Details** **Power analysis** The number of participants necessary to show a reduction of 50% in fetal distress was 1840 in each group, α=0.05, β=0.05. **Statistical analyses** Analyses done by Student's t test and χ2 test, depending on the variable.	**Results** **Critical outcomes** **Admission to neonatal unit** Neonatal transfer- Number (%) Intervention: 188/1950 (9.6) Control: 159/1948 (8.2) **Perinatal mortality**	**Limitations** **Cochrane risk of bias tool V2:** Randomisation process: Low risk. (Participants randomised by block randomisation by consecutive numbers. Allocation concealment by sealed envelope).

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Ref Id 1149149 **Country/ies where the study was carried out** France **Study type** Randomised controlled trial **Aim of the study** To evaluate the effect on management and outcome of pregnancy of routine umbilical Doppler examination in low risk populations. **Study dates** March 1988 to June 1990 **Source of funding** Association Franqaise pour le Depistage et la Prevention des Handicaps de l'Enfant' (R. Boschetti, M.L. Briard).	Intervention: 27.9 (5.2) Control: 27.8 (4.9) Primiparae- Number (%) Intervention: 881 (45.2) Control: 819 (42.0) **Inclusion criteria** • All women who came for routine visit between 28 and 34 weeks; • All women with normal ultrasound scan (fetal biometry above the 10th centile of the reference curve). **Exclusion criteria** • Women who had indications for umbilical doppler (e.g. medical history of hypertension or diabetes, an obstetric history of fetal death, intrauterine growth retardation (IUGR), hypertensive disorder of pregnancy, or		**Intention-to-treat analysis** Not mentioned.	Perinatal or neonatal deaths- Number Intervention: 3/1950 Control: 9/1948 Stillbirths- Number Intervention: 2/1950 Control: 5/1948 Neonatal deaths- Number Intervention: 1/1950 Control: 4/1948 **Important outcomes** **Mode of birth** Vaginal birth-Spontaneous- Number (%) Intervention: 1373/1950 Control: 1397/1948 Vaginal birth- Assisted- Number (%) Intervention: 329/1950 Control: 300/1948 Caesarean section-Elective- Number (%) Intervention: 134/1950 (6.9) Control: 126/1948 (6.5) Caesarean section-Emergency- Number (%) Intervention: 114/1950 (5.85) Control: 124/1948 (6.37)	Deviations from intended interventions (assignment): Low risk. (Blinding of participants and personnel was not feasible for this study). Missing outcome data: Low risk. (<6% lost to follow-up overall). Measurement of the outcome: Low risk. (Outcomes reported were objective). Selection of the reported result: Some concerns. (No trial protocol reported). Other bias: Low risk. (No other bias detected). Overall risk: Low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	such conditions during the first two trimesters of the current pregnancy as hypertension, treatment by beta agonists, or insulin-dependent diabetes). • Women who had undergone an umbilical doppler before 28 weeks for any reason whatsoever.				
Full citation Duff, G. B., A randomized controlled trial in a hospital population of ultrasound measurement screening for the small for dates baby, Australian & New Zealand Journal of Obstetrics & Gynaecology, 33, 374-8, 1993 **Ref Id** 408576 **Country/ies where the study was carried out** New Zealand **Study type** Randomised controlled trial	**Sample size** N=1527 Intervention: n=763 Control: n=764 **Characteristics** There were no significant differences between two groups. **Inclusion criteria** • Women < 24 weeks' gestation **Exclusion criteria**	**Interventions** Intervention: routine care (scan at 16-24 weeks) + ultrasound at 32-36 weeks Control: routine care and additional scans on clinical indication	**Details** **Power analysis** Not mentioned **Statistical analyses** Analysis was by the χ^2 test, t test, or Mann-Whitney-U test, depending on the variable. **Intention-to-treat analysis** Not mentioned	**Results** **Critical outcomes** **Admission to neonatal unit** Admission to Neonatal Unit among study groups-Number (%) Intervention: 107/759 (14.1) Control: 94/763 (12.3) **Perinatal mortality** Outcome of pregnancy-Stillbirth + Neonatal death-Number (%) Intervention: 10/761 (1.31) Control: 4/764 (0.52)	**Limitations** **Cochrane risk of bias tool V2:** Randomisation process: Low risk. (Participants were randomised based on a computer generated random study number. Allocation concealment was done using the envelope method). Deviations from intended interventions (assignment): Low risk. (Blinding of participants and personnel was not feasible for this study). Missing outcome data: Some concerns. (Unclear how many participants were lost to follow up overall). Measurement of the outcome:

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Aim of the study To compare the number of perinatal outcomes between women with a 2-stage examination and women with a 1-stage examination. **Study dates** Not mentioned **Source of funding** Foundation for the Newborn	• Women with multiple pregnancy were excluded on diagnosis				Low risk. (Outcomes reported were objective). Selection of the reported result: Some concerns. (No trial protocol reported). Other bias: Low risk. (No other bias apparent). Overall risk: Some concerns
Full citation Eik-Nes, S. H., Salvesen, K. A., Okland, O., Vatten, L. J., Routine ultrasound fetal examination in pregnancy: the 'Alesund' randomized controlled trial, Ultrasound in Obstetrics & Gynecology, 15, 473-8, 2000 **Ref Id** 758177 **Country/ies where the study was carried out** Norway **Study type**	**Sample size** N=1628 Intervention: n=825 Control: n=803 **Characteristics** Mean age (years) Intervention: 26 Control: 26 Nulliparous (%) Intervention: 33 Control: 35 Non-smoking (%) Intervention: 64 Control: 69 **Inclusion criteria**	**Interventions** Intervention: routine care (ultrasound at 18 weeks) + ultrasound at 32 gestational weeks (+additional examination at 35 weeks' gestation if breech presentation Control: routine care + selective examination for clinical indication	**Details** **Power analysis** The sample size was calculated so that a 50% difference in the incidence of post-term induced labour could be detected (α=0.05, β=0.10). **Statistical analyses** Analyses were carried out with SPSS. Analysis was done by χ2 statistics, t-tests, and Mann-Whitney tests. **Intention-to-treat analysis** Not mentioned.	**Results** **Critical outcomes** **Perinatal mortality** Perinatal mortality (singletons only)- Number Intervention: 4/774 Control: 8/750 OR 0.48 [95% CI: 0.15 to 1.60]. **Important outcomes** **Mode of birth** Vaginal birth- Induced labour- Number Intervention: 34/722 Control: 77/686 OR 0.39 [95% CI 0.26 to 0.59] Caesarean section- Elective- Number Intervention: 43/722	**Limitations** **Cochrane risk of bias tool V2:** Randomisation process: Some concerns. (No details provided on random sequence generation. Envelope method used for allocation concealment). Deviations from intended interventions (assignment): Low risk. (It was not feasible to blind participants due to study design). Missing outcome data: Some concerns. (Unclear how many participants were lost to follow-up overall).

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Randomised controlled trial **Aim of the study** To evaluate the possible benefits of the routine use of ultrasound screening in pregnancy. **Study dates** May 1979 to September 1981 **Source of funding** Not mentioned.	Not mentioned. **Exclusion criteria** Not mentioned.			Control: 27/686	Measurement of the outcome: Low risk. (Outcomes reported were objective). Selection of the reported result: Some concerns. (No trial protocol reported). Other bias: Low risk. (No other bias detected). Overall risk: Some concerns **Other information** This trial was reported in letter form only in 1984. It subsequently became clear that there were inconsistencies in results, and the data were subsequently re-analysed. The data entered in this review are derived from more recent unpublished and published reports.
Full citation Ewigman, B. G., Crane, J. P., Frigoletto, F. D., LeFevre, M. L., Bain, R. P., McNellis, D., Effect of prenatal ultrasound screening on perinatal outcome. RADIUS Study Group, N Engl J MedThe	**Sample size** N=15530 (15151 analysed) Intervention: n=7812 (7617 analysed) Control: n=7718 (7534 analysed) **Characteristics**	**Interventions** Intervention: routine care (scan at 15-22 gestational weeks) + ultrasound at 31 to 35 weeks Control: routine care only	**Details** **Power analysis** Sample size was based on the assumption that the proportion of women in control group with an adverse perinatal outcome would be at least 5%; the change in this percentage would be 20% or more in the ultrasound-screening	**Results** **Critical outcomes** **Perinatal mortality** Perinatal mortality- Number Intervention: 52/7685 Control: 41/7596 Stillbirth- Number Intervention: 34/7685 Control: 23/7596 Neonatal deaths- Number	**Limitations** **Cochrane risk of bias tool V2:** Randomisation process: Low risk. (Participants randomised by computer-generated sequence. Allocation concealment performed after stratification by practice site).

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
New England journal of medicine, 329, 821-7, 1993 **Ref Id** 1131370 **Country/ies where the study was carried out** USA **Study type** Randomised controlled trial **Aim of the study** To test whether the routine screening with standardised ultrasonography on two occasions would reduce perinatal morbidity and mortality. **Study dates** November 1987 to May 1991. **Source of funding** Supported under cooperative agreements with the National Institute of Child Health and Human Development.	Age (years)- <20 years- Number Intervention: 224/7812 Control: 208/7718 Age (years)- 20-35 years- Number Intervention: 7425/7812 Control: 7349/7718 Age (years)- >35 years- Number Intervention: 163/7812 Control: 161/7718 Primiparous- Number Intervention: 2770/7812 Control: 2762/7718 Current smoking- Number Intervention: 1002/7812 Control: 976/7718 **Inclusion criteria** • Age >17 years; • English speaking; • Last menstrual period known within 1 week; • Gestational age <18 weeks; • No plans to change providers. **Exclusion criteria** • Previous ultrasonography		group; the rate of non-compliance would be 10% or less; and the level of significance would be 5%. **Statistical analyses** SAS was used for all data management and analysis. Analysis was used was Fisher's exact test, χ2 test, and Wilcoxon rank-sum test. **Intention-to-treat analysis** ITT analysis used.	Intervention: 18/7685 Control: 18/7596 *Outcomes pooled for analysis as perinatal mortality. **Important outcomes** **Method of birth** Caesarean section- Number Intervention: 1205/7617 Control: 1135/7534	Deviations from intended interventions (assignment): Low risk. (Blinding of participants and personnel was not feasible for this study). Missing outcome data: Low risk. (<2.5% lost to follow-up overall). Measurement of the outcome: Low risk. (Outcomes reported were objective). Selection of the reported result: Some concerns. (No trial protocol reported). Other bias: Low risk. (No other bias detected). Overall risk: Low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	during this pregnancy; • Previous stillbirth; • Irregular menstrual cycle; • Last menstrual period induced by an oral contraceptive agent; • Fertility-drug use in current cycle; • Discrepancy between size and dates >3 weeks; • Previous small-for-gestational-age infant; • Diabetes mellitus; • Chronic hypertension; • Chronic renal disease; • Pelvic mass; • Fetal death; • Ectopic pregnancy; • Molar pregnancy; • Multiple gestation; • Planned termination of pregnancy; • Planned amniocentesis; • Planned cervical cerclage; • Planned ultrasonography				

