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Title	Risk factors for surgical site infection following Caesarean section: a retrospective cohort study
Authors	Felicia Ketcheson MSc, Christy Woolcott PhD, Victoria Allen MD, Joanne M. Langley MD
Reviewer 1	R.K. Morris
Institution	Obstetrics & Gynaecology, University of Birmingham
General comments (author response in bold)	1. This should include a description of the cohorts population i.e., North America **We have added to the Methods section: "This study took place in the Canadian province of Nova Scotia" (line 57).** 2. The data for the CS SSI rate in USA is 10 years old, more up to date data is available. **We have updated our reference (line 32).** 3. Reference 8 is quoted to show a BMI and SSI relationship yet does not attempt to explain why the SSI are so greatly different with a 10x higher rate in the Wloch paper. **Discussion on the reason for this difference has been added to the interpretation section: "For example, Wloch et al. found a considerably higher SSI rate than the current paper possibly due to higher prevalence of comorbidities such as diabetes and active follow-up" (lines 176-177).** 4. Need more details of the background health of Nova Scotia to determine why the rate is at the lower end of the rates quoted in the literature. Social deprivation? IMD? **Added to the interpretation section: "While we do not know why Nova Scotia rates are at the lower end of this range, contributing factors could be universal access to healthcare, standardized antibiotic administration prior to C/S, and the salutary effect of a provincial reproductive care program that sets quality standards and provides education to all obstetric healthcare providers." (lines 169-172)** 5. For international readers more explanation of "Women with a provincial health card" as the population needs expansion **This has been clarified in the Methods: "In Nova Scotia, everyone is eligible for a health card if they can provide proof of citizenship or immigration." (lines 65-66)** 6. Antibiotics at CS – procedure and which antibiotics **Unfortunately, we are unable to distinguish whether non-GBS antibiotics were for perioperative prophylaxis or for other reasons (e.g. treatment) in the dataset available to us. We have added this clarification in the Results section: "We were unable to distinguish between these indications in the data available. From 2003-2012, we were able to determine that the indication was Group B Streptococcus in 8.2% of women receiving antibiotics." (lines 136-139)** 7. Skin preparation – betadine or chlorohexidine **Chlorhexidine use began partway through the study period and is mentioned in in the interpretation section :"Possible reasons for these temporal trends include quality improvement interventions such as surgical checklists, use of 2% chlorhexidine skin antisepsis..." (lines 180-181).** 8. Dressing – standard dressing, specialist dressing (negative pressure) **We were unable to obtain dressing type from the database.** 9. Other techniques employed to reduce the SSI rate should be discussed. **Added. Please see lines 180-185.** 10. It involved the linkage of a number of databases but all of these relied on the use of ICD 10 codes of either diagnosis at discharge or billing codes for treatment at a physicians office post discharge and linkage with a perinatal database that included records of SSI clinically diagnosed pre-discharge. There are two issues when using databases in this way – how accurate are the records in that those recorded as having an SSI actually had one (i.e. PPV) SSI and how many cases of infection might be missed by using these records i.e. those that had CS and no episode recorded prior to discharge or at physicians office (i.e. NPV). The authors quote a study by Daneman et al 2011 (ref 18) that validate d population-based hospital, emergency room, and physician claim databases for the detection of surgical site infections against the reference standard of clinical surveillance and quotes the sensitivity for detection of SDSI as 77.3%. Daneman et al however conclude that "...although these data sets are highly specific and could be used to define research cohorts, their low sensitivity and positive predictive value make them inadequate for use as quality indicators." This requires further discussion as a limitation. **This limitation has been expanded upon (lines 217-222).** 11. The authors then quote a systematic review by Goto et al 2014 (ref 19) to show that the risk of misclassification of SSI

	is low. This SR is out of date and has been replaced by BMJ Open. 2015 Aug 27;5(8):e008424. doi: 10.1136/bmjopen-2015-008424. "Accuracy of administrative data for surveillance of healthcare-associated infections: a systematic review." van Mourik MS1, van Duijn PJ2, Moons KG2, Bonten MJ3, Lee GM4. This highlights the variable accuracy of administrative databases and in particular the poor PPV. **Thank you for the reference. It has been updated (lines 219-222) alongside with more discussion of the advantages and disadvantages of using administrative data (lines 230-236).** 11. The statistical methods are appropriate. The authors mention missing data but do not say why they did not consider multiple imputation for the missing data? **We did not consider multiple imputation due to our large sample size. Estimates from analyses using five datasets with missing values imputed using chained equations were very similar. See lines 119-122 in the Methods section: "We did not use multiple imputation for our primary analyses due to the large size of our dataset. Estimates from analyses using five datasets with missing values imputed with chained equations were very similar to those shown herein."