# 4-year surveillance (2017) – summary of new evidence <u>Caesarean section (2011)</u> NICE guideline CG132

# Woman-centred care

132 – 01 Provision of information

# **Recommendations derived from this question**

- 1.1.1.1 Pregnant women should be offered evidence-based information and support to enable them to make informed decisions about childbirth. Addressing women's views and concerns should be recognised as being integral to the decision-making process. [2004].
- 1.1.1.2 Give pregnant women evidence-based information about CS during the antenatal period, because about one in four women will have a CS. Include information about CS, such as:
  - indications for CS (such as presumed fetal compromise, 'failure to progress' in labour, breech presentation)
  - what the procedure involves
  - associated risks and benefit
  - implications for future pregnancies and birth after CS. [new 2011]
- 1.1.1.3 Communication and information should be provided in a form that is accessible to pregnant women, taking into account the information and cultural needs of minority communities and women whose first language is not English or who cannot read, together with the needs of women with disabilities or learning difficulties. [2004]

# **Surveillance decision**

This review question should not be updated.

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

# 4-year surveillance summary

Three references from two randomised controlled trials (RCT) were identified <sup>1-3</sup>. These RCTs assessed interventions to reduce childbirth fear during pregnancy <sup>1-3</sup>.

One RCT compared a psychoeducational intervention (six sessions of group therapy during pregnancy, one after childbirth) with control group (standard care with community nurses and referral if needed) in 271 nulliparous women with a Wijma Delivery Expectancy Questionnaire (W-DEQ-A) >100 (severe fear of childbirth). The psychoeducational intervention was associated with a reduction of caesarean section (CS), higher rate of spontaneous vaginal deliveries (VD) and better delivery experiences compared with controls. The other RCT compared a midwife psychoeducational intervention with standard care in pregnant women with a W-DEQ-A score >66 (n=339) <sup>3</sup>. Details about intervention and standard care were not provided in the abstract. The psychoeducational intervention was not associated with reduction of CS (including emergency CS). Women that received the intervention reported a reduction of childbirth fear. No differences were identified in other important outcomes. This study reported more that 20% of loss of follow-up.

# Women preferences

Two qualitative systematic reviews (SR) were identified in this area and are summarised in the question  $132 - 02^{4,5}$ .

# Topic expert feedback

One stakeholder highlighted a need for NICE guideline CG132 to be more explicit about what women should be told in terms of obstetric risk in both vaginal and CS deliveries. It was in

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132

relation to the Montgomery versus Lanarkshire Health Board case and the need to ensure that the person know all the risk and benefits of a recommended treatment and any alternative options. The person has the right to decide which option is best base on the risk they are willing to run.

# Impact statement

Stakeholders highlighted a need to place more emphasis in the discussion about the risks and benefits of CS and any alternative options. NICE guideline CG132 recommends give pregnant women evidence-based information about CS including the associated risks and benefits of the intervention and support them in the decision making process about childbirth. However new evidence is considered unlikely to have an impact on NICE guideline CG132 recommendations.

New evidence is unlikely to change guideline recommendations

# 132 – 02 Planning mode of birth - What are the risks and benefits of planned CS compared with planned vaginal birth for both women and babies?

# **Recommendations derived from this question**

- 1.1.2.1 Discuss the risks and benefits of CS and vaginal birth with women, taking into account their circumstances, concerns, priorities and plans for future pregnancies (including the risks of placental problems with multiple CS) (see box A and 1.7.1.8). [new 2011]
- Box A Planned caesarean section compared with planned vaginal birth for women with an uncomplicated pregnancy and no previous caesarean section

Planned caesarean section may reduce the risk of the following in women:

- perineal and abdominal pain during birth and 3 days postpartum
- · injury to vagina
- early postpartum haemorrhage
- obstetric shock.

Planned caesarean section may increase the risk of the following in babies:

- neonatal intensive care unit admission.
- Planned caesarean section may increase the risk of the following in women:
- longer hospital stay
- · hysterectomy caused by postpartum haemorrhage
- cardiac arrest.

Please refer to tables 1 and 2 in appendix C for full details, including the absolute and relative risks for each effect.

- 1.1.2.2 Consent for CS should be requested after providing pregnant women with evidence-based information and in a manner that respects the woman's dignity, privacy, views and culture, while taking into consideration the clinical situation. [2004]
- 1.1.2.3 A pregnant woman is entitled to decline the offer of treatment such as CS, even when the treatment would clearly benefit her or her baby's health. Refusal of treatment needs to be one of the woman's options. [2004, amended 2011]
- 1.1.2.4 When a decision is made to perform a CS, a record should be made of all the factors that influence the decision, and which of these is the most influential. [2004, amended 2011]

# Surveillance decision

This review question should be updated.

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 2 of 95

# 2-year surveillance (2014) and Evidence Update (2013)

# Planned caesarean section compared with planned vaginal delivery

A Dutch prospective cohort study (n=2552) assessed the risk of Severe Acute Maternal Morbidity (SAMM) related to mode of delivery <sup>6</sup>.

SAMM was classified according to 5 categories: intensive care unit admission, uterine rupture, eclampsia, major obstetric haemorrhage, and miscellaneous. Deliveries were classified as VD, planned CS, and unplanned CS.

A total of 1479 women with SAMM had VD, and 1073 had CS: 565 planned and 508 unplanned. The overall incidence of SAMM was significantly higher for CS compared with VD. Woman in the planned CS group had higher incidence of SAMM compared to the planned VD group.

Regarding the incidence of SAMM possibly relating to mode of delivery, CS group had a higher incidence compared with VD group. Similar results were found when comparing the incidence of SAMM possibly related to planned CS to planned VD.

The authors stated that some of the decisions for excluding deliveries in which SAMM was not clearly related to mode of delivery may be contentious. Also, study bias by indication could not be totally excluded, although the selected groups reflected actual practice.

The results were considered broadly consistent with NICE guideline CG132 in showing that CS is associated with higher risk of maternal morbidity than vaginal birth, and unlikely to impact on NICE guideline CG132.

# **4-year surveillance summary** *Ectopic pregnancy*

One SR assessed the risk of ectopic pregnancy after a CS compared with VD <sup>7</sup>. They included cohort and case controlled studies that reported the mode of delivery and the development of ectopic pregnancy afterwards (n=61,978; 13 studies). Among the studies found only five adjusted by confounder factors. CS did not increase the risk of ectopic pregnancy but the quality of the studies included was considered low. Authors concluded that there is a need for more research in the area.

# Stillbirth or miscarriage

A SR evaluated the risk of stillbirth or miscarriage after CS compared with VD 8. The authors identified a total of 19 studies (cohorts and case controlled studies) including 1,961,829 pregnancies and 7,803 events for stillbirth (11 studies), and 147,017 pregnancies and 12,682 for miscarriage (8 studies). Women with a previous CS have an increased risk of stillbirth. Subgroup analyses showed similar results for unexplained stillbirths, explained stillbirth but not for antepartum stillbirths where no statistically significant differences were found. The authors reported that the studies assessing miscarriage were low quality and only one reported adjusted results. They suggested that women with previous CS may have an increased risk of stillbirths, but more research is needed in the area.

# Sub-fertility

A meta-analysis examined the association between CS and sub-fertility through the assessment of the subrogate outcome time to next pregnancy or birth<sup>9</sup>. The authors included cohort, case-control and cross-sectional studies in the review. They identified a total of 11 studies but only 5 adjusted their results by confounders and they were included in the meta-analysis of the results (n=750,407). Women with a previous CS may have an increased risk of sub-fertility. Subgroup analysis performed by parity, publication date, length of follow-up, indication for mode of delivery, cohort size, and definition of subfertility (including type of variable used in the analysis) showed similar results. The authors concluded that CS may have a link in the increased risk of sub-fertility but given the low quality of the evidence found more research is needed to identify the causes.

A SR published in the same year found similar results with low pregnancy rates and low birth rates after CS compared with vaginal birth <sup>10</sup>. Authors also highlight the lack of adjustments by important outcomes in the vast majority of the studies included.

# Cerebral palsy

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 3

A SR studying the link between CS and cerebral palsy was identified <sup>11</sup>. A total of 13 studies, both cohort and case-control studies, were included (n=1,696,390; 3,810 cases and 1,692,580 controls). CS (elective or emergency) was not associated with increased risk of cerebral palsy. Subgroup analysis showed that emergency CS but not planned CS was associated with higher cerebral palsy. CS (planned or emergency) in babies at term was associated with higher risk of cerebral palsy. But in preterm babies or breech presentation CS (planned or emergency) was not associated with increased risk of cerebral palsy. Authors concluded that there is no evidence to recommend the use of CS to prevent cerebral palsy.

# Childhood obesity

We identified four SRs published in the last three years assessing the relationship between CS and childhood and adult obesity<sup>12-15</sup>. The most recent one also explored the effect of the variability of the different studies characteristics (settings, designs, and adjustment by confounders) on the results <sup>14</sup>. The authors of this study found that CS is related to an increased risk of childhood obesity compared with VD but the results were heterogeneous and at high risk of bias (residual confounding and publication bias). The other SRs showed similar results<sup>12,13,15</sup> and most of them remarked the possible influence of confounding factors on these findings<sup>13,15</sup>.

# Childhood asthma

A SR evaluated whether the type of delivery (planned and emergency CS, spontaneous and operative VD) increases the risk of childhood asthma <sup>16</sup>. A total of 26 studies were included but the type of studies was not reported in the abstract. The authors reported an increased risk of childhood asthma associated with CS compare to VD. Similar findings were identified when they analysed the results by type of CS (planned or emergency CS) compare with VD. The authors also found an increased risk of asthma linked to operative VD but the results were heterogeneous.

# Placental transfusion and iron-related haematological indices

A SR assessed the relation between CS and the reduction of placental transfusion and haematological indices in the new born compared with VD <sup>17</sup>. According to the authors, these outcomes had been associated with the development of iron-deficiency anaemia in infancy. They included a total of 15 studies (n= 8,477). VD was associated with higher placental residual blood volume, and to lower levels of haematocrit, haemoglobin and erythrocytes. Authors concluded that CS could be associated with a reduction of placental transfusion and poor haematological indices. This could be linked to the development of iron deficiency anaemia during infancy.

# Childhood bowel disease

We identified two SRs assessing the role of the CS in the development of childhood bowel disease <sup>18,19</sup>. Both SRs were published in the same year but they arrived to different conclusions.

The first one assessed the risk of inflammatory bowel disease (IBD) in those delivered by CS <sup>19</sup>. The SR included in total seven cohort and case-control studies (n= 12,709) and they did not identify a relationship between the mode of delivery and the risk of IBD.

The other SR performed a subgroup analysis by type of IBD: Crohn's disease (CD) and ulcerative colitis (UC) <sup>18</sup>. The authors identified nine studies and found that CS increased the risk of CD but not the risk of UC. They did not find an increased risk of IBD associated with CS.

# Women preferences

We identified two qualitative SRs about women birthing preferences <sup>4,5</sup>.

One SR explored the factors influencing women's choice between CS and VD<sup>4</sup>. They included observational and gualitative studies assessing the childbirth preferences in women with low-risk pregnancies (excluding preferences for place of birth). The authors performed a meta-synthesis of the results and identified three major factors impacting on the decision: 1) fear of childbirth, pain, and recovery after delivery; 2) information provided by health care professionals; and 3) women's expectations of childbirth. The authors concluded that these three factors were influential in the women's decision making process regardless of the mode of birth preferred. They also highlighted the need for more studies to investigate the influence of CS on long-term outcomes in women's decision makina.

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 **4** of **95**  The second SR did a meta-synthesis of qualitative studies assessing women's experience with CS <sup>5</sup>. They included 10 qualitative studies and six overarching themes emerged: scared to death, in your hands, out of control, broken body and soul, empty heart and arms, and shattered dreams. Scared to death and in your hand were identified by the authors as themes that show women knowledge in this area and a need to provide more information about the CS process.

# **Topic expert feedback**

Topic experts raised concerns about the longterm impact on the infant of CS. This issue is not being addressed properly in clinical practice, and still unknown to parents.

Topic experts highlighted one observational study that assessed the link between the mode of delivery (planned CS or VD) and the development of childhood health problems or death (all-causes death by age 21 years)<sup>20</sup>. The study assessed chronic conditions as asthma (requiring hospital admission), obesity at 5 years old, type 1 diabetes, IBD, cancer, among others. They used population-base data of 312,287 term singleton first born in Scotland (UK).

They found that planned CS increases the risk of type 1 diabetes compared with unplanned CS but they did not detected any statistical significant difference in the risk of any of the other outcomes assessed.

Regarding planned CS, they found an increased risk of asthma requiring hospital

admission, salbutamol inhaler prescription at 5 years old, and death but not the risk of type 1 diabetes, IBD, obesity at 5 years old, and cancer.

The authors concluded that more research is needed to study the causality link between planned CS and the results in long-term outcomes found.

A observational study that evaluated the association between CS and the body mass index until the adolescence was also highlighted <sup>21</sup>. This study was analysed in two of the SRs included in the 4-year evidence summary <sup>14,15</sup>, therefore it is not discuss further.

# Impact statement

Topic experts highlighted there is a need to consider these long-term outcomes when planning the mode of birth. We identified evidence about CS and its impact on maternal outcomes (risk of future ectopic pregnancy, stillbirth or miscarriage, sub-fertility) and infant outcomes (cerebral palsy, childhood obesity, asthma, bowel disease, and iron-related haematological indices). Some of these outcomes are not included in the current version of NICE guideline CG132. The evidence identified from SRs is limited given the low quality of the studies included.

New evidence identified that may change current recommendations.

# Planned CS

# 132 – 03 Breech presentation

# **Recommendations derived from this question**

- 1.2.1.1 Women who have an uncomplicated singleton breech pregnancy at 36 weeks' gestation should be offered external cephalic version. Exceptions include women in labour and women with a uterine scar or abnormality, fetal compromise, ruptured membranes, vaginal bleeding or medical conditions. [2004].
- 1.2.1.2 Pregnant women with a singleton breech presentation at term, for whom external cephalic version is contraindicated or has been unsuccessful, should be offered CS because it reduces perinatal mortality and neonatal morbidity. [2004].

# Surveillance decision

This review question should not be updated.

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence was identified.

# **4-year surveillance summary** *External cephalic version*

A SR assessed the mode of delivery after a successful external cephalic version (ECV) <sup>22</sup>. The authors included 11 studies, both cohort and case-control studies, (n= 46,641) and found that 21% of the women have a CS after a successful ECV. Women after a successful ECV for breech presentation were more likely to have a CS for dystocia and CS for fetal distress. Women were also more likely to have operative VD. Authors concluded that despite the increased risk for assisted delivery (CS or operative); ECV is an efficient procedure to prevent CS (number to treat of three).

We identified an update of a Cochrane review that assessed ECV in term breech presentation pregnancies <sup>23</sup>. A total of eight studies were included (n=1305 women). ECV reduced significantly the risk of non-cephalic presentation at birth, vaginal cephalic birth not achieved, and CS without an increased risk of short time complications (Apgar score rating below seven at one minute or five minutes, low umbilical vein pH levels, neonatal admission, or perinatal death). The authors highlighted that the quality of the evidence was low or very low, and that more research is needed to identify the impact on long term outcomes.

### Preterm breech presentation

We identified an updated of a Cochrane review <sup>24</sup>. This updated included five RCT comparing ECV before term (37 weeks of gestation) to no ECV attempt or ECV attempted at term <sup>24</sup>. ECV before term was associated with significantly reduced risk of non-cephalic presentation at birth, failure to achieve vaginal cephalic birth, and vaginal breech delivery but increased risk of pre-term labour compared with ECV after 37 weeks. No differences were observed in short term complications (Apgar score or perinatal death).

Caesarean section compared with vaginal delivery in breech presentations

We identified two SRs that compared CS with VD in breech presentations <sup>25,26</sup>.

A Cochrane review assessed the impact of planned CS compared with planned VD for singleton breech presentation at term on different pregnancy outcomes <sup>25</sup>. The authors included three randomised trials (n=2396) and found that planned CS reduced significantly the risk of perinatal or neonatal mortality and increased the risk of short-term maternal morbidity. Data for other short term outcomes (urinary incontinence, pain, abdominal pain and perineal pain at three months) and long term outcomes (death or neurodevelopmental delay, infant medical problems at 2 years) were informed by few studies (only one) and in some cases included a low number of events (birth trauma and brachial plexus injury). In general, planned CS was associated with increased risk of abdominal pain and risk of infant medical problems at two years, and with a reduction of urinary incontinency, and perineal pain. Authors concluded that planned CS was associated with reduced risk of perinatal or neonatal death but increased maternal morbidity. More studies are needed to assess the impact of the planned CS on pregnancy outcomes and long-term infant outcomes.

The other SR identified included observational studies that compared the impact of CS compared with VD on breech presentations between 25 [+0] and 36 [+6] weeks of gestational age on neonatal mortality <sup>26</sup>. They included seven studies (n=3557) and found that CS was associated with significantly reduced risk of neonatal mortality.

#### **Topic expert feedback**

Topic experts highlighted that this is an area where new evidence needs to be reviewed.

One stakeholder highlighted that NICE guideline CG132 needs to place more emphasis in the discussion about the risk and benefits of this intervention and the alternatives to help women in the decision making process.

### Impact statement

Evidence is consistent with the current guideline, which recommends ECV in uncomplicated singleton pregnancies at 36

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132

weeks gestation (exceptions described) and CS in case of unsuccessful ECV or contraindication. Few studies assessed the impact of CS for breech presentation on longterm outcomes. One of them indicated an increased risk of infant medical problems two years after a CS for breech presentation. But given the low quality of the study, it seems unlikely to have an impact on the current recommendation. Most of the studies included highlighted a need of further research in this area and in particular the impact of CS for breech presentation on long term outcomes.

New evidence is unlikely to change guideline recommendations.

# 132 – 04 Multiple pregnancy

# **Recommendations derived from this question**

- 1.2.2.1 In otherwise uncomplicated twin pregnancies at term where the presentation of the first twin is cephalic, perinatal morbidity and mortality is increased for the second twin. However, the effect of planned CS in improving outcome for the second twin remains uncertain and therefore CS should not routinely be offered outside a research context. [2004]
- 1.2.2.2 In twin pregnancies where the first twin is not cephalic the effect of CS in improving outcome is uncertain, but current practice is to offer a planned CS. [2004]

# **Surveillance decision**

This review question should not be updated.

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

### 4-year surveillance summary

We identified five references related this question: two Cochrane reviews <sup>27,28</sup> and one RCT (the Twin Birth Study) with three different publications <sup>29-31</sup>. This RCT was included in the SR.

One Cochrane review assessed in women with twin pregnancies the impact of planned CS on short and long-term pregnancy outcomes <sup>27</sup>. Two RCTs were included (n=2864). Planned CS did not increase significantly the risk of maternal death or serious morbidity, or perinatal or neonatal death or serious neonatal morbidity compared with planned VD. No statistical differences were found in the risk of failure to breastfeed or postnatal depression. No data in long-term outcomes were reported in the studies included and authors stated that they are awaited. They concluded that there is not enough evidence to recommend the routine use of planned CS for term twin pregnancies with first twin in cephalic presentation and more research is needed in this area.

The Twin Birth Study was included in the Cochrane review. We identified a reference published after the review<sup>29</sup>. This paper reported on breastfeeding, quality of life, depression, fatigue and urinary incontinence at 3 months of follow-up. The authors did not identify differences in none of these outcomes between the groups (planned CS compared with planned VD).

# Timing of planned CS for twin pregnancy

One Cochrane review assessed the impact on different pregnancy outcomes of an elective birth policy for women with uncomplicated twin pregnancies from 37 weeks of gestation compared with an expectant approach <sup>28</sup>. The authors identified two RCTs including 271 women (542 infants). There were no differences in the risk of CS, perinatal or

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132

serious perinatal morbidity or maternal death or serious maternal morbidity. Other maternal and infant secondary outcomes were assessed but no significant differences were identified (maternal haemorrhage, operative VD, Apgar score, admission to neonatal intensive care, neonatal encephalopathy, and respiratory distress syndrome, among others). Authors concluded that an elective birth at 37 weeks' gestations in uncomplicated twin pregnancies is an intervention that does not seems to have a negative effect on the different pregnancy outcomes studied.

### **Topic expert feedback**

One stakeholder highlighted that NICE guideline CG132 needs to place more

emphasis in the discussion about the risk and benefits of this intervention and the alternatives to help women in the decision making process about the mode of delivery.

### Impact statement

The evidence identified is consistent with the current recommendations. There is not enough evidence to support the use of planned CS for term uncomplicated twin pregnancies with a first twin in a cephalic position.

New evidence is unlikely to change guideline recommendations.

# 132 – 05 Preterm birth and CS

# **Recommendations derived from this question**

1.2.3.1 Preterm birth is associated with higher neonatal morbidity and mortality. However, the effect of planned CS in improving these outcomes remains uncertain and therefore CS should not routinely be offered outside a research context. [2004]

# Surveillance decision

No new information was identified at any surveillance review.

This question should not be updated.

# 132 – 06 Small for gestational age and CS

# **Recommendations derived from this question**

1.2.4.1 The risk of neonatal morbidity and mortality is higher with 'small for gestational age' babies. However, the effect of planned CS in improving these outcomes remains uncertain and therefore CS should not routinely be offered outside a research context. [2004]

# Surveillance decision

No new information was identified at any surveillance review.

This question should not be updated.

# 132 – 07 Placenta praevia

# **Recommendations derived from this question**

1.2.5.1 Women with a placenta that partly or completely covers the internal cervical os (minor or major placenta praevia) should be offered CS. [2004, amended 2011]

# Surveillance decision

No new information was identified at any surveillance review.

This question should not be updated.

# 132 – 08 What is the accuracy of imaging techniques (colour flow ultrasound [US] and magnetic resonance imaging [MRI]) for diagnosis of a morbidly adherent placenta in pregnant women who have had a previous CS and are currently diagnosed with placenta praevia?

# **Recommendations derived from this question**

- 1.2.6.1 If low-lying placenta is confirmed at 32–34 weeks in women who have had a previous CS, offer colour-flow Doppler ultrasound as the first diagnostic test for morbidly adherent placenta. [new 2011]
- 1.2.6.2 If a colour-flow Doppler ultrasound scan result suggests morbidly adherent placenta:
  - discuss with the woman the improved accuracy of magnetic resonance imaging (MRI) in addition to ultrasound to help diagnose morbidly adherent placenta and clarify the degree of invasion
  - explain what to expect during an MRI procedure
  - inform the woman that current experience suggests that MRI is safe, but that there is a lack of evidence about any long-term risks to the baby
  - offer MRI if acceptable to the woman. [new 2011]
- 1.2.6.3 Discuss the interventions available for delivery with women suspected to have morbidly adherent placenta, including cross matching of blood and planned CS with a consultant obstetrician present. [new 2011]

# Surveillance decision

This question should not be updated.

# 2-year surveillance (2014) and Evidence Update (2013)

A retrospective review of clinical data evaluated whether magnetic resonance imaging (MRI) after ultrasound for women with or at risk of placenta accreta had an effect on rates of CS with immediate hysterectomy (n=139) <sup>32</sup>. Women who had placenta accreta confirmed by

ultrasound or documented operative diagnosis, or at least 1 risk factor for placenta accreta were included.

