# 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

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**Cite this as:** *BMJ* 2025;391:e084312
http://dx.doi.org/10.1136/bmj-2025-084312

**Accepted:** 15 August 2025

## ABSTRACT

### OBJECTIVE

To evaluate the effect of prophylactic antibiotics on the risk of wound complications after episiotomy or second degree tear.

### DESIGN

Single centre, double blind, placebo controlled randomised trial.

### SETTING

One university hospital in the Capital Region of Denmark. Participants were enrolled between March and December 2023. All initial clinical consultations were conducted between March 2023 and January 2024, and all long term follow-up consultations were conducted between March and November 2024. This article reports only data from the first consultation.

### PARTICIPANTS

442 women with episiotomies or second degree tears were consecutively recruited at delivery. Exclusion criteria included treatment allergy (or risk of cross reactivity with related antibiotics), antibiotic use within 24 hours of delivery, non-Danish speakers, caesarean section, or episiotomy extension.

### INTERVENTION

A computer generated program randomised participants to either three doses of amoxicillin (500 mg) with clavulanic acid (125 mg) or placebo starting within six hours post partum and repeated at eight hour intervals. Follow-up was conducted four to 14 days post partum. Physicians, the steering committee, and participants were blinded.

### MAIN OUTCOME MEASURES

Wound complications (primary outcome) and clinically relevant wound complications (secondary outcome).

### RESULTS

The study ended as planned, in December 2024. 433 women completed follow-up and were included in the primary analysis. No significant difference was observed in overall wound complications (antibiotic 47/218, 22%; placebo 62/215, 29%; P=0.10), with a risk difference of −7.2% (95% confidence interval (CI) −15.4% to 0.8%) and a relative risk of 0.75 (0.54 to 1.04). For clinically relevant wound complications, significantly fewer events occurred in the treatment group (19/218, 9% *v* 36/215, 17%; P=0.01), with a risk difference of −8.0% (95% CI −14.3% to −1.8%) and a relative risk of 0.52 (0.31 to 0.88). For clinically relevant wound complications, the number needed to treat was 12 (95% CI 7 to 56). Exploratory outcomes show that the treatment group reported better self-evaluated health, received fewer additional antibiotic treatments, and had smaller average wound dehiscence among patients with dehiscence. No serious adverse reactions occurred.

### CONCLUSION

Although no significant effect was seen for overall wound complications, prophylactic antibiotics significantly reduced the risk of clinically relevant wound complications in women with episiotomies and second degree tears and should be considered in postpartum care.

### TRIAL REGISTRATION

Clinical Trials Information System (euclinicaltrials.eu) 2022-501930-49-00 and ClinicalTrials.gov NCT05830162.

## WHAT IS ALREADY KNOWN ON THIS TOPIC

Knowledge about wound complications in women with second degree tears is limited

Use of prophylactic antibiotics in instrumental deliveries is recommended by the World Health Organization, based on evidence suggesting a reduction in infection including wound complications

## WHAT THIS STUDY ADDS

This study demonstrates that oral prophylactic antibiotics significantly reduce the risk of clinically relevant wound complications in women with episiotomy or second degree tear

The protective effect of prophylactic antibiotics is also significant in low risk populations (eg, body mass index <30, non-instrumental delivery, no episiotomy)

The findings provide evidence to support updating postpartum care guidelines to reduce the risk of clinically relevant wound complications for women with episiotomy or second degree tear

## Introduction

Obstetric tears after vaginal delivery are common and affect millions of women annually across the globe. Prevention and treatment of complications relating to healing are not thoroughly investigated, and incidence varies substantially across studies (0.1% to 25%).[1] A Cochrane review evaluated prophylactic antibiotics for obstetric anal sphincter injury,[2] but included only one randomised controlled trial, which reported a reduction in healing complications from 24% to 8% following a single intravenous dose of antibiotics.[3] The loss to follow-up was high, prompting the authors to recommend cautious data interpretation. Even less data are available on the effect of prophylactic antibiotics after the most common obstetric tears: episiotomies and second degree tears. A 2017 Cochrane review evaluated antibiotic use after episiotomy[4] but included only one study with methodological limitations.[5] The

review concluded that evidence was not sufficient to recommend prophylactic antibiotic use. No Cochrane review on antibiotic use for second degree tears currently exists.

