



**TITLE:** Antibiotics for the Prevention of Post-Cesarean Section Complications: Clinical Evidence and Safety

**DATE:** 07 February 2013

## RESEARCH QUESTIONS

1. What is the clinical evidence regarding the effectiveness and safety of antibiotic prophylaxis administered before or after clamping during cesarean sections for the prevention of maternal post-surgical infections?
2. What is the clinical evidence regarding the effects of antibiotic prophylaxis administered before or after clamping during cesarean section on neonatal health and antibiotic resistance?

## KEY MESSAGE

Four systematic reviews and meta-analyses, four randomized controlled trials, and five non-randomized studies were identified regarding the timing of antibiotic administration for the prevention of post-cesarean section maternal and neonatal complications.

## METHODS

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2012, Issue 12), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. The search was also limited to English language documents published between Jan 1, 2008 and Jan 23, 2013. Internet links were provided, where available.

The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.

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## RESULTS

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials and non-randomized studies.

Four systematic reviews and meta-analyses, four randomized controlled trials, and five non-randomized studies were identified regarding the timing of antibiotic administration for the prevention of post-cesarean section maternal and neonatal complications. No relevant health technology assessment reports were identified. Additional references of potential interest are provided in the appendix.

## OVERALL SUMMARY OF FINDINGS

### *Maternal Health*

All of the included studies examined the effect of antibiotic administration on maternal health.<sup>1-13</sup> Evidence from one systematic review<sup>2</sup> and one non-randomized study<sup>11</sup> suggested that compared to no antibiotic prophylaxis, antibiotic administration was beneficial in reducing post cesarean section infectious complications. With respect to the timing of prophylaxis, the evidence was mixed. The authors of two systematic reviews<sup>1,4</sup> and four non-randomized studies<sup>9,10,12,13</sup> found differences in rates of infections and concluded that pre-operative administration reduced rates of post-cesarean section complications<sup>1,4,10</sup> and recommended pre-operative antibiotic administration.<sup>9,12,13</sup> The authors of one systematic review<sup>3</sup> and four randomized trials<sup>5-8</sup> found that the administration of antibiotics was effective in reducing infectious complications following cesarean section, but that the timing of administration was not a factor in reducing infections. The authors of one study recommended that for elective cesarean section, antibiotics should be used after clamping, but that for non-elective cesarean section they should be used prior to incision.<sup>7</sup>

### *Neonatal Health*

The majority of the included studies were either underpowered to detect neonatal events<sup>1,2</sup> or did not examine the effects of the antibiotics on neonatal health.<sup>3,6,10,11,13</sup> The studies that did examine neonatal events found that antibiotics, administered either before skin incision or after cord clamping, had no effect on neonatal outcomes following cesarean section.<sup>4,5,7-9,12</sup> Further study regarding neonatal outcomes was recommended.<sup>2,3</sup>

### *Antibiotic Resistance*

Little information was identified regarding antibiotic resistance. Methicillin-resistant *Staphylococcus aureus* was the most common organism found in maternal wound infections in one study<sup>10</sup> and further study was recommended by the authors of that study, as well as the authors of one of the included systematic reviews.<sup>3</sup>

Further detail regarding the included studies is provided in Table 1.

**Table 1: Summary of Included Studies**

Author, Date	Study Objectives	Results	Conclusions
<i>Systematic Reviews and Meta-Analyses</i>			
Baaqeel & Baaqeel, 2012 <sup>1</sup>	Compare the rates of maternal and neonatal infections when antibiotics are administered either preoperatively or after cord clamping.	Pre-operative administration was associated with a 41% reduction in endometritis compared to administration after cord clamping. There were non-significant reductions: in wound infections, maternal febrile morbidity, neonatal sepsis, and NICU admission.	Pre-operative administration of antibiotics significantly reduced the rate of endometritis following c-section. There was limited power to detect neonatal events.
Smaill & Gyte, 2010 <sup>2</sup>	Assess the effects of antibiotics versus no antibiotic prophylaxis on infectious morbidity in women undergoing c-section.	Antibiotic prophylaxis resulted in substantial reductions in fevers, wound infections, endometritis, serious infections, and infection-related complications. There were no reports of neonatal complications, however thrush was not assessed. Results were similar for administration before or after cord clamping.	Antibiotic prophylaxis for women undergoing c-section was found to be beneficial for maternal health, however there was no certainty regarding neonatal events.
Tita et al., 2009 <sup>3</sup>	To examine different strategies for antibiotic prophylaxis for the prevention of infections in women undergoing c-section.	The use of pre-operative cefazolin administration and the use of extended spectrum antibiotics (with azithromycin or metronidazole) after cord clamping resulted in up to a 50% reduction in maternal infections. Studies comparing the two strategies were not identified.	Both antibiotic regimens were found to be effective in reducing maternal infections. Future studies examining neonatal outcomes and antibiotic resistance were suggested.
Constantine et al., 2008 <sup>4</sup>	To examine the effects of timing of antibiotic prophylaxis during c-section.	Pre-operative administration of antibiotics significantly reduced the risk of post-partum endometritis and the total number of maternal infections. There was a trend toward lower incidence of wound infections. Pre-operative administration had no effect on neonatal sepsis (suspected or confirmed) or on admissions to the NICU.	Antibiotic administration prior to incision resulted in lower risk of endometritis and infections without having negative neonatal outcomes.
<i>Randomized Controlled Trials</i>			
Macones et al., 2012 <sup>5</sup>	To compare the effects of antibiotics administered either prior to incision or after cord clamping on both maternal and neonatal health.	The timing of antibiotic administration resulted in no difference in a composite of maternal infectious morbidity (postoperative fever, wound infection, endomyometritis, urinary tract infection). Neonatal outcomes were similar in both groups.	The authors concluded that both pre-operative and post-clamping administration of antibiotics were reasonable regimens for the prevention of post-c-section complications.
Witt et al., 2011 <sup>6</sup>	To compare the effectiveness of cefazolin administered pre-	There were no statistically significant differences between pre-operative administration and post-clamping administration in maternal infectious	Authors concluded that while the timing of cefazolin administration was not important,