The final operative diagnosis was highly correlated with both ultrasound and MRI diagnosis and either scan was significantly associated with CS and immediate

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132

hysterectomy. Positive imaging diagnoses were also significantly associated with higher transfusion requirements.

The authors noted that the results from ultrasound and MRI and the operative and final diagnoses were not independent variables so they could not assess the accuracy of the interventions. Other limitations were the absence of a blinded reinterpretation of each woman's ultrasound and MRI or a pathological confirmation of the final diagnosis, the smaller number of MRIs compared with the number of ultrasounds, and the duration of the study (over 13 years so the technology and experience of imagers may have developed in this time). The population was from a high risk obstetric centre so may be biased towards more complex cases.

The results of this study suggest that the addition of MRI to ultrasound examination does not change delivery mode in patients at risk of placenta accreta. Although this was considered inconsistent with NICE guideline CG132 (MRI should be offered if acceptable to the woman) the results were considered unlikely to change guidance because of the limitations of the evidence found.

# 4-year surveillance summary

No relevant evidence identified.

# **Topic expert feedback**

Comments received via topic expert feedback:

- MRI scanning compared with colour flow Doppler. In the current practice more value is place on MRI scanning than on colour flow Doppler. This needs to be reviewed.
- Diagnostic techniques in morbidly adherent placenta need to be reviewed but probably there is little new, high quality, evidence available in this moment.

# Impact statement

Topic experts highlighted this area as an important area to be reviewed. But no new evidence was identified and the previous one found in the 2-year surveillance (2014) and Evidence Update (2013) was considered unlikely to have an impact on current recommendations.

New evidence is unlikely to change guideline recommendations.

132 – 09 Does a diagnosis of morbidity adherent placenta using imaging techniques lead to improved outcomes in pregnant women with a previous caesarean section currently diagnosed with placenta praevia?

# **Recommendations derived from this question**

- 1.2.6.4 When performing a CS for women suspected to have morbidly adherent placenta, ensure that:
  - a consultant obstetrician and a consultant anaesthetist are present
  - an experienced paediatrician is present
  - a senior haematologist is available for advice
  - a critical care bed is available
  - sufficient cross-matched blood and blood products are readily available. [new 2011]
- 1.2.6.5 When performing a CS for women suspected to have morbidly adherent placenta, the consultant obstetrician should decide which other healthcare professionals need to be consulted or present. [new 2011]
- 1.2.6.6 All hospitals should have a locally agreed protocol for managing morbidly adherent placenta that sets out how these elements of care should be provided. [new 2011]

# Surveillance decision

This question should not be updated.

# 2-year surveillance (2014) and Evidence Update (2013)

A French retrospective cohort evaluated the fertility and obstetric outcomes after conservative management of placenta accreta in 2 tertiary maternity centres (n=46) <sup>33</sup>. Fertility was assessed only for women who had conservative management with all or part of the placenta left in the uterus.

The placenta was left partially in situ in 30 women, and completely in situ in 16 women. Twenty women had a planned CS, 23 had unplanned CS and 3 had spontaneous VD. Conservative management was unsuccessful for 6 women, all of whom needed hysterectomy. Of the 40 women successfully managed conservatively, 35 were women followed-up, and 14 women wanted further pregnancies: 12 had at least 1 more, with 15 pregnancies occurring in total. Six pregnancies did not last beyond the first trimester (5 spontaneous abortions and 1 planned termination). Eight pregnancies were normal until term and 1 was complicated by intrauterine growth restriction. Two women had a recurrence of placenta accreta, one of whom had a hysterectomy, and the other was managed conservatively.

The authors described several limitations of the study as its retrospective design, the lack of confirmation of placenta accreta in most cases, and the low number of women who wanted further pregnancies that could impact on the high morbidity results found.

This study suggests that conservative management of placenta accreta may preserve fertility. Because NICE guideline CG132 does not have specific recommendations for the management of placenta accreta this study was considered unlikely to have an impact on guidance.

# Prophylactic pelvic artery catheterisation

An Israeli retrospective study evaluated prophylactic pelvic artery catheterisation, balloon occlusion and embolisation before CS in women with ultrasound findings consistent with, or significant clinical risk factors for, placenta accreta (n=30) <sup>34</sup>.

A multidisciplinary team that included an obstetrician, an anaesthetist, an invasive radiologist and a neonatologist examined and counselled the women before surgery. All participants had at least 1 previous CS. During surgery, morbidly adherent placenta was identified in 25 women: 13 women had placenta percreta and 12 had placenta increta or placenta accreta. Embolisation was performed on 23 women.

Median estimated blood loss was 2000 ml (range 500–900 ml). Median blood loss and surgery did not differ depending on port of entry, number of previous CS, or whether the woman had placenta increta, accreta or percreta.

Major post-operative complications were a vesicouterine fistula and a tubo-ovarian abscess. Other complications included fever and pulmonary congestion. There were no major catheter-related complications. Minor catheter-related complications included subcutaneous haematoma, and transient leg ischaemia, which resolved spontaneously.

The authors noted that the lack of a control group was a major limitation of this study. Another limitation was the unavoidable lack of pathological confirmation of the diagnosis in all cases that the uterus was preserved.

The results of this study provide limited evidence for the safe and effective use of prophylactic pelvic artery catheterisation in women with placenta accreta, but the sample size was small. This study was considered unlikely to have an impact on NICE guideline CG132 because further research is needed. This was in line with a research recommendation in the full version of NICE guideline CG132, on the effectiveness of treatments for reducing morbidity associated with maternal blood loss during surgery for morbidly adherent placenta.

#### Blood cell salvage

A retrospective study of case records reviewed the effectiveness of blood cell salvage used during both planned (102 women) and unplanned CS (5 women) <sup>35</sup>. Salvaged blood

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 11 of 95

was reinfused only when the collection of fluid was more than 800 ml.

Of the 107 women, 36 had salvaged blood reinfused. The remaining 71 did not have sufficient blood loss to collect and reinfuse. The mean volume of blood lost from the 36 women was 1275 ml (planned mean=830 ml, unplanned mean=1897 ml). The proportion of reinfused salvaged blood was higher in the planned group compared with the unplanned group. This was because of the higher volume of blood lost and loss of blood before cell salvage was set up in the unplanned group.

The results of this small study provide limited support for the use of cell salvage in high-risk planned and unplanned CS. These results were considered unlikely to affect recommendations in NICE guideline CG132.

### 4-year surveillance summary

Prophylactic pelvic artery catheterisation

One RCT evaluated the effect of balloon catheters (BC) used as prophylaxis of bleeding in women with prenatal diagnosis of placenta accreta <sup>36</sup>. A total of 27 women were randomised to intervention (BC placed in the anterior division of the internal iliac arteries) or control group. There were no significant differences in the number of CS hysterectomies between the groups (46.2% compare to 50.0%, respectively), in the number of units of blood transfused or in the calculated blood loss. They did not find significant differences in any of the other outcomes assessed (number of plasma products transfused, duration of surgery. peripartum complications, or hospitalisation stay). Two women had minor adverse events related to catheter insertion. The authors concluded that the use of a BC as prophylaxis of bleeding in women with prenatal diagnosis of placenta accreta did not reduce the number of red blood cells units transfused.

# **Topic expert feedback**

Topic experts highlighted a change in clinical practice. There is an increased use of prophylactic interventional radiology procedures. They are being seeing as a 'default practice'. These services are not always available. So, there is a need to provide evidence-based guidance in this area and if they are safe, provide appropriate networks for their use.

# Impact statement

In the previous 2-year surveillance (2014) and Evidence Update (2013) new evidence was identified about conservative management of placenta accreta, prophylactic pelvic artery catheterisation and blood cell salvage. It was considered unlikely to have an impact on NICE guideline CG132 recommendations. In the 4year surveillance review, we identified one RCT assessing the effectiveness of prophylactic pelvic artery catheterisation in women with prenatal diagnosis of placenta accreta. This was a small study that included a low number of participants. The primary outcome was the number of units of blood transfused. Blood loss was considered as an important outcome in NICE guideline CG132 but only if it gives information to identify the number of women where blood loss could be potentially lifethreatening. This outcome was not reported in the study. Other outcomes were reported but no significant differences were identified between the groups. The results of this study provide limited evidence and are unlikely to have an impact on the current recommendations.

New evidence is unlikely to change guideline recommendations.

# 132 – 10 Predicting CS for cephalopelvic disproportion in labour

# **Recommendations derived from this question**

1.2.7.1 Pelvimetry is not useful in predicting 'failure to progress' in labour and should not be used in decision making about mode of birth. [2004]

1.2.7.2 Shoe size, maternal height and estimations of fetal size (ultrasound or clinical examination) do not accurately predict cephalopelvic disproportion and should not be used to predict 'failure to progress' during labour. [2004]

# Surveillance decision

No new information was identified at any surveillance review.

This question should not be updated.

# 132 – 11 Mother-to-child transmission of maternal infections

# **Subquestion**

What is the effectiveness of planned CS compared with planned vaginal birth at decreasing the motherto-child transmission of the virus in pregnant women with HIV, for both low and high viral load?

# **Recommendations derived from this question**

- 1.2.8.1 As early as possible give women with HIV information about the risks and benefits for them and their child of the HIV treatment options and mode of birth so that they can make an informed decision. [new 2011]
- 1.2.8.2 Do not offer a CS on the grounds of HIV status to prevent mother-to-child transmission of HIV to.
  - women on highly active anti-retroviral therapy (HAART) with a viral load of less than 400 copies per ml or
  - women on any anti-retroviral therapy with a viral load of less than 50 copies per ml.
- Inform women that in these circumstances the risk of HIV transmission is the same for a CS and a vaginal birth. [new 2011]
- 1.2.8.3 Consider either a vaginal birth or a CS for women on anti-retroviral therapy (ART) with a viral load of 50-400 copies per ml because there is insufficient evidence that a CS prevents mother-to-child transmission of HIV. [new 2011]
- 1.2.8.4 Offer a CS to women with HIV who:
  - are not receiving any anti-retroviral therapy or
  - are receiving any anti-retroviral therapy and have a viral load of 400 copies per ml or more. [new 2011]
- 1.2.8.5 Researchers and national bodies responsible for the collection of UK population data should continue to collect data about HIV diagnoses in pregnant women, including treatment, mode of birth, and mother-to-child transmission rates. [new 2011]

# Surveillance decision

This question should not be updated.

2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

4-year surveillance summary

No relevant evidence identified.

# **Topic expert feedback**

Topic experts highlighted that after the publication of NICE guideline CG132, British

4-year surveillance 2017 summary of new evidence - Caesarean section (2011) NICE guideline CG132

HIV Association (BHIVA) guidelines have added detail and more evidence in this field. So, NICE guideline CG132 recommendations in this area have been superseded by BHIVA and probably are now redundant.

### Impact statement

We did not identify new evidence that would affect recommendations. Topic experts mentioned that BHIVA guidelines provide more detailed and updated information in this field that NICE guideline CG132. BHIVA is a NHS Evidence accredited provider. BHIVA guideline was published in 2012 and reviewed in 2014. It will be fully updated and revised in 2017.

New evidence is unlikely to change guideline recommendations.

# **Hepatitis B virus**

### **Recommendations derived from this question**

1.2.8.6 Mother-to-child transmission of hepatitis B can be reduced if the baby receives immunoglobulin and vaccination. In these situations pregnant women with hepatitis B should not be offered a planned CS because there is insufficient evidence that this reduces motherto-child transmission of hepatitis B virus. [2004]

# Surveillance decision

This question should not be updated.

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

# 4-year surveillance summary

Two SRs compared CS with VD on prevention of mother-to-child transmission of hepatitis B <sup>37,38</sup>.

The first SR identified RCTs, cohort and casecontrol studies and included a total of 10 studies <sup>37</sup>. The odds ratio of hepatitis B virus (HBV) transmission was significantly lower in CS compared with VD but the results were heterogeneous. The heterogeneity was explained by the variation in the hepatitis B immune globulin (HBIG) administration. In women with a hepatitis B e-antigen positive CS did not reduce the odds of HBV transmission. The authors concluded that CS may have a role in the prevention of vertical transmission of the HBV but a final conclusion cannot be drawn given the heterogeneity of the results.

The other SR included RCTs and non-RCTs that compared any of the following groups: HBIG administration, antiviral treatment,

placebo, planned CD, and VD <sup>38</sup>. The HBIG administration was associated with a significant reduction of incidence of HBV intrauterine infection and the number of infants with chronic hepatitis B. There was also a reduction of the incidence of infant HBV transmission and the infant serum HBsAg positivity with the antiviral treatment. As to the latter, it was not significant difference in the infant serum HBsAg positivity at birth or at 6-7 months between CS and VD groups. The authors reported a higher incidence of infant chronic hepatitis B infection in the VD group.

### **Topic expert feedback**

None identified relevant to this question.

### Impact statement

We identified two SRs in this area. Both of them included RCTs and observational studies but the number and type of studies finally included was unclear. One SR identified a reduction in the mother-to-child transmission of hepatitis B with CS compared with VD, but the results were heterogeneous. The other SR did not identify such a differences but an increased risk of the infant chronic hepatitis B infection in

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 14 of 95

the VD group. They also found a positive impact on the infant outcomes with the HBIG administration and antiviral treatment. The HBIG administration is in line with NICE guidance. NICE guideline CG132 does not recommend planned CS because there is a lack of evidence about its efficacy to reduce vertical HBV transmission. The evidence found shows conflicting results but the quality of the included studies in the SRs and the influence of certain variables as for example HBIG administration on the results remains unclear. It is considered that the studies identified provide limited evidence and do not affect the current recommendations.

New evidence is unlikely to change guideline recommendations.

# **Hepatitis C virus**

### **Recommendations derived from this question**

- 1.2.8.7 Women who are infected with hepatitis C should not be offered a planned CS because this does not reduce mother-to-child transmission of the virus. [2004]
- 1.2.8.8 Pregnant women who are co-infected with hepatitis C virus and HIV should be offered planned CS because it reduces mother-to-child transmission of both hepatitis C virus and HIV. [2004]

# Surveillance decision

No new information was identified at any surveillance review.

This question should not be updated.

# Herpes simplex virus

### **Recommendations derived from this question**

- 1.2.8.9 Women with primary genital herpes simplex virus (HSV) infection occurring in the third trimester of pregnancy should be offered planned CS because it decreases the risk of neonatal HSV infection. [2004]
- 1.2.8.10 Pregnant women with a recurrence of HSV at birth should be informed that there is uncertainty about the effect of planned CS in reducing the risk of neonatal HSV infection. Therefore, CS should not routinely be offered outside a research context. [2004]

# Surveillance decision

No new information was identified at any surveillance review.

This question should not be updated.

132 – 12 Maternal request for CS- What is the appropriate care pathway for women who request a primary CS where there is no obstetric or medical indication?

# **Recommendations derived from this question**

- 1.2.9.1 When a woman requests a CS explore, discuss and record the specific reasons for the request. [new 2011]
- 1.2.9.2 If a woman requests a CS when there is no other indication, discuss the overall risks and benefits of CS compared with vaginal birth and record that this discussion has taken place (see box A). Include a discussion with other members of the obstetric team (including the obstetrician, midwife and anaesthetist) if necessary to explore the reasons for the request, and ensure the woman has accurate information. [new 2011]
- 1.2.9.3 When a woman requests a CS because she has anxiety about childbirth, offer referral to a healthcare professional with expertise in providing perinatal mental health support to help her address her anxiety in a supportive manner. [new 2011]
- 1.2.9.4 Ensure the healthcare professional providing perinatal mental health support has access to the planned place of birth during the antenatal period in order to provide care. [new 2011]
- 1.2.9.5 For women requesting a CS, if after discussion and offer of support (including perinatal mental health support for women with anxiety about childbirth), a vaginal birth is still not an acceptable option, offer a planned CS. [new 2011]
- 1.2.9.6 An obstetrician unwilling to perform a CS should refer the woman to an obstetrician who will carry out the CS. [new 2011]

# Surveillance decision

This question should not be updated

# 2-year surveillance (2014) and Evidence Update (2013)

CS for non-medical reasons

A Cochrane review evaluated the effects of planned CS compared with planned vaginal birth in women with no clear clinical indication for CS <sup>39</sup>. All RCTs containing pregnant women in their first pregnancy, with cephalic presentation at term, with no medical indication for CS were to be included. They did not identify RCTs that met the eligibility criteria for inclusion in the review.

A Swedish prospective cohort study compared maternal outcomes in healthy women who were giving birth to their first child, after planned CS (n=247) or planned VD (n=294)<sup>40</sup>. Medical outcomes were compared at 3 months, including the risk of infection and excess blood loss. The CS group included breech

presentation (n=132) and maternal request (n=115).

There were no differences in estimated blood loss, rate of blood transfusions, or rate of infections between the planned CS or planned VD groups. No significant differences were noted in rates of infection or in reported pain of any kind at 3-month follow-up. This study had several limitations: small sample size, visual estimation of blood loss is unreliable, and the complication rate for planned VD was higher than previously reported (findings reported by intended mode of delivery and not by actual delivery mode).

The results of this study suggested that there is no difference between planned VD and planned CS in first pregnancy in terms of medical complications after 3 months. This study did not cover the outcomes of actual

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 16 of 95

vaginal birth or CS and so it was considered that it was unlikely to have an impact on NICE guideline CG132.

# 4-year surveillance summary Childbirth fear

Two RCTs were identified in this area and are summarised in the question  $132 - 01^{1-3}$ .

# Women preferences

Two qualitative SRs were identified in this area and are summarised in the question 132 - 02<sup>4,5</sup>. Both qualitative SRs highlighted the importance to provide appropriate information and support to women in the decision-making process.

# **Topic expert feedback**

Comments received via expert feedback:

- Current recommendations are not fully adopted.
  - 'The current recommendations are ignored in most units, or are not fully adopted entailing variations in clinical practice. This leads to a total mismatch between a NICE recommendation and actual practice. It results in regular conflicts between commissioners, providers and service users'.
- More information is needed about appropriate interventions to manage women who request CS. The current recommendations have led to variations in clinical practice, so more clearly recommendations are needed.
- Perinatal mental health interventions to help maternal choice of delivery options.
  - 'This particularly relates to the role of 'perinatal mental health professional' and what interventions they should provide'.
- There is a need to review predictions models for success of elective CS.
- Recommendation 1.2.9.3

When a woman requests a CS because she has anxiety about childbirth, offer referral to a healthcare professional with expertise in providing perinatal mental health support to help her address her anxiety in a supportive manner [new 2011]'. There is not perinatal mental health support (little or no access) in whole regions. So units either: do CS because they cannot provide the recommended service, ignore women who request CS, or sent them to see a midwife who does not have relevant information, skills or expertise. This recommendation needs to be reinforced.'

'Further clarification is required [in the] current guideline due to varied interpretation in practice'.

'Increasingly elective caesarean sections are being carried out based on 'enhanced recovery' models. There are currently NO RCT's in this area but some observational data'.

 One stakeholder highlighted that NICE guideline CG132 needs to be more explicit about what women should be told in terms of obstetric risk in both vaginal and CS deliveries. It was in relation to the Montgomery versus Lanarkshire Health Board case and the need to ensure that the people know all the risk and benefits of a recommended treatment and any alternative options. The person has the right to decide which option is best base on the risk they are willing to run.

# Impact statement

Topic experts highlighted variation in the clinical practice in this area. Most of the comments were linked to issues with the implementation of NICE guideline CG132 recommendations. Mainly due to problems related to access to perinatal mental health support and a lack of clarification about what to do when these services are not available. They highlighted a need for more detailed information about the interventions that might work to manage women who request CS.

In this surveillance review, we did not identify new evidence related to interventions to help women's decision making. We identified two qualitative SRs that highlighted the importance

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 17 of 95

of this process and also two RCTs that evaluated psychoeducative interventions to reduce women's childbirth fear.

New evidence is unlikely to change guideline recommendations.

# 132 – 13 Body mass index

# **Recommendations derived from this question**

1.2.10.1 Do not use a body mass index (BMI) of over 50 alone as an indication for planned CS. [new 2011]

# Surveillance decision

No new information was identified at any surveillance review.

This question should not be updated.

# Factors affecting likelihood of CS during intrapartum care

# 132 – 14 Place of birth

# **Recommendations derived from this question**

No recommendations made in this area, only research recommendations (RR - 19 and RR - 20)

# **Surveillance decision**

No new information was identified at any surveillance review.

This question should not be updated.

# 132 – 15 Factors reducing the likelihood of CS

# **Recommendations derived from this question**

- 1.3.2.1 Women should be informed that continuous support during labour from women with or without prior training reduces the likelihood of CS. [2004]
- 1.3.2.2 Women with an uncomplicated pregnancy should be offered induction of labour beyond 41 weeks because this reduces the risk of perinatal mortality and the likelihood of CS. [2004]
- 1.3.2.3 A partogram with a 4-hour action line should be used to monitor progress of labour of women in spontaneous labour with an uncomplicated singleton pregnancy at term, because it reduces the likelihood of CS. [2004]

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 18 of 95

- 1.3.2.4 Consultant obstetricians should be involved in the decision making for CS, because this reduces the likelihood of CS. [2004]
- 1.3.2.5 Electronic fetal monitoring is associated with an increased likelihood of CS. When CS is contemplated because of an abnormal fetal heart rate pattern, in cases of suspected fetal acidosis, fetal blood sampling should be offered if it is technically possible and there are no contraindications. [2004]

# Surveillance decision

This question should not be updated.

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

# 4-year surveillance summary Partogram

We identified an update of a Cochrane review that assessed the impact of partogram on perinatal and maternal morbidity and mortality <sup>41</sup>. The review included RCTs and guasi-RCTs that compared the use or not use of a partogram or that compared different partogram designs. A total of six studies were included (n=7,706). They did not identify significant differences in the risk of CS, operative delivery or Apgar score (less than seven at five minutes) between partogram compared with no partogram. Four-line action line was associated with higher requirement of oxytocin augmentation compared with two-hour action line. Four-line action partogram was associated with decreased risk of CS when compared with three-action line partogram. Partogram with a latent phase was also related to a lower rate of CS when compared with a partogram without latent phase. The evidence found did not support the use of partogram but given that it is a common practice and the quality of the evidence was weak; the authors concluded that

the use of the partogram must be determinate at the local level.

# **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

# Impact statement

New evidence identified did not support the use of the partogram. The results showed no impact of the partogram on the risk reduction of CS, operative VD and Apgar score less than seven at 5 minutes. NICE guideline CG132 recommendations support the use of 4-hour action partogram based in the risk reduction of CS. The evidence shows that 4-hour action line reduced the risk of CS compared with 2-hour action partogram. This is in line with NICE guideline CG132 recommendations. However, the final impact of the use of the partogram on maternal and infant outcomes needs to be determinate. Authors suggested that the use of the partogram should be determined at the local level because it is a widespread practice and more high quality evidence is needed.

New evidence is unlikely to change guideline recommendations.