Since the 2017 Cochrane review,[4] a few original studies have been published. Two randomised controlled trials from India found no protective effect from a prophylactic antibiotic treatment lasting five days.[6 7] One trial did not define wound dehiscence,[6] and the other trial was not placebo controlled.[7] Both studies had very low infection numbers. A recent Turkish study found that rifampicin irrigation reduced infections after episiotomy but did not describe allocation of patients to the intervention or the placebo.[8] The ANODE trial, a large multicentre randomised controlled trial, reported that a single dose of intravenous antibiotics reduced wound infection or wound dehiscence (or both) in instrumental deliveries.[9] Accordingly, the World Health Organization (WHO) now recommends this treatment.[10] The primary outcome of the ANODE trial was suspected maternal infection based on records, questionnaires, and telephone interviews conducted six weeks post partum, without scheduled clinical consultation. A recent systematic review discussed whether the effect of antibiotics seen in the ANODE trial was driven by the large number of obstetric tears in the individuals in the trial rather than mode of delivery.[11]

The REPAIR study evaluated whether three doses of prophylactic oral amoxicillin (500 mg) and clavulanic acid (125 mg) during the first day post partum could reduce wound dehiscence or infection (or both) following episiotomy or second degree tear regardless of mode of vaginal delivery.

## Methods

### Study design

The REPAIR study was a double blind, parallel, placebo controlled randomised trial investigating the effect of prophylactic antibiotic versus placebo (1:1) following episiotomy or second degree tear. The study was conducted at one centre at the Department of Gynaecology and Obstetrics, Herlev Hospital, Copenhagen, Denmark. Approved on 2 February 2023 (EU-CT 2022-501930-49-00) and registered at ClinicalTrials.gov (NCT05830162), the study was monitored by the national Danish Good Clinical Practice Unit. Methodological details are published in the protocol paper,[12] while the present study adheres to the CONSORT 2010 guidelines.[13]

### Participants

Participants were included if they were Danish speaking women aged 18 years or older who had a second degree tear or mediolateral episiotomy (episiotomy with extension to the anal sphincter was excluded) and were sutured at our institution. We excluded women with treatment allergy (or risk of cross reactivity with related antibiotics), women who had undergone a caesarean section, and women who had been treated with antibiotics within 24 hours of delivery, regardless of indications (group B streptococcus or other delivery or non-delivery related indications). Herlev Hospital follows a strict screening protocol for group B streptococcus to minimise the use of antibiotics. In this study, "women" refers to people of female sex; all genders were eligible for inclusion. All women received written digital information about the study during pregnancy, and verbal information during prenatal classes. Within six hours of delivery, a maternity ward clinician provided final written and oral information and obtained consent from the participants (for participant flow through the study, see supplementary file S1).

### Intervention

The treatment group received three doses of oral antibiotics: amoxicillin (500 mg) with clavulanic acid (125 mg). The first tablet was taken within six hours post partum, and subsequently at eight hour intervals. Thus, the intervention stopped after a maximum of 22 hours post partum. The placebo group received three placebo tablets (calcium) matching the active drug in size, shape, and colour.

### Outcome

Clinical consultations performed by KP and HJ were conducted four to 14 days post partum, with long term follow-up at nine to 12 months. This paper only provides results from the initial consultations.

The primary outcome was wound dehiscence or wound infection (or both; hereafter referred to collectively as wound complications) assessed in the lithotomy position. Wound complications were defined as wound dehiscence (diastasis exceeding 5 mm measured with a disposable measuring tape)[14 15] or wound infection (ongoing infection with substantial purulent discharge or abscess), or both.[16] During the preparatory phase, KP and HJ conducted joint clinical assessments to align evaluation practice. They observed that wound dehiscence defined as more than 5 mm would lead to the inclusion of a large number of women with superficial dehiscence considered part of normal healing, as opposed to a complication. Consequently, we introduced a secondary outcome—clinically relevant wound dehiscence—before the inclusion of the first participant. If wound dehiscence of more than 5 mm was observed, we secondarily categorised it as clinically relevant if it required clinical follow-up because of the extent of the dehiscence (typically ≥10 mm), severity of pain (typically visual analogue scale score ≥5 or patient reported affected daily life), or infection. The assessment was a clinical evaluation with no strict cut-off value, owing to a lack of support in the literature. The outcome was included in the REDCap database before initiation of the study (supplementary file S2) and updated in ClinicalTrials.gov before completion and unblinding. To align terminology with the primary outcome, the secondary outcome will hereafter be referred to as clinically relevant wound complications. In cases of diagnostic uncertainty by one investigator, a second

opinion was obtained from another coinvestigator or, if unavailable, a senior physician from the urogynaecology department.