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	for reasons other than screening.				
Full citation Hammad, I. A., Chauhan, S. P., Mlynarczyk, M., Rabie, N., Goodie, C., Chang, E., Magann, E. F., Abuhamad, A. Z., Uncomplicated Pregnancies and Ultrasounds for Fetal Growth Restriction: A Pilot Randomized Clinical Trial, AJP Reports, 6, e83-e90, 2015 **Ref Id** 1112829 **Country/ies where the study was carried out** USA **Study type** Randomised controlled trial **Aim of the study** To determine the feasibility of randomising uncomplicated pregnancies (UPs) to have third trimester ultrasonographic exams (USE) versus routine prenatal care to improve the detection of SGA.	**Sample size** N=149 (N=145 analysed) Intervention: n=74 (n=71 analysed) Control: n=75 (n=74 analysed) **Characteristics** Mean age (years)- Mean (±SD) Intervention: 25.6 (5.4) Control: 26.5 (5.3) Nulliparous- Number (%) Intervention: 39/74 (53) Control: 38/75 (51) Gestational age at randomisation- Mean (±SD) Intervention: 28.3 (2.0) Control: 28 (2.1) **Inclusion criteria** • Nonanomalous singleton; • Fetal anatomy ultrasound by 22 weeks; • Expected third trimester care and delivery at one of	**Interventions** Intervention: routine care + ultrasound at 30 to 32 weeks gestation and 36 to 37 weeks gestation Control: routine care only	**Details** **Power analysis** Not mentioned. **Statistical analyses** Data analysed by independent sample t-tests, Wilcoxon rank sum test, χ2test, or Fisher exact test, depending on the variable. **Intention-to-treat analysis** ITT principle was used.	**Results** **Critical outcomes** **Admission to neonatal unit** NICU admission- Number (%) Intervention: 2/71 (3) Control: 2/74 (3) **Important outcomes** **Mode of birth** Spontaneous vaginal birth- Number (%) Intervention: 53/71 (74) Control: 54/74 (73) p=1.00 RR 1.01 (95% CI 0.69 to 1.57) Operative vaginal birth- Number (%) Intervention: 2/71 (3) Control: 5/74 (7) p=0.44 RR 0.57 (95% CI 0.10 to 1.44) Caesarean section- Number (%) Intervention: 16/71 (23) Control: 15/74 (20) p=0.84 RR 1.07 (95% CI 0.66 to 1.55)	**Limitations** **Cochrane risk of bias tool V2:** Randomisation process: Low risk. (Block randomisation from computer randomisation. No details provided for allocation concealment) Deviations from intended interventions (assignment): Low risk. (It was not feasible to blind participants due to study design). Missing outcome data: Low risk. (<3% participants lost to follow-up overall). Measurement of the outcome: Low risk. (Outcomes reported were objective). Selection of the reported result: Low risk. (Study trial protocol reported). Other bias: Low risk. (No other biases detected). Overall risk: Low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study dates June 1 2012 to July 10 2014 **Source of funding** Not mentioned.	the participating hospitals. **Exclusion criteria** • Autoimmune disorders (antiphospholipid antibody, lupus, rheumatoid arthritis, scleroderma); • Cerclage in the index pregnancy; • Diabetes mellitus—gestational or pregestational; • Enrollment in another RCT; • Hematologic disorders (coagulation defects, sickle cell disease, thrombocytopenia, thrombophilia); • Hypertension (chronic or pregnancy induced) before randomization; • HIV (human immunodeficienc virus); • Institutionalised individuals (prisoners);				

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	• Obesity, defined as body mass index above 40 kg/m2 at first prenatal visit; • Prior obstetric history of intrauterine growth restriction, preterm birth before 34 weeks, severe preeclampsia, eclampsia, HELLP syndrome, or stillbirth after 24 weeks or neonatal death; • Preterm labour or ruptured membranes before randomisation; • Psychiatric disorder (bipolar, depression) on medication; • Placenta previa/third trimester bleeding; • Renal insufficiency (serum creatinine > 1.5 mg/dL); • Restrictive lung disease; • Fetal red blood cell isoimmunisation;				

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	• Seizure disorder on medication; • Thyroid disease on medication.				
Full citation Henrichs, J., Verfaille, V., Jellema, P., Viester, L., Pajkrt, E., Wilschut, J., van der Horst, H. E., Franx, A., de Jonge, A., Iris study group, Effectiveness of routine third trimester ultrasonography to reduce adverse perinatal outcomes in low risk pregnancy (the IRIS study): nationwide, pragmatic, multicentre, stepped wedge cluster randomised trial, BMJBmj, 367, l5517, 2019 **Ref Id** 1135693 **Country/ies where the study was carried out** The Netherlands **Study type** Cluster-randomised trial **Aim of the study** To investigate the effectiveness of routine ultrasonography in the third	**Sample size** Clusters: 60 midwifery practices enrolled 59 midwifery practices randomised Pregnant women: N=13520 (N=13046 analysed) Intervention: n=7372 (n=7067 analysed) Control: n=6148 (n=5979 analysed) **Characteristics** Maternal age (years)- Mean (SD) Intervention: 31.0 (4.5) Control: 31.0 (4.3) Parity status (Nulliparous)- Number (%) Intervention: 3368 (47.7) Control: 2928 (49.0) Parity status (Multiparous)- Number (%) Intervention: 3632 (51.4) Control: 3004 (50.2) Parity status (missing)- Number (%) Intervention: 67 (0.9) Control: 47 (0.8) Ethnicity (Dutch)- Number (%)	**Interventions** Intervention: Usual care + two biometry ultrasound scans at 28-30 and 34-36 weeks gestation. A third of practices randomised to intervention after 3, 7, and 10 months. Control: Usual care (serial fundal height measurements with clinically indicated ultrasonography).	**Details** **Power analysis** Assuming an intracluster correlation coefficient of 0.0003 based on previous literature, and an a priori assumed average cluster size (ie, practice size of 250 women annually), the study authors aimed to include 15000 pregnant women (7500 for each strategy) to be able to take possible clustering effects into account. **Statistical analyses** Univariable logistic regression analyses was conducted to investigate the association between routine ultrasonography in the third trimester and a reduction in severe adverse perinatal outcomes and adverse secondary neonatal and maternal outcomes. A multilevel multivariable logistic regression analyses was conducted for the dichotomous primary and secondary outcomes. For continuous secondary outcomes, multivariable	**Results** **Critical outcomes** **Perinatal mortality** Perinatal death, 28 weeks' gestational age to 7 days postnatal- Number Intervention: 14/7066 Control: 15/5977 OR (95% CI): 0.79 (0.38 to 1.64) **Obstetric anal sphincter injury (OASIS)** Third or fourth degree perineal trauma- Number Intervention: 186/7065 Control: 134/5979 OR (95% CI): 1.18 (0.94 to 1.48) Adjusted* OR (95% CI): 1.17 (0.92 to 1.47)% **Important outcomes** **Mode of birth** Vaginal birth- Spontaneous- Number Intervention: 2974/6663 Control: 2650/5827 OR (95% CI): 0.97 (0.90 to 1.04) Adjusted* OR (95% CI): 1.00 (0.92 to 1.08) Vaginal birth- Assisted- Number Intervention: 538/7065 Control: 506/5979	**Limitations** **Cochrane risk of bias tool V2:** Randomisation process: Low risk. (Participants randomised by computer-generated sequence. No details on allocation concealment provided). Deviations from intended interventions (assignment): Low risk. (Blinding of participants and personnel was not feasible for this study). Missing outcome data: Low risk. (3.5% lost to follow-up overall). Measurement of the outcome: Low risk. (Outcomes reported were objective). Selection of the reported result: Some concerns. (No trial protocol reported). Other bias: Low risk. (No other bias detected). Overall risk: Low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
trimester in reducing adverse perinatal outcomes in low risk pregnancies compared with usual care and the effect of this policy on maternal outcomes and obstetric interventions **Study dates** 1st February 2015 to 29th February 2016 **Source of funding** A grant from the Netherlands Organisation for Health Research and Development (ZonMw; grant No 209030001).	Intervention: 5096 (72.1) Control: 4684 (78.4) Ethnicity (Other Western)-Number (%) Intervention: 766 (10.8) Control: 576 (9.6) Ethnicity (Non-Western)-Number (%) Intervention: 1202 (17.0) Control: 714 (11.9) Ethnicity (Missing)-Number (%) Intervention: 3 (0.0) Control: 5 (0.1) **Inclusion criteria** • Women with a low risk pregnancy; • Antenatal care in a participating midwifery practice at enrolment; • Aged 16 years or older; • A singleton pregnancy; • No major obstetric or medical risk factors; • Reliable expected date of delivery based on a dating scan or a reliable first day of last menstrual period.		linear mixed models were conducted. The cluster randomised design meant midwifery practices were included as a random effect in the multilevel regression models. Time of inclusion, divided into four groups according to the crossover from usual care to the intervention strategy, was considered as a fixed factor. The main analyses were adjusted for potential confounders selected a priori and based on previous literature. Analyses were performed on complete case analysis given that less than 5% of th data on confounders were missing. A multilevel analysis was performed only if the expected number of events per cluster was at least one. **Intention-to-treat analysis** ITT analysis performed.	OR (95% CI): 0.89 (0.79 to 1.01) Adjusted* OR (95% CI): 0.90 (0.78 to 1.04) Caesarean section-Number Intervention: 969/7065 Control: 814/5979 OR (95% CI): 1.01 (0.91 to 1.12) Adjusted* OR (95% CI): 1.00 (0.90 to 1.11) **adjusted for clustering, midwifery practice size (potential fixed factor), and potential confounders, including maternal age; body mass index; smoking, alcohol, or recreational drug use; parity; educational level; employment status; marital status; sex of infant; and midwifery practice size. In the various multilevel, multivariable models, the amount of missing values for potential confounders was ≤4.4*	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	Exclusion criteria Not mentioned				
Full citation Mason, G. C., Lilford, R. J., Porter, J., Nelson, E., Tyrell, S., Randomised comparison of routine versus highly selective use of Doppler ultrasound in low risk pregnancies, British Journal of Obstetrics and Gynaecology, 100, 130-133, 1993 **Ref Id** 545734 **Country/ies where the study was carried out** United Kingdom **Study type** Randomised controlled trial **Aim of the study** To help answer the question: should Doppler ultrasound of the umbilical circulation be made available to all pregnant women as part of their routine antenatal care?	**Sample size** N=2145 (n=2025 analysed) Intervention: n=1073 (n=1020 analysed) Control: n=1072 (n=1005) **Characteristics** Mean maternal age (years)- Mean (±SD) Intervention: 25.27 (5.04) Control: 25.07 (5.12) **Inclusion criteria** • Primagravida women with a negative medical and gynaecological history and physical examinations were identified at booking clinic. **Exclusion criteria**	**Interventions** Intervention: routine care + doppler at 28 weeks + doppler at 34 weeks Control: routine care only	**Details** **Power analysis** An analysis based on the stillbirth rate in our hospital demonstrated that over 60 000 women would be required to show a realistic reduction in stillbirth and/or neonatal death. **Statistical analyses** Not mentioned. **Intention-to-treat analysis** Not mentioned.	**Results** **Critical outcomes** **Admission to neonatal unit** Neonatal unit admissions- Number Intervention: 29/1015 Control: 31/1001 **Perinatal mortality** Perinatal deaths- Number Intervention: 4/1015 Control: 5/1001 Neonatal death- Number Intervention: 1/1015 Control: 0/1001 **Important outcomes** **Mode of birth** Vaginal birth- Assisted (Induction)- Number Intervention: 180/1015 Control: 177/1001 Caesarean section- Elective- Number Intervention: 29/1015 Control: 36/1001	**Limitations** **Cochrane risk of bias tool V2:** Randomisation process: Low risk. (Participants randomised by block randomisation using a table of random numbers. Allocation concealment by opaque numbered envelopes). Deviations from intended interventions (assignment): Low risk. (Blinding of participants and personnel was not feasible for this study). Missing outcome data: Low risk. (<6% lost to follow-up overall). Measurement of the outcome: Low risk. (Outcomes reported were objective). Selection of the reported result: Some concerns. (No trial protocol reported). Other bias: Low risk. (No other bias detected). Overall risk: Low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study dates January 1988 to June 1990 **Source of funding** Not mentioned.	• Twin pregnancies.				**Other information** Data included 9 sets of twins: 5 in the intervention group and 4 in the control group, which has been excluded from the analysis.
Full citation McKenna,D., Tharmaratnam,S., Mahsud,S., Bailie,C., Harper,A., Dornan,J., A randomized trial using ultrasound to identify the high-risk fetus in a low-risk population, Obstetrics and Gynecology, 101, 626-632, 2003 **Ref Id** 217519 **Country/ies where the study was carried out** UK **Study type** Randomised controlled trial **Aim of the study**	**Sample size** N=1998 (n=1993 analysed) Intervention: n=999 (n=994 analysed) Control: n=999 **Characteristics** Age (years)- Mean Intervention: 27.7 Control: 27.3 Parity- 0- Number Intervention: 413 Control: 388 Parity- 1 to 2- Number Intervention: 465 Control: 457 Parity- 3 to 4- Number Intervention: 94 Control: 134 Parity- ≥5- Number Intervention: 24 Control: 22 **Inclusion criteria**	**Interventions** Intervention: routine care + ultrasound at 30-32 gestational weeks and 36-37 gestational weeks Control: routine care	**Details** **Power analysis** A recruitment target of 2000 patients enabled the study to have 80% power to detect as statistically significant (p<.05) a 35% reduction in small for gestational age infants among the ultrasound scan group, relative to a 10% rate of small for dates in the control group. **Statistical analyses** Data management and analysis were performed by Epi-Info 6 and SPSS. Primary outcome measures were compared between groups using χ2 test with Yates' correction, and relative risks with 95% confidence limits were also calculated. **Intention-to-treat analysis** Not mentioned.	**Results** **Critical outcomes** **Admission to neonatal unit** Admissions to neonatal unit- Number (%) Intervention:28/994 (2.8) Control: 34/999 (3.4) RR 0.83 (95% CI 0.51 to 1.35) p=0.532 **Perinatal mortality** Stillbirth- Number Intervention: 2/994 Control: 1/999 **Important outcomes** **Mode of birth** Vaginal birth-Spontaneous- Number (%) Intervention: 671/994 (67.5) Control: 711/999 (71.2) RR 1.00 Vaginal birth- Assisted- Number (%) Intervention: 133/994 (13.4) Control: 131/999 (13.3) RR 1.06 (95% CI 0.85 to 1.33) p=0.36	**Limitations** **Cochrane risk of bias tool V2:** Randomisation process: Low risk. (Participants randomised by computer-generated sequence. Allocation concealment performed by sealed numbered envelopes). Deviations from intended interventions (assignment): Low risk. (Blinding of participants and personnel was not feasible for this study). Missing outcome data: Low risk. (0.25% lost to follow-up in intervention arm only). Measurement of the outcome: Low risk. (Outcomes reported were objective). Selection of the reported result: Some concerns. (No trial protocol reported). Other bias:

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
To evaluate the effect of introducing two biophysical ultrasound examinations in a low-risk antenatal population. **Study dates** Not mentioned **Source of funding** This study was funded by a £29,500 sterling grant from the Northern Ireland Mother and Baby Appeal (registered charity number XN75792/1).	• Singleton pregnancies with gestational age confirmed by early ultrasound examination; • And/or 18–20 week anomaly scan. **Exclusion criteria** • Known maternal medical problems or previous obstetric complications identified at booking (eg, diabetes, essential hypertension, or previous severe pregnancy-induced hypertension); • The identification of risk factors including pregnancy-induced hypertension, rhesus isoimmunization, and intrauterine growth restriction before 30 weeks'			<u>Caesarean section- Elective- Number (%)</u> Intervention: 91/994 (9.2) Control: 75/999 (7.5) RR 1.25 (95% CI 0.94 to 1.67) <u>Caesarean section- Emergency- Number (%)</u> Intervention: 92/994 (9.2) Control: 77/999 (7.7) RR 1.23 (95% CI 0.93 to 1.64)	Low risk. (No other bias detected). Overall risk: Low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	gestation in present pregnancy; • Multiple pregnancy; • Uncertain gestational age; • Late booking (after 20 weeks' gestation); • Or known fetal abnormality.				
Full citation Neilson, J. P., Munjanja, S. P., Whitfield, C. R., Screening for small for dates fetuses: A controlled trial, British Medical Journal, 289, 1179-1182, 1984 **Ref Id** 962829 **Country/ies where the study was carried out** UK **Study type** Randomised controlled trial **Aim of the study** Not mentioned	**Sample size** N=877 Intervention: n=433 Control: n=444 **Characteristics** Mean age (years- Mean (±SD) Intervention: 27.3 (5.1) Control: 27.4 (4.9) Nulliparous- Number (%) Intervention: 190 (46) Control: 178 (40) **Inclusion criteria** • Women with uncomplicated singleton pregnancies at between 34 to	**Interventions** Intervention: ultrasound <24 gestational weeks + ultrasound at 34-36.5 gestational weeks- REVEALED Control: ultrasound <24 gestational weeks + ultrasound at 34-36.5 gestational weeks- CONCEALED	**Details** **Power analysis** Not mentioned. **Statistical analysis** Analysis by $\chi 2$ or t tests. **Intention-to-treat analysis** Not mentioned.	**Results** **Critical outcomes** **Perinatal mortality** Number of neonatal deaths- Number Intervention: 0/433 Control: 1/444 Stillbirths- Number Intervention: 0/433 Control: 0/444 **Important outcomes** **Mode of birth** Vaginal birth- Spontaneous- Number Intervention: 259/433 Control: 282/444 Vaginal birth- Assisted- Number Intervention: 120/433 Control: 106/444 Caesarean section- Elective- Number Intervention: 54/433 Control: 56/444 Caesarean section- Emergency- Number	**Limitations** **Cochrane risk of bias tool V2:** Randomisation process: High risk. (Participants randomised from hospital index numbers. No details provided for allocation concealment). Deviations from intended interventions (assignment): Low risk. (Blinding of participants and personnel was not feasible for this study). Missing outcome data: Low risk. (High retention and no reported loss to follow-up overall). Measurement of the outcome: Low risk. (Outcomes reported were objective). Selection of the reported result:

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study dates Not mentioned **Source of funding** The study was supported by a project grant from the Medical Research Council.	36.5 weeks gestation; as confirmed by first stage ultrasound examination before 24 weeks. **Exclusion criteria** • High risk pregnancies, including any in whom there had already been some reason to start fetoplacental monitoring or in whom a clinical suspicion that the fetus might be small for dates had been noted at any time.			Intervention: 37/433 Control: 32/444	Some concerns. (No trial protocol reported). Other bias: Low risk. (No other bias detected). Overall risk: High risk
Full citation Newnham,J.P., Evans,S.F., Michael,C.A., Stanley,F.J., Landau,L.I., Effects of frequent ultrasound during pregnancy: a randomised controlled trial, Lancet, 342, 887-891, 1993 **Ref Id**	**Sample size** N=2834 (n=2801 analysed) Intervention: n=1415 (n=1402 analysed) Control: n=1419 (n=1399 analysed) **Characteristics** Age (years)- Mean (±SD)	**Interventions** Intervention: ultrasound at 18 gestational weeks + Doppler flow at 24, 28, 34, and 38 weeks Control: ultrasound at 18 gestational weeks	**Details** **Power analysis** Calculations estimated that a sample size of 2800 women would have a 90% power to detect a difference in the duration of neonatal stay of 0.25 days in those who delivered at term (α=0.05; SD=2 days), and a power of 80% to detect a	**Results** **Critical outcomes** **Perinatal mortality** Stillborn- Number Intervention: 10/1415 Control: 12/1419 Neonatal deaths- Number Intervention: 3/1415 Control: 10/1419 **Important outcomes**	**Limitations** **Cochrane risk of bias tool V2:** Randomisation process: Low risk. (Participants randomised by computer-generated random numbers. Allocation concealment by sealed-envelope technique). Deviations from intended interventions (assignment):

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
97234 **Country/ies where the study was carried out** Australia **Study type** Randomsied controlled trial **Aim of the study** To test the hypothesis that intensive use of ultrasound imaging and Doppler flow studies would improve pregnancy outcome. **Study dates** May 1989 to November 1991 **Source of funding** Supported by grants from the Raine Research Foundation of the University of Western Australia, National Health and Medical Research Council of Australia, and The King Edward Memorial Hospital Research Foundation.	Intervention: 27.4 (5.9) Control: 27.3 (6.0) Nulliparous- Number Intervention: 685 Control: 692 **Inclusion criteria** • Gestational age between 16 and 20 weeks; • Sufficient proficiency in English to understand the implication of participation; • An expectation to deliver at the study hospital; • An intention to remain in Western Australia in the coming years such that childhood follow up was feasible. **Exclusion criteria** Not mentioned.		reduction in the preterm birth rate from 7% to 4.5%. **Statistical analyses** Differences between the groups were tested by the t-test, Fisher's exact test, Pearson $\chi 2$, and Mantel-Haenszel $\chi 2$, for different variables. **Intention-to-treat analysis** Not mentioned.	**Length of neonatal stay in neonatal unit** Duration of neonatal stay (days)- Median [IQR] Intervention: 5 [4-6] Control: 5 [4-6] p=0.26 **Mode of birth** Vaginal birth-Spontaneous- Number Intervention: 774/1415 Control: 770/1419 p=0.86 Vaginal birth- Assisted-Number Intervention: 459/1415 Control: 450/1419 p=0.86	Low risk. (Blinding of participants and personnel was not feasible for this study). Missing outcome data: Low risk. (<2% lost to follow-up overall). Measurement of the outcome: Low risk. (Outcomes reported were objective). Selection of the reported result: Some concerns. (No trial protocol reported). Other bias: Low risk. (No other bias detected). Overall risk: Low risk
Full citation Proud,J., Grant,A.M., Third trimester placental grading	**Sample size** N=2000 Intervention: n=1000 Control: n=1000	**Interventions** Intervention: routine early pregnancy ultrasound + 2 routine scans in 3rd	**Details** **Power analysis** If the true prevalence of this combination of measures of	**Results** **Critical outcomes** **Admission to neonatal unit**	**Limitations** **Cochrane risk of bias tool V2:** Randomisation process:

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
by ultrasonography as a test of fetal wellbeing, British Medical Journal Clinical Research Ed., 294, 1641-1644, 1987 **Ref Id** 305656 **Country/ies where the study was carried out** UK **Study type** Randomised controlled trial **Aim of the study** To investigate whether clinical action taken on the basis of placental grading improved perinatal outcome. **Study dates** Not mentioned **Source of funding** East Anglian Regional Health Authority	**Characteristics** Maternal age (years)- Mean (±SD) Intervention: 25.8 (5.5) Control: 25.3 (5.1) Nulliparity- Number Intervention: 487 Control: 509 **Inclusion criteria** Not mentioned. **Exclusion criteria** Not mentioned.	trimester (3rd US for placental grading)- REVEALED Control: routine early pregnancy ultrasound + 2 routine scans in 3rd trimester (3rd US for placental grading)- CONCEALED	adverse outcome was 8%, a trial of this size had a 65% chance of a significant result (α=0.05) if the real effect was a reduction by a third; the power was 85% if the true reduction was by 40% **Statistical analyses** Analysis was one by χ2 and Student's t tests, where appropriate. **Intention-to-treat analysis** Not mentioned.	Admission to special care nursery- Number (includes multiple pregnancy data) Intervention: 48/1014 Control: 60/1011 **Perinatal mortality** Total perinatal deaths- Number Intervention: 4/1014 Control: 13/1011 **Important outcomes** **Mode of birth** Vaginal birth- Spontaneous- Number Intervention: 727/1000 Control: 709/1000 Vaginal birth- Assisted- Number Intervention: 133/1000 Control: 143/1000 Caesarean section- Elective- Number Intervention: 62/1000 Control: 59/1000 Caesarean section- Emergency- Number Intervention: 73/1000 Control: 81/1000	Some concerns. (No details provided on how participants were randomised. Allocation concealment performed by numbered, sealed opaque envelopes). Deviations from intended interventions (assignment): Low risk. (Blinding of participants and personnel was not feasible for this study). Missing outcome data: Low risk. (High retention and no reported loss to follow-up overall). Measurement of the outcome: Low risk. (Outcomes reported were objective). Selection of the reported result: Some concerns. (No trial protocol reported). Other bias: Low risk. (No other bias detected). Overall risk: Some concerns
Full citation Skrastad,R.B., Eik-Nes,S.H., Sviggum,O., Johansen,O.J., Salvesen,K.A.,	**Sample size** N=6780 (n=6399 analysed) Intervention: n=3355 (n=3175 analysed)	**Interventions** Intervention: ultrasound at 18 gestational weeks and at 33 gestational weeks	**Details** **Power analysis** The power analysis was based on the assumption that 30% of SGA infants	**Results** **Critical outcomes** **Admission to neonatal unit**	**Limitations** **Cochrane risk of bias tool V2:** Randomisation process:

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Romundstad,P.R., Blaas,H.G., A randomized controlled trial of third-trimester routine ultrasound in a non-selected population, Acta Obstetricia et Gynecologica Scandinavica, 92, 1353-1360, 2013 **Ref Id** 308745 **Country/ies where the study was carried out** Norway **Study type** Randomised controlled trial **Aim of the study** To compare detection rates of small-for-gestational-age fetuses, large-for-gestational-age fetuses, congenital anomalies and adverse perinatal outcomes in pregnancies randomized to third-trimester routine ultrasound or ultrasound on clinical indication. **Study dates** 1989 to 1992 **Source of funding**	Control: n=3425 (n=3224 analysed) **Characteristics** Mean age (years)- Mean (±SD) Intervention: 27 (5) Control: 27 (5) p=0.4 Nulliparous- Number (%) Intervention: 1448 (45) Control: 1501 (46) p=0.4 **Inclusion criteria** Not mentioned. **Exclusion criteria** Not mentioned.	Control: ultrasound at 18 gestational weeks and on clinical indication	would be detected in the control group and 60% in the study group, with α=0.05 and β=0.2. This gave a sample size of 3107 women in each group. **Statistical analyses** Data analysis by Student's t-test, Mann-Whitney U-test, chi-squared test and Fisher's exact test, for appropriate variables. **Intention-to-treat analysis** Groups were analysed according to the intention-to-treat principle.	Transfer to NICU- Number (%) Intervention: 333/3163 (10.5) Control: 320/3213 (10.0) p=0.5 **Perinatal mortality** Perinatal death- Number (%) Intervention: 17/3175 (0.5) Control: 14/3224 (0.4) p=0.6 Neonatal death- Number (%) Intervention: 2/3163 (0.06) Control: 1/3213 (0.03) p=0.6 **Important outcomes** **Mode of birth** Vaginal birth- Assisted (Vacuum extraction + Forceps)- Number Intervention: 138/3190 Control: 226/3236 Caesarean section- Elective- Number Intervention: 237/3190 Control: 278/3236 Caesarean section- Emergency- Number (%) Intervention: 119/3190 Control: 131/3236 p=0.5	Some concerns. (No details provided for random sequence generation. Allocation concealment performed by sealed envelopes). Deviations from intended interventions (assignment): Low risk. (Blinding of participants and personnel was not feasible for this study). Missing outcome data: Low risk. (<6% lost to follow-up overall). Measurement of the outcome: Low risk. (Outcomes reported were objective). Selection of the reported result: Some concerns. (No trial protocol reported). Other bias: Low risk. (No other bias detected). Overall risk: Some concerns

