A Report on "Risk of infection and wound dehiscence after use of prophylactic antibiotics in episiotomy or second degree tear (REPAIR study): single centre, double blind, placebo controlled randomised trial" by Perslev et al. (2025)

Reviewer 2

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> I am wiser than this person; for it is likely that neither of us knows anything fine and good, but he thinks he knows something when he does not know it, whereas I, just as I do not know, do not think I know, either. I seem, then, to be wiser than him in this small way, at least: that what I do not know, I do not think I know, either.
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> Plato, *The Apology of Socrates*, 21d

> To err is human. All human knowledge is fallible and therefore uncertain. It follows that we must distinguish sharply between truth and certainty. That to err is human means not only that we must constantly struggle against error, but also that, even when we have taken the greatest care, we cannot be completely certain that we have not made a mistake.
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> Karl Popper, 'Knowledge and the Shaping of Reality'

Overview

Citation: Perslev, K., Klarskov, N., Bergholt, T., & Jangö, H. (2025). Risk of Infection and Wound Dehiscence After Use of Prophylactic Antibiotics in Episiotomy or Second Degree Tear (REPAIR Study): Single Centre, Double Blind, Placebo Controlled Randomised Trial. *BMJ*, Vol. 391, e084312.

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Abstract Summary: This study aimed to evaluate the effect of prophylactic antibiotics on the risk of wound complications after episiotomy or second-degree tear. The findings suggest that while there was no significant effect on overall wound complications, prophylactic antibiotics significantly reduced the risk of clinically relevant wound complications.

Key Methodology: Single-center, double-blind, placebo-controlled randomized trial.

Research Question: What is the effect of prophylactic antibiotics on the risk of wound complications after episiotomy or second-degree tear?

Summary

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Perslev et al. present the REPAIR study, a single-center, double-blind, placebo-controlled randomized trial evaluating the use of prophylactic antibiotics for women with episiotomies or second-degree tears. The authors claim that a short course of oral amoxicillin-clavulanic acid significantly reduces the risk of "clinically relevant wound complications" (p. 1). Based on this finding, they conclude that prophylactic antibiotics should be considered in routine postpartum care and provide evidence to support updating clinical guidelines. They also highlight exploratory findings suggesting the treatment is effective even in low-risk populations, such as women with a body mass index under 30, those who had non-instrumental deliveries, or those with spontaneous tears (pp. 1, 6).

While the trial addresses an important gap in postpartum care, its headline claims are significantly overstated due to outcome switching and subjective measurement. The study actually failed to find a statistically significant reduction in its pre-specified primary outcome, which was the overall rate of wound complications defined by a strict measurement of dehiscence exceeding 5 mm or the presence of infection characterized by purulent discharge or abscess (p. 2). The overall complication rate was 22% in the antibiotic group versus 29% in the placebo group, yielding a non-significant p-value of 0.10 (p. 1).

Despite this primary failure, the authors elevate a secondary outcome—clinically relevant wound complications—to the status of their main finding. This secondary outcome was significantly reduced in the treatment group, occurring in 9% of the antibiotic group versus 17% of the placebo group (p. 1). However, relying on a secondary outcome after a primary outcome fails is a recognized form of spin that distorts the strength of the evidence. This is particularly problematic because the

trial was not prospectively powered to detect a difference in this secondary measure; a post-hoc calculation specifically for this outcome revealed a power of only 71%, which falls below the conventional threshold for an adequately powered study (p. 5).

Furthermore, the definition of this successful secondary outcome introduces a high degree of subjectivity. Unlike the primary outcome's strict 5 mm cut-off for dehiscence, clinically relevant wound complications were assessed based on clinical evaluations without strict thresholds. While the authors did provide guidelines—such as dehiscence "typically ≥10 mm" or a visual analog scale pain score "typically ≥5"—they explicitly state there was "no strict cut-off value" (p. 2). This reliance on "typical" presentations rather than rigid criteria makes the outcome vulnerable to observer bias. This vulnerability is compounded by the fact that the study did not formally assess the integrity of its double-blind design. While the authors employed robust allocation concealment procedures (p. 3), they did not ask participants or investigators to guess their allocation at the end of the trial. Consequently, it remains unknown whether the blinding was compromised by the known gastrointestinal side effects of the antibiotics.