**Table 1: Summary of Included Studies**

Author, Date	Study Objectives	Results	Conclusions
	operatively, post-clamping, or placebo for the prevention of post-c-section complications	morbidity following elective c-section.	antibiotics were more effective than placebo at preventing infectious morbidity following elective c-section.
Nokiani et al., 2009 <sup>7</sup>	To compare the effectiveness of cefazolin administered pre-operatively or post-clamping for the prevention of post-c-section complications.	There were no significant differences between the two groups with respect to neonatal complications.	Authors recommended that for elective c-section, cefazolin should be used after clamping but that for non-elective c-sections, it should be used prior to incision.
Yildirim et al., 2009 <sup>8</sup>	To determine whether the timing of antibiotic prophylaxis has an effect on maternal and neonatal outcomes following c-section.	There were no significant differences found between groups regarding total infectious morbidity or endometritis and no increases in neonatal sepsis, sepsis workup, need for neonatal intensive care, or intensive care stay.	Authors concluded that the timing of antibiotic prophylaxis did not affect maternal or neonatal outcomes.
<i>Non-Randomized Studies</i>			
Brown et al., 2013 <sup>9</sup>	To evaluate the differences in post-c-section complications before and after a policy change regarding the timing of antibiotic prophylaxis.	There rates of post-c-section complications dropped from 10.8% to 2.8% in the year following the policy change from antibiotic administration after cord clamping, to administration prior to incision, with no difference in adverse events on neonates.	Authors concluded that antibiotics should be given prior to incision in Australia and New Zealand.
Thurman et al., 2010 <sup>10</sup>	To compare post-c-section infection rates before and after the implementation of a preoperative antibiotic administration policy.	After the policy implementation, the rates of post-c-section infectious complications decreased from 20.7% to 8.5%. MRSA was the most common organism present in wound infections.	Authors recommended further study regarding optimal antibiotic regimens and antibiotic resistance.
Dinsmoor et al., 2009 <sup>11</sup>	To examine the efficacy of antibiotic administration in non-labouring women undergoing c-section.	Antibiotic administration was associated with lower rates of endometritis (2.0% vs. 2.6%) and wound infection (0.52% vs. 0.96%) versus no antibiotics.	Authors concluded that antibiotic administration significantly reduced the rates of endometritis and wound infections in non-labouring women undergoing c-section.
Owens et al., 2009 <sup>12</sup>	To examine the effects of a change in the timing of antibiotic administration for the prevention of post-c-section complications.	Pre-incision administration resulted in lower rates of endometritis (2.2% vs. 3.9%) and wound infection (2.5% vs. 3.6%) compared with administration following cord clamping without having any negative effects on neonatal infection rates or health.	Authors concluded that antibiotic administration should occur prior to skin incision.
Kaimal et al., 2008 <sup>13</sup>	To examine the effect of a policy change in	SSI rates fell from 6.4% (post-cord clamp administration) to 2.5% (pre-	Authors concluded that antibiotic administration

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Author, Date	Study Objectives	Results	Conclusions
	the timing of antibiotic prophylaxis for the prevention of post-c-section SSIs.	incision administration). There was also a decrease in the rates of endometritis and a trend toward decreased cellulitis.	prior to c-section incision lead to a significant decrease in SSIs.

c-section = cesarean section; MRSA = methicillin-resistant *Staphylococcus aureus*; NICU = neonatal intensive care unit; SSI = surgical site infections; vs = versus

## REFERENCES SUMMARIZED

### Health Technology Assessments

No literature identified.

### Systematic Reviews and Meta-analyses

1. Baaqeel H, Baaqeel R. Timing of administration of prophylactic antibiotics for caesarean section: a systematic review and meta-analysis. BJOG. 2012 Nov 6. [Epub ahead of print] [PubMed: PM23126271](#)
2. Smaill FM, Gyte GM. Antibiotic prophylaxis versus no prophylaxis for preventing infection after cesarean section. Cochrane Database Syst Rev. 2010;(1):CD007482. [PubMed: PM20091635](#)
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### Randomized Controlled Trials

5. Macones GA, Cleary KL, Parry S, Stamilio DM, Cahill AG, Odibo AO, et al. The timing of antibiotics at cesarean: a randomized controlled trial. Am J Perinatol. 2012 Apr;29(4):273-6. [PubMed: PM22135154](#)
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### Non-Randomized Studies

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[PubMed: PM23102816](#)
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[PubMed: PM20627452](#)
11. Dinsmoor MJ, Gilbert S, Landon MB, Rouse DJ, Spong CY, Varner MW, et al. Perioperative antibiotic prophylaxis for nonlaboring cesarean delivery. *Obstet Gynecol* [Internet]. 2009 Oct [cited 2013 Jan 29];114(4):752-6. Available from:  
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2863989>
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[PubMed: PM19701037](#)
13. Kaimal AJ, Zlatnik MG, Cheng YW, Thiet MP, Connatty E, Creedy P, et al. Effect of a change in policy regarding the timing of prophylactic antibiotics on the rate of postcesarean delivery surgical-site infections. *Am J Obstet Gynecol.* 2008 Sep;199(3):310-5.  
[PubMed: PM18771995](#)

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**APPENDIX – FURTHER INFORMATION:**

**Guidelines and Recommendations**

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**Surveys of Clinical Practice**

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