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
The trial was supported by National Center for Fetal Medicine, Department of Obstetrics and Gynecology, St Olav's Hospital, Trondheim University Hospital and Department of Laboratory Medicine Children's and Women's Health, Faculty of Medicine, Norwegian University of Science and Technology, Trondheim, Norway.					
Full citation Whittle,M.J., Hanretty,K.P., Primrose,M.H., Neilson,J.P., Screening for the compromised fetus: a randomized trial of umbilical artery velocimetry in unselected pregnancies, American Journal of Obstetrics and Gynecology, 170, 555-559, 1994 **Ref Id** 224327 **Country/ies where the study was carried out** UK **Study type** Randomised controlled trial	**Sample size** N=2986 Intervention: n=1642 Control: n=1344 **Characteristics** Mean age (years)- Mean Intervention: 27.9 Control: 27.2 Parity- Mean (±SD) Intervention: 0.8 (0.95) Control: 0.8 (0.95) **Inclusion criteria** • Unselected population. • Women attending the AN before 26 weeks' gestation, there was no attempt at	**Interventions** Intervention: routine care + doppler at 26-30 weeks + doppler at 34-36 weeks Control: routine care + doppler at 26-30 weeks + doppler at 34-36 weeks (concealed)	**Details** **Power analysis** The number of recruited women was not determined by power calculations but by the predetermined duration of funding of the project. **Statistical analyses** Student t and χ2 tests were used to assess statistical significance, and odds ratios with confidence limits were calculated. **Intention-to-treat analysis** Not mentioned.	**Results** **Critical outcomes** **Admission to neonatal unit** Admission to SCBU/NICU- Number Intervention: 196/1642 Control: 161/1344 **Perinatal mortality** Stillbirth- Number Intervention: 3/1642 Control: 8/1344 Perinatal death (potentially preventable deaths)- Number Intervention: 3/1642 Control: 6/1344 **Important outcomes** **Mode of birth** Vaginal birth- Assisted (operative vaginal birth)- Number Intervention: 652/1642 Control: 530/1344 Caesarean section- Elective- Number	**Limitations** **Cochrane risk of bias tool V2:** Randomisation process: Low risk. (Participants randomised by random number tables. Allocation concealment by numbered, sealed opaque envelopes). Deviations from intended interventions (assignment): Low risk. (Blinding of participants and personnel was not feasible for this study). Missing outcome data: Low risk. (High retention and no reported loss to follow-up overall). Measurement of the outcome: Low risk. (Outcomes reported were objective). Selection of the reported result:

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Aim of the study To address the impact on outcome of umbilical artery velocimetry in a non-selected population (i.e. as a screening test in low-risk and high-risk pregnancies). **Study dates** 1987 to 1989 **Source of funding** Birthright	selection, so women were eligible for inclusion, regardless of whether they had high-risk features. **Exclusion criteria** • Multiple pregnancies			Intervention: 86/1642 Control: 64/1344	Some concerns. (No trial protocol reported). Other bias: High risk. (Authors mention problem with randomisation that led to unequal numbers of participants in the arms). Overall risk: High risk

CI: confidence interval; ICU: intensive care unit; ITT; intention to treat; IVF: in vitro fertilisation; NICU; neonatal intensive care unit; OR: odds ratio; RR: risk ratio; SCBU; special care baby unit; SD: standard deviation.

Appendix E – Forest plots

Forest plots for review question: Is routine ultrasound in women from 28 weeks effective?

This section includes forest plots only for outcomes that are meta-analysed. Outcomes from single studies are not presented here, but the quality assessment for these outcomes is provided in the GRADE profiles in appendix F.

Figure 2: Routine care plus third trimester ultrasound scan versus Routine care- Outcome: Admission to neonatal care

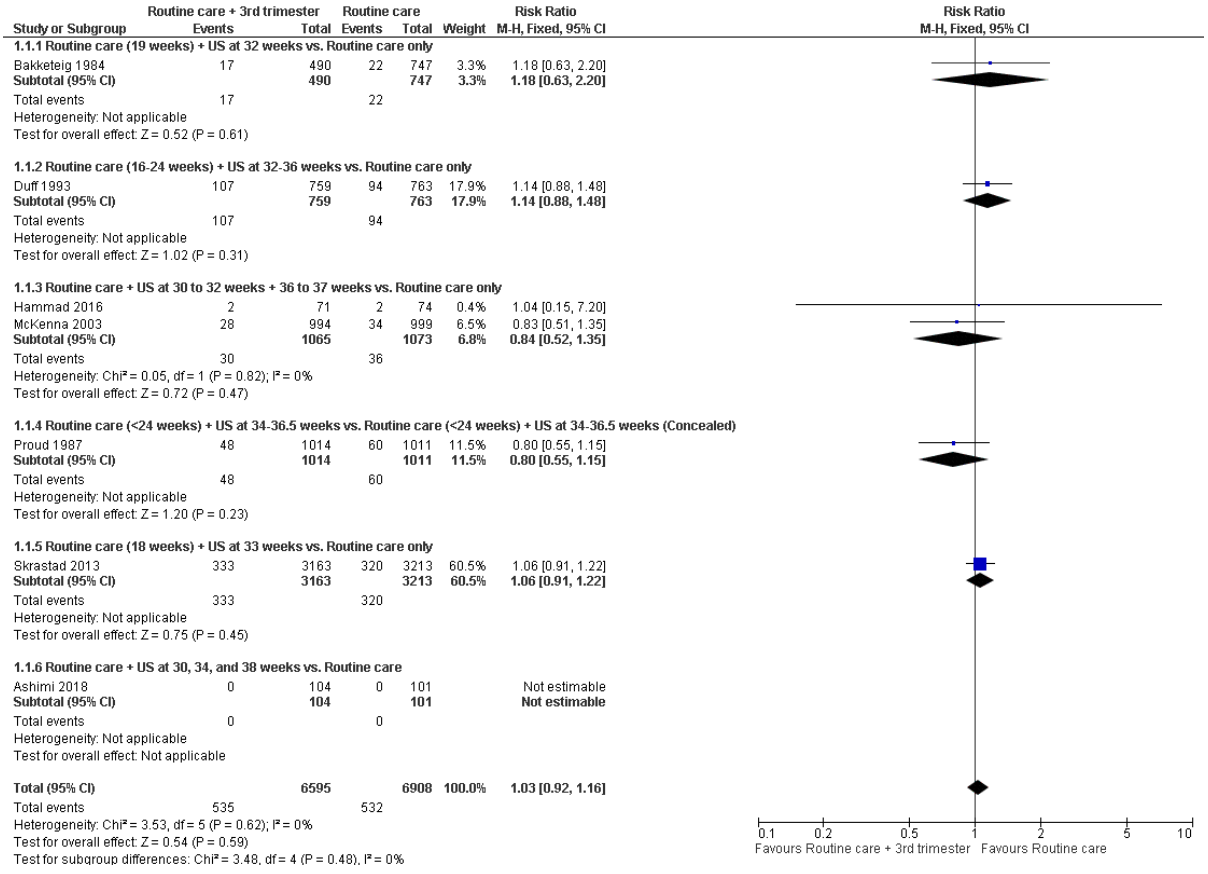


Figure 3: Routine care plus third trimester ultrasound scan versus Routine care- Outcome: Perinatal mortality

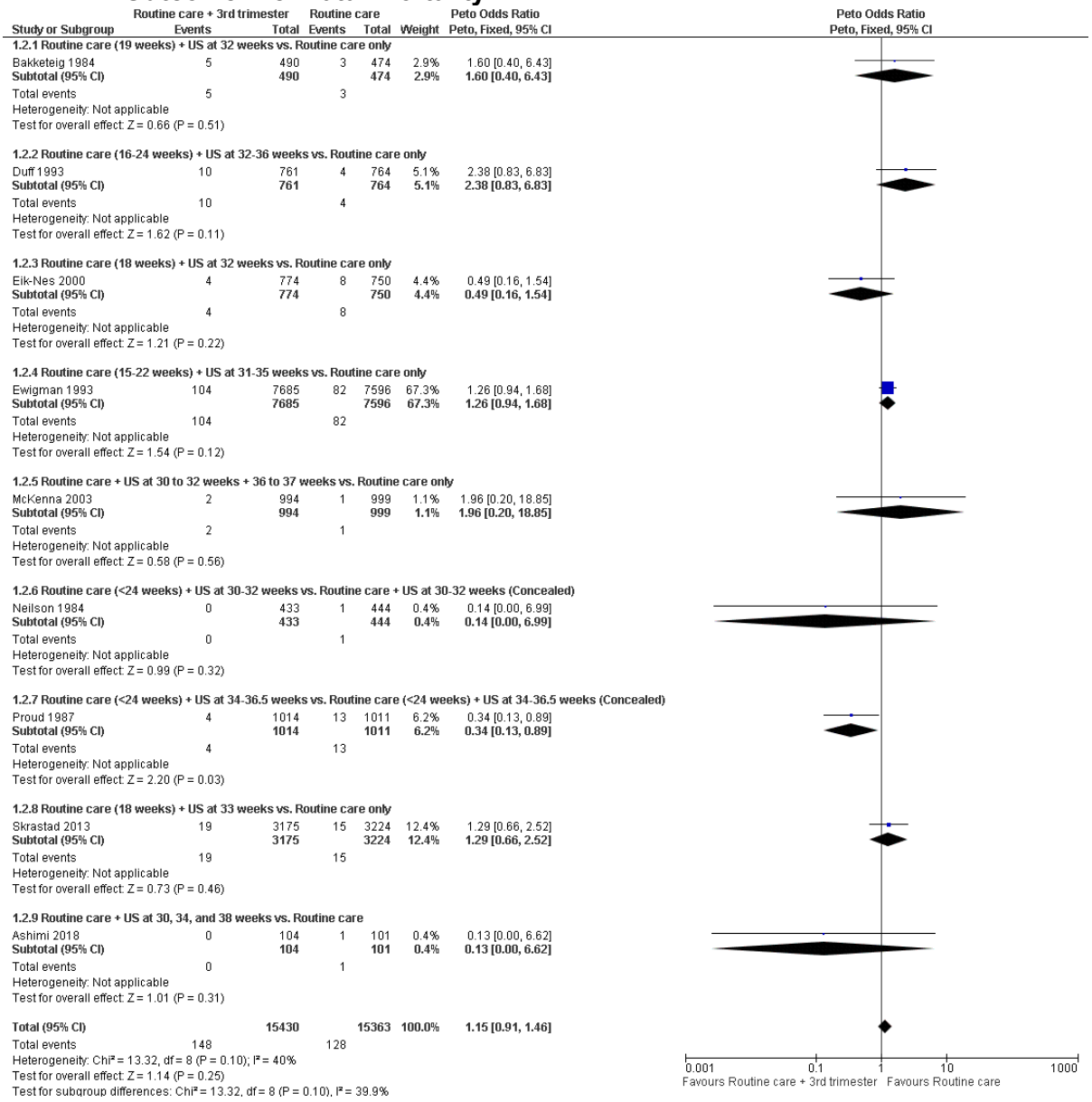


Figure 4: Routine care plus third trimester ultrasound scan versus Routine care- Outcome: Mode of birth- Spontaneous vaginal birth