# 132 – 16 No influence on likelihood of CS

# **Recommendations derived from this question**

1.3.3.1 Women should be informed that the following interventions during intrapartum care have not been shown to influence the likelihood of CS, although they may affect other outcomes that are outside the scope of this guideline:

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 19 of 95

- walking in labour
- non-supine position during the second stage of labour
- immersion in water during labour
- · epidural analgesia during labour
- the use of raspberry leaves. [2004]
- 1.3.3.2 Women should be informed that the effects on the likelihood of CS of complementary therapies used during labour (such as acupuncture, aromatherapy, hypnosis, herbal products, nutritional supplements, homeopathic medicines, and Chinese medicines) have not been properly evaluated and further research is needed before such interventions can be recommended. [2004]

# Surveillance decision

This question should not be updated.

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

# **4-year surveillance summary** *Immersion in water in labour*

One SR assessed the impact of immersion in water during labour and water birth on different outcomes related to pregnancy (maternal, neonatal, caregiver) 42. A total of 12 RCTs were included (n=3,243). None of trials assessed the management of third state of labour. Immersion in water during the first stage of labour was associated with a significant reduction of regional anaesthesia and duration of the first stage compared with controls. No significant differences were identified in VD, CS, use of uterotonics, perineal trauma, and maternal infections or in neonatal outcomes (Apgar score less than 7 at 5 minutes, neonatal unit admissions, or neonatal infection). Immersion in water during the second stage was

associated with an increase of satisfaction with the birth experience compared with no immersion. Authors concluded that the immersion in water during the first stage of labour might reduce the anaesthesia use, but the evidence available is limited and low quality. They did not identify evidence about maternal or neonatal adverse events and highlighted a need for more research in the area.

#### **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

### Impact statement

New evidence found is consistent with NICE guideline CG132 recommendations.

New evidence is unlikely to change guideline recommendations.

# 132 – 17 'Failure to progress' in labour and CS

# **Recommendations derived from this question**

- 1.3.4.1 The following aspects of intrapartum care have not been shown to influence the likelihood of CS for 'failure to progress' and should not be offered for this reason, although they may affect other outcomes which are outside the scope of this guideline:
  - active management of labour

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 20 of 95

early amniotomy. [2004]

# Surveillance decision

This question should not be updated.

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

### 4-year surveillance summary

One Cochrane review assessed if the active management of labour was related with a reduction of CS in women with normal pregnancies <sup>43</sup>. They included a total of seven RCTs (n=5390). Active management of labour was not related with a reduction of CS rates. In further analyses, authors excluded one study with a large loss to follow-up and the reduction of CS rates reached the statistical significance (relative risk [RR] 0.77; 95% CI 0.63 to 0.94). Authors concluded that the quality of the studies included was varied and it is possible that some interventions included in the active management package might be more effective than others. There is a need for more research in this area.

A Cochrane review evaluated the effect of early amniotomy and early oxytocin augmentation on CS rates and other maternal and neonatal outcomes when they were used to treat (or prevent) prolonged VD <sup>44</sup>. A total of 14 studies were included (n=8033).

When early amniotomy and oxytocin was used to treat prolonged VD, it was not associated with a reduction of CS rates. When these interventions were used to prevent it, early augmentation was associated with a small reduction of CS rates compared with standard care.

One Cochrane review compared the effect of operative delivery in theatre with CS in the second stage for failure to progress <sup>45</sup>. They did not identify studies that meet the inclusion criteria.

# **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

# Impact statement

New evidence was considered unlikely to affect current recommendations.

New evidence is unlikely to change guideline recommendations.

# 132 – 18 Eating during labour

# **Recommendations derived from this question**

- 1.3.5.1 Women should be informed that eating a low-residue diet during labour (toast, crackers, low-fat cheese) results in larger gastric volumes, but the effect on the risk of aspiration if anaesthesia is required is uncertain. [2004]
- 1.3.5.2 Women should be informed that having isotonic drinks during labour prevents ketosis without a concomitant increase in gastric volume. [2004]

# Surveillance decision

This question should not be updated.

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 21 of 95

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

# 4-year surveillance summary

A Cochrane review assessed the impact of eating during labour on different maternal and neonatal outcomes <sup>46</sup>. The review included RCTs and quasi-RCTs comparing a restriction in solid and liquids with no restriction during labour.

A total of 5 studies were included (n=3,310) all of them in women with low risk of general anaesthesia. A restriction in solids and liquids during labour was not associated with increased risk of CS, operative VD, and Apgar score less than seven at five minutes. Only one study included (with a small sample size) identified an increased risk of CS associated with the consumption of carbohydrate drinks during labour. Authors concluded that there is no evidence to support the restriction of solid and liquids during the labour in women with low-risk pregnancies.

# Topic expert feedback

No topic expert feedback was relevant to this evidence.

# Impact statement

The guideline reported than in UK more than 95% maternity hospital have a policy of restricted intake during labour. New evidence is against this practice given that an unrestricted diet does not seem to have a harmful effect on maternal or neonatal outcomes. NICE guideline CG132 does not have a specific recommendation about diet restriction during labour.

New evidence is unlikely to change guideline recommendations.

# **Procedural aspects of CS**

# 132 – 19 Timing of planned CS

# **Recommendations derived from this question**

1.4.1.1 The risk of respiratory morbidity is increased in babies born by CS before labour, but this risk decreases significantly after 39 weeks. Therefore planned CS should not routinely be carried out before 39 weeks. [B] [2004]

# Surveillance decision

This question should not be updated.

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

# 4-year surveillance summary

A RCT compared the impact of CS before 39+3 days with 38 week + 3 day on rates of neonatal intensive care unit (NICU) admission rates,

neonatal oxygen treatment more than one day, and maternal bleeding more than 500 ml<sup>47</sup>. Women included have singleton uncomplicated pregnancies (n=1,273). The authors did not identify statistical differences in any of the outcomes included.

# **Topic expert feedback**

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 22 of 95

One of the topic experts highlighted that:

'An implication of work in this area [impact on the infant after delivery by CS] might be that all current elective CS would best be performed after the onset of labour'

# Impact statement

We identified one randomised open label controlled trial that compared planned CS at 39 weeks with planned CS at 38 in uncomplicated singleton pregnancies. The authors reported no significant differences between the two groups in NICU admission rates, use of neonatal oxygen treatment or maternal bleeding. They did not clarify the reason of NICU admission (for example respiratory syndrome or transient tachypnoea of the new born) and report a subrogate outcome of respiratory morbidity (oxygen treatment more than one day). NICE guideline CG132 recommends carrying out the CS after 39 given the increased risk of respiratory morbidity if it is done before. It is considered that the new study identified provides limited evidence and do not affect the current recommendations.

New evidence is unlikely to change guideline recommendations.

# 132 – 20 Classification of urgency

# **Recommendations derived from this question**

- 1.4.2.1 The urgency of CS should be documented using the following standardised scheme in order to aid clear communication between healthcare professionals about the urgency of a CS:
- 1. immediate threat to the life of the woman or fetus
- 2. maternal or fetal compromise which is not immediately life-threatening
- 3. no maternal or fetal compromise but needs early delivery
- 4. delivery timed to suit woman or staff. [2004]

# Surveillance decision

No new information was identified at any surveillance review.

This question should not be updated.

# 132 – 21 What is the appropriate decision-to-delivery interval (DDI) for unplanned caesarean section?

# **Recommendations derived from this question**

- 1.4.3.1 Perform category 1 and 2 CS\* as quickly as possible after making the decision, particularly for category 1. [new 2011]
- 1.4.3.2 Perform category 2 CS\* in most situations within 75 minutes of making the decision. [new 2011]

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 23 of 95

- 1.4.3.3 Take into account the condition of the woman and the unborn baby when making decisions about rapid delivery. Remember that rapid delivery may be harmful in certain circumstances. [new 2011]
- 1.4.3.4 Use the following decision-to-delivery intervals to measure the overall performance of an obstetric unit:
  - 30 minutes for category 1 CS\*
  - both 30 and 75 minutes for category 2 CS.
- Use these as audit standards only and not to judge multidisciplinary team performance for any individual CS. [new 2011]
- \*Category 1 CS is when there is immediate threat to the life of the woman or fetus, and category 2 CS is when there is maternal or fetal compromise which is not immediately life-threatening

# Surveillance decision

This question should not be updated.

# 2-year surveillance (2014) and Evidence Update (2013)

A prospective observational cohort study evaluated the target decision-to-delivery intervals (DDI) for unplanned CS <sup>48</sup>. The primary objective was to assess the impact of DDI on neonatal condition in women undergoing CS for unplanned indications (59 category 1 and 532 category 2).

Category 1 deliveries were achieved within a significantly shorter DDI than intrapartum category 2 deliveries, and 68% were achieved within 30 minutes of decision. For category 2 CS, delivery was achieved within 75 minutes in 66% and 180 minutes in 93%. Category 2 deliveries were more likely to be within the 75 minute target if the primary indication was fetal distress during labour.

The DDI for babies born with acidosis was significantly shorter than for babies born without acidosis. For category 1, deliveries within the target time did not reduce the odds of acidosis. The DDI for babies born with asphyxia was not significantly different compared with the babies born without asphyxia.

Six babies died none related to the DDI. Five of the surviving neonates had neurological impairment, 3 had conditions thought to be related to perinatal ischaemia and were category 2 deliveries within target. The authors noted a selection bias: clinicians act more quickly in cases of greater urgency. They also noted that the allocation to CS categories has considerable heterogeneity and they suggest that consensus is needed.

The authors concluded that the 30 minute target for category 1 deliveries is appropriate, but suggested splitting category 2 deliveries into a 75 minute target for concerns about fetal health or placental bleeding, and a 180 minute target for other category 2 indications. This evidence is broadly supportive of NICE guideline CG132 and so it was considered unlikely to have an impact on the guidance.

# Rapid review (2015)

NICE conducted a rapid surveillance review of this question in 2015. Two SRs and three primary studies were identified considering the DDI for category 1 CS. One of the primary studies was already summarised in 2-year surveillance (2014) and Evidence Update (2013) section <sup>48</sup>.

The first SR aimed to determine the optimal DDI for emergency  $CS^{49}$ . The SR also considered the range of DDI and influences on DDI. The SR did not identify any strong evidence improved outcomes being linked to a DDI 30 minutes or less. The SR did identify some evidence, which was confounded by the indications for the emergency CS, that a DDI of 30 - 75 minutes may confer benefit. The SR concluded that emergency CS should be

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 24 of 95

conducted as soon as possible but did not identify evidence to support defining what the DDI should be.

The second SR aimed to consider if there are differences in neonatal outcomes between DDI for category 1 and category 2 deliveries <sup>50</sup>. The SR also considered the proportion of emergency CS accomplished in 30 minutes and the mean time from decision-to-incision or delivery. Thirty-four studies were included (n=22,936). Analysing the 13 studies that included neonatal outcomes, shorter delivery intervals were associated with a higher risk of Apgar score less than 7 and with a lower umbilical artery pH level (less than 7.10). The SR showed that for category 1 only CS, there was no statistically significant difference between DDIs for risk of Apgar score less than 7 or umbilical artery pH level less than 7.10. The SR showed that 79% of the category 1 and 36% of the category 2 deliveries were performed within 30 minutes interval. The SR concluded that for category 1 and category 2, the delivery intervals are not being followed adequately and it was uncertain what clinical effect a DDI of longer than 30 minutes would have.

The first primary study was an observational study that evaluated the impact of DDI on neonatal outcomes (n=336)<sup>51</sup>. The study found the DDI had no significant difference in umbilical cord arterial pH (less than 7.05) and base excess (less than -12) or the Apgar score at 5 min less than 5. The study concluded that there was no impact on neonatal outcomes if the DDI was under 20 minutes.

The second primary study evaluated the effect of shortening the DDI on maternal and neonatal outcomes (n=593) <sup>52</sup>. The study included emergency CS where non reassuring fetal heart rate was the only indication. During the study the DDI was reduced from 21.7 +/- 9.1 minutes to 12.3 +/- 3.8 minutes. The study found that with the shorter DDI there was a significant decrease in the rate of cord pH <7.1, Apgar score at 5 min less than 7, worse composite neonatal outcome. The study reported that worse neonatal outcome was dependent on time period (longer DDI) and on gestational age at delivery. For maternal outcomes there was no difference in composite maternal outcome. The study concluded that reducing the DDI improved early neonatal outcomes without changing maternal complications.

# 4-year surveillance summary

No relevant evidence identified.

# Topic expert feedback

Rapid Review (2015)

In the Rapid Review, topic expert highlighted that current practice is to carry out a category 1 CS as quickly as possible and within 30 minutes, and the importance of taking into account maternal risk when carrying out a category 1 CS and balancing this with fetal risk. They also highlighted that recommendation 1.4.3.4 was being interpreted as audit criteria and not as the DDI that should be used for any particular individual.

### 4-year surveillance

No topic expert feedback was relevant to this evidence.

### Impact statement

It is considered that the evidence identified in the Evidence Update (2013), 2-year surveillance (2014), and Rapid Review (2015) as well as clinical feedback supports the current guideline recommendations. No new evidence was identified in this 4-year surveillance review.

New evidence is unlikely to change guideline recommendations.

# 132 – 22 Preoperative testing and preparation for CS

### **Recommendations derived from this question**

- 1.4.4.1 Pregnant women should be offered a haemoglobin assessment before CS to identify those who have anaemia. Although blood loss of more than 1000 ml is infrequent after CS (it occurs in 4–8% of CS) it is a potentially serious complication. [2004]
- 1.4.4.2 Pregnant women having CS for antepartum haemorrhage, abruption, uterine rupture and placenta praevia are at increased risk of blood loss of more than 1000 ml and should have the CS carried out at a maternity unit with on-site blood transfusion services. [2004]
- 1.4.4.3 Pregnant women who are healthy and who have otherwise uncomplicated pregnancies should not routinely be offered the following tests before CS:
  - grouping and saving of serum
  - cross-matching of blood
  - a clotting screen
  - preoperative ultrasound for localisation of the placenta, because this does not improve CS morbidity outcomes (such as blood loss of more than 1000 ml, injury of the infant, and injury to the cord or to other adjacent structures). [2004]
- 1.4.4.4 Women having CS with regional anaesthesia require an indwelling urinary catheter to prevent over-distension of the bladder because the anaesthetic block interferes with normal bladder function. [2004

# Surveillance decision

This question should not be updated.

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

# 4-year surveillance summary

Indwelling bladder catheterisation

One Cochrane review assessed the use of indwelling bladder catheterisation in CS <sup>53</sup>. They included a total of 17 RCTs (n=1,065). Compare with no catheter, indwelling bladder catheter was associated with reduction of the risk of bladder distention at the end of the surgery, retention of urine and need for catheterisation. It was associated with an increase of the time to first voiding, pain and discomfort (linked to the catheter insertion), time to ambulation, and a longer stay in the hospital. They did not find differences in the risk of urinary tract infection between the interventions. Authors highlighted that the main outcome of the SR (bladder injury during

operation and UTI) were not reported or not adequately reported in most of the studies. They also highlighted that most of the findings were heterogeneous, came from studies of moderate quality and need to be interpreted with caution. The authors concluded that there is limited evidence to assess the impact of indwelling bladder catheter on important outcomes in women undergoing to CS.

One other RCT was identified in our searches but it was included in the dates of searches of the Cochrane review described previously <sup>54</sup>.

#### **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

# Impact statement

The evidence found is in the line with the guideline recommendations.

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 26 of 95

# 132 – 23 Anaesthesia for CS

# **Recommendations derived from this question**

- 1.4.5.1 Pregnant women having a CS should be given information on different types of post-CS analgesia so that analgesia best suited to their needs can be offered (see recommendation 1.6.3.1). [2004]
- 1.4.5.2 Women who are having a CS should be offered regional anaesthesia because it is safer and results in less maternal and neonatal morbidity than general anaesthesia. This includes women who have a diagnosis of placenta praevia. [2004]
- 1.4.5.3 Women who are having induction of regional anaesthesia for CS should be cared for in theatre because this does not increase women's anxiety. [2004, amended 2011]
- 1.4.5.4 Women who are having a CS under regional anaesthesia should be offered intravenous ephedrine or phenylephrine, and volume pre-loading with crystalloid or colloid to reduce the risk of hypotension occurring during CS. [2004]
- 1.4.5.5 Each maternity unit should have a drill for failed intubation during obstetric anaesthesia. [2004]
- 1.4.5.6 To reduce the risk of aspiration pneumonitis women should be offered antacids and drugs (such as H2 receptor antagonists or proton pump inhibitors) to reduce gastric volumes and acidity before CS. [2004]
- 1.4.5.7 Women having a CS should be offered antiemetics (either pharmacological or acupressure) to reduce nausea and vomiting during CS. [2004]
- 1.4.5.8 General anaesthesia for unplanned CS should include preoxygenation, cricoid pressure and rapid sequence induction to reduce the risk of aspiration. [2004, amended 2011]
- 1.4.5.9 Intravenous ephedrine or phenylephrine should be used in the management of hypotension during CS. [2004]
- 1.4.5.10 The operating table for CS should have a lateral tilt of 15°, because this reduces maternal hypotension. [2004]

# **Surveillance decision**

This question should not be updated.

One amendment is proposed to recommendation 1.4.5.4:

• A footnote is to be added with reference to the HES products drug safety update.

One amendment is proposed to recommendation 1.4.5.6:

 A footnote is to be added explaining that proton pump inhibitors are not licensed for this indication.

# General compared with regional anaesthesia for CS

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

#### 4-year surveillance summary

We identified 12 studies relevant to this area: one update of a Cochrane review published in 2006<sup>55</sup>, one SR <sup>56</sup> and ten RCTs <sup>57-66</sup>.

Some studies compared general anaesthesia with regional anaesthesia <sup>55-57,64-66</sup>. Others compared general anaesthesia with spinal anaesthesia <sup>58-61,63</sup>.

The Cochrane review included a total of 29 RCTs (n=1,793) and guasi-RCTs published until 2012 comparing regional anaesthesia with general anaesthesia in CS for any indication <sup>55</sup>. The authors found that women who received regional anaesthesia (epidural or spinal anaesthesia) had less blood loss compared with general anaesthesia, lower differences between pre and postoperative haematocrit levels but were more likely to be satisfied and they will use the same technique in following pregnancies if needed. There were no differences in other neonatal outcomes (Apgar of six or less, and four or less at 5 minutes; and need of resuscitation with oxygen). Authors highlighted that main outcomes as for example maternal death, post-delivery wound infection, other infections (endometritis or urinary tract infection) or neonatal death were not reported in the studies included. They concluded that there is no evidence that one technique is superior to the other but more research is needed to assess the impact of general anaesthesia and regional anaesthesia on other important maternal and neonatal outcomes.

One other SR found similar findings when assessed the blood loss outcome <sup>56</sup>. General anaesthesia was associated with higher blood loss compared with regional anaesthesia but the need of transfusion was similar between the two interventions. So, the authors questioned the clinical relevance of these findings.

Nine RCTs assessed general anaesthesia compared with regional (spinal and epidural)

anaesthesia in women who underwent to planned CS. They included an average 180 women (range 47 to 418) and assessed the following outcomes:

Neonatal outcomes

- Oxygen and acid-base status <sup>58,66</sup>. One study identified found that spinal anaesthesia was associated with higher pH levels in umbilical artery blood <sup>58</sup>. The other study identified the pH levels in umbilical artery blood were better with general anaesthesia compared with regional anaesthesia <sup>66</sup>.
- Total antioxidant status, total oxidant status, oxidative stress <sup>63</sup>. No differences were identified between general, epidural and spinal anaesthesia except for total oxidant status that was lower in general anaesthesia compared with epidural anaesthesia.
- Apgar scores <sup>58,59,61</sup>. One study did not identify differences between general anaesthesia compared with spinal anaesthesia <sup>59</sup>. The other two studies were in favour of regional anaesthesia <sup>58,61</sup>.
- Neonatal thyroid and liver functions <sup>59</sup>. No differences were identified between general anaesthesia and spinal anaesthesia.
- Neurological and adaptative capacity score <sup>64</sup>. No differences were identified between the general, epidural or spinal anaesthesia.

Maternal outcomes

- Blood loss <sup>65</sup>, haemoglobin and haematocrit differences <sup>61</sup>. Less blood loss and better haematocrit and haemoglobin values were identified with spinal anaesthesia compared with general anaesthesia.
- Shoulder tip pain <sup>57</sup>. More prevalent with general anaesthesia compared with spinal anaesthesia.
- Breastfeeding <sup>60</sup>. Delayed with general anaesthesia compared to epidural and spinal anaesthesia.
- Mean bowel sounds and gas discharge time were greater with general anaesthesia<sup>61</sup>. Urine volume 1h post-surgery and time until the first analgesia requirement was higher with spinal anaesthesia <sup>61</sup>.

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 28 of 95

One RCT compared general anaesthesia with spinal anaesthesia (low doses) in women with pre-eclampsia who underwent emergency CS <sup>62</sup>. They did not identify differences in neonatal umbilical artery blood gases but women who received spinal anaesthesia required more epinephrine than those that received general anaesthesia. The proportion of new-borns with an Apgar superior to 7 was higher in the spinal anaesthesia group. Authors concluded that spinal anaesthesia is a safe option in women with pre-eclampsia who need an emergency CS.

### **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

# Impact statement

One Cochrane review did not identify differences between general anaesthesia and regional anaesthesia but authors highlighted that more research is needed to assess the impact of these techniques in other important maternal and neonatal outcomes. RCTs published after the Cochrane review showed conflicting results regarding the impact of these interventions on some of the neonatal outcomes and maternal outcomes assessed. Some of the outcomes were not considered when NICE guideline CG132 recommendations were made (for example outcomes related to oxidative stress, neonatal thyroid and liver function, maternal shoulder tip pain, breastfeeding or recovery of maternal gastrointestinal function). But considering other outcomes, blood loss seems to be lower and haematocrit and haemoglobin values seems to higher with regionals techniques compared with general anaesthesia. Findings on Apgar scores and delay in breastfeeding seem to favour regional anaesthesia over general anaesthesia. It is considered that new evidence is unlikely to impact on NICE guideline CG132 recommendations.

New evidence is unlikely to change guideline recommendations.

# Procedures to avoid hypotension

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

#### 4-year surveillance summary

Intravenous ephedrine or phenylephrine

A total of 13 studies were identified (1 SR and 12 RCTs).

A SR assessed the ephedrine and phenylephrine as a prophylactic treatment of maternal hypotension due to spinal anaesthesia in CS <sup>67</sup>. A total of 15 studies were included (n=742). Authors concluded that both interventions were effective as preventive treatments of maternal hypotension induced by spinal anaesthesia.

Seven RCTs compared phenylephrine with ephedrine as prophylactic treatment of the maternal hypotension inducted by CS <sup>68-74</sup>.

Most of the studies assessed maternal hemodynamic parameters (for example mean blood pressure, systolic blood pressure, heart rate, cardiac output, cardiac index, or systemic vascular resistance) and neonatal outcomes (for example Apgar score, umbilical or cord blood pH, heart rate). They included between 24 and 200 women undergoing to planned CS. Only one study compared phenylephrine, ephedrine and placebo <sup>74</sup>, and another one compared phenylephrine, ephedrine and metaraminol <sup>71</sup>.

In summary, four RCTs reported that phenylephrine was associated with better maternal hemodynamic outcomes compared with ephedrine <sup>68,69,72,74</sup> or placebo <sup>74</sup>. The other three RCTs did not identify differences in these outcomes between the interventions assessed<sup>70,73,74</sup>.