The authors also present several exploratory and subgroup analyses, claiming consistent benefits in low-risk populations and improved self-evaluated health (p. 6). However, these analyses were not adjusted for multiple comparisons, increasing the risk that the statistically significant findings within these subgroups are merely chance artifacts. Additionally, the study lacks crucial microbiological context, providing no data on the specific pathogens responsible for the infections or the local antibiotic resistance patterns. While the authors note that the hospital follows a strict screening protocol for group B streptococcus (p. 2), the absence of specific pathogen data severely limits the generalizability of the results to other hospital settings where resistance patterns may differ.

Ultimately, the recommendation to update postpartum care guidelines is premature.

Recommending widespread prophylactic antibiotic use based on a single-center trial that failed its primary objective and relies on an underpowered, subjectively measured secondary outcome risks encouraging antibiotic overuse without robust evidence of clinical benefit.

The Bottom Line

The REPAIR study claims that prophylactic antibiotics significantly reduce clinically relevant wound complications after common obstetric tears, suggesting a need to update postpartum care guidelines. However, this conclusion relies entirely on a subjectively defined secondary outcome, as the trial failed to demonstrate a statistically significant benefit for its pre-specified primary outcome. Given the single-center design, the lack of statistical power for the highlighted finding, and the absence of microbiological data, the evidence is not robust enough to support widespread changes to clinical practice or antibiotic prescribing guidelines.

Potential Issues

Outcome reporting and interpretation: The study's main positive conclusion is based on a secondary outcome, while the pre-specified primary outcome was not statistically significant. The trial failed to show a significant effect for its primary outcome of "overall wound complications" (22% in the antibiotic group vs. 29% in the placebo group; $p = 0.10$). Despite this, the abstract, the "What This Study Adds" box, and the conclusion all prominently feature the statistically significant finding for the secondary outcome, "clinically relevant wound complications" (9% vs. 17%; $p = 0.01$) (pp. 1, 5). While the authors do transparently report the non-significant primary finding in the abstract (p. 1), the framing of the conclusion and recommendations around the secondary outcome may mislead readers about the overall strength of the evidence. Elevating a secondary outcome to the main takeaway after the primary outcome fails to reach statistical significance is a form of "spin" that can distort the interpretation of trial results.

Subjectivity of the main outcome measure: The study's only statistically significant main finding relies on a secondary outcome that is defined with considerable subjectivity. The outcome, "clinically relevant wound complications," was assessed based on a "clinical evaluation with no strict cut-off value." Although the authors provided guidelines—such as the extent of dehiscence ("typically ≥10 mm") or severity of pain ("typically visual analogue scale score ≥5")—the use of ambiguous terms like "typically" and the explicit lack of a strict cutoff introduce a high potential for observer bias (p. 2). This is a significant concern for the study's internal validity, particularly because the more objective, pre-specified primary outcome (defined by a strict dehiscence measurement of >5 mm or infection) was not statistically significant. The authors acknowledge this issue, stating the subjective definition was due to a "lack of support in the literature," and describe steps to align investigator judgment, but this does not fully neutralize the risk of bias (p. 2).

Lack of detail on the clinical significance of prevented events: The article does not provide sufficient detail to assess the practical importance of the complications prevented by the intervention. The main positive finding is a reduction in a composite outcome, "clinically relevant wound complications," which was triggered by large dehiscence, severe pain, or infection (p. 2). While some data on the individual components are available elsewhere in the article, such as the overall infection rate (p. 5), a clear breakdown of the specific events that constituted the 55 cases of this composite outcome is not provided. It is therefore unclear whether the treatment effect was driven primarily by a reduction in infections, large dehiscences, or patient-reported pain. Furthermore, while the outcome was defined as requiring "clinical follow-up," the article does not specify the nature or severity of this follow-up (e.g., outpatient visit, re-suturing, hospitalization). This omission makes it difficult to interpret the clinical value of the reported Number Needed to Treat of 12 (p. 5).

Potential for compromised blinding: The study's double-blind design may have been weakened by the failure to formally assess its effectiveness. The manuscript does not report any assessment of blinding integrity, such as asking participants or investigators to guess treatment allocation at the end of the trial. While the authors describe a procedure where a non-study provider repackaged tablets to conceal allocation (p. 3), this does not guarantee that blinding was maintained given the known gastrointestinal side effects of amoxicillin-clavulanate. This is a methodological weakness, particularly given the subjective nature of the secondary outcome that produced the positive result.