Additional outcomes derived from questionnaires completed the day before consultation were considered exploratory, as the definitions and analysis plan were not prespecified. The additional outcomes included pain (yes/no and visual analogue scale), use of analgesics (yes/no), breastfeeding (full or partial/no), urinary incontinence (yes/no), additional antibiotic use (yes/no), side effects of treatment/placebo (yes/no and type), self-evaluated health status (better than expected, as expected, or worse than expected), and unplanned contact with a doctor. Selected responses were clarified during the consultation and verified in medical records.

### Sample size

The incidence estimate was based on a Danish study that found 18% risk of wound dehiscence and 9% risk of wound infection.[15] From these proportions, we established a combined incidence of 20% for wound complications post partum. Without a well established minimal clinically important difference for wound complications, we chose a 50% reduction, similar to the effect seen in the ANODE trial, as a clinically meaningful and achievable target for sample size estimation.[9] Accounting for an anticipated drop-out rate of 10%, a significance level of 0.05, and a power of 80%, the study required 442 women for inclusion, with a 1:1 allocation ratio.

Once 50% of consultations were completed, we conducted an interim analysis without unblinding to evaluate the complication rate. We anticipated an average complication incidence of 15% (treatment group 10%; placebo group 20%). The study would proceed as planned with a complication incidence rate of 15% or more, but the sample size would be recalculated and the study extended if the complication rate was substantially lower than 15%. We performed a post hoc power calculation based on the results for the secondary outcome (clinically relevant wound complications).

### Statistical analysis

We used R Studio version 4.4.1 to perform statistical analyses.[17] For baseline data, amount and percentages were provided for categorical data, while continuous data were evaluated for normal distribution with visual evaluation (histograms and Q-Q plots). Variables with normal distribution were summarised using means and standard deviations (SDs). Non-normally distributed data were presented as medians with interquartile ranges. We used Fisher's exact test for categorical variables while continuous variables were analysed using the t test when normally distributed and using the Mann-Whitney U test when not normally distributed. $P<0.05$ was considered significant. We also calculated the risk difference, relative risk, and number needed to treat with 95% confidence intervals (CIs). Analysis followed the intention-to-treat principle, with participants included regardless of protocol adherence. A per protocol analysis was also conducted, only including women who took all three tablets and attended the consultation within four to 14 days post partum.

To assess the robustness of the intention-to-treat results in the women lost to follow-up, we performed post hoc analysis in two extreme case scenarios: one assuming that all nine women lost to follow-up had wound complications, and another assuming that none did.

We conducted a post hoc subgroup analysis to assess whether the overall results for clinically relevant wound complications were solely driven by patients at high risk of wound complications (women with a body mass index ≥30, women who had an instrumental delivery, women who had an episiotomy).[15 18 19] We therefore evaluated the treatment effect in patients without these risk factors.

### Randomisation

The Capital Region Pharmacy conducted randomisation using a computer generated random number sequence (1:1 allocation) in variable block sizes of six, eight, 10, and 12. The sequence was securely stored at the pharmacy throughout the study. The pharmacy used sealed containers labelled with identification numbers containing either three antibiotic tablets in blister packs for shelf stability, or three placebo tablets stored loose, as they were unavailable in blister packs. The pharmacy advised that a healthcare provider not involved in the study remove the blister packs, repackage the tablets, and return the container to the enrolling doctor without revealing its contents. Randomisation therefore occurred before enrolment and remained blinded to the staff (except repacking individuals), the steering committee (comprising all authors), and the patients until unblinding. Baseline characteristics and delivery related parameters were extracted from electronic medical records, based on documentation from midwives and doctors. This information included maternal age, parity, body mass index, gestational diabetes, pre-eclampsia, and previous or current psychological difficulties (eg, anxiety, stress, depression). Delivery related variables included mode of delivery (including instrumental), duration of the active phase (defined as cervical dilation >4-6 cm with regular contractions), membrane rupture, duration of active second stage (from onset of pushing to birth), and tear characteristics based on procedural descriptions of affected structures (eg, perineal skin, rectovaginal fascia, transverse and bulbocavernosus muscles).