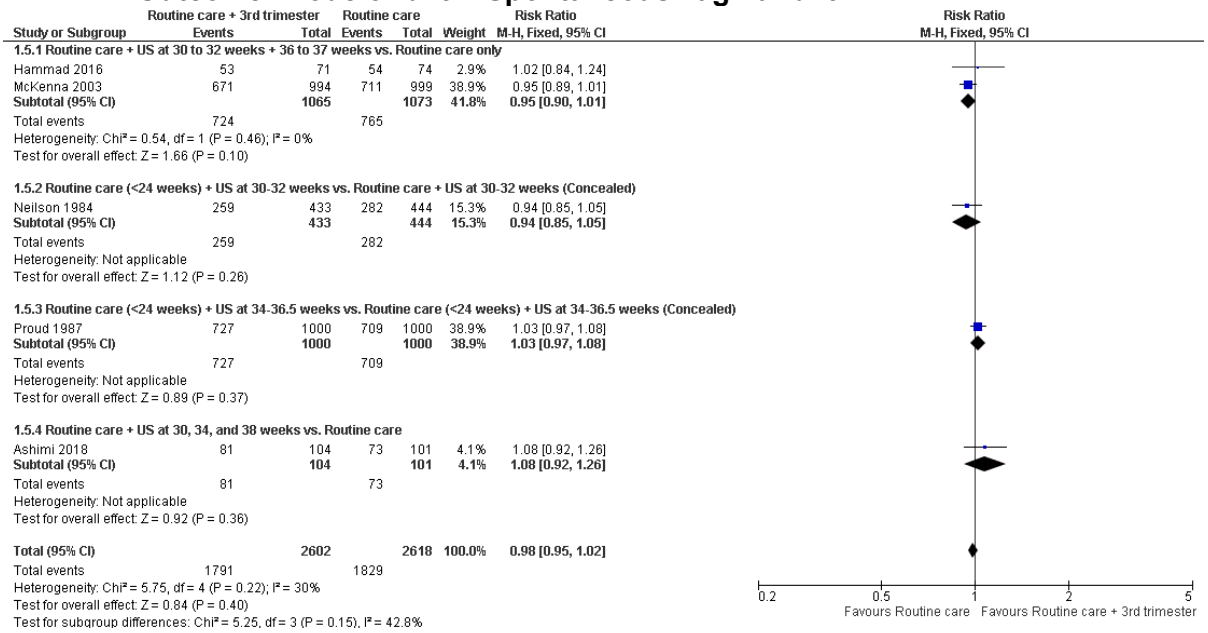


Figure 5: Routine care plus third trimester ultrasound scan versus Routine care- Outcome: Mode of birth- Assisted vaginal birth

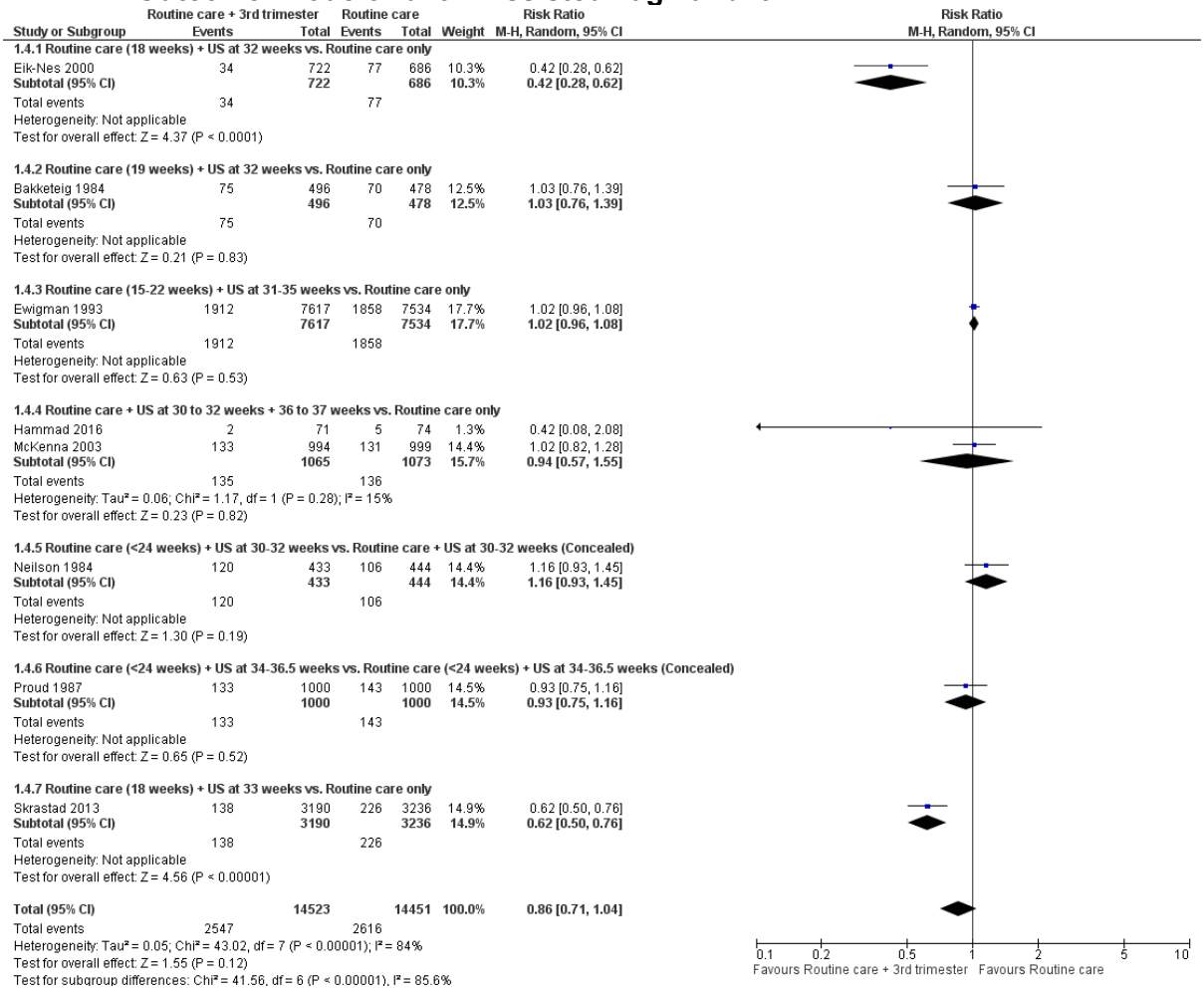


Figure 6: Routine care plus third trimester ultrasound scan versus Routine care- Outcome: Elective caesarean section

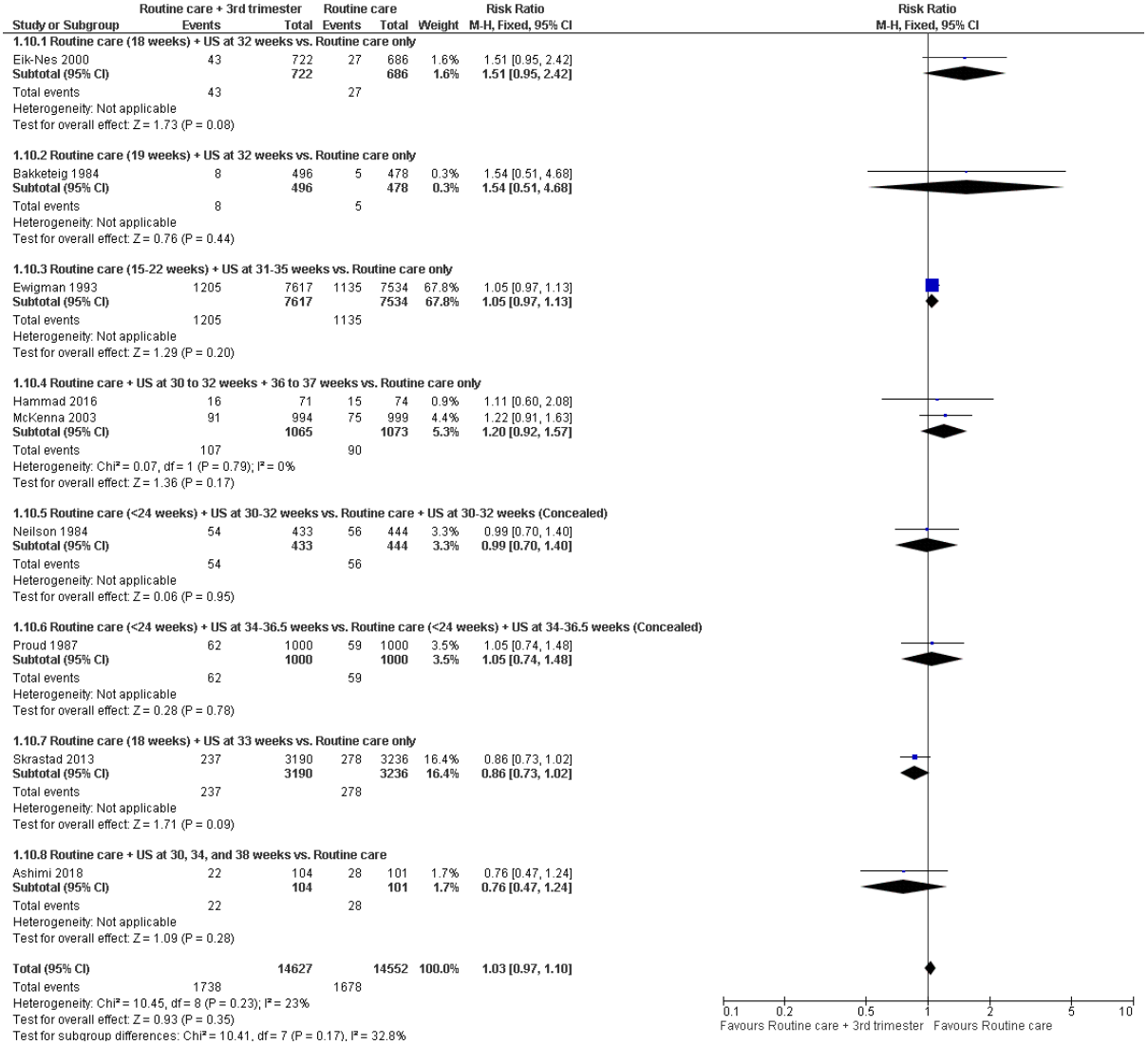


Figure 7: Routine care plus third trimester ultrasound scan versus Routine care- Outcome: Emergency caesarean section

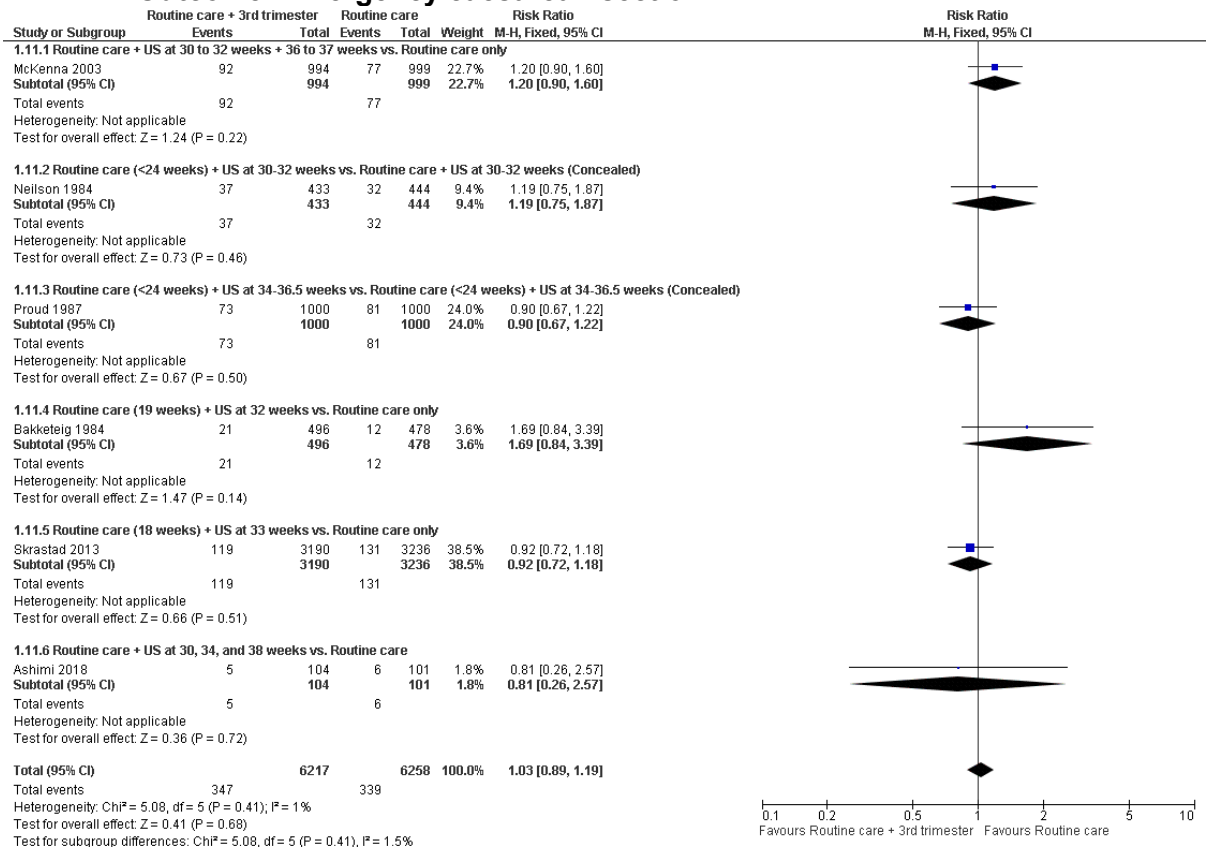


Figure 8: Routine care plus third trimester Doppler scan versus Routine care- Outcome: Admission to neonatal care