** 12. It is very interesting that the rate decreased from 5.2% in 1997 to 2.0% in 2012 this appears slightly incongruous as BMI and diabetes has increased in this time. Therefore, attempts to explain the change in rate need to be discussed. This should include standardisation of the CS procedure and the guidelines at the lead maternity unit where over 50% of the procedures are performed. **Added to the interpretation section - see lines 180-185** 13. Needs to better explain the low rate the sentences on page 11 line 32 is not sufficient. With much more information of the practices within the local maternity units. More discussion of the individual risk factors and how they are mitigated for in current practice. **Reasons for the low rate, in comparison to the review that is mentioned, have been added: "For example, Wloch et al. found a considerably higher SSI rate than the current paper possibly due to higher prevalence of comorbidities such as diabetes and active follow-up" (lines 176-177). . Due to word limits, there is not enough space to allow for further discussion on individual risk factors (lines 188-199).** 14. The section on limitations of the use of retrospective databases and their sensitivity and specificity needs expanding as discussed above. **Expanded as suggested (lines 217-223).**
Reviewer 2	Dana Sumilo
Institution	Institute of Applied Health Research, University of Birmingham
General comments (author response in bold)	1. In the introduction (page 4, para 2), the authors mention some of the risk factors that have been studied, but are there other risk factors that have been identified previously? **There have been other risk factors identified previously. However, due to word limits we are unable to review these comprehensively.** 2. In the introduction, it would be beneficial to emphasise the research gaps and what this study aims to add to the current body of knowledge. **Research gaps have been added to lines 45-48: "There are several gaps in the literature: 1) few studies examine SSI to 30 days, 2) many potential risk factors have been poorly studied or not studied including hospital size, anticoagulation therapy, and smoking, and 3) no study has examined whether risk factors significantly differ based on time of SSI presentation."** 3. There seem to be some errors/ inconsistencies in the way the results are presented. E.g. only 37% had antibiotic therapy according to Tables 2 and 3, contradicting data in Appendix 1 where the majority had antibiotic 'prophylaxis'. **Thank you for noticing this. The numbers for antibiotic prophylaxis 'yes' and 'no' were erroneously switched in Tables 2 and 3. This has been fixed as has the terminology in Appendix 1 to also say antibiotic 'therapy'.** 4. The discussion of the significant findings is slightly selective and would benefit from further comparison with the literature and interpretation in the light of Canadian healthcare policies. **Please see lines 88-199 for comparison with the literature.** 5. Abstract: it needs to be clarified what the SSI rate of 2.72% is (e.g. is it the average annual incidence (p3, lines 27-29))? **2.72% represents the 16-year average incidence. This has been clarified in line 11 "The 16-year SSI rate of 2.72%..."** 6. Abstract: The last sentence of the results paragraph is not clear (p3, lines 37-44). **This sentence has been clarified as follows (lines 15-19): "Women delivering earlier in the study period, and in a hospital with 130-1249 C/S deliveries per year, were at a significantly higher risk of SSI pre-discharge; and women who smoked, had a C/S during first stage of labour, and multiple gestations were at a**

	significantly higher risk of SSI post-discharge." 7. Abstract: P3, lines 36-37: did you mean 130-1249 instead of 130-949 C/Ss? **Yes, we did. Corrected (line 16).** 8. Abstract: Interpretation (p3, lines 46-51) of the results is very generic and does not include interpretation of the results for all of the aims of the study. **Interpretation has been expanded to be less generic and include the third objective : "Most risk factors are known pre-delivery (e.g. pre-pregnancy weight) and some are potentially modifiable (e.g. weight gain). Several risk factors differ between pre- and post-discharge SSI. While the rate of SSI has decreased, the rate of C/S warrants attention to preventive interventions to reduce the burden of illness associated with SSI." (lines 20-23).** 9. It would be good to explain if all women have a Nova Scotia health card (or if there are any exceptions) to readers not familiar with the Canadian health system (p 6, para 2). **Clarification added (see response to Reviewer 1, #5).** 10. What is the rationale for studying the births between 1997-2012? Were more recent data (2013 onwards) not available? **These years were chosen as the physician billings database only recorded one diagnostic code pre-1997 and the discharge and physician billings databases hadn't been linked from 2013 onwards.** This explanation has not been added to the manuscript. 