### Medication and side effects

Participants allocated to intervention received three doses of amoxicillin (500 mg) with clavulanic acid (125 mg), a well known combination considered to be safe for breastfeeding women.[20] The intervention was given within 22 hours post partum, before lactation onset,[21] suggesting minimal infant exposure. Owing

to the short treatment duration, few maternal side effects were expected. According to Danish prescribing guidelines, no dose adjustment is required for treatment duration of less than one week regardless of kidney function. After assessment in questionnaires and consultations, we classified maternal side effects as drug related (adverse reaction) or unrelated (adverse event), as well as serious or non-serious.

### Unblinding

The study was completed when the final long term consultations (9-12 months post partum; results not included in this article) were conducted in November 2024. The Good Clinical Practice Unit approved the study, including a locked analysis plan, in December 2024. The study was partially unblinded, with the pharmacy disclosing group allocation without revealing treatment. All analyses and main conclusions were completed and saved in a non-editable file before final unblinding on 8 January 2025. This two step process aimed to minimise bias when interpreting the results. The participants will be informed of their allocation and the main study results once these have been published.

### Patient and public involvement

During the planning phase, we interviewed five women who recently experienced an obstetric tear. They shared their views on postpartum antibiotic use and how they would prefer to receive information about the study. They also evaluated the questionnaires to assess the time burden and identify missing aspects. Their suggestions were incorporated, and all five found the inclusion process acceptable.