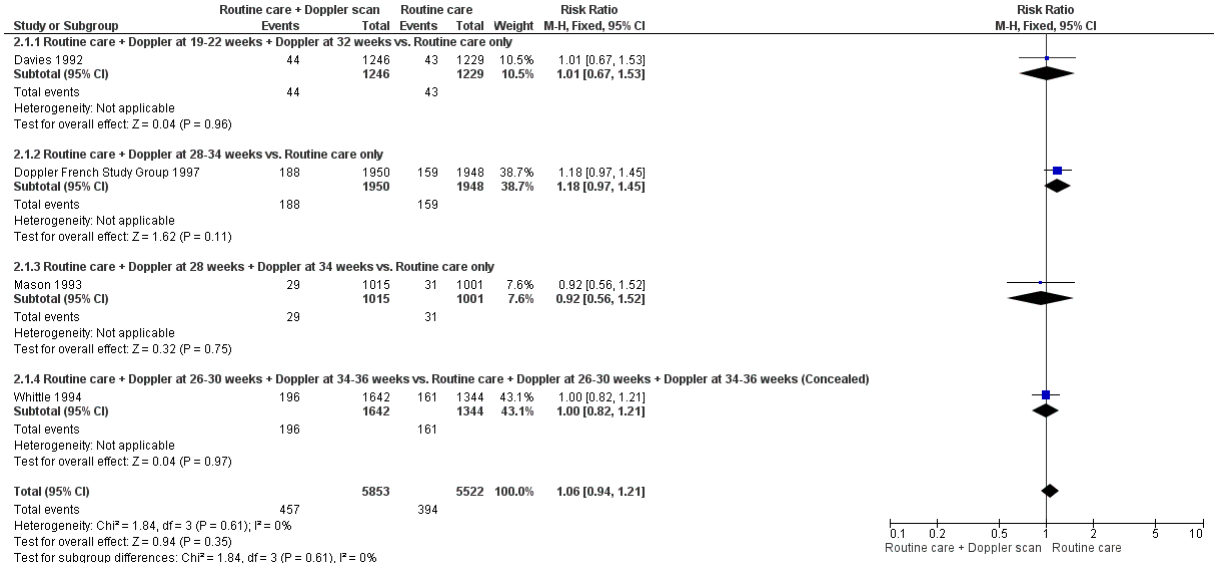


Figure 9: Routine care plus third trimester Doppler scan versus Routine care- Outcome: Perinatal mortality

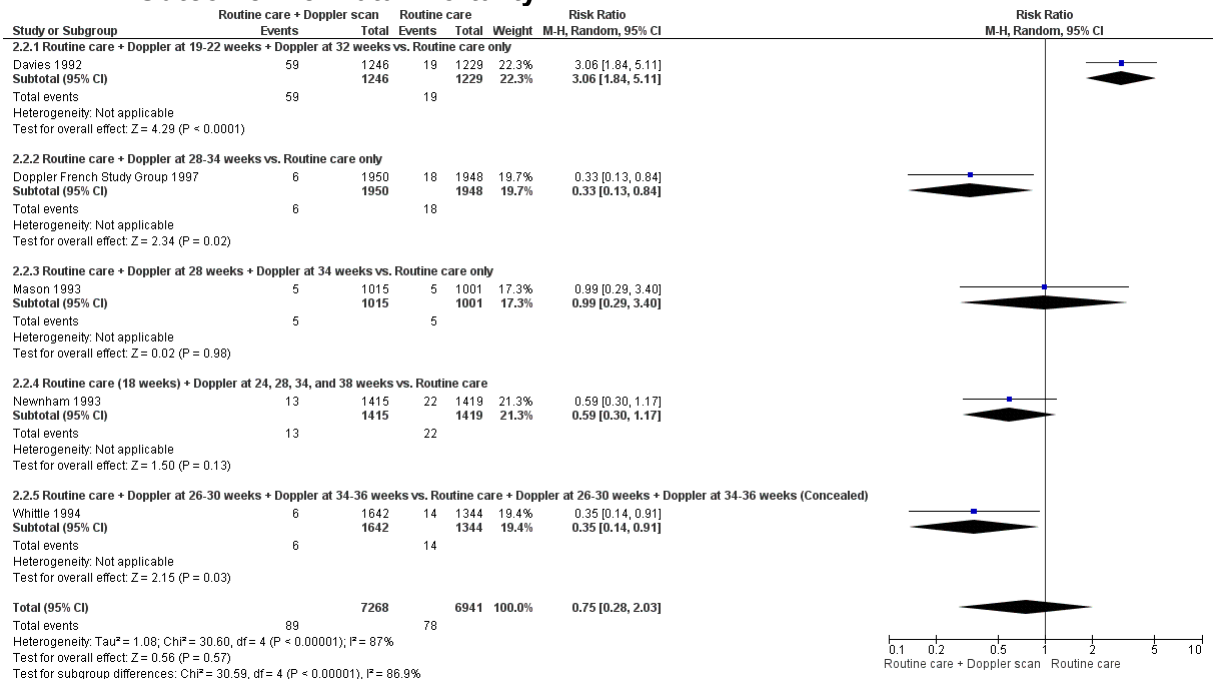


Figure 10: Routine care plus third trimester Doppler scan versus Routine care- Outcome: Mode of birth- Spontaneous vaginal birth

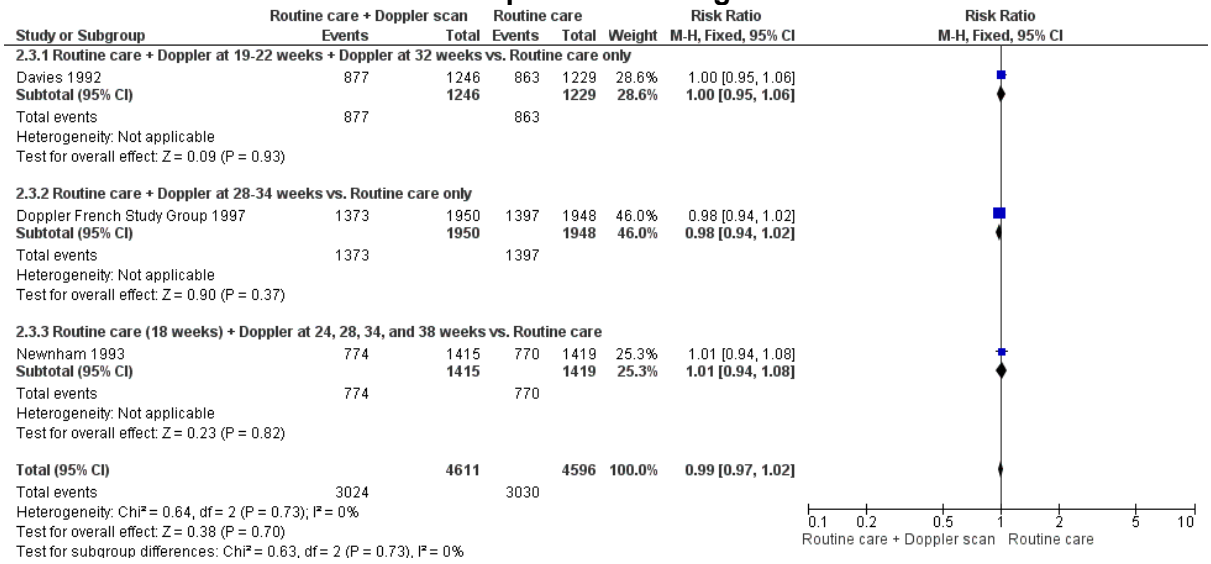


Figure 11: Routine care plus third trimester Doppler scan versus Routine care- Outcome: Mode of birth- Assisted vaginal birth

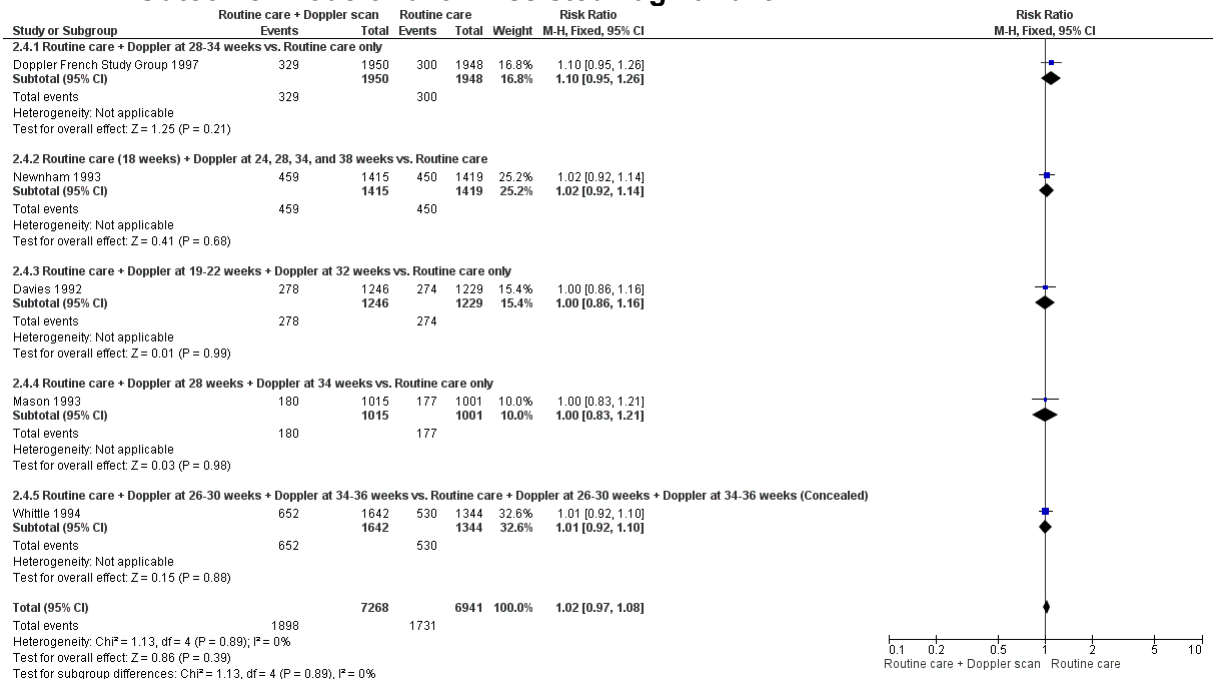


Figure 12: Routine care plus third trimester Doppler scan versus Routine care- Outcome: Mode of birth- Elective caesarean section