Two studies reported less incidence of nausea or vomiting with phenylephrine compared with ephedrine <sup>68,74</sup>.

Regarding neonatal outcomes, two studies reported that phenylephrine reduced neonatal acidosis compared with ephedrine <sup>68</sup> and placebo <sup>74</sup>. The other studies did not identify

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 29 of 95

differences in the umbilical cord blood pH <sup>70,71</sup>, Apgar scores <sup>68,70,74</sup> or fetal heart rate <sup>73</sup> between the interventions assessed.

Metaraminol seems to be equally effective than phenylephrine or ephedrine in the prevention of maternal hypotension induced by spinal anaesthesia but produces more reactive hypertension compared with other groups <sup>71</sup>.

We identified two RCTs that assessed the optimal administration of phenylephrine <sup>75,76</sup>.

The first study compared an intermittent bolus administration of phenylephrine with a fixed-rate infusion. The authors did not identify differences between the groups <sup>75</sup>.

The second study compared a phenylephrine infusion associated with rescue boluses with rescue boluses alone. An infusion phenylephrine associated with rescue bolus seems to improve hemodynamic maternal outcomes but no differences were identified in neonatal outcomes between the groups <sup>76</sup>.

We identified one study that compared ephedrine with 15 degree left lateral tilt in pregnant women with a positive supine stress test undergoing to planned CS <sup>77</sup>. No differences were identified in maternal hemodynamic outcomes or neonatal outcomes between the groups compared.

A study compared norepinephrine (computercontrolled infusion) with phenylephrine <sup>78</sup> (n=104). They found that both interventions were similar in prevent maternal hypotension but maternal heart rate and cardiac output were greater norepinephrine with less episodes of bradycardia. Authors concluded that more research is needed to determine safety and efficacy of norepinephrine in obstetric population.

The last study assessed the addition of glycopyrrolate previous to phenylephrine induction to prevent the decrease of cardiac output and bradycardia events due to phenylephrine <sup>79</sup> (n-104). Glycopyrrolate improved some hemodynamic maternal outcomes (heart rate and cardiac output) but produced more hypertension and less control of blood pressure.

We identified two SRs 80,81 and nine RCTs 82-90.

One SR published in 2015 assessed the impact of colloids compared with crystalloids on the prevention of hypotension caused by spinal anaesthesia in planned CS<sup>80</sup>. They included a total 11 RCTs (n=990) and found that the incidence of hypotension was lower with the use of colloids compared with crystalloids. No differences were identified in the incidence of nausea and vomiting between the interventions compared. The other SR identified included a total of ten RCTs (n=853) and reported similar results<sup>81</sup>.

Regarding the RCTs, the studies were published between 2012 and 2016. They included between 55 and 167 women undergoing to CS. They assessed the incidence of hypotension with colloids (mainly Hydroxyethylstarch [HES]) compared with Ringer's lactate (or HES and Ringer's lactate)<sup>82,87-89</sup>, saline solution <sup>86</sup> or ephedrine <sup>90</sup>. They also assessed different infusion rates of gelofusine <sup>83</sup> and the preload or co-load effect of crystalloids <sup>85</sup> or colloids <sup>84</sup> on the incidence of hypotension.

In summary, RCTs reported that colloids alone or in combination with crystalloids seemed to be superior to crystalloids alone for the prevention of hypotension induced by spinal anaesthesia<sup>82,86-89</sup>.

No differences in hemodynamic parameters were identified between colloids and ephedrine <sup>90</sup>.

The time of administration of colloids (preloading or coloading) have not impact on prevention of hypotension<sup>77</sup>. In the case of crystalloids, coload seems to have better results than preloading on the incidence of hypotension during spinal anaesthesia<sup>84,85</sup>.

In December 2014, the Medicines and Healthcare products Regulatory Agency (MHRA) released a drug safety update related to HES products. They warned an increased risk of kidney dysfunction and mortality with HES products compared with crystalloids (<u>https://www.gov.uk/drug-safety-</u> <u>update/hydroxyethyl-starch-intravenous-</u> <u>infusions</u>). They advised that HES products should be used only in cases of acute blood

Fluids

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 30 of 95

loss when crystalloids were not sufficient to reestablish the blood volume. They also described contraindications for their use and other information related to the administration and monitoring of people receiving HES treatment.

# Operating table position

One Cochrane review assessed the effect of the mother position during CS on different maternal outcomes (risk of air embolism, hypotensive episodes, and changes in mean systolic and diastolic blood pressure, pulse rate maternal blood pH) and neonatal outcomes (Apgar score and cord blood pH) <sup>91</sup>.

The operating table positions assessed were: head up, horizontal, left lateral tilt (full and 15degree tilt), right lateral tilt, right lumbar pelvic wedge, right pelvic wedge, head down tilt, and use of manual displacers. A total of 11 RCTs were included.

Left lateral tilt position was associated with a reduction of hypotensive episodes compared with right lateral tilt position. Manual displacers were associated with a decreased fall in mean systolic blood compared with left lateral tilt position. No differences were identified in neonatal outcomes between the interventions assessed. Authors highlighted that the evidence available is limited to support any final recommendation.

# Other interventions

We identified two publications of one RCT that compared combined spinal-epidural anaesthesia with spinal anaesthesia to reduce spinal induced hypotension during CS (n=60) <sup>92,93</sup>. Spinal-epidural anaesthesia was associated with less maternal hypotension, less ephedrine supplementation and better neonatal outcomes.

The other RCT assessed the use of a sequential compression mechanical pump to prevent spinal induced hypotension during CS (n=100) <sup>94</sup>. This intervention was associated with a decreased of the incidence of hypotension.

Seven RCTs assessed the effect of 5HT3 receptor antagonists on the spinal induced hypotension in women undergoing to CS <sup>95-101</sup>.

However, 5HT3 receptor antagonists are not licensed for this indication and NICE guideline CG132 advices to avoid their use during pregnancy and breastfeeding.

### **Topic expert feedback**

A topic expert suggested that the recommendation 1.4.5.4 needs to be amended to be clearer to assure that any patient receiving spinal anaesthesia also receive a preventive treatment of hypotension.

# Impact statement

Intravenous ephedrine or phenylephrine

New evidence comparing ephedrine or phenylephrine shows conflicting results mainly in maternal hemodynamic outcomes. Overall most of the studies did not identify differences between these two interventions. This is consistent with current NICE guideline CG132 recommendations.

New evidence was identified regarding the optimal administration of phenylephrine. NICE guideline CG132 does not recommend a specific procedure for optimal administration. The evidence found is limited and considered unlikely to impact the current recommendations.

Few studies compared the use of other interventions (for example norepinephrine or metaraminol) with phenylephrine as prophylactic treatments for maternal hypotension due to CS. But the evidence is limited and considered unlikely to impact the current recommendations.

# Fluids

NICE guideline CG132 recommends that women undergoing to CS under regional should receive volume pre-loading with crystalloid or colloid and intravenous ephedrine or phenylephrine to reduce the risk of hypotension occurring during CS.

New evidence is in favour the use of colloids (alone or in combination with crystalloids) over crystalloids. If crystalloids are used, coloading infusion seems to be superior to preloading in the reduction of hypotension in CS. NICE guideline CG132 recommends the use of crystalloids or colloids. Although this new evidence is inconsistent with the guideline

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 31 of 95

recommendation, the studies have major limitations.

Most of the RCTs identified in this area had small sample sizes and evaluated HES products. A drug safety update released in 2014 by MHRA warned about the higher risk of kidney dysfunction and mortality with HES treatment mainly in people with certain conditions (critically ill people, sepsis, burns, among others). They advised to use HES products only in cases of acute blood loss when crystalloids were not sufficient to reestablish the blood volume. A footnote is to be added with reference to the HES products drug safety update.

New evidence was found about the use 15 degree left lateral tilt during CS to reduce maternal hypotension, which is consistent with current recommendations. Left lateral tilt and manual displacers seem to have a benefit in the reduction of hypotensive episodes compared with other positions. Manual displacers seem to be better than left lateral tilt but the evidence found is limited to arrive to a final conclusion. It is considered unlikely that the new evidence found could have an impact on current recommendations.

New evidence is unlikely to change guideline recommendations

Operating table position

# Procedures to manage hypotension

2-year surveillance (2014) and Evidence Update (2013) No relevant evidence identified.

### 4-year surveillance summary

We identified one RCT (n=200) that compared phenylephrine with ephedrine for the treatment of hypotension due to spinal anaesthesia for CS <sup>102</sup>. Both phenylephrine and ephedrine were effective in the management of hypotension. Results in neonatal outcomes were comparable between these two interventions evaluated.

### **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

# Impact statement

New evidence is consistent with NICE guideline CG132 recommendation.

New evidence is unlikely to change guideline recommendations

# Use of antacids before CS

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

#### 4-year surveillance summary

One Cochrane review and two publications of one RCT were identified <sup>103-105</sup>.

The Cochrane review assessed the impact of different interventions on the risk of aspiration pneumonitis in women with low risk pregnancies undergoing to CS under general anaesthesia <sup>105</sup>. Authors included a total of 32 RCTs and concluded that a combination of antacids and H2 antagonists are associated with a higher reduction of the risk of intragastric 4-year surveillance 2017 summary of new evidence - Caesarean section (2011) NICE guideline CG132

pH less than 2.5 compared with no intervention or antacids alone but the quality of the evidence was poor.

The RCT compared tramadol with ranitidine in the reduction of the pH gastric secretion during CS with general anaesthesia <sup>103,104</sup>. Tramadol was associated with higher volume, lower intragastric pH, lower Apgar score and less requirement of opioid treatment compared with ranitidine. Tramadol is not licensed for this indication in the UK.

# **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

### Impact statement

32 of 95

NICE guideline CG132 recommends that antacids and drugs (H2 receptor antagonists or proton pump inhibitors) should be offered to reduce gastric volumes and acidity before CS. New evidence was identified to support the use of antacids and H2 receptor antagonists. No new evidence was identified regarding the combination of antacids and proton pump inhibitors. It is considered that the new evidence identified is consistent with NICE guideline CG132 recommendation.

New evidence is unlikely to change guideline recommendations

# Use of antiemetics

2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

# 4-year surveillance summary

One Cochrane review assessed nausea and vomiting prophylactic pharmacological and no pharmacological treatments for women undergoing to regional anaesthesia for CS <sup>106</sup>. They included a total 52 studies (n=5046) evaluating a number of interventions (5HT3 receptor antagonist, dopamine receptors antagonists, corticosteroids<sup>1</sup>, acupressure, antihistamines or anticholinergics). Dopamine antagonists, 5HT3 antagonists, and sedatives were highlighted as effective in at least three of the primary outcomes assessed in the review (nausea and vomiting both during and after CS). The authors did not identify that one intervention was superior to another and concluded that different interventions could be effective in the prevention of nausea and vomiting in women undergoing to regional anaesthesia for CS.

We identified a further 13 RCTs related to antiemetic prophylactic treatment. The studies included between 66 and 300 women undergoing to CS.

One RCT assessed acupressure, metoclopramide and placebo and concluded that acupressure is as effective as metoclopramide in the reduction of nausea and vomiting after CS <sup>107</sup>.

Three other RCTs assessed the effect of dexamethasone on prevention nausea and vomiting <sup>108-110</sup> (in two studies women went to CS under spinal anaesthesia with morphine) <sup>109,110</sup>. One of the studies concluded that dexamethasone is ineffective and increase the risk of post-dural headache <sup>108</sup>. The other two concluded that dexamethasone reduce the incidence of nausea and vomiting <sup>109,110</sup>.

Eight RCTs evaluated 5HT3 antagonists (ondansetron, granisetron). These studies compared 5HT3 antagonists with placebo <sup>111</sup> or other antiemetic drugs alone or in combination (midazolam<sup>2</sup>, dexamethasone, fentanyl intrathecal<sup>3</sup> or glycopyrrolate<sup>4</sup>)<sup>112-118</sup>. NICE quideline CG132 advices to avoid the use of 5HT3 receptor antagonists during pregnancy and breastfeeding therefore they are not discussed further.

A final study compared a ginger preparation with placebo and no differences were identified between the groups <sup>119</sup>.

# **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

# Impact statement

New evidence is consistent with NICE guideline CG132 recommendations.

New evidence is unlikely to change guideline recommendations

#### NQ - 01 Procedures to prevent and manage hypothermia and shivering

# **Recommendations derived from this question**

There are currently no recommendations in the guideline in relation to this guestion.

<sup>2</sup> Off-label indication.

<sup>3</sup> Off-label route of administration and indication. <sup>4</sup> Off-label indication

4-year surveillance 2017 summary of new evidence - Caesarean section (2011) NICE guideline CG132

34 of 95

<sup>&</sup>lt;sup>1</sup> Off-label indication.

# Surveillance decision

This question should be added.

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence was identified.

# **4-year surveillance summary** Forced air warming or warming fluid

One SR assessed the effect of different warming activities on maternal and neonatal outcomes <sup>120</sup>. The interventions assessed were forced air warming or warming fluid within 30 minutes of regional anaesthesia. The authors included a total of 13 RCTs (n=789). Active warming interventions were associated with less hypothermia and shivering during CS and a higher umbilical artery pH. Two other RCTs assessed the effect of forced air warming <sup>121</sup> and warming fluid on prevention of intraoperative hypothermia <sup>122</sup> and found similar results.

# Changes in the temperature and density of local anaesthesia agents

One RCT was identified (n=80) <sup>123</sup> compared the effects of the administration of the bupivacaine stored at two different temperatures (23 degrees Celsius or 37 degrees Celsius) during spinal anaesthesia on sensory block and shivering in patients undergoing to CS. A higher temperature was associated with a lower incidence of shivering and with a more rapid block (sensory and motor).

# Opioids

A RCT (n=80) compared intrathecal fentanyl<sup>1</sup> 25 micrograms combined with hyperbaric bupivacaine 0.5% 2.5ml with hyperbaric bupivacaine combined with normal saline as prophylaxis of shivering in women receiving spinal anaesthesia <sup>124</sup>. Fentanyl was associated with a lower incidence (during and after CS) and lower severity of shivering.

Two RCTs compared the use of meperidine (pethidine)<sup>2</sup> as prophylactic treatment of shivering during CS under spinal anaesthesia <sup>125,126</sup>. One compared hyperbaric lidocaine 5%

75 mg combined with meperidine (0.2 mg/kg) with hyperbaric lidocaine combined with placebo (n=100)  $^{125}$ . The other compared bupivacaine 0.5% 10 mg combined with meperidine with bupivacaine combined with placebo (n=110)  $^{126}$ . In both studies meperidine was associated with a reduction of the incidence and severity of shivering due to spinal anaesthesia during CS.

Finally a RCT evaluated the addition of intravenous 5HT3 antagonist to regional anaesthesia as prophylaxis of shivering in women undergoing to CS <sup>127</sup>. NICE guideline CG132 advices to avoid use of 5HT3 receptor antagonists during pregnancy and breastfeeding therefore this study not discussed further.

# Vasopressors

One RCT assessed the impact of ephedrine given as a treatment of maternal hypotension during CS on maternal temperature and neonatal outcomes (n=110)<sup>128</sup>. The study compared intravenous ephedrine 5 mg in bolus followed by ephedrine infusion with intravenous ephedrine 5 mg in bolus followed by infusion of normal saline in women under spinal anaesthesia with heavy bupivacaine (12.5 mg) plus fentanyl (15 micrograms) for CS. An initial bolus of ephedrine followed by ephedrine infusion was associated with higher maternal temperatures, less incidence of maternal and neonatal hypothermia than ephedrine bolus alone.

The other RCT compared intravenous ephedrine 6 mg with intravenous meperidine 15 mg for prophylaxis of shivering in women under spinal anaesthesia for CS (n=96) <sup>129</sup>. Ephedrine was similar to meperidine to prevent shivering during spinal anaesthesia for CS.

# Other interventions

One RCT compared two different doses of intravenous ketamine<sup>3</sup> (0.25 mg/kg or 0.5 mg/kg) with placebo for prophylaxis of shivering in women undergoing to CS with spinal anaesthesia <sup>130</sup>. Both doses were related with a

<sup>&</sup>lt;sup>1</sup> Off-label route of administration.

<sup>&</sup>lt;sup>2</sup> Off label indication.

<sup>&</sup>lt;sup>3</sup> Off-label indication.

higher temperature and with a reduction of shivering in women having spinal anaesthesia for CS.

One RCT <sup>131</sup> (n=116) and one cluster randomised trial <sup>132</sup> (n=484) assessed the effect of warming mattress on the reduction of hypothermia during CS compared with control <sup>131</sup> or usual care (warmed intravenous and irrigation fluids, warmed blankets, heat retaining caps) <sup>132</sup>. Both studies found that warming mattress reduced the incidence of hypothermia. One of them also observed that warming mattress reduced the mean of haemoglobin change but no differences were identified in the incidence of shivering <sup>131</sup>. In the other one, the effects on maternal temperature were not sustained after CS (post-anaesthesia care unit) <sup>132</sup>.

# **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

# Impact statement

NICE guideline CG132 does not include guidance about prophylaxis and management of hypothermia and shivering in women undergoing to CS. In NICE guideline CG65 Hypothermia: prevention and management in adults having surgery; pregnant women are out of scope. In the previous surveillance review of NICE guideline CG65 they considered that the best place to address this issue is in NICE guideline CG132.

New evidence is likely to impact on the guideline.

# 132 – 24 Surgical techniques for CS

# Methods to prevent HIV transmission in theatre

# **Recommendations derived from this question**

- 1.4.6.1 Healthcare professionals should wear double gloves when performing or assisting at CS on women who have tested positive for HIV, to reduce the risk of HIV infection of healthcare professionals during surgery. [2004]
- 1.4.6.2 General recommendations for safe surgical practice should be followed at CS to reduce the risk of HIV infection of staff. [2004]

# Surveillance decision

No new information was identified at any surveillance review.

This question should not be updated.

# Abdominal wall incision

# **Recommendations derived from this question**

- 1.4.6.3 CS should be performed using a transverse abdominal incision because this is associated with less postoperative pain and an improved cosmetic effect compared with a midline incision. [2004]
- 1.4.6.4 The transverse incision of choice should be the Joel Cohen incision (a straight skin incision, 3 cm above the symphysis pubis; subsequent tissue layers are opened bluntly and, if necessary, extended with scissors and not a knife), because it is associated with shorter operating times and reduced postoperative febrile morbidity. [2004]

## Surveillance decision

This question should not be updated.

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

### 4-year surveillance summary

One Cochrane review evaluated different abdominal wall incisions for CS <sup>133</sup>. The review included four RCTs (n=666) comparing Joel-Cohen incision, Pfannenstiel incision, muscle cutting incisions Mouchel incision (two compared Joel-Cohen with Pfannenstiel incision [n=411]). Joel-Cohen incision was associated with a reduction of the operative time, post-operative pain (painkiller requirement and more time to the first dose), blood loss, post-operative febrile morbidity and hospital stay compared with Pfannenstiel incision. No differences were identified between Maylard muscle cutting incisions and Pfannenstiel incision in maternal outcomes (febrile morbidity, blood transfusion, wound infection, hospital stay and muscle strength at three months of CS). Authors highlighted that there is no evidence about the impact of abdominal wall incisions on long term outcomes.

Two other RCTs were identified <sup>134,135</sup>. One of the RCTs (n=302) compared a modified Joel-

Cohen incision with Pfannenstiel incision for CS and found similar results to the Cochrane review <sup>134</sup>. The other RCT (n=323) compared Misgav-Ladach technique with Pfannenstiel incision and found that Misgav-Ladach technique was associated with a reduction of the operative time, post-operative pain, blood loss, and post-operative complications compare with Pfannenstiel incision <sup>135</sup>.

### **Topic expert feedback**

Comments received via expert feedback:

 Area that need to be reviewed: Collapsible disposable retractors (for example Alexis Oring retractors) to improve safety of the CS in women with obesity or morbidly obesity.

### Impact statement

New evidence is consistent with NICE guideline CG132 recommendations. No evidence was found relating to collapsible disposable retractors.

New evidence is unlikely to change guideline recommendation.

### Instruments for skin incision

### **Recommendations derived from this question**

1.4.6.5 The use of separate surgical knives to incise the skin and the deeper tissues at CS is not recommended because it does not decrease wound infection. [2004]

# Surveillance decision

This question should not be updated.

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

### 4-year surveillance summary

One RCT compared the use of scalpel with diathermy for abdominal incision during CS in women with a previous CS (n=130) <sup>136</sup>. Electrosurgery was associated with a reduction

of the blood loss and operative time but no effects were identified in terms of postoperative pain or wound complications between the groups.

### **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

### Impact statement

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 37 of 95

New evidence is consistent with NICE guideline CG132 recommendation.

New evidence is unlikely to change guideline recommendation.

### Extension of the uterine incision

### **Recommendations derived from this question**

1.4.6.6 When there is a well formed lower uterine segment, blunt rather than sharp extension of the uterine incision should be used because it reduces blood loss, incidence of postpartum haemorrhage and the need for transfusion at CS. [2004]

### Surveillance decision

This question should not be updated.

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

#### 4-year surveillance summary

We identified one Cochrane review that assessed different surgical techniques for uterine incision and closure during CS<sup>137</sup>. The Cochrane review identified five RCTs that compared blunt with sharp dissection (n=2141). Blunt incision was related with a significant reduction of the need for blood transfusion and no differences were identified in the risk of febrile morbidity between the interventions compared. The Cochrane review also reported results of a single trial that compared transverse with cephalad-caudad blunt extension. Transverse extension was associated with less blood loss mean difference 42 mL) but the clinical relevance of the findings were considered uncertain.

The other SR including a total of six RCTs (n=2908) also comparing these two methods of expanding uterine incisions reported similar findings in favour of blunt expansion<sup>138</sup>. Similar results were identified in a RCT that compared these techniques in women undergoing to CS (n=1706) <sup>139</sup>. Blunt incision was associated with a lower incidence of unintended extension and blood loss. The authors did not identify differences in transfusions and need for additional uterotonics.

### **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

### Impact statement

New evidence is consistent with NICE guideline CG132 recommendation.

New evidence is unlikely to change guideline recommendation

# **Fetal laceration**

### **Recommendations derived from this question**

1.4.6.7 Women who are having a CS should be informed that the risk of fetal lacerations is about 2%. [2004]

### Surveillance decision

This question should not be updated.

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 38 of 95

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

### 4-year surveillance summary

No relevant evidence identified.

### **Topic expert feedback**

Comments received via expert feedback:

• 'CG132 recommends that parents should be aware about the 1-2% risk of fetal lacerations. They continue to occur, they are largely preventable with appropriate techniques, and they cause upset to parents and occasionally result in litigation and pay-outs from NHS-LA'.

### Impact statement

Topic experts highlighted that fetal lacerations could be avoided using adequate techniques. We did not identify new evidence.

New evidence is unlikely to change guideline recommendation.

### **Use of forceps**

### **Recommendations derived from this question**

1.4.6.8 Forceps should only be used at CS if there is difficulty delivering the baby's head. The effect on neonatal morbidity of the routine use of forceps at CS remains uncertain. [2004]

### Surveillance decision

No new information was identified at any surveillance review.

This question should not be updated.

### **Cord clamping**

### **Recommendations derived from this question**

This area does not have recommendations.

### Surveillance decision

This question should not be updated.