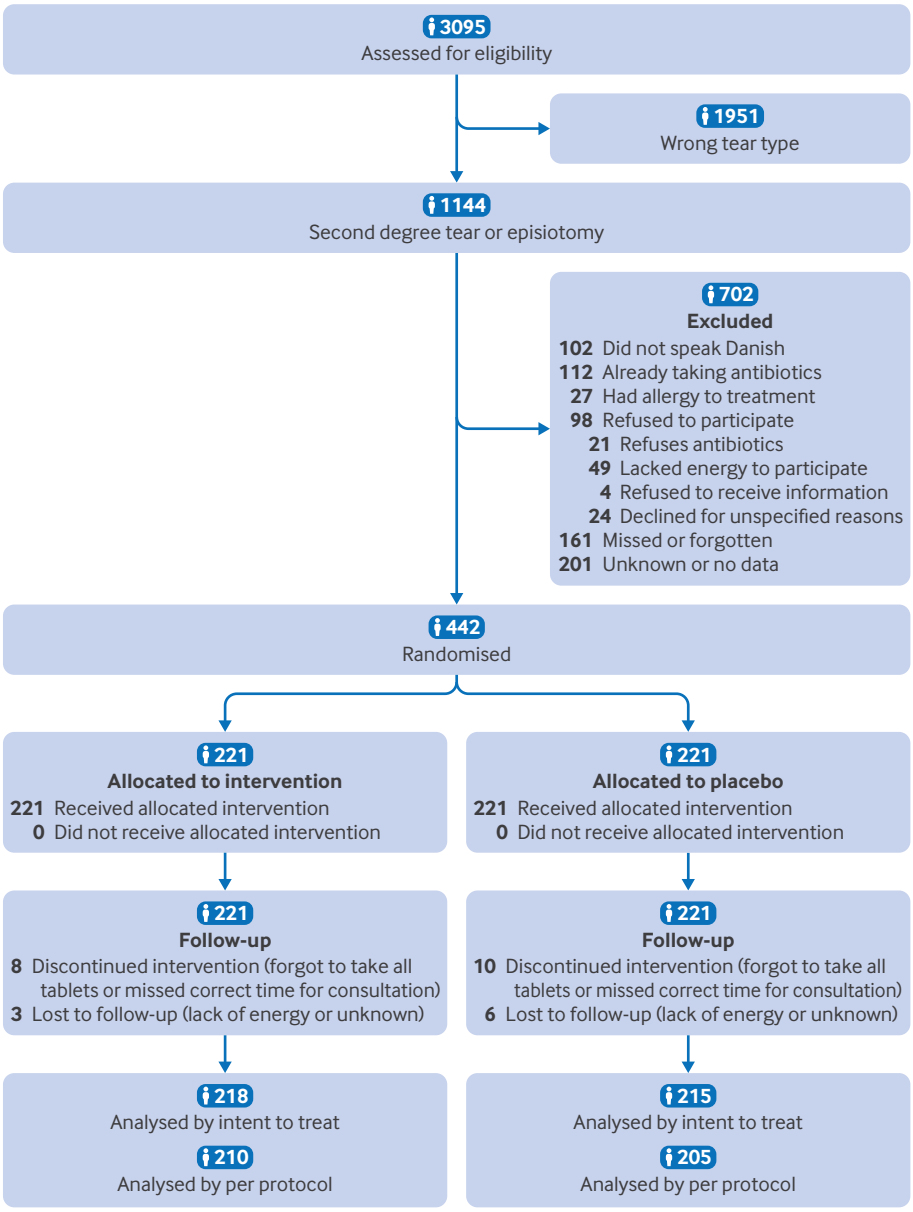


**Fig 1 | CONSORT flowchart of REPAIR study participants**

**Table 1 | Baseline characteristics of women in the REPAIR study (n=433)**

| Characteristic | No of participants with missing information* | Antibiotics (n=218) | Placebo (n=215) |
|---|---|---|---|
| Mean (SD) age (years) | 0 | 31 (4.6) | 32 (4.1) |
| Primiparous women | 0 | 147 (67) | 144 (67) |
| Previous obstetric anal sphincter injury | 0 | 8 (3.7) | 4 (1.9) |
| Previous caesarean section | 0 | 7 (3.2) | 5 (2.3) |
| Median (IQR) body mass index | 20 | 22.8 (20.3-25.2) | 23.1 (20.7-25.8) |
| Gestational diabetes mellitus | 0 | 9 (4.1) | 10 (4.7) |
| Hypertension/pre-eclampsia | 0 | 14 (6.4) | 6 (2.8) |
| Current/previous psychological difficulties | 1 | 50 (23.0) | 56 (26.0) |
| Method of induction of labour: | 0 | 60 (27.5) | 42 (19.5) |
| Misoprostol | 0 | 40 (18.3) | 30 (14.0) |
| Cervical ripening with balloon catheter | 0 | 5 (2.3) | 2 (0.9) |
| Oxytocin | 0 | 23 (10.6) | 9 (4.2) |
| Median time (IQR) spent in active labour (hours) | 34 | 5 (2-8) | 5 (2-8) |
| Stimulation with oxytocin | 0 | 67 (30.7) | 70 (32.6) |
| Median time (IQR) spent in active second stage (minutes) | 11 | 32 (16-60) | 30 (15-53) |
| Median duration (IQR) of rupture of membranes (hours) | 13 | 6 (1-12) | 5 (2-11) |
| Epidural | 0 | 91 (42.7) | 74 (34.4) |
| Mean (SD) fetal birth weight (g) | 1 | 3574 (472) | 3629 (427) |
| Fetal presentation: | 14 | | |
| Occiput anterior | | 199 (93.9) | 198 (95.6) |
| Occiput posterior | | 11 (5.2) | 8 (3.9) |
| Breech | | 2 (0.9) | 1 (0.5) |
| Vacuum delivery† | 0 | 44 (20.2) | 35 (16.3) |
| Median duration (IQR) of postpartum haemorrhage (mL) | 1 | 350 (250-500) | 350 (250-450) |
| Reason for episiotomy: | 0 | 37 (17.0) | 32 (14.9) |
| Tear of bulbocavernosus and transversus | 7 | 15 (7.0) | 16 (7.6) |
| Tear of rectovaginal fascia | 4 | 4 (1.9) | 2 (0.9) |
| Structures affected by spontaneous second degree tear: | 0 | 181 (83.0) | 183 (85.1) |
| Bulbocavernosus and transversus | 12 | 111 (52.6) | 99 (47.1) |
| Perineal skin | 9 | 151 (71.6) | 149 (70) |
| Rectovaginal fascia | 6 | 19 (8.9) | 20 (9.4) |
| Doctor involved in suturing | 0 | 39 (17.9) | 30 (14.0) |
| Suturing done in operating theatre | 0 | 4 (1.8) | 2 (0.9) |

Data are number (%) of women unless stated otherwise. IQR=interquartile range; SD=standard deviation.
*For some variables, it was not possible to achieve the necessary information for all women. The number of women not included in the specific analysis are stated here.
†No forceps deliveries took place in the study and forceps are only used in case of entrapment of head in vaginal breech delivery in our setting.