11. It is not entirely clear what is meant by a physician's office (p7, para 1) – does this database capture both outpatient consultations and consultations in primary care? **By physician's office we mean any physician, including family doctors, obstetricians, and nurse practitioners. This has been clarified in lines 81-82: "to capture insured service encounters rendered by a physician"** 12. Potential sources of biases are not discussed in the methods section. **A discussion including reference to literature on validation of administrative claims databases to detect health care associated infections and risk of misclassification has been added to the discussion under limitations. XX.** 13. Table 1 (p18): overall very few variables appear to have missing data >5%; it might be helpful to explain a bit more about how data is collected in NSAPD and comment on its completeness. **Additional information on the NSAPD has been added "The NSAPD is regularly analyzed for accuracy and reliability." (lines 72-73).** 14. Reconsider the use of the term incidence 'rate' given the denominator used to calculate % **We have changed the term 'incidence' to 'incidence rate' throughout the manuscript.** 15. Variables and tables: consider grouping the variables in categories (e.g. maternal characteristics, pregnancy etc.) to guide the reader. Are all the variables listed in Table 1 potential risk factors for SSI? **Thank you for the suggestion. All tables have been categorized. Many of the potential risk factors in Table 1 have been studied in the literature previously. Others had not and were studied as to determine whether they are risk factors and if they should be examined in future research.** 16. Perhaps it is implied that the same principles were used, but how were the variables selected for examining the risk factors for pre-and-discharge SSI (p8, para 2)? **The following is now provided in the methods : "A number of potential risk factors for SSI were examined based on literature review and variables available in the NSAPD (see Table 1)."(lines 95-96)** 17. The tables only include the adjusted estimates, but do not show the unadjusted ORs. **We had opted to show only adjusted ORs to minimize the size of our tables. All unadjusted estimates have been included in online appendices.** 18. Neighbourhood level income quintiles: it would be interesting to see the results separately also for quintiles 2-5. **The odds of SSI were significantly different among women in quintiles 1 and 2 but not for quintiles 3-5. As such, we have added an additional category for quintile 2.** 19. Smoking during pregnancy: if data are available, it would be interesting to see separately the results for women who

	did not quit smoking during pregnancy. **We agree that this would be interesting. However, smoking was not always recorded at each timepoint by health care providers and we opted to combine them as one variable to represent any smoking in pregnancy.** 20. Weight gain during pregnancy: 10-30 kg is a very broad category; consider splitting. **The 10-30 kg category has been split into 10-19.9 kg and 20-29.9 kg.** 21. Table 2 and Appendix 1 refer to 'antibiotic therapy' and 'antibiotic prophylaxis' respectively; it would be good to have consistency throughout the paper where appropriate. Do the authors mean antibiotic therapy at any time during pregnancy or only around the time of delivery? **Appendix 1 has been changed to 'antibiotic therapy' as have all instances thereof within the manuscript. Antibiotic therapy was for that during labour and delivery, which has been clarified in Appendix 1 and Tables 1 - 3. We were unable to distinguish between antibiotic 'therapy' and antibiotic 'prophylaxis' (e.g. for group B streptococcus or for surgical prophylaxis, as it is not labelled as such in the database.). This has been added in the Results: "We were unable to distinguish between these indications in the data available. From 2003-2012, we were able to determine that the indication was Group B Streptococcus in 8.2% of women receiving antibiotics." (136-139).** 22. Information regarding any changes in antibiotic prophylaxis policy (including timing and composition) over the period of the study would be helpful. **Information on antibiotic guidelines has been added to the Interpretation section: "...increased administration of appropriate prophylactic antibiotics following published guidelines by the CDC in 1999 (21), American College of Obstetricians and Gynecologists in 2003 (22), and Canadian Society of Obstetricians and Gynaecologists in 2010 (10)." (lines 182-185).** 23. In the methods section (p5, para 1), it is stated that 'approximately half of deliveries are performed at the regional and tertiary care centre based in the capital city', but in the tables ¾ of Caesarean sections appear to be in hospitals with fewer than 1,250 sections per year? **The total number of deliveries in Nova Scotia is low (approximately 8000-9000 annually). Therefore, low 'number of C/S per hospital per year' is not unexpected.** 24. In the interpretation section (p11) it is stated that a higher % of SSIs presented post-discharge but there is no discussion regarding changes in the incidence of post-discharge SSIs over time and possible explanation. **Added to the Interpretation section line 161-162 and 180-185.** 25. There is no discussion in the interpretation section regarding some of the statistically significant variables e.g. the number of caesarean sections per hospital. **We would ideally like to comment on all the statistically significant variables; however, we are unable to due to the word limit. Full results will be communicated to the Nova Scotia Reproductive Care Program which aims to standardize and improve care across the province.**