### 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

### 4-year surveillance summary

One RCT including 24 women undergoing to planned CS were randomised to immediate clamping or umbilical cord milking <sup>140</sup>. Umbilical cord milking was associated with lower placental blood volume and higher haematocrit levels (at 36 to 48 hours) compared with immediated clamping. The authors reported that four babies had an immediated haematocrit level indicative of anaemia (lower than 47%) in the immediate cord clamping group.

#### **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

#### Impact statement

New evidence suggests that umbilical cord milking might have benefit in terms of maternal and neonatal outcomes compared with immediate cord clamping. The evidence

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 39 of 95

supporting these findings is limited. It comes from one single study with a small sample size, and assessed short term and subrogates outcomes. These results were considered unlikely to affect recommendations in NICE guideline CG132 because further research is needed to determine the effect of delayed cord clamping on important maternal and neonatal outcomes as described in the research recommendation number 33 (RR – 33).

New evidence is unlikely to change guideline recommendation.

### **Use of uterotonics**

### **Recommendations derived from this question**

1.4.6.9 Oxytocin 5 IU by slow intravenous injection should be used at CS to encourage contraction of the uterus and to decrease blood loss. [2004]

### **Surveillance decision**

This question should not be updated.

# 2-year surveillance (2014) and Evidence Update (2013)

A double-blind placebo-controlled RCT assessed the effects of adding an oxytocin infusion (over 4 hours) to bolus oxytocin (5 UI) in terms of blood loss at planned CS in healthy women at term (the Elective Caesarean Section Syntocinon [oxytocin] Infusion Trial, n=2069)<sup>141</sup>.

Major obstetric haemorrhage (>1000ml) did not differ significantly between the bolus plus infusion group and the bolus plus placebo group. Stratifying the results by the experience of the obstetricians, in junior doctors the infusion of oxytocin was related to lower rates of major obstetric haemorrhage. Women in the bolus plus infusion group were less likely to need an additional uterotonic agent than those in the bolus plus placebo group.

A limitation stated by the authors was that they could have included a third comparison group that reflected current US clinical practice (use of a placebo bolus with an oxytocin infusion), but this approach would have deviated from hospital protocols. Also, because clinicians intervene if uterine atony occurs, the use of an additional uterotonic agent could have been considered as an important outcome in itself. The study results suggest that the addition of an oxytocin infusion to oxytocin bolus may reduce the need for additional uterotonic agents, but may not affect the frequency of major obstetric haemorrhage. This evidence was considered unlikely to have an impact on NICE guideline CG132.

#### 4-year surveillance summary

We identified SR and RCTs that compared the use of different uterotonics at CS.

#### Oxytocin administration

One RCT compared oxytocin 10UI<sup>8</sup> in bolus with oxytocin 10UI in infusion (during 5 minutes) in planned CS (n=50) <sup>142</sup>. Infusion over 5 minutes seems to produce less haemodynamic chages in the mother without an impact on the other outcomes (blood loss).

A RCT (n=60) assessed the addition of different doses of calcium chloride (200 mg or 400 mg) to oxytocin regime to prevent adverse effects associated with oxytocin administration (hypotension, tachycardia, nausea) in planeed CS <sup>143</sup>. They compared three different interventions: 1) oxytocin 5UI with calcium chloride 200 mg, 2) oxytocin 5UI with calcium chloride 400 mg, and 3) oxytocin 5UI alone. The use of calcium chloride did not reduce the

<sup>&</sup>lt;sup>8</sup> Licensed dose for prevention of uterine atony after CS is 5 UI.

risk of adverse effects associated with oxytocin administration.

A RCT (n=40) assessed the use of phenylephrine as prophylactic treatment of the hypotension due to oxytocin administration <sup>144</sup>. Intravenous phenylephrine 50 micrograms was admistrated previously to oxytocin (3UI)<sup>9</sup> in planned CS. Phelyphrine did not reduce the risk of hypotension or tachycardia compared with placebo.

### Misoprostol compared with placebo

Three RCTs compared misoprostol<sup>10</sup> with placebo <sup>145-147</sup>.

The first RCT evaluated the impact of misoprostol in women undergoing to planned or emergency CS on the risk of intraoperative blood loss,need of additional uterotonic agents, and fall in the haemoglobin levels (n=174)<sup>145</sup>. Misoprostol 400 micrograms sublingual was administrated at the time of cord clamping. Misoprostol was associated with a reduction of the risk of all the outcomes assessed compared with placebo.

The second RCT evaluated a similar dose of misoprostol sublingual compared with placebo. Misoprostol was administrated after intubation in women under general anaesthesia with isoflurane for CS (n=366) <sup>146</sup>. Misoprostol was associated with a reduction of perioperative estimated blood loss, need of additional uterotonic agents, and higher haematocrit levels. More women in the misoprostol group had shivering. No differences were identified in other neonatal outcomes (Apgar score) or maternal outcomes (nausea, vomiting, pyrexia).

Similar findings were reported in the last RCT identified (n=200) <sup>147</sup>. This RCT evaluated misoprostol 400 micrograms administred intrarectalyl during planned CS (before skin incision). Misoprostol was associated with a reduction of blood loss, better heamatocrit levels compared with placebo. No differences in the Apgar scores were identified between the groups compared.

One RCT compared the administration of misoprostol 400 micrograms intrarectal before or after a planned CS (n=348) <sup>148</sup>. Misoprostol administred before CS was associated with a

greater reduction of the blood loss compared with its admistration after CS.

### Misoprostol compared with oxytocin

One SR <sup>149</sup> and three RCTs compared misoprostol with oxytocin <sup>150-152</sup> as prophylatic treatment of postpartum haemorrhage. Two RCTs used an oxytocin regimen not recommended in NICE guideline CG132; therefore they are not discussed further <sup>151,152</sup>.

A meta-analysis (n=646) found that misoprostol was associated with lower estimated blood loss than oxytocine but no differences were identified in terms of haemoglobin levels, additional uterotonic agents or blood transfusion requirements between the two interventions compared <sup>149</sup>. Misoprostol was significantly associated with shivering and pyrexia after CS. This SR did not report in the abstract the number and type of studies included.

One RCT compared misoprostol 400 micrograms intrarectal with oxytocin (oxytocin regimen not described in the abstract) in planned CS (n=100) <sup>150</sup>. No differences were identified in blood loss or fall of haemoglobin levels. Misoprostol was associated with shivering compared with oxytocin but oxytocin was associated with respiratory distress and changes in mean arterial pressure and heart rate.

### Misoprostol plus oxytocin

Four RCTs compared the combination of misoprostol plus oxytocin compared with: 1) misoprostol and oxytocin alone <sup>153</sup>, 2)oxytocin alone <sup>154,155</sup>, or 3) carbetocin <sup>156</sup> for the prevention of postpartum haemorrage after CS. Two of these studies used an oxytocin regimen not recommended in NICE guideline CG132; therefore they are not discussed further <sup>155,156</sup>.

One RCT compared three different regimens (n=150) <sup>153</sup>: 1) 20 UI infusion of oxytocin, 2) misoprostol 400 micrograms sublingual, and 3) misoprostol 200 micrograms plus oxytocin 5UI in bolus after delivery. Misoprostol plus oxytocin was associated a reduction of the blood loss compared with the other two groups without an increase of adverse events.

The other RCT compared misoprostol 400 micrograms sublingual plus intravenous

<sup>10</sup> Off-label indication. No rectal preparation is available in the UK.

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 41 of 95

<sup>&</sup>lt;sup>9</sup> Licensed dose for prevention of uterine atony after CS is 5 UI.

oxytocin 20UI with intravenous oxytocin 20UI alone after cord clamping (n=120) <sup>154</sup>. The combination of misoprostol and oxytocin was associated with lower blood loss and need of additional uterotonic agents but increasing the risk of shivering and pyrexia compared with oxytocin alone.

### Oxytocin compared with carbetocin

We identified a SR that evaluated the use of carbetocin for the prevention of postpartum haemorrhage <sup>157</sup>. The abstract did not report the number of studies included (or sample sizes). No significant differences were found in the postpartum haemorrage, mean estimated blood loss and adverse events between carbetocin and oxytocin. Carbetocin was related with a risk reduction of the need of additional uterotonics compared with oxytocin (relative risk [RR] 0.68, confidence interval 0.55 to 0.84). The SR also compared carbetocin with syntometrine (ergometrine plus oxytocine) but NICE guideline CG132 did not included ergometrine because its use is not common practice in uncomplicated CS.

A RCT compared intravenous oxytocin 5UI with carbetocin 100 microgrammes or placebo in women undergoing to CS under spinal anaesthesia (n=76) <sup>158</sup>. No significant differences were identified in any of the maternal haemodinamic parameters assessed (mean systolic arterial pressure, heart rate, cardiac output) between oxytocin and carbetocin.

One RCT assessed the effect on uterine contraction reached with different dose of carbetocin (80, 90, 100, 110 and 120 microgrammes) in planned CS <sup>159</sup>. Doses between 80 and 120 microgrammes showed a similar effective uterine tone but the authors highlighted a high incidence of hypotension in all the groups compared. The dose licensed in UK is 100 microgrammes.

### Oxytocin compared with other drugs

One RCT compared carboprost<sup>11</sup> (alone or in combination with oxytocin) with oxytocin as a prophylactic treatment of postpartum haemorrhage (n=117) in women with high risk of postpartum haemorrhage (multiple pregnancies, polyhydramnios, placenta praevia, fetal macrosomia) undergoing to CS <sup>160</sup>. Carboprost alone was associated with

lower blood loss and higher incidence of vomiting compared with the other two groups.

### **Topic expert feedback**

Comments received via expert feedback:

 Areas that need to be reviewed: oxytocin compared to misoprostol and carbetocin to reduce the risk and volume of bleeding at CS.

Topic experts highlighted a RCT that compared intravenous carbetocin 100 micrograms (in bolus) with oxytocin 20 IU (6 hours infusion) for the prevention of postpartum haemorrhage (n=1210) <sup>161</sup>. Carbetocin was related with a reduction of blood loss and blood loss exceeding 500 ml compared with oxytocin. It was also related with a reduction of use of uterotonics and fluids. No differences were identified in terms of blood transfusions or severe post CS haemorrhage between the interventions or in other outcomes.

### Impact statement

New evidence was identified about oxytocin and it was considered consistent with NICE guideline CG132 recommendations.

Misoprostol is not licensed for prevention of uterine atony following delivery by CS. New evidence found suggests that misoprostol is an effective prophylactic treatment of postpartum haemorrhage when compared with placebo. A greater reduction of blood loss appears to be related with its administration before CS.

When comparing misoprostol with oxytocin, one SR found differences in the estimated blood loss (in ml) favouring the use of misoprostol over oxytocin but the clinical relevance of these differences remains unclear (weighted mean difference -64.09, 95% CI -119.3 to -8.31). Misoprostol was more associated with shivering compared with oxytocin.

Limited evidence from small RCTs was identified comparing the combination of misoprostol plus oxytocin. This combination was associated with lower blood loss and need of additional uterotonic agents compared with single administration of these drugs but it was also related with an increase of shivering and pyrexia.

Regarding carbetocin, most of the studies did not identify differences between carbetocin and

<sup>&</sup>lt;sup>11</sup> Off-label indication.

oxytocin in important outcomes. A SR reported that carbetocin was associated with a reduction of the use additional of uterotonics compared with oxytocin, but no differences were identified in terms of postpartum haemorrhage, blood loss or adverse events. The need for additional oxytocic was considered as a surrogate outcome in NICE guideline CG132. Two other RCTs were identified. One of them did not identify differences between carbetocin and oxytocin. The other one identified differences in terms of reduction of blood loss, blood loss exceeding 500 ml and reduction of use of uterotonics and fluids. It is not clear if these RCTs were included in the SR. At the time NICE guideline CG132 was published, carbetocin was licensed but not launched in UK. The expected basic NHS price for carbetocin was £12-15 per vial compared with oxytocin cost £1.40 for a 5UI or 10UI vial.

Currently, BNF report a NHS indicative price for carbetocin of £88.20 per five ampoules (£17.60 per ampoule of 100 micrograms) and for oxytocin £4.01-4.67 per five ampoules of 5UI or 10 UI. It is considered that new evidence is consistent with current recommendations.

Carboprost is licensed in UK as a postpartum haemorrhage treatment when other options did not work (ergometrine and oxytocin). Limited evidence from a single trial with a small sample size suggested that carboprost might be better than oxytocin (alone or in combination with carboprost) in the reduction of blood loss. New evidence in this area is considered unlikely to have an impact on current recommendations.

New evidence is unlikely to change guideline recommendation.

### Method of placental removal

### **Recommendations derived from this question**

1.4.6.10 At CS, the placenta should be removed using controlled cord traction and not manual removal as this reduces the risk of endometritis. [2004]

### Surveillance decision

This question should not be updated.

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

### 4-year surveillance summary

One RCT compared two methods of placental removal (manual or spontaneous) in women undergoin to CS throught lower segment transverse incision and general anaesthesia (n=100)<sup>162</sup>. No differences were identified between the two methods of placental removal in terms of blood loss (need of blood transfusion or change in hemoglobine levels) or development of endometritis after CS.

### **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

### Impact statement

New evidence was found but it comes from a single RCT with a small sample size. New evidence was limited and considered unlikely to have an impact on the current recommendation.

New evidence is unlikely to change guideline recommendation.

### Exteriorisation of the uterus

### **Recommendations derived from this question**

1.4.6.11 Intraperitoneal repair of the uterus at CS should be undertaken. Exteriorisation of the uterus is not recommended because it is associated with more pain and does not improve operative outcomes such as haemorrhage and infection. [2004]

### Surveillance decision

This question should not be updated.

# 2-year surveillance (2014) and Evidence Update (2013)

A Turkish prospective randomised trial compared uterine repair performed in situ with extra-abdominal repair following CS in women of at least 36 weeks' gestation<sup>163</sup>. The primary outcome was intraoperative blood loss, measured as the difference in the woman's haemoglobin levels before and after CS.

The difference between preoperative and postoperative haemoglobin levels were similar between groups. Uterine atony was higher in women who had intraperitoneal repair compared with women who had exteriorised repair, but they had less wound infection.

Women in the external uterine repair had higher risk of ovarian vein rupture, compared with intraperitoneal uterine repair group, and needed additional analgesia. Four women with uterine atony in the exteriorised repair group had hysterectomies. No significant differences were seen in bowel, bladder or ureteral injury, and rates of endometritis.

The authors did not discuss possible limitations of their study. However an exteriorised repair of the uterus was associated with more pain, and did not improve rates of haemorrhage or infection. The results were considered consistent with NICE guideline CG132.

### 4-year surveillance summary

One SR assessed the effect of uterine exteriorization on maternal outcomes compared with in situ repair after CS <sup>164</sup>. This SR included 16 RCTs (n=19,439). Uterine exteriorization was associated with a reduction of the fall in haemoglobin levels and blood loss but the clinical relevance of these differences remains uncertain. In situ repair was associated with a reduction of the time of bowel function recovery. No differences were identified in

intraoperative nausea, vomiting, pain or endometritis between the two interventions compared.

Three other RCTs were identifed <sup>165-167</sup>. The SR did not report the dates of searches so it is not clear if these RCTs were included in their analysis.

The first RCT (n=100) found that uterus exteriorization repair was associated with less surgical time but with more moderated pain at seis hours after CS than insitu repair <sup>167</sup>.

Another RCT (n=15,935) (CORONIS Trial) did not identify differences in the composite outcome of death, maternal infectious morbidity, further operative procedures, or blood transfusion between the two procedures <sup>165</sup>.

The last RCT (n=1000) comparing these two techniques of uterine repair found that insitu uterine repair was associated with less surgical time, pain and need for additional analgesia, and a rapid bowel recovery compared with exteriorisation repair <sup>166</sup>.

#### Topic expert feedback

No topic expert feedback was relevant to this evidence.

#### Impact statement

NICE guideline CG132 recommends intraperitoneal repair over exteriorisation given that exteriorisation is associated with more pain and do not improve other outcomes. New evidence from a SR and a large RCT did not identify differences in pain between the interventions. Two other RCTs found that exteriorisation repair was associated with more pain and need for additional analgesia than in situ repair. Differences in other outcomes also showed conflicting results. NICE guideline CG132 summarised the results of a survey of

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 44 of 95

surgical practice in the UK. They reported that in UK most of the surgeons repair the uterus intraperitoneally and rarely do an exterior repair.

New evidence is unlikely to change guideline recommendation.

### **Closure of the uterus**

### **Recommendations derived from this question**

1.4.6.12 The effectiveness and safety of single layer closure of the uterine incision is uncertain. Except within a research context, the uterine incision should be sutured with two layers. [2004]

### Surveillance decision

This question should not be updated.

# 2-year surveillance (2014) and Evidence Update (2013)

A meta-analysis evaluated the association between use of single-layer or 2-layer closure of the uterus after CS and risk of uterine rupture during a trial of labour in a subsequent pregnancy <sup>168</sup>. The primary outcome was uterine rupture.

Nine studies were included (1 RCT, 6 cohort studies, and 2 case-control studies) with all studies containing data on uterine rupture during a trial of labour (n=5810).

The difference in risk of uterine rupture between previous single-layer closure of the uterus was not significantly higher compared with double-layer closure. Sensitivity analysis did not find heterogeneity or significant differences due to study design, trial size, or whether the trial of labour was before or after 2002. However, a locked single-layer closure was associated with an increased risk of uterine rupture compared with a double-layer closure. There was significant heterogeneity across studies, which was mainly attributable to the 2 types of single-layer closure (locked vs unlocked).

Some of the limitations were: most of the included studies were retrospective; possible variation in the closure techniques within hospitals, information on the suture type was usually not available, and no study compared locked with unlocked single-layer sutures.

The CAESAR RCT reported by the CAESAR study collaborative group (2010) assessed 3

pairs of alternative CS techniques in women having a first CS: single-layer closure compared with double-layer closure of the uterine incision; closure compared with nonclosure of the pelvic peritoneum; and liberal compared with restricted use of a subrectus sheath drain <sup>169</sup>. The primary outcome was maternal infectious morbidity, during the postnatal hospital stay, endometritis, or wound infection treated with antibiotics.

The risk of maternal infectious morbidity was similar between groups. Twelve serious adverse events were reported, spread equally among arms.

Subgroup analysis showed an association between closure of the peritoneum and use of a subrectus sheath drain. Women allocated to liberal use of a subrectus sheath drain had a higher risk of maternal infectious morbidity associated with non-closure of the pelvic peritoneum compared with closure. Women allocated to restricted use of a subrectus sheath drain had a lower risk of maternal infectious mortality with non-closure of the peritoneum compared with closure of the peritoneum compared with closure of the peritoneum.

A limitation of the study stated by the authors was lower than anticipated recruitment and the study had to be closed prematurely. However, they stated that the power for detecting the main effects of the trial should not have been affected, but the power to detect interactions was low. The study by the Caesar collaborative group (2010) suggests that levels of postoperative maternal infection did not seem to be affected by the choice of single compared with double layers of sutures, closure or non-closure of pelvic peritoneum, or use of a subrectus drain. These findings were considered unlikely to affect recommendations in NICE guideline CG132 because further research into the safety and effectiveness of these surgical techniques is needed. The meta-analysis by Roberge et al. (2011) suggested that locked, but not unlocked single-layer closures may be associated with a higher risk of uterine rupture in a subsequent pregnancy compared with double-layer closure, which was consistent with NICE guideline CG132. This study also suggested that unlocked single-layer closure may have a rate of uterine rupture in future pregnancy similar to that of double-layer closure, but further research is needed to confirm these findings.

#### 4-year surveillance summary

We identified one Cochrane review that assessed different surgical techniques for uterine incision and closure during CS <sup>137</sup>. A meta-analisis of 14 studies (n=13,890) that compared single layer with dobule layer closure of the uterus did not identify statistical differences in terms of febrile morbidity and risk of blood transfusion between the interventions assessed. A significant difference was identified in the reduction in mean blood loss in favour of single layer closure but the results were heterogeneous. Two other RCTs were identified <sup>170,171</sup>. The first one compared single with doble layer uterine repair (locked/unlocked sutures) in terms of healing of the uterine scare and other maternal outcomes (n=36) <sup>170</sup>. Single layer closure tecnique was associated with higher risk of poor uterine scar healing (six month after CS). No other differences were identified between the groups (estimated blood loss, operation time, haemostatic suture).

The other RCT compared the doble layer uterine suture with a Turan technique (doble layer string uterine closure) in women undergoing to CS (n=168) <sup>171</sup>. No differences were identified in short term outcomes between the interventions (operating time, hospital stay, haemoglobine values). Turan technique was associated with less scar defects at 6 weeks after CS. At 2-years follow-up 11 women were pregnant again (5 turan technique, 6 double layer) and no complications were reported.

### Topic expert feedback

No topic expert feedback was relevant to this evidence.

### Impact statement

Further research is needed to identify the effect of these surgical techniques on short and long term outcomes.

New evidence is unlikely to change guideline recommendations.

### **Closure of the peritoneum**

#### **Recommendations derived from this question**

1.4.6.13 Neither the visceral nor the parietal peritoneum should be sutured at CS because this reduces operating time and the need for postoperative analgesia, and improves maternal satisfaction. [2004]

### Surveillance decision

This question should not be updated.

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

4-year surveillance summary

One Cochrane review assessed the impact of non-closure (non-closure of viseral peritoneum, parietal peritoneum or both) compared with closure of both peritoneal surfaces on different outcomes <sup>172</sup>. Twenty-nine RCTs were included

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 46 of 95

(n=15,480). Non-clousure was associated with less operative time and hospital stay after CS (except in the non-closure of parietal peritoneum subgroup were no differences were identified). In terms of adhesion formation the evidence identified was limited to draw final conclusions.

Three other RCTs comparing closure with nonclosure of the peritoneum were identified <sup>173-175</sup>. Two of them did not reported differences between the interventions <sup>173,174</sup>. The other one reported benefits of non-closure of peritoneum in short term outcomes (pain post CS, analgesic requirement, bowel transit time) <sup>175</sup>.

### **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

### Impact statement

New evidence identified is consistent with NICE guideline CG132 recommendation.

New evidence is unlikely to change guideline recommendations.

### Closure of the abdominal wall

### **Recommendations derived from this question**

1.4.6.14 In the rare circumstances that a midline abdominal incision is used at CS, mass closure with slowly absorbable continuous sutures should be used because this results in fewer incisional hernias and less dehiscence than layered closure. [2004]

### Surveillance decision

No new information was identified at any surveillance review.

This question should not be updated.

### **Closure of subcutaneous tissue**

### **Recommendations derived from this question**

1.4.6.15 Routine closure of the subcutaneous tissue space should not be used, unless the woman has more than 2 cm subcutaneous fat, because it does not reduce the incidence of wound infection. [2004]

### Surveillance decision

This question should not be updated.

### 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

### 4-year surveillance summary

Two RCTs assessed the impact of closure or non closure of subcutaneous tissue in CS  $^{176,177}$ . One study included women undergoing to CS (n=361)<sup>176</sup>. The other study included women undergoing to planned or unplanned CS (n=116)<sup>177</sup>. No differences were identified in terms of superficial site infections, superficial wound dehiscense, deep wound dehiscense, length of hospital stay between the interventions compared in the studies identified.