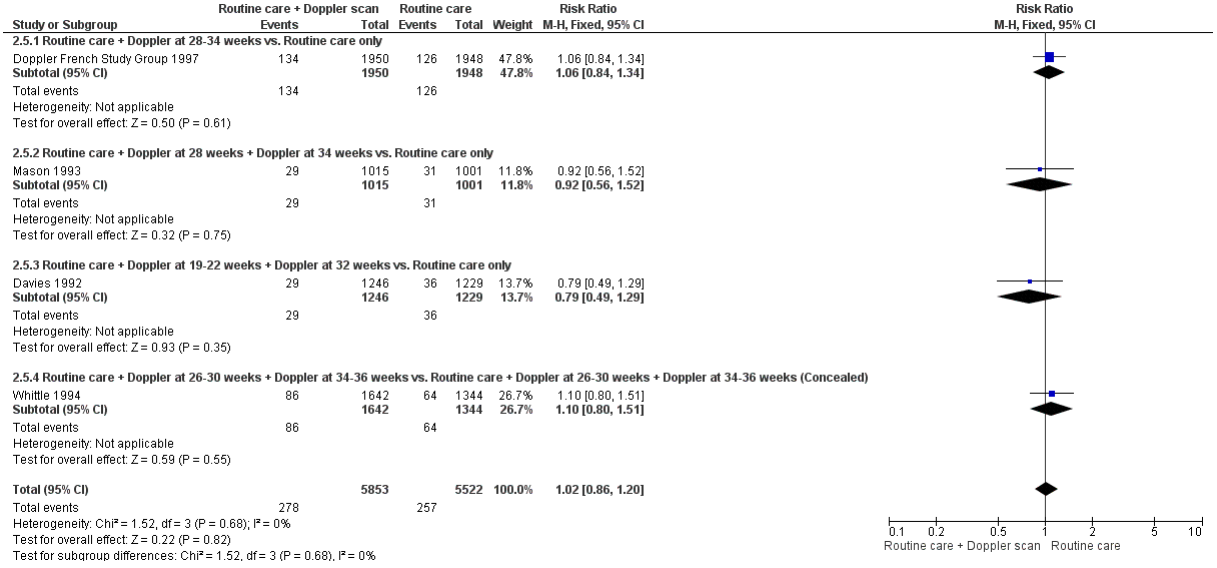
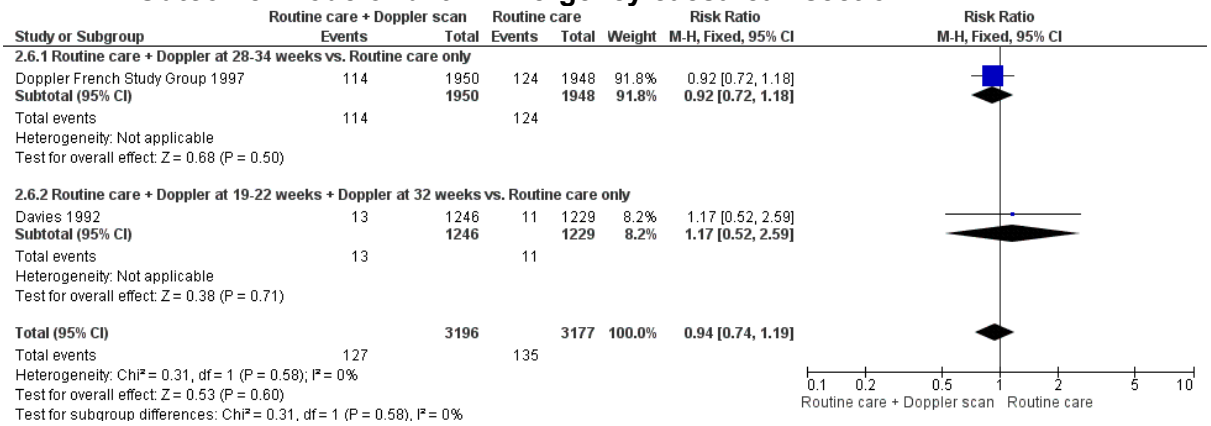


Figure 13: Routine care plus third trimester Doppler scan versus Routine care- Outcome: Mode of birth- Emergency caesarean section



Appendix F – GRADE tables

GRADE tables for review question: Is routine ultrasound in women from 28 weeks effective?

Table 5: Clinical evidence profiles for routine care plus third trimester ultrasound scan versus routine care

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Routine care + 3rd trimester ultrasound scan	Routine care	Relative (95% CI)	Absolute		
Admission to neonatal care												
7‡	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	535/6595 (8.1%)	532/6908 (7.7%)	RR 1.03 (0.92 to 1.16)	2 more per 1000 (from 6 fewer to 12 more)	⊕⊕⊕O MODERATE	CRITICAL
Perinatal mortality												
9‡	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	148/15430 (0.96%)	128/15363 (0.83%)	Peto OR 1.15 (0.91 to 1.46)	1 more per 1000 (from 1 fewer to 4 more)	⊕OOO VERY LOW	CRITICAL
Perinatal mortality												
1 (Henrichs 2019)	cluster randomised trials	serious	no serious inconsistency	no serious indirectness	very serious[4]	none	14/7066 (0.2%)	15/5977 (0.25%)	OR 0.79 (0.38 to 1.64)	1 fewer per 1000 (from 2 fewer to 2 more)	⊕OOO VERY LOW	CRITICAL
Obstetric anal sphincter injury (OASIS)												
1 (Henrichs 2019)	cluster randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	186/7065 (2.6%)	134/5979 (2.2%)	OR 1.18 (0.94 to 1.48)	4 more per 1000 (from 1 fewer to 10 more)	⊕⊕⊕O MODERATE	CRITICAL
Mode of birth- Vaginal birth (spontaneous)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Routine care + 3rd trimester ultrasound scan	Routine care	Relative (95% CI)	Absolute		
5‡	randomised trials	very serious[5]	no serious inconsistency	no serious indirectness	no serious imprecision	none	1791/2602 (68.8%)	1829/2618 (69.9%)	RR 0.98 (0.95 to 1.02)	14 fewer per 1000 (from 35 fewer to 14 more)	⊕⊕OO LOW	IMPORTANT
Mode of birth- Vaginal birth (spontaneous)												
1 (Henrichs 2019)	cluster randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	2974/6663 (44.6%)	2650/5827 (45.5%)	OR 0.97 (0.9 to 1.5)	8 fewer per 1000 (from 26 fewer to 101 more)	⊕⊕⊕O MODERATE	IMPORTANT
Mode of birth- Vaginal birth (assisted)												
8‡	randomised trials	very serious[6]	very serious[7]	serious	serious[3]	none	2547/14523 (17.5%)	2616/14451 (18.1%)	RR 0.86 (0.71 to 1.04)	25 fewer per 1000 (from 52 fewer to 7 more)	⊕OOO VERY LOW	IMPORTANT
Mode of birth- Vaginal birth (assisted)												
1 (Henrichs 2019)	cluster randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	538/7065 (7.6%)	506/5979 (8.5%)	OR 0.89 (0.79 to 1)	9 fewer per 1000 (from 17 fewer to 0 more)	⊕⊕⊕O MODERATE	IMPORTANT
Mode of birth- Caesarean section (elective)												
9‡	randomised trials	very serious[6]	no serious inconsistency	no serious indirectness	no serious imprecision	none	1738/14627 (11.9%)	1678/14552 (11.5%)	RR 1.03 (0.97 to 1.1)	3 more per 1000 (from 3 fewer to 12 more)	⊕⊕OO LOW	IMPORTANT
Mode of birth- Caesarean section (emergency)												
6‡	randomised trials	very serious[8]	no serious inconsistency	no serious indirectness	no serious imprecision	none	347/6217 (5.6%)	339/6258 (5.4%)	RR 1.03 (0.89 to 1.19)	2 more per 1000 (from 6 fewer to 10 more)	⊕⊕OO LOW	IMPORTANT
Mode of birth- Caesarean section												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Routine care + 3rd trimester ultrasound scan	Routine care	Relative (95% CI)	Absolute		
1 (Henrichs 2019)	cluster randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	969/7064 (13.7%)	814/5979 (13.6%)	OR 1.01 (0.91 to 1.12)	1 more per 1000 (from 11 fewer to 14 more)	⊕⊕⊕⊕ HIGH	IMPORTANT

CI: confidence interval; OR: odds ratio; RR: risk ratio
[1] Evidence downgraded by 1 level due to unclear risk of selection bias in 3 studies, unclear risk of attrition bias in 1 study, unclear risk of reporting bias in 5 studies, and unclear risk of other bias in 1 study.
[2] Evidence downgraded by 2 levels due to high risk of selection bias in 1 study and unclear risk of selection bias in 5 studies; unclear risk of attrition bias in 2 studies; and unclear risk of reporting bias in all studies.
[3] Evidence downgraded by 1 level because 95% CI crosses 1 MID for dichotomous outcomes (0.8 or 1.25).
[4] Evidence downgraded by 2 levels because 95% CI crosses 2 MIDs for dichotomous outcomes (0.8 and 1.25).
[5] Evidence downgraded by 2 levels due to high risk of selection bias in 1 study and unclear risk of selection bias in 3 studies; and unclear risk of reporting bias in 3 studies.
[6] Evidence downgraded by 2 levels due to high risk of selection bias in 1 study and unclear risk of selection bias in 6 studies; unclear risk of attrition bias in 1 study; and unclear risk of reporting bias in 7 studies.
[7] Evidence downgraded by 2 levels due to very serious heterogeneity (i2=84%).
[8] Evidence downgraded by 2 levels due to high risk of selection bias in one study and unclear risk of selection bias in 4 studies; and unclear risk of reporting bias in all studies.
‡ For references see corresponding Forest plots

Table 6: Routine care plus third trimester Doppler scan versus Routine care

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Routine care + Doppler scan	Routine care	Relative (95% CI)	Absolute		
Admission to neonatal care												
4‡	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	457/5853 (7.8%)	394/5522 (7.1%)	RR 1.06 (0.94 to 1.21)	4 more per 1000 (from 4 fewer to 15 more)	⊕⊕OO LOW	CRITICAL
Perinatal mortality												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Routine care + Doppler scan	Routine care	Relative (95% CI)	Absolute		
5‡	randomised trials	serious[1]	very serious[2]	no serious indirectness	very serious[3]	none	89/7268 (1.2%)	78/6941 (1.1%)	RR 0.75 (0.28 to 2.03)	3 fewer per 1000 (from 8 fewer to 12 more)	⊕OOO VERY LOW	CRITICAL
Length of neonatal stay in neonatal unit (median)												
1 (Newnham 1993)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	1415	1419	-	routine care median 5 (IQR 4 to 6), routine care + Doppler median 5 (IQR 4 to 6), p =0.26[4]	⊕⊕⊕⊕ HIGH	IMPORTANT
Mode of birth- Vaginal birth (spontaneous)												
3‡	randomised trials	serious[5]	no serious inconsistency	no serious indirectness	no serious imprecision	none	3024/4611 (65.6%)	3030/4596 (65.9%)	RR 0.99 (0.97 to 1.02)	7 fewer per 1000 (from 20 fewer to 13 more)	⊕⊕⊕O MODERATE	IMPORTANT
Mode of birth- Vaginal birth (assisted)												
5‡	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	1898/7268 (26.1%)	1731/6941 (24.9%)	RR 1.02 (0.97 to 1.08)	5 more per 1000 (from 7 fewer to 20 more)	⊕⊕⊕O MODERATE	IMPORTANT
Mode of birth- Caesarean section (elective)												
4‡	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	278/5853 (4.7%)	257/5522 (4.7%)	RR 1.02 (0.86 to 1.2)	1 more per 1000 (from 7 fewer to 9 more)	⊕⊕⊕O MODERATE	IMPORTANT
Mode of birth- Caesarean section (emergency)												
2‡	randomised trials	serious[5]	no serious inconsistency	no serious indirectness	serious[6]	none	127/3196 (4%)	135/3177 (4.2%)	RR 0.94 (0.74 to 1.19)	3 fewer per 1000 (from 11 fewer to 8 more)	⊕⊕OO LOW	IMPORTANT

CI: confidence interval; RR: risk ratio

[1] Evidence downgraded by 2 levels due to unclear risk of reporting bias in all studies, high risk of other bias in 1 study and unclear risk of other bias in 1 study.

[2] Downgraded by 2 levels due to very serious heterogeneity (i2=87%).

[3] Evidence downgraded by 2 levels because 95% CI crosses 2 MIDs for dichotomous outcomes (0.80 and 1.25).
[4] No 95% CI reported. Median and IQR.
[5] Evidence downgraded by 1 level due to unclear risk of reporting bias in all studies and unclear risk of other bias in 1 study.
[6] Evidence downgraded by 1 level because 95% CI crosses 1 MID for dichotomous outcomes (0.8).
‡ For references see corresponding Forest plots

Appendix G – Economic evidence study selection

Economic evidence study selection for review question: Is routine ultrasound in women from 28 weeks effective?

A single economic search was undertaken for all topics included in the scope of this guideline. One economic study was identified which was applicable to this review question. See supplementary material 2 for details.

Appendix H – Economic evidence tables

Economic evidence tables for review question: Is routine ultrasound in women from 28 weeks effective?