Reliance on an underpowered secondary analysis: The trial was not prospectively powered to detect a difference in its key secondary outcome, "clinically relevant wound complications," which forms the basis of the article's main conclusion. The sample size calculation was based on the primary outcome (p. 3). The authors report a post-hoc power calculation specifically for this secondary outcome of 71%, which is below the conventional 80% threshold for an adequately powered study (p. 5).

While the authors did conduct an interim analysis to monitor the overall complication rate (p. 3), drawing firm conclusions from a statistically significant result in an analysis the trial was not originally designed for carries a higher risk of being a chance finding (Type I error) or an overestimation of the true effect size.

Overstatement of exploratory and subgroup analyses: The study presents findings from post-hoc subgroup and exploratory analyses in a way that may overstate their evidentiary value. The authors report a "consistently significant effect" in three low-risk subgroups (BMI <30, spontaneous tear, non-instrumental delivery) without performing a formal statistical test for interaction to compare the effect between subgroups or adjusting for multiple comparisons (pp. 6, S4). Similarly, several exploratory outcomes are reported as statistically significant in the abstract and results tables without adjustment for multiple testing (pp. 1, 6). The authors acknowledge in the discussion that these results "should be interpreted cautiously because of a lack of prespecification... and lack of multiple testing" (p. 6). However, presenting these potentially fragile findings prominently in the abstract and "What This Study Adds" box without sufficient caveats may give a misleading impression of their robustness.

Potential over-extrapolation of recommendations: The study's recommendations may be stronger than what the evidence can support. The authors conclude that their findings "provide evidence to support updating postpartum care guidelines" and that antibiotics "should be considered in postpartum care" (p. 1). These recommendations are based on short-term outcomes (4–14 days) from a single university hospital in Denmark that excluded non-Danish speakers (pp. 1, 2). The authors transparently acknowledge these limitations, noting that generalizability may be limited and that long-term follow-up data is not yet available (p. 6). However, there appears to be a mismatch between these acknowledged limitations and the strength of the recommendations for widespread changes in clinical practice.

Absence of microbiological context: For a trial investigating prophylactic antibi-

otics, the article provides no microbiological data. It does not report on the specific pathogens responsible for the observed wound infections or the local antibiotic resistance patterns at the study hospital. While the authors explain that the hospital follows a strict screening protocol for group B streptococcus and excluded women receiving intrapartum antibiotics (pp. 2, 6), the lack of specific pathogen data limits the applicability of the results. Clinicians in other settings cannot determine if the chosen antibiotic, amoxicillin-clavulanate, is appropriate for their local context or if the results would hold in populations with different resistance profiles.

Minor reporting and transparency issues: Several minor issues related to presentation and transparency are present in the manuscript. First, the CONSORT flow diagram contains a minor discrepancy; the itemized reasons for exclusion sum to 701, while the stated total is 702, likely due to a single patient misclassification or rounding error (p. 4). Second, the rationale provided for the decision to continue the trial after an interim analysis is convoluted, shifting between different outcomes and expected event rates (pp. 3, 5). Finally, the "Data sharing" section states that the analysis code "can be found in the supplemental files," but no code is visible in the provided supplementary documents (Supplementary Files 1–5); it is uncertain whether this is an error or if the code is available as a separate digital file not included in the reviewed PDF (p. 7).

Future Research

Objective outcome measures: Future trials should establish and power studies based on strictly defined, objective criteria for clinically relevant wound complications. Relying on clinical evaluations that lack strict cut-offs introduces observer bias, so developing standardized, measurable endpoints is essential for producing reliable evidence.

Multicenter trials with microbiological profiling: To support broad guideline changes regarding antibiotic prophylaxis, future research must be conducted across multiple centers and include detailed microbiological data. Understanding local pathogen profiles and antibiotic resistance patterns is necessary to determine if the findings are generalizable beyond a single hospital setting.

Validation in low-risk populations: The exploratory findings suggesting benefits in low-risk subgroups, such as women with spontaneous tears and a low body mass index, require validation. Future trials should be specifically powered to detect differences in these populations and utilize appropriate statistical adjustments for multiple comparisons to ensure the observed effects are not chance findings.

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