## Results

### Participant flow

We included 442 women between 22 March 2023 and 24 December 2023 (consecutively recruited at delivery), stopping enrolment in the study once the target sample size was reached. Figure 1 shows the inclusion flow. The continuous inclusion timeline and wound complication rates are shown in supplementary file S3. We performed the interim analysis after 230 women had completed the consultation: 53 of 230 (23%) had a wound complication and 30 of 230 (13%) had a clinically relevant wound. The drop-out rate was lower than expected (five women, 2% *v* expected 10%), and the primary outcome rate was higher than anticipated (23% *v* expected 15%). Based on the low drop-out rate and an event rate of 13% for clinically relevant complications, we assumed sufficient power, and the study continued without modifications. After unblinding, a post hoc power calculation based on the clinically relevant outcome found a power of 71%.

The initial consultations presented in this paper were conducted between 30 March 2023 and 4 January 2024. Of 442 women included, 433 attended the consultation (2% drop-out rate): 218 participants in the treatment group and 215 participants in the placebo group. Most women (427/433, 98.8%) were seen within the prespecified timeframe (four to 14 days post partum, median eight days post partum). Baseline characteristics showed a higher incidence of induction in the treatment group (P=0.06), but this did not affect overall delivery time. No other baseline differences were found between groups (table 1). Age, parity, and type of tear in the nine women lost to follow-up were comparable to the main study population. The study ended as planned, in December 2024.

### Outcomes

Among the 433 women who completed follow-up, 109 (25%) had wound complications, including 19 infections, and 55 women (13%) had a clinically relevant wound complication. Wound complications were non-significantly lower in the treatment group (22% *v* 29%, P=0.10), while clinically relevant wound complications were significantly reduced (9% *v* 17%, P=0.01; table 2). The number needed to treat was 12 (95% CI 7 to 56). Table 2 compares the health status of

Table 2 | Primary, secondary, and exploratory outcomes in the REPAIR study (intention to treat analysis; n=433), one week post partum

| Outcome | Antibiotic (n=218) | Placebo (n=215) | P value | Risk difference (%; 95% CI) | Relative risk (95% CI) |
|---|---|---|---|---|---|
| **Primary outcome** | | | | | |
| Wound complications* | 47 (21.6) | 62 (28.8) | 0.10 | −7.2 (−15.4 to 0.8) | 0.75 (0.54 to 1.04) |
| **Secondary outcome** | | | | | |
| Clinically relevant wound complications† | 19 (8.7) | 36 (16.7) | 0.01 | −8.0 (−14.3 to −1.8) | 0.52 (0.31 to 0.88) |
| **Exploratory outcomes** | | | | | |
| Median (IQR) wound dehiscence (mm) | 7 (6-10) | 10 (7-12) | <0.001 | −3.0 (−3.8 to −2.2)‡ | — |
| Urinary incontinence | 47 (21.6) | 37 (17.2) | 0.28 | 4.4 (−3.1 to 11.8) | 1.25 (0.85 to 1.85) |
| Pain (yes) | 141 (64.7) | 145 (67.4) | 0.61 | −2.8 (−11.7 to 6.2) | 0.96 (0.84 to 1.10) |
| Median (IQR) VAS score for pain | 4 (3-5) | 4 (2-5) | 0.68 | 0.0 (−0.4 to 0.4)‡ | — |
| Use of painkillers | 84 (38.5) | 93 (43.3) | 0.30 | −4.7 (−14.0 to 4.5) | 0.89 (0.81 to 1.12) |
| Self-evaluation of healing process: | | | | | |
| Worse | 26 (11.9) | 41 (19.1) | 0.05 | −7.1 (−0.35 to −13.9) | 0.63 (0.40 to 0.98) |
| As expected | 86 (39.4) | 100 (46.5) | 0.15 | −7.1 (−16.4 to 2.2) | 0.85 (0.68 to 1.05) |
| Better | 106 (48.6) | 74 (34.4) | 0.003 | 14.2 (5.0 to 23.4) | 1.43 (1.12 to 1.78) |
| Breastfeeding | 212 (97.2) | 207 (96.3) | 0.60 | 1.0 (−2.4 to 4.3) | 1.01 (0.98 to 1.05) |
| Doctor contact before REPAIR visit | 20 (9.2) | 31 (14.4) | 0.10 | −5.2 (−11.3 to 0.8) | 0.64 (0.37 to 1.08) |
| Antibiotics before REPAIR visit | 4 (1.9) | 12 (5.6) | 0.04 | −3.8 (−7.3 to −0.2) | 0.33 (0.10 to 1.01) |
| Antibiotics before or at REPAIR visit | 8 (3.7) | 19 (8.8) | 0.03 | −5.1 (−9.7 to −0.6) | 0.42 (0.18 to 0.93) |