#### **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

### Impact statement

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 47 of 95

New evidence was limited and considered unlikely to impact current NICE guideline CG132 recommendations.

New evidence is unlikely to change guideline recommendation.

### Use of superficial wound drains

### **Recommendations derived from this question**

1.4.6.16 Superficial wound drains should not be used at CS because they do not decrease the incidence of wound infection or wound haematoma. [2004]

### Surveillance decision

This question should not be updated.

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

#### 4-year surveillance summary

One Cochrane review evaluated the impact of using different wound drains on maternal outcomes and health resourse use <sup>178</sup>. A total of ten trials were included (n=5248). It did not identify any benefit of the use of drains in the outcomes assessed (wound complications, febrile morbidity or pain). One trial reported an increased risk of wound infection with the use of subcutaneous drains compared with sub-

sheath drain. No differences were identified between subcutaneous procedures (drainage or suturing) in the outcomes assessed.

#### **Topic expert feedback**

No topic expert feedback was relevant to this evidence

### Impact statement

New evidence is consistent with NICE guideline CG132 recommendations.

New evidence is unlikely to change guideline recommendation.

### **Closure of the skin**

### **Recommendations derived from this question**

1.4.6.17 Obstetricians should be aware that the effects of different suture materials or methods of skin closure at CS are not certain. [2004]

### Surveillance decision

This question should not be updated.

# 2-year surveillance (2014) and Evidence Update (2013)

A meta-analysis evaluated whether staples or subcuticular sutures were associated with a higher risk of wound complications when used for transverse skin incisions following CS <sup>179</sup>. The primary outcome was wound complication, defined as the occurrence of wound infection or separation.

Six studies were included (5 RCTs and 1 prospective cohort study) with a total of 803 wounds closed with staples and 684 closed with subcuticular sutures. All RCTs were of 'fairly good' quality but the prospective cohort

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 48 of 95

study was of poor quality. The meta-analysis indicated that staple closure was associated with a higher risk of either wound infection or separation compared with sutures. The rates of wound infection were similar between the groups, but staple closure was associated with a significantly higher risk of wound separation. The 2 closure techniques were judged to be equivalent with regard to postoperative pain (3 RCTs), cosmetic outcome (3 RCTs), and patient satisfaction (5 RCTs).

An updated Cochrane review also compared the effects of skin closure techniques and materials on maternal and operative outcomes after CS <sup>180</sup>. Of the 6 studies evaluating the primary comparison (absorbable subcuticular sutures compared with non-absorbable staples), 5 RCTs were included in the metaanalysis by Tuuli et al. (2011) and their conclusions were similar. Wound infection rates did not differ significantly between absorbable sutures and non-absorbable staples. These results did not differ when analysis was limited to the 5 studies in which Pfannenstiel incision was used. Subgroup analysis suggested that staples may have a different effect depending on the type of incision (vertical or Pfannenstiel). Incisions closed by staples were more likely to become separated. However, most studies did not define a minimum width for the definition of separation. No significant differences were seen for other outcomes including pain and cosmetic outcome.

The Cochrane review (2012) and Tuuli et al. (2011) both reported no significant difference in rates of infection between sutures and staples. Similarly, they both reported that staples were significantly more likely to cause skin separation. These studies also provide further information from RCTs on the lack of significant difference between staples and sutures on postoperative pain and cosmetic appearance, as requested in a research recommendation in the full version of NICE guideline CG132. Overall, these results suggest that sutures may be more effective than staples for skin closure and it was considered may have a potential impact on NICE guideline CG132, although the details of any impact were outside the scope of the Evidence Update.

### 4-year surveillance summary

One SR <sup>181</sup> and nine RCTs were identified<sup>182-</sup> <sup>190</sup>. All of them published before the SR.

The SR compared subcuticlar absorbable sutures with metal staples for skin closure during CS <sup>181</sup>. A total of 12 RCTs were included (n=3112). Skin closure with suture was associated with a reduction of the risk of wound complications (subgroup analysis in people with obesity showed similar results), risk of wound separation and with a longer operating time compared with staples closure. No differences were identified in other outcomes assessed (pain perception, patient satisfaction, cosmetic assessment).

### Topic expert feedback

No topic expert feedback was relevant to this evidence

### Impact statement

New evidence suggests that skin closure with sutures might reduce the risk of wound complications and wound separation. There is an overlap between this question and NICE guideline CG74 Surgical site infection guideline. In the Evidence Update it was considered to be more efficient to cover this area in a larger question that includes more than one type of operation. This new evidence will be considered in the next surveillance review of NICE guideline CG74.

New evidence is unlikely to change guideline recommendation.

### **Umbilical artery pH measurement**

#### **Recommendations derived from this question**

1.4.6.18 Umbilical artery pH should be performed after all CS for suspected fetal compromise, to allow review of fetal wellbeing and guide ongoing care of the baby. [2004]

### Surveillance decision

No new information was identified at any surveillance review.

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 49 of 95

This question should not be updated.

# **Use of antibiotics**

### **Recommendations derived from this question**

There are currently no recommendations in the guideline in relation to this question.

### Surveillance decision

This question should be updated.

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

# 4-year surveillance summary Methods to reduce infectious morbidity at CS

Different methods to reduce infection morbidity during CS were listed in the full version of the guideline under the subsection use of antibiotics. These interventions were: preoperative skin preparation, vaginal preparation with povidone iodine, intraabdominal lavage with saline, and intrauterine lavage with antibiotics. No evidence was identified at that time in terms of benefits in the prevention of infectious morbidity.

We identified new evidence related to some of these areas: preoperative skin preparation, vaginal preparation, and intra-abdominal irrigation.

### Preoperative skin preparation

One Cochrane review <sup>191</sup> and two RCTs assessed different intervention for skin preparation previous to CS<sup>192,193</sup>. One of the RCT was already included in the SR <sup>192</sup>. The Cochrane review included a total of six studies (n=1522). The main comparisons assessed were: drape compared with no drape, alcohol scrub and iodophor drape compared with iodophor scrub without drape, parachlorometaxylenol plus iodine compared with iodine alone, chlorhexidine gluconate compared with povidone-iodine. No differences were identified in the risk of endometritis or wound infection. Authors concluded that evidence available was low quality to evaluate the different interventions properly. They highlighted that there is a need for more high quality RCT that describe in detail the

characteristics of the interventions assessed (time, duration, type of antiseptic agent, planned CS or non-planned CS, etc.). The other RCT compared skin preparation with chlorhexidine (with alcohol) with povidoneiodine (with alcohol) in women undergoing to CS (n=1404) <sup>193</sup>. They did not identify differences in any of the outcomes evaluated between the interventions.

#### Vaginal preparation

One Cochrane review assessed the impact of vaginal preparation on post CS infectious morbidity <sup>194</sup>. They included a total of five studies (n=1766). Vaginal preparation with povidone-iodine solution immediately before CS reduces the risk of endometritis particularly in women with rupture of membranes. No other differences in any other outcomes were identified. No adverse events due to intervention were described. We identified another RCT relevant to this area <sup>195</sup>. This study was published before the Cochrane review; therefore it is not dicussed further.

#### Intra-abdominal irrigation

Two RCTs assessed the effect of intraabdominal irrigation on maternal outcomes in women undergoing to CS <sup>196,197</sup>. One RCT included 430 women <sup>196</sup>, the other one 236 women <sup>197</sup>. None of studies identified benefits of the intra-abdominal irrigation in terms of reduction of post CS infectious morbidity. In both studies intra-abdominal wall irrigation was associated with an increase of intra operative nausea and vomiting compared with no irrigation.

### **Topic expert feedback**

No topic expert feedback was relevant to this evidence

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 50 of 95

### Impact statement

We identified new evidence in three areas: preoperative skin preparation, vaginal preparation, and of intra-abdominal irrigation. Only the vaginal preparation immediately before CS was related with a reduction of risk of endometritis. This reduction was more important in women with a rupture of membranes. NICE guideline CG132 does not have a recommendation regarding vaginal preparation and it is considered that this new evidence may have an impact on current recommendations.

New evidence identified that may change current recommendations.

### Timing of antibiotic administration

What is the effectiveness of antibiotics given prior to clamping of the cord compared to antibiotics given after clamping of the cord during a planned or unplanned caesarean section?

### **Recommendations derived from this question**

- 1.4.6.19 Offer women prophylactic antibiotics at CS before skin incision. Inform them that this reduces the risk of maternal infection more than prophylactic antibiotics given after skin incision, and that no effect on the baby has been demonstrated. [new 2011]
- 1.4.6.20 Offer women prophylactic antibiotics at CS to reduce the risk of postoperative infections. Choose antibiotics effective against endometritis, urinary tract and wound infections, which occur in about 8% of women who have had a CS. [new 2011]
- 1.4.6.21 Do not use co-amoxiclav when giving antibiotics before skin incision. [new 2011]

### Surveillance decision

This review question should not be updated

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

### 4-year surveillance summary

One Cochrane review assessed antibiotic prophylactic treatment in CS <sup>198</sup>.

A total of 95 RCTs and guasi RCTs were included (n=15,000). Prophylactic treatment with antibiotics was associated with a reduction of the risk of wound infection, endometritis, and maternal serious complications compared with placebo. Subgroup analysis by planned CS found similar results in the incidence of wound infections and endometritis. Similar findings were identified when it was compared preclamp with post-clamp administration of antibiotics, and in the majority of antibiotic regimens analysed. Authors highlighted that most of the studies included did not report neonatal outcomes (for example adverse infant outcomes or impact on infant immune system) or maternal adverse events.

Three RCTs were identified <sup>199-201</sup>. All of them were published before the Cochrane review; therefore they are not discussed further.

# Preoperative compared with post-cord clamp administration of antibiotics

We identified one Cochrane review <sup>202</sup>, three SRs <sup>203-205</sup> and seven RCTs relevant to this area <sup>206-212</sup>. Two SRs <sup>203,204</sup> and five RCTs <sup>206-210</sup> were published before the Cochrane review; therefore they are not dicussed further.

The Cochrane review included a total of 10 RCTs (n=5041). Preoperative administration of antibiotic prophylactic treatment was associated with a reduction of the maternal infectious morbidity compared with intravenous post-clamp administration. These differences were mainly related to a reduction of the risk of endometritis and wound infection. No differences were identified in other neonatal outcomes (including neonatal sepsis) or other maternal outcomes. Authors highlighted that the risk of bias of the studies was considered low, and the quality of the evidence was assessed as high in most of the outcomes included.

One RCT with meta-analysis compared the effect of the administration of antibiotic prophylactic treatment before skin incision with administration after cord clamping in planned CS (n=205) <sup>205</sup>. The results of the RCT were combiend with other 8 RCTs (number of participants not reported) and no differences were identified in terms of incidence of endometritis, wound infection, neonatal sepsis, admission to intermediate neonatal intensive care unit and other outcomes analysed (total puerperal morbidity, septic workup). Authors concluded that both interventions were effective.

Two other RCTs conducted in low-resource settings showed conflictiving results  $^{211,212}$ . One of them did not identify significant differences between administration of the antibiotic prophylactic treatment before the skin incision and after cord clamping (n=100)  $^{211}$ . The other one showed that the administration of the antibiotic prophylactic treatment before the skin incision was associated with a reduction of postopertive infection (mainly endometritis) compared with the administration after skin incision (n=464)  $^{212}$ .

### Antibiotic type

One Cochrane review was identified comparing different antibiotic regimens used as prophylactic treatments in CS <sup>213</sup>. They included a total of 35 RCTs (n=7697). No differences were identified between cephalosporins compared with penicillins in terms of maternal sepsis, endometritis, wound infections, and urinary tract infections. Authors highlighted that none of the studies included reported neonatal outcomes,or events after hospital discharge (for example infections) and they were unable to assess the impact of these interventions on the development of antibiotic resistance.

Two other RCTs were identified <sup>214,215</sup>. They were published before the Cochrane review, therefore they are not dicussed further.

### Topic expert feedback

Comments received via expert feedback:

 Antibiotic administration (range, timing, single or multiple dosing) to prevent surgical type infection in women with obesity or morbid obesity.

> 'I'm not sure that the evidence has changed much since the last guideline update, but I remember that the guideline changed at that time (from post-delivery to preincision) largely on expert consensus. In my view the expert consensus is changing again!'

#### Impact statement

New evidence of high quality support current recommendations about pre-cord clamp administration of the antibiotic prophylactic treatment. We did not identify new evidence in terms of antibiotic administration (range, timing, single or multiple dosing) in women with obesity or morbidly obesity.

No differences were identified between different antibiotic types but the evidence was low quality. The recommendation against the use of co-amoxiclav when giving antibiotics before skin incision was based on indirect evidence from women with pre-labour rupture of membranes and women with suspected preterm labour in which the exposure to coamoxiclav was related with an increased risk of necrotising enterocolitis in the baby. We did not identify new evidence that could have an impact on this recommendation.

New evidence is unlikely to change guideline recommendation.

### **Thromboprophylaxis for CS**

### **Recommendations derived from this question**

1.4.6.22 Women having a CS should be offered thromboprophylaxis because they are at increased risk of venous thromboembolism. The choice of method of prophylaxis (for example, graduated stockings, hydration, early mobilisation, low molecular weight heparin) should take

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 52 of 95

into account risk of thromboembolic disease and follow existing guidelines\*. [2004, amended 2011]

For more information see 'Venous thromboembolism: reducing the risk' (NICE clinical guideline 92).

### Surveillance decision

This question should not be updated.

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

### 4-year surveillance summary

One Cochrane review assessed thromboprofilaxis in pregnant women considered at risk of venous thromboembolism (VTE) <sup>216</sup>. A total of 16 RCTs were included in the meta-analysis (n=2592). Six of them assessed different methods of tromboprophylaxis during the antenal period (heparin, low molecular weight heparin [LWMH], unfractionated heparin [UFH]), nine after CS (heparin, LMWH, UFH, hydroxyethyl starch [HES], 5 days course compared with 10 days couse of LMWH) and one assessed prophylaxis with UFH in the postnatal period (including VD). The outcomes reported were: maternal mortality, symptomatic tromboembolic events (TE), symptomatic pulmonary embolism (PE), symptomatic deep venous thrombosis (DVT), fetal lossses, adverse effects sufficient to stop treatment, bleeding (number of bleeding episodes, bleeding during or at delivery or other bleeding).

In antenatal prophylaxis, no differences were identified in symptomatic TE, symptomatic PE, and symptomatic DVT between LMWH, UFH or placebo. The studies included did not report maternal mortality. LMWH reduced the risk of adverse effects sufficient to stop the treament, fetal losses and bleeding episodes compared with UFH. Trials with small sample sizes reported results in other secondary outcomes (injection haematomas, bleeding during delivery or other bleeding) favoring LMWH over UFH but authors highlighted that these results need to be interpreted with caution given the low quality of the studies.

In post CS or postnatal prophylaxis no differences were identified between LMWH or UFH compared with placebo (post CS), LMWH compared with UFH (post CS), 5 days compared with 10 days course of LMWH, UFH compared with no treatment (postnatal period) in vast majority of the primary outcomes assessed (symptomatic thrombolic events, symptomatic PE, and symptomatic DVT). Only one study reported no deaths.

After CS the combination of UFH and physiotherapy was associated with an increased risk of bleeding complications than physiotherapy alone. No differences in bleeding episodes were identified when compared LMWH with placebo or in seconday outcomes when comparing LMWH with UFH post CS, HES with UFH post CS, UFH with no heparine postnatally or 5 days LMWH with 10 days LMWH post CS.

Authors concluded that the evidence was limited and came from non-high quality trials.

#### Topic expert feedback

No topic expert feedback was relevant to this evidence.

#### Impact statement

New evidence identified comes from a SR that concluded that there is not enough evidence to recommend any particular prophylactic treatment in pregnant women (and in the early postnatal period). Most of the studies included were in women given birth by CS and they were considered not high quality. NICE guideline CG132 recommends the use of thromboprophylaxis in women having CS. The choice of the method needs to be based on the risk of thromboembolic disease and in accord with current guidelines (NICE guideline CG92: Venous thromboembolism: reducing the risk for patients in hospital). NICE guideline CG92 is currently being updated and pregnant women admitted to hospital are included within the scope. The new evidence identified will be transferred to check if this has been considered for the update.

New evidence is unlikely to change guideline recommendation.

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 53 of 95

### Women's preferences during CS

### **Recommendations derived from this question**

1.4.6.23 Women's preferences for the birth, such as music playing in theatre, lowering the screen to see the baby born, or silence so that the mother's voice is the first the baby hears, should be accommodated where possible. [2004]

### Surveillance decision

No new information was identified at any surveillance review.

This question should not be updated.

# Care of the baby born by CS

### 132 – 25 Presence of paediatrician at CS

#### **Recommendations derived from this question**

1.5.1.1 An appropriately trained practitioner skilled in the resuscitation of the newborn should be present at CS performed under general anaesthesia or where there is evidence of fetal compromise. [2004]

### Surveillance decision

No new information was identified at any surveillance review.

This question should not be updated.

## 132 – 26 Thermal care for babies born by CS

### **Recommendations derived from this question**

1.5.2.1 Babies born by CS are more likely to have a lower temperature, and thermal care should be in accordance with good practice for thermal care of the new born baby. [2004]

### **Surveillance decision**

No new information was identified at any surveillance review.

This question should not be updated.

### 132 – 27 Maternal contact (skin-to-skin)

### **Recommendations derived from this question**

1.5.3.1 Early skin-to-skin contact between the woman and her baby should be encouraged and facilitated because it improves maternal perceptions of the infant, mothering skills, maternal behaviour, and breastfeeding outcomes, and reduces infant crying. [2004

### Surveillance decision

This question should not be updated.

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

### 4-year surveillance summary

One RCT assessed the impact skin-to-skin contact during one hour on neonatal hypothermia compared with routine care (n= 90) <sup>217</sup>. In the control group, newborns were dressed and placed in a cot to receive standard care. Skin-to-skin contact was no associated with neonatal hypothermia. No differences in

other outcomes assessed were identified between the groups.

#### Topic expert feedback

No topic expert feedback was relevant to this evidence.

#### Impact statement

New evidence is consistent with NICE guideline CG132 recommendation.

New evidence is unlikely to change guideline recommendation.

### 132 – 28 Breastfeeding

### **Recommendations derived from this question**

1.5.4.1 Women who have had a CS should be offered additional support to help them to start breastfeeding as soon as possible after the birth of their baby. This is because women who have had a CS are less likely to start breastfeeding in the first few hours after the birth, but, when breastfeeding is established, they are as likely to continue as women who have a vaginal birth. [2004]

### Surveillance decision

This question should not be updated.

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

### 4-year surveillance summary

One RCT compared an early breastfeeding intervention (breastfeeding started within 2 hours following a CS under general anaesthesia with the help of a midwife) with no intervention (n=110) <sup>218</sup>. No differences were identified in the exclusive breastfeeding rate at 3 months of follow-up.

We identified another RCT that evaluated the use of domperidone for four days (dose not described in the abstract) to increase breast

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 55 of 95

milk production in women after CS (n=45) <sup>219</sup>. Domperidone increase significantly the breast milk production compared with placebo. Minor adverse events were reported only in the intervention group.

### **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

### Impact statement

New evidence from a single study with a small sample found that early breastfeeding initiation after CS under general anaesthesia does not have an impact on exclusive breastfeeding at 3 month of follow-up. The other study found that domperidone increase the breast milk production after CS. Domperidone is not license in UK for this use. The clinical relevance of this intervention in healthy women without breastfeeding problems and the differences found remains to be established. There is also a safety warning on domperidone risk of cardiac side-effects

### (https://www.gov.uk/drug-safetyupdate/domperidone-risks-of-cardiac-side-

effects). It is considered that the new evidence is limited, and unlikely to have an impact on current NICE guideline CG132 recommendation.

New evidence is unlikely to change guideline recommendation.

# Care of the woman after CS

### 132 – 29 High dependency unit/intensive therapy unit admission

### **Recommendations derived from this question**

1.6.1.1 Healthcare professionals caring for women after CS should be aware that, although it is rare for women to need intensive care following childbirth, this occurs more frequently after CS (about 9 per 1000). [2004]

### Surveillance decision

No new information was identified at any surveillance review.

This question should not be updated.

# 132 – 30 Routine monitoring after CS

### **Recommendations derived from this question**

- 1.6.2.1 After CS, women should be observed on a one-to-one basis by a properly trained member of staff until they have regained airway control and cardiorespiratory stability and are able to communicate. [2004]
- 1.6.2.2 After recovery from anaesthesia, observations (respiratory rate, heart rate, blood pressure, pain and sedation) should be continued every half hour for 2 hours, and hourly thereafter provided that the observations are stable or satisfactory. If these observations are not stable, more frequent observations and medical review are recommended. [2004]
- 1.6.2.3 For women who have had intrathecal opioids, there should be a minimum hourly observation of respiratory rate, sedation and pain scores for at least 12 hours for diamorphine and 24 hours for morphine. [2004]

1.6.2.4 For women who have had epidural opioids or patient-controlled analgesia with opioids, there should be routine hourly monitoring of respiratory rate, sedation and pain scores throughout treatment and for at least 2 hours after discontinuation of treatment. [2004]

### Surveillance decision

This question should not be updated

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

### 4-year surveillance summary

No relevant evidence identified.

### Topic expert feedback

Comments received via expert feedback:

Intrathecal opioids use in CS.

'The current recommendation notes that women need to be monitored minimum every hour checking respiratory rate, sedation and pain scores for at least 12 hours (for diamorphine) and 24 hours (for morphine). The concern is late onset of respiratory depression after intrathecal opioids, but seems that this adverse event has been reported in a different population not covered in this CG. So, many units do not adhere to this recommendation (they curtail the observations period) or they do not use intrathecal opioids because they cannot provide the observation required (even if there is good evidence for the analgesic action of this intervention).'

### Impact statement

NICE guideline CG132 recommendation 1.6.2.4 is a good practice point. One topic expert highlighted some issues but they are related to the implementation of the recommendation. No new evidence was identified.

New evidence is unlikely to change guideline recommendation.

# 132 – 31 Pain management after CS

### **Recommendations derived from this question**

- 1.6.3.1 Women should be offered diamorphine (0.3–0.4 mg intrathecally) for intra- and postoperative analgesia because it reduces the need for supplemental analgesia after a CS. Epidural diamorphine (2.5–5 mg) is a suitable alternative. [2004]
- 1.6.3.2 Patient-controlled analgesia using opioid analgesics should be offered after CS because it improves pain relief. [2004]
- 1.6.3.3 Providing there is no contraindication, non-steroidal anti-inflammatory drugs should be offered post-CS as an adjunct to other analgesics, because they reduce the need for opioids.[2004]

### **Surveillance decision**

This question should not be updated

An amendment is proposed to recommendation 1.6.3.1:

 A footnote is to be added explaining that injectable formulations of diamorphine aren't licensed for intrathecal or epidural use (off-label).