Table 7: Economic evidence tables

Study country and type	Intervention and comparator	Study population, design and data sources	Costs and outcomes (descriptions and values)	Results	Comments
Author and year: Wastlund 2019 Country: UK Type of economic analysis: Cost utility analysis Source of funding: NIHR - HTA	Interventions: Universal ultrasound scanning at 36 weeks of gestation Comparator: Selective ultrasound scanning (stated as current practice).	Population characteristics: Nulliparous women in 3rd trimester of pregnancy Modelling approach: Decision tree Source of baseline data: 'Pregnancy and outcome (POP)' study. Source of effectiveness data: 'Pregnancy and outcome (POP)' study & selective inclusion of clinical inputs which best reflect UK practice. Source of cost data: NHS reference costs. Where a code doesn't exist, costs have been evaluated 'bottoms up' by allocating unit costs	Costs (type): NHS perspective. Mean cost per participant: Intervention: Selective US & induction: £2826 Selective US & planned CS: £2833 Universal US & expectant: £2933 Universal US & induction: £2939 Universal US & planned CS: £2955 Control: Selective US & expectant: £2821 Primary measure of outcome: Quality adjusted life years (QALYs)	Costs ranked from least expensive strategy. ICER calculated from least expensive alternative to next most expensive, non-dominated option. Selective US & induction: £904 Selective US & planned CS: Dominated Universal US & expectant: Dominated Universal US & induction: £52,719 Universal US & planned CS: Dominated Probability of being cost effective: Not listed in tabular form for exact results. Included CEAC demonstrates that Selective US & expectant management	Currency: GBP Cost year: 2017 Time horizon: 20 years from birth Discounting: 3.5% for cost and QALYs Applicability: Directly Applicable Limitations: Potentially serious limitations Other comments: the net monetary benefit is incorrectly calculated as displayed in the study. The study undertakes a health perspective so does not consider medico-legal costs. It may be that a more societal sensitivity analysis will have great alter conclusions about cost effectiveness. The health care costs for serious adverse events

Study country and type	Intervention and comparator	Study population, design and data sources	Costs and outcomes (descriptions and values)	Results	Comments
		to resource use estimates from included clinical studies.	Mean outcome per participant: Intervention: Intervention: Selective US & induction: 27.446 Selective US & planned CS: 27.417 Universal US & expectant: 27.441 Universal US & induction: 27.448 Universal US & planned CS: 27.396 Control: 27.441	is roughly 80% cost effective at a £20,000 threshold Sensitivity analysis: Results expressed in the form of a probabilistic sensitivity analysis (PSA). Threshold analysis on key input parameters such as the cost of scan for the universal ultrasound arm to be cost effective was £27. This is someway lower than the reported NHS reference cost input of £107.	such as brachial plexus injury are derived from US studies and may be a conservative reflection of the cost of such injuries over a lifetime horizon. Such costs, if included in the model may alter conclusions regarding the cost effectiveness of universal US

CS: caesarean section
US: ultrasound
CEAC: Cost effectiveness acceptability curve

Appendix I – Economic evidence profiles

Economic evidence profiles for review question: Is routine ultrasound in women from 28 weeks effective?

Table 8: Economic evidence profiles

Study and country	Limitations	Applicability	Other comments	Incremental costs	Incremental effects	ICER	Uncertainty
Author and year: Wastlund 2019 Country: UK	Potentially serious limitations[1]	Directly applicable[2]	Type of economic analysis: Cost utility analysis Time horizon: 20 years for costs and QALYs Primary measure of outcome: Diagnostic outcomes and perinatal mortality and morbidity.	Selective ultrasound & induction versus Selective ultrasound sound & expectant management: £5 Selective ultrasound & planned caesarean section versus Selective ultrasound sound & induction: £7 Universal ultrasound & expectant management versus Selective ultrasound sound & induction: £107 Universal ultrasound &	Selective ultrasound & induction versus Selective ultrasound sound & expectant management: 0.005 Selective ultrasound & planned caesarean section versus Selective ultrasound sound & induction: -0.029 Universal ultrasound & expectant management versus Selective ultrasound sound & induction: -0.005	Costs from least expensive strategy. ICER calculated from least expensive alternative to net most expensive, non-dominated option. Selective ultrasound & induction versus Selective ultrasound sound & expectant management: 904 (reported in study) Selective ultrasound & planned caesarean section versus Selective ultrasound sound &	Deterministic sensitivity analyses: Reported univariate sensitivity analysis in the narrative text shows that universal screening is cost effective if the cost of ultrasound is £27 or lower. It is not clear which particular policy is being compared for this threshold analysis however. PSA: Monte Carlo simulation (n=100,000). Specified probability distributions appear to be appropriate to

Study and country	Limitations	Applicability	Other comments	Incremental costs	Incremental effects	ICER	Uncertainty
				induction versus Selective ultrasound sound & induction: £113 Universal ultrasound & planned caesarean versus universal ultrasound & induction: £16	Universal ultrasound & induction versus Selective ultrasound sound & induction: 0.002 Universal ultrasound & planned caesarean versus universal ultrasound & induction: -0.052	induction: Dominated Universal ultrasound & expectant management versus Selective ultrasound sound & induction: Dominated Universal ultrasound & induction versus Selective ultrasound sound & induction: £52,719 Universal ultrasound & planned caesarean versus universal ultrasound & induction: Dominated	the relevant parameter.

Deterministic analysis no reported. Net Monetary benefit incorrectly calculated. Costs for serious adverse events may be very conservative. Some input parameters are not from best available source.
Population and interventions match protocol. UK context. Includes QALYs derived from preference-based utilities

Appendix J – Economic analysis

Economic evidence analysis for review question: Is routine ultrasound in women from 28 weeks effective?

No economic analysis was conducted for this review question.

Appendix K – Excluded studies

Excluded studies for review question: Is routine ultrasound in women from 28 weeks effective?

Clinical studies

Table 9: Excluded studies and reasons for their exclusion

Study	Reason for Exclusion
Al-hafez, L., Quist-Nelson, J., Ashimi Balogun, O. A., Hammad, I., Chauhan, S. P., Berghella, V., 1017: Third trimester ultrasound in low-risk pregnancies and perinatal death: A systematic review and meta-analysis, American Journal of Obstetrics and Gynecology, 222 (1 Supplement), S632-S633, 2020	Relevant articles from systematic review checked and included if appropriate.
Belanger, K., Hobbins, JC., Muller, JP., Howard, S., Neurological testing in ultrasound exposed infants, American Journal of Obstetrics and Gynecology, 174, 413, 1996	Conference abstract.
Henrichs, J., Verfaille, V., Jellema, P., Viester, L., Pajkrt, E., Wilschut, J., Van Der Horst, H. E., Franx, A., De Jonge, A., Effectiveness of routine third trimester ultrasonography to reduce adverse perinatal outcomes in low risk pregnancy (the IRIS study): nationwide, pragmatic, multicentre, stepped wedge cluster randomised trial, The BMJ, 367 (no pagination), 2019	Duplicate
Imboden, S., Muller, M., Raio, L., Mueller, M. D., Tutschek, B., Clinical significance of 3D ultrasound compared to MRI in uterine malformations, Ultraschall in der Medizin, 35, 440-4, 2014	Article unavailable in English.
Kagan, K. O., Wagner, P., Hoopmann, M., First trimester screening based on ultrasound and cfDNA vs. first-trimester combined screening - A randomized controlled study, European journal of obstetrics gynecology and reproductive biology, 234, e135-e136, 2019	Conference abstract.
Malin, G., Bugg, G., Takwoingi, Y., Thornton, J., Jones, N., Comparison of MRI and ultrasound to detect fetal macrosomia at term: a systematic review and meta-analysis, Archives of disease in childhood. Fetal and neonatal edition, 99, A97-A100, 2014	Conference abstract.
Milner, J., Arezina, J., The accuracy of ultrasound estimation of fetal weight in comparison to birth weight: A systematic review, Ultrasound, 26, 32-41, 2018	This study does not focus on the effectiveness of routine ultrasound to assess fetal wellbeing.
Mohsen, L. A., Amin, M. F., 3D and 2D ultrasound-based fetal weight estimation: a single center experience, Journal of Maternal-Fetal and Neonatal Medicine, 30, 818-825, 2017	This study does not focus on the effectiveness of routine ultrasound to assess fetal wellbeing.

Study	Reason for Exclusion
Okido, M. M., Valeri, F. L., Martins, W. P., Ferreira, C. H., Duarte, G., Cavalli, R. C., Assessment of foetal wellbeing in pregnant women subjected to pelvic floor muscle training: a controlled randomised study, International urogynecology journal, 26, 1475-81, 2015	This study does not focus on the effectiveness of routine ultrasound to assess fetal wellbeing.
Pagani, G., Palai, N., Zatti, S., Fratelli, N., Prefumo, F., Frusca, T., Fetal weight estimation in gestational diabetic pregnancies: comparison between conventional and three-dimensional fractional thigh volume methods using gestation-adjusted projection, Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology, 43, 72-76, 2014	This study does not focus on the effectiveness of routine ultrasound to assess fetal wellbeing.
Ray, C. L., Grange, G., Routine third trimester ultrasound in low risk pregnancy confers no benefit!: AGAINST: Arguments for a routine third trimester ultrasound: what the meta-analysis does not show!, 123, 1122, 2016	The study design is not a RCT.
Revankar, K. G., Dhumale, H., Pujar, Y., A randomized controlled study to assess the role of routine third trimester ultrasound in low-risk pregnancy on antenatal interventions and perinatal outcome, Journal of SAFOG, 6, 139-143, 2014	Study not conducted in a high-income country.
Roberts, R. P., Sibai, B. M., Blackwell, S. C., Chauhan, S. P., Timing of Serial Ultrasound in at Risk Pregnancies: a Randomized Controlled Trial (SUN Trial), American Journal of Obstetrics and Gynecology, 218, S3-S4, 2018	Conference abstract.
Roma, E., Arnau, A., Berdala, R., Bergos, C., Montesinos, J., Figueras, F., Ultrasound screening for fetal growth restriction at 36 vs 32 weeks' gestation: A randomized trial (ROUTE), Ultrasound in Obstetrics and Gynecology, 46, 391-397, 2015	The study does not match the protocol of this review.
Salvesen, K. A., Bakketeig, L. S., Eik-nes, S. H., Undheim, J. O., Okland, O., Routine ultrasonography in utero and school performance at age 8-9 years, LancetLancet (London, England), 339, 85-9, 1992	This study does not focus on the effectiveness of routine ultrasound to assess fetal wellbeing.
Sharp, G. C., Stock, S. J., Norman, J. E., Fetal assessment methods for improving neonatal and maternal outcomes in preterm prelabour rupture of membranes, Cochrane Database of Systematic Reviews, 10, CD010209, 2014	The study population specifically focuses on women with prelabour rupture of membranes.
Skrastad,R.B., Eik-Nes,S.H., Sviggum,O., Johansen,O.J., Salvesen,K.A., Romundstad,P.R., Blaas,H.G.K., A randomized controlled trial of third-trimester routine ultrasound in a nonselected population, Obstetrical and Gynecological Survey, 69, 185-187, 2014	The study design is not a RCT.

Study	Reason for Exclusion
Smith, G. C. S., A critical review of the Cochrane meta-analysis of routine late-pregnancy ultrasound, BJOG: An International Journal of Obstetrics and Gynaecology., 2020	Commentary on Cochrane review.
Stoch, Y. K., Williams, C. J., Granich, J., Hunt, A. M., Landau, L. I., Newnham, J. P., Whitehouse, A. J., Are prenatal ultrasound scans associated with the autism phenotype? Follow-up of a randomised controlled trial, J Autism Dev DisordJournal of autism and developmental disorders, 42, 2693-701, 2012	This study does not focus on the effectiveness of routine ultrasound to assess fetal wellbeing.
Tort, Sera, Martinâ-Lopez, Juliana Ester, How does routine ultrasound in late pregnancy affect maternal and infant outcomes?, Cochrane Clinical Answers, 2015	The study design is not a RCT.
Uyar, I., Kurt, S., Demirtas, O., Gurbuz, T., Aldemir, O. S., Keser, B., Tasyurt, A., The value of uterine artery Doppler and NT-proBNP levels in the second trimester to predict preeclampsia, Archives of Gynecology & ObstetricsArch Gynecol Obstet, 291, 1253-8, 2015	The study design is not a RCT.
van Dyke,B., Motto,J.A., Buchmann,E.J., The value of routine mid-trimester ultrasound in low-risk pregnancies at primary care level, Health SA Gesondheid, 13, 41-49, 2008	Study conducted in a low/middle income country.
Wanyonyi,, Osoro, D. M., Temmerman, M., P06.01: routine late trimester ultrasound for the detection of small-for-gestational-age and growth-restricted fetus in low-risk pregnancy: a randomised controlled trial, Ultrasound in Obstetrics & Gynecology, 54, 169-170, 2019	Study conducted in a low/middle income country.
Wladimiroff, J. W., Laar, J., Ultrasonic Measurement of Fetal Body Size: A Randomized Controlled Trial, Acta Obstetricia et Gynecologica Scandinavica, 59, 177-179, 1980	No usable data could be extracted from this paper.

Economic studies

One excluded list was created for all economic studies in this guideline. See supplementary material 2 for further information.

Appendix L – Research recommendations

Research recommendations for review question: Is routine ultrasound in women from 28 weeks effective?

No research recommendations were made for this review question.