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

### 4-year surveillance summary Regional analgesia

### Fentanyl<sup>12</sup>

Three RCTs assessed the use of fentanyl intrathecal or epidural for intra- and postoperative analgesia <sup>220-222</sup>. One study compared an intrathecal administration of fentanyl 20 micrograms (0.4 ml) added to 0.5% heavy bupivacaine 2.4 ml with 0.5% heavy bupivacaine 2 ml alone in planned CS (n=70) <sup>220</sup>. The second RCT compared a combination of 7.5 mg of hyperbaric bupivacaine and 25 micrograms with 10 mg of hyperbaric bupivacaine alone also in planned CS (n=50) <sup>221</sup>. The third study assessed the use of fentanyl 50 micrograms during epidural anaesthesia with 0.5% bupivacaine 10 ml for planned CS (n=64) 222. All three studies found that fentanyl was associated with an improvement in the duration of analgesia without an increase of adverse events (maternal or neonatal).

One RCT compared different doses of intrathecal fentanyl (0, 5, 10, or 25 micrograms) in women under spinal anaesthesia with hyperbaric bupivacaine (12 mg) and intrathecal morphine (200 micrograms) for CS (n=40)<sup>223</sup>. Women receiving higher doses of fentanyl reported higher postoperative pain scores. These findings suggest that the addition of fentanyl could lead on an acute tolerance to opioids but more research is needed in this area to support these results.

### Fentanyl<sup>13</sup> compared with other drugs

One RCT compared intrathecal fentanyl 10 micrograms with oral gabapentin<sup>14</sup> 300 mg two hours before planned CS in women under spinal anaesthesia with 0.5% heavy bupivacaine 12.5 mg (n=70)<sup>224</sup>. Gabapentin was associated with a higher use of opioids in

24 hours, more women's satisfaction and less pain at follow-up compared with fentanyl. Follow-up time was not described in the abstract and it is unclear if the pain reduction was related to the higher use of opioids in 24 hours after CS.

A RCT compared intrathecal fentanyl 25 micrograms with intrathecal meperidine<sup>15</sup> 25 mg (pethidine) and placebo in women under spinal anaesthesia with lidocaine and epinephrine for planned CS (n=195) <sup>225</sup>. Fentanyl and meperidine were associated with an increase of the mean duration of analgesia. Meperidine was associated with better sensory and motor block, and less frequency of sedation compared with fentanyl. No differences were identified in Apgar scores between the interventions.

Three RCTs compared the use of intrathecal clonidine<sup>16</sup> with intrathecal fentanyl in spinal anaesthesia for improvement of analgesia after CS <sup>226-228</sup>. One study compared clonidine 75 micrograms with intrathecal fentanyl 0.5 ml (dosage not described in the abstract) in women under spinal anaesthesia with bupivacaine 10 mg for planned CS (n=90) <sup>226</sup>. The other compared a similar dose of clonidine intrathecal with fentanyl 25 micrograms intrathecal (n=90) <sup>227</sup>. The third one compared clonidine 50 micrograms with clonidine 75 micrograms and with fentanyl 25 micrograms (n=105). All the groups received 2 ml of 0.5% hyperbaric bupivacaine intrathecal <sup>228</sup>.

One of the studies reported that clonidine was associated with a prolongation of the mean duration of postoperative analgesia compared with fentanyl but no differences were identified in terms of analgesic requirement during the first day after CS <sup>226</sup>. The other study did not find differences in the prolongation of postoperative analgesia between the groups. Clonidine was associated with an increase of hypotension, nausea and vomiting <sup>227</sup>. The last study found that clonidine 75 micrograms was

<sup>&</sup>lt;sup>12</sup> Off-label route of administration.

<sup>&</sup>lt;sup>13</sup> Off-label route of administration.

<sup>&</sup>lt;sup>14</sup> Off-label indication.

 <sup>&</sup>lt;sup>15</sup>Off-label route of administration.
<sup>16</sup>Off-label route of administration and indication.

associated with a longer duration of post CS analgesia compared with clonidine 50 micrograms and fentanyl 25 micrograms. They did not identify differences in the incidence of hypotension, or neonatal outcomes. Nausea and pruritus was more related with the use of fentanyl <sup>228</sup>.

A RCT compared the effect of intrathecal ketamine<sup>17</sup> (25 mg) with intrathecal fentanyl (25 micrograms) as an adjunct analgesic of spinal anaesthesia with 2 ml of 0.5% hyperbaric bupivacaine in planned CS (n=100)<sup>229</sup>. Ketamine decreased the time to optimal blockade (sensory and motor) but no differences were identified in terms of prolongation of analgesia. Sedation was more associated with ketamine and pruritus with fentanyl.

### Intrathecal buprenorphine<sup>18</sup>

One RCT assessed the effects of the administration of intrathecal buprenorphine 0.2 ml (dosage not described in the abstract) in women under spinal anaesthesia with 5% lidocaine 65-70 mg for CS (n=442) <sup>230</sup>. Buprenorphine was associated with a prolongation of the duration of analgesia without an increase of adverse events compared with placebo.

#### Intrathecal tramadol<sup>19</sup>

A RCT evaluated the use of tramadol intrathecal for analgesia post CS (n=80) <sup>231</sup>. The study compared intrathecal tramadol 10 mg with fentanyl 10 micrograms in people undergoing to planned CS under spinal anaethesia with 0.5% bupicavaine 10 mg. Findings suggested that tramadol is superior to fentanyl in prolonging the mean duration of postoperative analgesia with less adverse events (shivering).

### Intrathecal midazolam<sup>20</sup>

One RCT evaluated the use of midazolam intrathecal (2 mg/ml) during spinal anaesthesia with bupivacaine (10 mg) in planned CS (n=62) <sup>232</sup>. Midazolam was not associated with reduction of pain four hours after CS compared with placebo.

There were no differences in terms of duration of effective analgesia time for regression of sensory analgesia. Midazolam use was more associated with nausea and vomiting.

### Magnesium sulfate (adyuvant)

We identified one SR <sup>233</sup> and one RCT <sup>234</sup> that evaluate the effect of magnesium sulfate used during spinal anaesthesia on post CS pain. The RCT was published before the SR, therefore it is not described further.

The SR included a total of 12 RCT (n=817) that compared the intrathecal use of magnesium sulfate<sup>21</sup> (50 mg or 100 mg) with placebo during spinal anaesthesia (or opiate) in CS <sup>233</sup>. The use of magnesium sulfate was associated with a prolonged effect of opiates without an increase of adverse events.

One other RCT also evaluated the effect of intravenous magnesium sulfate in bolus (50 mg/kg) but on women undergoing to planned CS with general anaesthesia  $(n=50)^{235}$ . Magnesium sulfate was associated with a reduction of the pain <24 hours after CS but not at 24 hours. It was also associated with a reduction of opioid requirement.

### Ketamine (adjuvant)22

One RCT evaluated the use of ketamine as adjuvant of spinal anaesthesia for CS on postoperative pain. The study compared intrathecal ketamine (0.1 mg/kg) with placebo in women under spinal anaesthesia with bupivacaine 10 mg intrathecally (n=60) <sup>236</sup>. Ketamine administration was associated with longer postoperative anaesthesia, an increase of time until analgesia requirement and a reduction of the total analgesic consumption <sup>236</sup>.

#### Patient-controlled analgesia

Three RCTs evaluated patient controlled analgesia (PCA) after CS <sup>237-240</sup>.

One study compared intravenous tramadol in PCA with a continuous tramadol infusion (n=40) <sup>238</sup>. In this study PCA was associated with lower analgesic consumption, higher women's satisfaction witout an increase of side effects.

<sup>&</sup>lt;sup>17</sup> Off-label route of administration.

<sup>&</sup>lt;sup>18</sup> Off-label route of administration.

<sup>&</sup>lt;sup>19</sup> Off-label route of administration.

<sup>&</sup>lt;sup>20</sup> Off-label route of administration.

<sup>&</sup>lt;sup>21</sup> Off-label route of administration and indication.

<sup>&</sup>lt;sup>22</sup> Off-label route of administration.

The other two studies evaluated patientcontrolled epidural analgesia (PCEA) after CS <sup>237,240</sup>. NICE guideline CG132 describes that PCEA is not common practice after CS in UK, therefore these studies are not described further.

### Wound infiltration with local anaesthetic

One SR evaluated the effect of local analgesia apply via wound catheters on the reduction of pain post CS <sup>241</sup>. A total of nine RCTs were included (n=512). Local wound infiltrations was associated with an reduction of the cumulative morphine consumption after CS (12 hours and 48 hours) and the incidence of post-operative nausea. Pain reductions were observed only at 12 hours after CS.

Six other RCTs were published after or in the year before this SR. They assessed local wound infiltration <sup>242-244</sup>, continuos wound infiltration<sup>245,246</sup>, or the volumen of local anaesthetic to use in wound infiltration <sup>247</sup>. Five other RCTs were identified<sup>248-252</sup>. They were published two years before the SR were identified, therefore they are not discussed further.

Local wound infiltration was associated with a decreased of postoperative analgesic consumption and pain <sup>243-245</sup>. There were no differences on the analgesic effect when comparing high concentration with low concentration (and high volume) of local anaesthetic <sup>247</sup>. Studies assessing continuos wound infiltration showed conflicting results: in one study it was associated with an increase of postoperative analgesic consumption and pain <sup>246</sup>. The other study showed a reduction of the incidence of these two outcomes <sup>245</sup>.

### Transversus abdominis plane block

One SR <sup>253</sup> and 10 RCTs were identified relevant to this area.

The SR included nine RCTs (number of women included was not described in the abstract) that assessed the effect of transversus abdominis plane (TAP) block on analgesia after CS. The comparisons assessed were: 1) TAP block with no TAP block, and 2) TAP block with intrathecal morphine. Studies comparing TAP block with no TAP block were analysed depending on the administration (or not) of intrathecal morphine. TAP block was associated with a reduction of analgesic comsumption 6 hours and 12 hours after CS and with a reduction of pain scores compared with not TAP block. These effects were reduced if intrathecal morphine was added. TAP block was also associated with a reduction in pain scores and opioid consumption at 24 hours post CS when compared with intrathecal morphine, but intrathecal morphine was associated with an increased time until analgesia requirement. More adverse events were associated with intrathecal morphine compared with TAP block.

The other RCTs were published in the same year or after this SR. They included between 40 and 90 women (only two included 90 women). The studies compared TAP block with:

- placebo <sup>254,255</sup>,
- no blockage <sup>256-258</sup>,
- intrathecal morphine <sup>259</sup>,
- TAP plus clonidine <sup>260</sup>.
- TAP plus dexamethasone <sup>261</sup>
- continuous wound infusion<sup>262</sup> or
- TAP plus wound infliltration <sup>263</sup>.

TAP block was associated with a lower supplemental analgesic requirements and lower pain scores when compared with no blockage or placebo <sup>254-258</sup>. It was associated with a higher requirement of opioids and higher pain levels when compared with intrathecal morphine but fewer side effects <sup>259</sup>.

TAP block effects were not improved with the addition of clonidine <sup>260</sup> but dexamethasone seems to prolong its effects <sup>261</sup>. One study was stopped early due to the onset of seizures in the TAP block group <sup>262</sup>. TAP block plus placebo was not associated with better results when compared with TAP block plus wound infiltration <sup>263</sup>.

### Inguinal and quadratus lumborum block nerve

One RCT compared bilateral iliohypograstic and ilioinguinal nerve block with placebo in 34 women which underwent to planned CS under spinal anaesthesia (bupivacaine, fentanyl and morphine) <sup>264</sup>. Iliohypograstic and ilioinguinal nerve block was associated with lower pain scores, an increased time until analgesia requirement and women satisfaction compared with placebo.

A RCT compared quadratus lumborum block with placebo <sup>265</sup>. Fifty women under spinal anaesthesia for planned CS were included. The intervention reduced opioid requirement during the first 12 hours after operation but not after 24 hours. It was also associated with a reduction of pain scores but not at 24 hours after CS.

### Non-steroidal anti-inflammatory analgesia

One Cochrane review evaluated different oral treatments for pain management after CS <sup>266</sup>. They included a total of eight RCTs (n=962) that compared: 1) opioid analgesics and nonopiod analgesics with placebo, 2) opiod analgesics with combination of analgesics, and 3) non-opiod with combination of analgesics. Authors highlighted that most of the studies included were at high risk of bias and with low sample sizes. The evidence found was limited to determine if any of the oral treatments was superior to other in terms of benefits and harms for the women and babys. Fice other RCTs were identified, two published before the Cochrane review <sup>267,268</sup>, and the other one afterwards <sup>269</sup>. This trial compared a combination of opioid (pentazocine 60 mg) and non-steroidal anti inflamatory analgesic (NSAID) (diclofenac sodium 50 mg) with opioid treatment alone (n=166) <sup>269</sup>. The combination of opioid and NSAID was associated with less pain during the first 48 hours post CS and a higher level of women's satisfaction.

### Other oral analgesics

One RCT assessed the oral administration of gabapentin<sup>23</sup> (600 mg pre CS then 200 mg every 8 hours per 2 days) for analgesia after CS (n=197) <sup>270</sup>. Gabapentin was associated with lower pain after CS compared with placebo but these differences were interpreted by authors as clinically irrelevant.

### Other analgesics treatments

We identified three other RCTs that compared various analgesic treatments administered by a different way from oral route <sup>271-273</sup>. These RCTs assessed:

- Acetaminophen (paracetamol), indomethacin diclofenac and placebo suppositories after CS (n=120)<sup>271</sup>
- Diclofenac suppossitory with tramadol or intravenous acetaminophen after spinal anaesthesia for CS (n=204) <sup>272</sup>.

 Intravenous paracetamol before general anaesthesia for CS (n=80) <sup>273</sup>

Indomethacin, diclofenac and acetaminophen (suppositories) were associated with a reduction of pain. This reduction was greater with indomethacin and diclofenac than with acetaminophen. All the interventions were also associated with a reduction of opioids use 271. Regarding the association of diclofenac with tramadol or acetaminophen, both were effective reducing pain after CS. The association of diclofenac with tramadol was more effective but it was also associated with an increase of side effects (nausea) 272. Finally, intravenous paracetamol before general anaesthesia was associated with less haemodynamic changes during intubation and with a reduction of opioid requirements after CS 273

We identified five references from four RCTs that assessed other type of interventions for pain management after CS. These interventions were: hand and food massage (n=80)<sup>274</sup>, transcrutaneous electrical nerve stimunation (n=100)<sup>275</sup>, surgical sponges (n=201) <sup>276</sup>, and bupivacaine-soaked spongostan (n=164) <sup>277,278</sup>. All the interventions except surgical sponges were associated with less pain post CS and with a reduction of analgesic consumption without been associated with an increase of adverse events.

### Complications following regional anaesthesia

One Cochanre review evaluated the effectiveness of different treatments to prevent post-dural headache in adults and children <sup>279</sup>. The review included a total of 10 RCTs (n=1611) most of them in pregnant women that received regional anaesthesia for VD or CS. Focusing on the last group (CS), intravenous amiophyline<sup>24</sup> was associated with a reduction of post-dural headache in women that underwent planned CS compared with no intervention. Dexamethasone was associated with an increase risk of post-dural headache in the same population compared with placebo.

Five other RCTs published after the Cochrane review were identified. One of them was published before the Cochrane review, therefore it is not describe further <sup>280</sup>. The other four studies assessed different interventions: intrathecal normal saline administration before intrathecal anaesthesia (n=100) <sup>281</sup>,

<sup>24</sup> Off-label use indication.

<sup>&</sup>lt;sup>23</sup> Off-label indication.

intravenous ondansetron 0.15 mg/kg (n=210) <sup>282</sup>, perioperative gabapentin (600 mg) (n=80) <sup>283</sup>, and dexamethasone (n=307) <sup>284</sup>. All the interventions were compared with placebo. The intrathecal administration of normal saline and intravenous ondansetron were the only interventions that were associated with a reduction of post-dural headache in the studies. However, 5HT3 receptor antagonists are not licensed for this indication and NICE guideline CG132 advices to avoid use during pregnancy and breastfeeding.

### **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

### Impact statement

Intrathecal analgesia

New evidence was identified regarding the use of drugs (fentanyl buprenorphine, tramadol, midazolam, magnesium sulfate, ketamine) for the management of pain after CS. Most of the studies included have major limitations. They have small sample sizes and assessed drugs that are not licensed for this use or route of administration in UK. None of the studies identified compared the drug assessed with diamorphine that is the drug recommended in the CG.

In summary, this new evidence was considered unlikely to have an impact on current recommendations.

### Patient-controlled analgesia

Few studies were identified. They support current NICE guideline CG132 recommendations.

### Wound infiltration with local anaesthetic

New evidence was found in this area but has major limitations. This in line with research recommendation 43 which says that more research is needed to determine the effect this intervention on the need for analgesia post CS.

### Nerve block

New evidence was identified suggests that transversus abdominis plane block might have an effect on the improvement of analgesia after CS. NICE guideline CG132 does not include recommendations about nerve block and most of the studies included have small sample sizes and major limitations. It is considered that this new evidence is unlikely to have an impact on current recommendations.

# Non-steroidal anti-inflammatory analgesia and other analgesic treatments

New evidence found is considered unlikely to change current recommendations.

Complications following regional anaesthesia

New evidence was identified regarding the use of aminophylline as a prophylactic treatment of post-dural headache in CS (off-label use). Although, this new evidence has major limitations and it is considered unlikely to have an impact on current recommendations.

New evidence is unlikely to change guideline recommendation.

## 132 – 32 Early eating and drinking after CS

### **Recommendations derived from this question**

1.6.4.1 Women who are recovering well after CS and who do not have complications can eat and drink when they feel hungry or thirsty. [2004]

### Surveillance decision

This question should not be updated.

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

### 4-year surveillance summary

Three SRs <sup>285-287</sup> and three RCTs comparing early with delayed eating were identified <sup>288-290</sup>.

The most recent SR published in 2016 included a total of 11 studies (n=1800). The type of studies included was not described in the abstract. Early oral feeding was associated with a reduction of the time of return of bowel motility compared with delayed oral feeding. No differences were identified in other outcomes compared (nausea, vomiting, abdominal distension, diarrhea, mild ileus symptoms).

The other two SRs found similar results about the benefits of early eating after cesarean section without identify potential harms associated with the intervention <sup>286,287</sup>.

All RCTs identified (published before the SR already described) showed similar findings infavour of early oral feeding <sup>288-290</sup>.

### Chewing gum

We identified one Cochrane review <sup>291</sup>, one SR <sup>292</sup>, and four RCTs <sup>293-296</sup> that assessed the effect of chewing gum on post CS outcomes related to the recovery of the gastrointestinal function. The SR and the RCTs identified were

published before the Cochrane review; therefore they are not discussed further.

The Cochrane review included a total of 81 studies (n=9072) in people receiving different types of surgery (colorectal surgery, CS, and other surgery). Chewing gum after CS was related to a significant reduction of the time to bowel sounds and time to bowel movements. Smaller differences were identified in terms of mortality, infection risk, and readmission between the interventions when analysing all the type of surgeries included.

### **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

### Impact statement

New evidence about early oral intake after CS was identified it was considered consistent with NICE guideline CG132 recommendation. New limited and low quality evidence about the use of chewing gum to help the recovery of gastrointestinal function was identified. Further research is needed in this area and it is considered that this new evidence is unlikely to have an impact on current recommendations.

New evidence is unlikely to change guideline recommendation.

### 132 – 33 Urinary catheter removal after CS

### **Recommendations derived from this question**

1.6.5.1 Removal of the urinary bladder catheter should be carried out once a woman is mobile after a regional anaesthetic and not sooner than 12 hours after the last epidural 'top up' dose. [2004]

### Surveillance decision

This question should not be updated.

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

#### 4-year surveillance summary

One RCT compared immediate urinary catherter removal with removal 12 hours after planned CS (n=300)<sup>297</sup>. Early urinary catheter

removal was associated with a reduction of the incidence of post CS significant bacterinuria, urinary simptoms (dysuria, burning during micturition, urinary frequency and urgency) and other outcomes (length of hospital stay, time for first voiding after CS, mean time to ambulation). No differences were identified in the incidence of retention of urine with need for recatheterisation.

### **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

### Impact statement

New evidence identified from a single trial provides limited evidence about the time of urinary catheter removal. The study suggests that remove urinary catheters immediately post-CS might be beneficial compared with delayed removal after 12 hours. Evidence identified in the original guideline came from two small RCTs, one of them in women undergoing gynaecological surgery (including CS). They did not identify differences urinary tract infections and other outcomes between immediate removal after surgery and removal the next day but conflicting results were found regarding urinary retention. More research is needed and it is considered that the new evidence identified is unlikely to have an impact on the current recommendation.

New evidence is unlikely to change guideline recommendation.

# 132 – 34 Respiratory physiotherapy after CS

### **Recommendations derived from this question**

1.6.6.1 Routine respiratory physiotherapy does not need to be offered to women after a CS under general anaesthesia, because it does not improve respiratory outcomes such as coughing, phlegm, body temperature, chest palpation and auscultatory changes. [2004]

### **Surveillance decision**

No new information was identified at any surveillance review.

This question should not be updated.

# 132 – 35 Length of hospital stay and readmission to hospital

### **Recommendations derived from this question**

1.6.7.1 Length of hospital stay is likely to be longer after a CS (an average of 3–4 days) than after a vaginal birth (average 1–2 days). However, women who are recovering well, are apyrexial and do not have complications following CS should be offered early discharge (after 24 hours) from hospital and follow-up at home, because this is not associated with more infant or maternal readmissions. [2004]

### Surveillance decision

This question should not be updated.

2-year surveillance (2014) and Evidence Update (2013) No relevant evidence identified.

no relevant evidence identilied.

4-year surveillance summary

One RCT comparing hospital discharge after one or two days after CS in low risk women was identified (n=360)<sup>298</sup>. No differences were identified in terms of patients satisfaction, exclusive breastfeeding at 6 weeks post CS, or

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 64 of 95

other outcomes assessed (maternal antibiotic use, anxiety, depression status, hospital readmission) between the groups.

### **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

### Impact statement

New evidence found is consistent with current NICE guideline CG132 recommendation.

New evidence is unlikely to change guideline recommendation.

# <u>Recovery following CS</u>

132 – 36 Recovery following CS

### **Recommendations derived from this question**

- 1.7.1.1 In addition to general postnatal care, women who have had a CS should be provided with:
  - specific care related to recovery after CS
  - care related to management of other complications during pregnancy or childbirth. [2004]
- 1.7.1.2 Women who have a CS should be prescribed and encouraged to take regular analgesia for postoperative pain, using:
  - for severe pain, co-codamol with added ibuprofen
  - for moderate pain, co-codamol
  - for mild pain, paracetamol. [2004]
- 1.7.1.3 CS wound care should include:
  - removing the dressing 24 hours after the CS
  - specific monitoring for fever
  - assessing the wound for signs of infection (such as increasing pain, redness or discharge), separation or dehiscence
  - encouraging the woman to wear loose, comfortable clothes and cotton underwear
  - · gently cleaning and drying the wound daily
  - if needed, planning the removal of sutures or clips\*. [2004]
- 1.7.1.4 Healthcare professionals caring for women who have had a CS and who have urinary symptoms should consider the possible diagnosis of:
  - urinary tract infection
  - stress incontinence (occurs in about 4% of women after CS)
  - urinary tract injury (occurs in about 1 per 1000 CS). [2004]
- 1.7.1.5 Healthcare professionals caring for women who have had a CS and who have heavy and/or irregular vaginal bleeding should consider that this is more likely to be due to endometritis than retained products of conception. [2004, amended 2011]
- 1.7.1.6 Women who have had a CS are at increased risk of thromboembolic disease (both deep vein thrombosis and pulmonary embolism), so healthcare professionals need to pay particular attention to women who have chest symptoms (such as cough or shortness of breath) or leg symptoms (such as painful swollen calf). [2004]
- 1.7.1.7 Women who have had a CS should resume activities such as driving a vehicle, carrying heavy items, formal exercise and sexual intercourse once they have fully recovered from the CS (including any physical restrictions or distracting effect due to pain). [2004]

- 1.7.1.8 Healthcare professionals caring for women who have had a CS should inform women that after a CS they are not at increased risk of difficulties with breastfeeding, depression, post-traumatic stress symptoms, dyspareunia and faecal incontinence. [2004]
- 1.7.1.9 While women are in hospital after having a CS, give them the opportunity to discuss with healthcare professionals the reasons for the CS and provide both verbal and printed information about birth options for any future pregnancies. If the woman prefers, provide this at a later date. [new 2011]
- \*For more recent recommendations on wound care see 'Surgical site infection' (NICE clinical guideline 74).

### **Surveillance decision**

This question should not be updated.

An amendment is proposed to recommendation 1.7.1.2

 A footnote is to be added explaining the two MHRA warnings related to the use of codeine and ibuprofen.

# 2-year surveillance (2014) and Evidence Update (2013)

No relevant evidence identified.

### 4-year surveillance summary

Two MHRA warnings relating to the recommendations on 1.7.1.2 were identified. There was one on the very rare risk of sideeffects of codeine (which co-codamol contains) in breast feed babies (https://www.gov.uk/drugsafety-update/codeine-very-rare-risk-of-sideeffects-in-breastfed-babies). This is related to people who are ultra-rapid metabolisers of the drug, doing a rapid conversion of codeine to morphine and therefore, having a higher risk of side-effects. According with this Drug Safety Update, in UK around 1%-2% of the people fall into this category and breastfeeding babies of women with this condition are a risk of adverse events.

The second MHRA warning is about the use of high dose of ibuprofen in people with significant risk factors for cardiovascular events (for example ischemic heart disease, peripheral arterial disease, cerebrovascular disease, congestive heart failure or uncontrolled hypertension) (<u>https://www.gov.uk/drug-safety-</u> <u>update/high-dose-ibuprofen-2400mg-day-</u> <u>small-increase-in-cardiovascular-risk</u>). This Drug Safety Updated did not include information directly related with pregnant women or breastfeeding.

### **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

### Impact statement

Two MHRA warnings were identified and an amendment in the form of footnotes is proposed to the recommendations on 1.7.1.2 to include this information.

New evidence is unlikely to change guideline recommendation.

# Pregnancy and childbirth after CS

### 132 – 37 Pregnancy and childbirth after CS

### **Recommendations derived from this question**

1.8.1 When advising about the mode of birth after a previous CS consider:

- maternal preferences and priorities
- the risks and benefits of repeat CS
- the risks and benefits of planned vaginal birth after CS, including the risk of unplanned CS. [new 2011]
- 1.8.2 Inform women who have had up to and including four CS that the risk of fever, bladder injuries and surgical injuries does not vary with planned mode of birth and that the risk of uterine rupture, although higher for planned vaginal birth, is rare. [new 2011]
- 1.8.3 Offer women planning a vaginal birth who have had a previous CS:
  - electronic fetal monitoring during labour
  - care during labour in a unit where there is immediate access to CS and on-site blood transfusion services. [2011]
- 1.8.4 During induction of labour, women who have had a previous CS should be monitored closely, with access to electronic fetal monitoring and with immediate access to CS, because they are at increased risk of uterine rupture\*. [2004, amended 2011]
- 1.8.5 Pregnant women with both previous CS and a previous vaginal birth should be informed that they have an increased likelihood of achieving a vaginal birth than women who have had a previous CS but no previous vaginal birth. [2004]
- \* For more information see 'Induction of labour' (NICE clinical guideline 70).

# Surveillance decision

This question should not be updated.

# 2-year surveillance (2014) and Evidence Update (2013)

Vaginal birth after CS

An Australian prospective restricted cohort study consisted of a patient-preference cohort study, and a small nested randomised study was identified<sup>299</sup>. The aim of the trial was to compare the benefits and risks of a planned repeat CS (n=10 randomised, n=1098 preference) with a planned vaginal birth after CS (n=12 randomised, n=1237 preference) in women who had a single prior CS and were pregnant with a live singleton in cephalic presentation, at 37 weeks gestation or more, and were considered suitable by their obstetrician for planned vaginal birth after CS.

The primary outcome was a composite of death or serious outcome for the infant, defined as death after study entry or before hospital discharge, or serious morbidity.

Of the women in the planned repeat CS group 98% delivered by CS and 2% by vaginal birth. In the planned vaginal birth after CS group 57% women had CS and 43% had vaginal birth. The risk of infant death before discharge or serious outcome was significantly reduced for infants born to women in the planned CS group compared with those in the planned vaginal birth group.

There was a significant reduction in the risk of serious morbidity in infants born to the planned CS group compared with the vaginal birth group. There were no significant differences between planned CS and planned vaginal birth for any of the other individual components of the primary outcome. No perinatal deaths occurred in the planned CS group, but unexplained 2 stillbirths occurred in the planned vaginal birth group.

An Australian retrospective cohort study assessed the outcomes of VD after CS (Ten Group Classification System [TGCS] group 5, n=423) compared with all cephalic singleton term births in women with no previous CS (TGCS groups 1–4, n=16,020) <sup>300</sup>. Primary outcomes were uterine rupture, post-partum haemorrhage, 3rd and 4th degree tears and neonatal morbidity.

Most women in TGCS group 5 delivered by CS (80%) and most women in TGCS groups 1-4 delivered vaginally (83%). Uterine rupture or dehiscence occurred in only 5 women overall (4 in TGCS group 5), but this low number resulted in insufficient power to detect statistical

significance. Post-partum haemorrhage following normal VD was significantly higher for women in TGCS group 5 compared with those in TGCS groups 1–4. The absolute number of 3rd and 4th degree tears was low. However, in women who had normal vaginal deliveries, there were significantly more tears in TGCS group 5 compared with TGCS groups 1–4, but this was not significant for instrumental VD. Admissions to the neonatal intensive care unit or special care nursery did not differ significantly between the TGCS groups for normal vaginal deliveries or instrumental vaginal deliveries. However, significant differences were noted for CS deliveries.

The authors highlighted that the results need to be considered in the context of the TGCS classifications, which do not control for variables such as birth weight or whether CS was planned or unplanned. Another limitation was the retrospective nature of the analysis.

The results of this study suggest that the risk of infant death before discharge or serious outcome for planned repeat CS is less than planned vaginal birth after CS <sup>300</sup>. However, the evidence from Crowther et al. (2012) suggested that many outcomes after vaginal birth after CS were not significantly different from those who had no previous CS <sup>299</sup>. This evidence was considered unlikely to have an impact on NICE guideline CG132, which recommends discussing the risks and benefits of planned vaginal birth and of repeat CS.

### Uterine rupture

An Australian retrospective cohort study aimed to quantify the risk of uterine rupture in women with 1 prior CS (n=29,008) <sup>301</sup>. The study was based on data from 1998 to 2000 and analysed only second singleton births with confirmed uterine rupture (n=48). Births were classified as: repeat CS without labour; spontaneous labour with augmentation with oxytocin; induction of labour with oxytocin only; induction with only prostaglandins; induction with both oxytocin and prostaglandins; and induction with neither oxytocin nor prostaglandins. Relative risks were calculated for the spontaneous labour without augmentation group compared with each of the other groups.

Of the 48 confirmed uterine ruptures, 37 were complete ruptures. For complete ruptures placental abruption was the only variable showing increased risk of uterine rupture for each subgroup compared with women who had spontaneous labour without augmentation with oxytocin. The overall rate of vaginal birth in the vaginal birth after CS group was 54%.

When all subgroups were compared with spontaneous labour without augmentation with oxytocin, planned CS had the lowest risk of uterine rupture and complete uterine rupture. The risk of uterine rupture was 3 to 5 times greater when labour was induced by any means. The highest risk of any uterine rupture was for oxytocin after spontaneous onset of labour.

There are a number of limitations stated by the authors. Although the increased risk associated with oxytocin is clinically relevant it is based on 12 cases of complete uterine rupture. There may also be differences in groups of women who have a trial of labour, those who have no trial of labour, and those who have unplanned CS after a trial of labour. The data did not allow study of perinatal death, the effect of the length of inter-pregnancy interval, the reason for first CS, or details of induction dosages and rates of drug administrations.

The study suggested that planned CS may be associated with lower risk of uterine rupture compared with spontaneous labour without augmentation, and that inducing labour increases the risk of uterine rupture. This was considered consistent with the recommendation in NICE guideline CG132 that women planning vaginal birth after CS should be offered care during labour in a unit with immediate access to CS because of the possibility of uterine rupture.

### **4-year surveillance summary** Decision making interventions or tools

One Cochrane review assessed different methods to support women in the decision making process of mode of delivery after CS <sup>302</sup>. There were included a total of three RCTs (n=2270) all of them done in high income countries. Authors identified studies evaluating independent (to be used only by the women) or mediated use tools (with help of independent support). None of the studies included evaluated sharing decision making tools. No differences were identified in the planned mode of birth, the proportion of women without a preferred delivery mode or adverse events between the interventions assessed. No differences the mode of birth preferred and

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 68 of 95

achieved were identified either. There was a higher proportion of unplanned CS. Decisional support was associated with less decisional conflict about delivery mode and with higher level of women knowledge compared with control. Authors concluded that the evidence available is limited and more research is needed to evaluate these t tools.

One RCT assessed two different tools to support mode of delivery decision in women with a previous CS <sup>303</sup>. One tool was an interactive decision aid and the other was a brochure with information (evidence based). Overall, women felt more informed with both interventions, but the interactive tool was associated with more clarity compared with brochures.

# Risk and benefits planned CS compared with planned VD

One Cochrane review assessed the differences between a planned CS and planned VD in women with a previous CS <sup>304</sup>. The review included two RCTs (n=320). Only 22 women were included in the analysis of important outcomes. No differences were identified in terms of maternal or infant death or serious maternal or infant morbidity between the interventions assessed. Given the low number of studies and participants included, authors highlighted that these results need to be interpreted with caution. A RCT was identified but it was published before the Cochrane review (and included) <sup>305</sup>.

# Risk and benefits planned CS compared with induction of labour

One Cochrane review evaluated planned CS or induction of labour in women with a previous CS <sup>306</sup>. The Cochrane review did not identify any RCTs.

### Women's experiences on VBAC

One metasynthesis of eight qualitative studies about women's experience after VD after CS was identified <sup>307</sup>. Emergent themes were related to difficulties facing the decision making process about mode of delivery, positive aspects of vaginal birth described by women, risks of VD after CS, and feelings of strong responsibility if a VD was decided. Authors concluded that more research in women's experiences is needed as well as more evidence-base information that includes risk and benefits of VD after CS.

### **Topic expert feedback**

No topic expert feedback was relevant to this evidence.

### Impact statement

New evidence identified is consistent with NICE guideline CG132 recommendations.

New evidence is unlikely to change guideline recommendation.

# **Research recommendations**

# Prioritised research recommendations

At 4-year and 8-year surveillance reviews of guidelines published after 2011, we assess progress made against prioritised research recommendations. We may then propose to remove research recommendations from the NICE version of the guideline and the <u>NICE database for research</u> <u>recommendations</u>. The research recommendations will remain in the full versions of the guideline. See NICE's <u>research recommendations</u> process and methods guide 2015 for more information.

These research recommendations were deemed priority areas for research by the Guideline Committee; therefore, at this 4-year surveillance review time point a decision will be taken on whether to retain the research recommendations or stand them down.

# RR – 28 What factors influence the decision-to-delivery interval when there is a category 1 level of urgency for CS?

No new information was identified at any surveillance review.

# Surveillance decision

No new evidence was found but it is not expected that this research recommendation would be answered by systematic reviews or RCTs. Therefore it is proposed to keep this research recommendation.

# RR – 29 A prospective study to determine whether the decision-to-delivery interval has an impact on maternal and neonatal outcomes when there is a category 2 level of urgency for CS.

New evidence identified and summarised in the question 132 - 21 but an update is not planned because the evidence supports the current guideline recommendations.

# Surveillance decision

The research recommendation will be retained and evidence from the ongoing research will be considered when results are published.

# RR – 30 Repeat of the National Caesarean Section Sentinel Audit.

No new information was identified at any surveillance review

# Surveillance decision

No new evidence was found but it is not expected that this research recommendation would be answered by systematic reviews or RCTs. Therefore it is proposed to keep this research recommendation.

# RR – 15 What support or psychological interventions would be appropriate for women who have a fear of vaginal childbirth and request a CS?

The research recommendation will be retained and evidence from the ongoing research will be considered when results are published.

# RR – 01 What are the medium- to long-term risks and benefits to women and their babies of planned CS compared with planned vaginal birth?

New evidence was found (132 - 02) and an update is planned.

# Surveillance decision

The research recommendation will be removed from the NICE version of the guideline and the NICE research recommendations database. If needed, a new research recommendation may be made as part of the update process.

# Other research recommendations

**Risks and benefits of CS** 

### RR – 01 See priority section.

RR – 02 Further evaluation is needed to determine the impact of demographic and clinical factors (such as ethnic group, increase in body mass index) and attitudinal factors on CS rates.

No new information was identified at any surveillance review.

### **Breech presentation**

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RR – 03 Further research is needed to determine the effect of caesarean section compared with vaginal birth for women with:
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- preterm breech,
- a breech presentation that is diagnosed in the second stage of labour.

New evidence was found in preterm breech (132 - 03) but an updated is not planned because the evidence support the current guideline recommendations.

### **Multiple pregnancy**

# RR – 04 RCTs are needed to evaluate the benefits and risks to mothers and babies of CS for delivery of twin and triplet pregnancies.

New evidence was found in preterm breech (132 - 04) but an updated is not planned because the evidence support the current guideline recommendations.

### Preterm birth and CS

RR – 05 RCTs are needed to evaluate the impact of CS on the benefits and risks to mothers and babies born preterm.

No new information was identified at any surveillance review.

# Small for gestational age

RR – 06 RCT evidence is needed to determine the effect of planned CS on neonatal mortality and morbidity for 'small for gestational age' babies.

No new information was identified at any surveillance review.

### Morbidly adherent placenta

# RR – 07 How accurate is 3D ultrasound compared with 2D ultrasound or MRI scanning for diagnosing morbidly adherent placenta?

No new information was identified at any surveillance review.

RR – 08 What is the effectiveness of procoagulant agents (such as recombinant factor VIIa, beriplex, tranexamic acid, fibrinogen concentrate) in reducing blood loss in women with morbidly adherent placenta?

No new information was identified at any surveillance review.

RR – 09 What is the effectiveness of point of care testing for haematological indices in women with an established postpartum haemorrhage and in cases of morbidly adherent placenta in reducing maternal morbidity?

No new information was identified at any surveillance review.

RR – 10 What is the effectiveness of the components of the package of care for morbidly adherent placenta such as imaging techniques (e.g. interventional radiology including balloon catheters), stenting of ureters, removal of the placenta, and cell salvage in reducing morbidity associated with maternal blood loss?

New evidence identified and summarised in the question 132 - 09, but an updated is not planned because the evidence support the current guideline recommendations.

# RR – 11 What is the appropriate gestational age of elective birth for babies of women with a morbidly adherent placenta?

No new information was identified at any surveillance review.

RR – 12 What is the effectiveness of performing an elective hysterectomy to reduce morbidity associated with blood loss in women with morbidly adherent placenta?

No new information was identified at any surveillance review.

### Mother-to-child transmission of maternal infections

# RR – 13 RCTs are needed to evaluate the effect of planned CS in addition to immunoglobulin and vaccination on MTCT of hepatitis B.

New evidence identified and summarised in the question 132 – 11, but an updated is not planned because the evidence support the current guideline recommendations.

# RR – 14 RCTs are needed to determine whether planned CS should be offered to prevent MTCT of HSV to women with recurrence of HSV at birth and in women in whom the primary HSV infection occurs in the first trimester of pregnancy.

No new information was identified at any surveillance review.

- RR 15 See priority section.
- RR 16 Medium to long term quality of life study comparing psychological and physical outcomes in women who have had a requested and given birth by CS compared with women who plan a vaginal birth.

No new information was identified at any surveillance review.

# RR – 17 Qualitative and quantitative research should be carried out to look at the reasons that lead to pregnant women's request for CS

No new information was identified at any surveillance review.

# RR – 18 The effect of counselling and other interventions such as second opinion and provision of support on the likelihood of CS for women who express a preference for CS need further evaluation.

No new information was identified at any surveillance review.

#### Place of birth

### RR – 19 RCTs comparing planned birth in a stand-alone birthing centre to birth in conventional maternity facilities or midwifery led units.

No new information was identified at any surveillance review.

### RR – 20 Qualitative research is needed to explore women's opinions on place of birth and the impact of place of birth on their birth experiences.

No new information was identified at any surveillance review.

### RR – 21 Further RCTs are needed to determine the effect of 'delayed admission in labour' on the likelihood of CS.

No new information was identified at any surveillance review.

#### Factors reducing the likelihood of CS

### RR – 22 RCT evidence is needed to determine the impact of partograms based on different curves of labour on CS rates and morbidity outcomes.

New information in this area is summarised in the question 132 – 15 but an update is not planned because the evidence supports the current guideline recommendations.

#### No influence on likelihood of CS

RR – 23 RCT evidence is required to evaluate the effect of parenteral analgesia (intramuscular and intravenous morphine based analgesia) used during childbirth on the likelihood of CS.

No new information was identified at any surveillance review.

### RR – 24 RCTs are needed to establish the safety and efficacy of complementary therapies used during labour.

No new information was identified at any surveillance review.

#### 'Failure to progress' in labour and CS

#### RR – 25 More RCTs are required to determine the effect of oxytocin augmentation as single interventions or as part of a package of interventions (such as "active management of labour") on the likelihood of CS and other outcomes including women's satisfaction with care.

New evidence identified and summarised in the question 132 – 17 but an update is not planned because the evidence supports the current guideline recommendations.

### RR – 26 Further research on the short and longer term health impacts of CS during the second stage compared to operative vaginal delivery are needed.

No new information was identified at any surveillance review.

#### Eating during labour

RR – 27 RCTs that evaluate the effects of eating during labour compared with restricting intake on labour outcomes are needed. Cohort or case control studies on the risk factors for aspiration and other morbidities for women having CS are needed.

New evidence identified and summarised in the question 132 – 18 but an update is not planned because the evidence supports the current guideline recommendations.

#### Decision-to delivery-interval for unplanned CS

RR – 28	See priority section.
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### RR – 29 See priority section

### RR – 30 See priority section

Surgical techniques for CS

RR – 31 RCTs are required to determine the effectiveness of adhesive drapes at CS in reducing blood spillage and cross infection and improving safety for staff in the operating room.

No new information was identified at any surveillance review.

RR – 32 RCTs are needed to evaluate the effectiveness of incisions made with diathermy compared with surgical knife in terms of operating time, wound infection, wound tensile strength, cosmetic appearance and women's satisfaction with the experience.

New evidence was found and summarised in the instruments for skin incision section (1.4.6<u>Surgical techniques for CS</u>) but an update is not planned because the evidence supports the current guideline recommendations.

## RR – 33 RCTs are needed to determine the effect of delayed cord clamping on neonatal outcomes including transient tachypnoea of the newborn and risk of maternal fetal transfusion in rhesus negative women for term and preterm births.

New evidence was found and summarised in the cord clamping section (<u>1.4.6 Surgical</u> <u>techniques for CS</u>) but an update is not planned because the evidence supports the current guideline recommendations.

## RR – 34 RCTs are required to determine the effectiveness of mass closure compared to layered closure of the abdominal wall incision at CS particularly for transverse abdominal incisions.

No new information was identified at any surveillance review.

# RR – 35 Research is required to assess the effect of the various surgical techniques for CS on future surgery such as repeat CS and the incidence of complications during future surgery such as hysterectomy and urogynaecological procedures.

New evidence was found and summarised in the abdominal wall incision section (1.4.6<u>Surgical techniques for CS</u>) but an update is not planned because the evidence supports the current guideline recommendations.

## RR – 36 More RCTs are needed to determine the effect of wound drainage of postoperative morbidity especially in women more at risk of this outcome such as obese women.

New evidence was found and summarised in the use of superficial wound drains section (<u>1.4.6 Surgical techniques for CS</u>) but an update is not planned because the evidence supports the current guideline recommendations.

## RR – 37 More RCTs are needed to determine the effect of staples compared to subcuticular sutures for skin closure at CS on postoperative pain, cosmetic appearance and removal of sutures and staples.

New evidence was found and summarised in the closure of the skin section 1.4.6 (<u>1.4.6</u> <u>Surgical techniques for CS</u>) but an update is not planned because the evidence supports the current guideline recommendations.

### RR – 38 What is the most effective antibiotic to prevent maternal infectious morbidity post-CS when given prior to incision?

New evidence was found and summarised in the timing of antibiotic administration (<u>1.4.6</u> <u>Surgical techniques for CS</u>) but an update is not planned because the evidence supports the current guideline recommendations.

### RR – 39 What is the physical, psychological and social impact of maternal infectious morbidity post-CS?

No new information was identified at any surveillance review.

## RR – 40 More evaluation of interventions such as seeing baby born via a lowered screen; music playing in theatre; silence in theatre so mother's voice is the first baby hears and lowering the lights in theatre during CS are needed.

No new information was identified at any surveillance review.

### Neonatal encephalopathy and cerebral palsy

### RR – 41 Further evaluation of the long and short term risks and benefits of CS compared with vaginal birth for babies is required.

New evidence was found and summarised in the question 132 – 02 but an update is not planned because the evidence supports the current guideline recommendations.

### Thermal care for babies born by CS

### RR – 42 Research is required to establish the thermal care requirements for babies born by CS.

No new information was identified at any surveillance review.

### Pain management after CS

### RR – 43 Further research is needed to determine the effect of wound infiltration with local anaesthetic at CS on the need for post-CS analgesia.

New evidence was found and summarised in the question 132 - 31 but an update is not planned because the evidence supports the current guideline recommendations.

### **Respiratory physiotherapy after CS**

### RR – 44 Research is needed to establish the effect of non-respiratory physiotherapy for women following CS on post-CS recovery.

No new information was identified at any surveillance review.

### Debriefing for women after CS

### RR – 45 More RCT evidence is required to determine the effect of midwifery-led debriefing following CS.

No new information was identified at any surveillance review.

### Pregnancy and childbirth after CS

#### RR – 46 A comparison of the long term psychological and physical outcomes between women who have chosen and/or been advised towards a VBAC or a planned repeat CS.

New evidence was found and summarised in the section <u>pregnancy and childbirth after CS</u>, but an update is not planned because the evidence supports the current guideline recommendations.

## RR – 47 An evaluation of the effectiveness of continuity of carer on the proportion of women planning and achieving a VBAC, and the short and long term psychological and physical outcomes of women following a planned VBAC.

No new information was identified at any surveillance review.

4-year surveillance 2017 summary of new evidence – Caesarean section (2011) NICE guideline CG132 76 of 95

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