Data are number (%) of women unless stated otherwise.
CI=confidence interval; IQR=interquartile range; VAS=visual analogue scale;
*Wound dehiscence or infection (or both).
†Wound complication requiring further follow-up based on the size, pain level, or infection of the wound.
‡Median (IQR) difference.

participants one week post partum by group, covering primary, secondary, and exploratory outcomes. Further, the treatment group required fewer additional consultations (32 *v* 54, P=0.03).

Post hoc subgroup analysis of women without high risk variables (body mass index ≥30, instrumental delivery, or episiotomy) showed a consistently significant effect (P<0.05 in all three subanalyses) of antibiotics regarding clinically relevant wound complications (supplementary file S4). Sensitivity results did not alter the beneficial effect of antibiotics regarding clinically relevant wound complications, nor did the per protocol analysis (supplementary file S5).

### Side effects

Eight women (four in each allocation group) experienced adverse reactions including diarrhoea, nausea, headache, and dizziness. Adverse and serious adverse events were reported by 14 women (seven in each group) and included mastitis, hypertension/pre-eclampsia, cholelithiasis, and endometritis. No serious adverse reactions were reported. KP and HJ evaluated serious adverse events. Among the nine women who missed the consultation, four completed the questionnaire and reported no side effects, and only one of the remaining five had received antibiotics.

## Discussion

### Principal findings

The primary outcome of this double blind randomised controlled trial (risk of wound complications) showed a non-significant reduction in the treatment group, while clinically relevant wound complications were significantly lower, suggesting that these complications are infection driven. Exploratory outcomes suggested better wellbeing in the treatment group, but results should be interpreted cautiously because of a lack of prespecification in trial registration and statistical analysis plan and lack of multiple testing. Unlike another study by Tandon and Dalal we found no difference in pain, possibly due to its high overall prevalence.[6] Subgroup analysis also showed a significant effect in low risk groups, whereas the ANODE trial found benefit to high risk women, prompting WHO to recommend antibiotic use for this group.[10]

### Strengths and limitations

Key strengths of the REPAIR study include a low drop-out rate, steady inclusion, and short timeframe, reducing the risk of change in clinical practice. All women included in the analysis had a clinical consultation, minimising the risk of underdiagnosis among those who might otherwise avoid medical care.[22] Another strength is the use of oral antibiotics, which WHO recognises as a practical alternative to intravenous treatment in settings with low resource availability.[10] One limitation is that the outcome of clinically relevant wound dehiscence was registered at ClinicalTrials.gov after study initiation, although it was defined before study initiation and assessed prospectively throughout. To align with the trial design and reduce selective reporting bias, we retained the original primary outcome and subsequently added the clinically relevant outcome as secondary.

Generalisability may be limited and selection bias introduced because of the single centre design, inclusion restricted to Danish-speaking women, and lack of ethnicity data. Exclusion of women receiving intrapartum antibiotics helped isolate the prophylactic effect but may reduce generalisability, as could differences in pathogens, resistance patterns, and obstetric practices such as episiotomy and instrumental delivery. However, consistent benefits

across subgroups support generalisability beyond high risk populations and the ANODE trial found a similar effect size.[9] Although tablets were not taste matched and only antibiotics were stored in blister packs, we handled these factors according to pharmacy guidelines, and we consider blinding was maintained and results valid.

We observed the significant reduction in clinically relevant wound complications despite treatment likely being given more than two hours post partum (the exact timepoint was not recorded), as treatment was given after the inclusion procedure. The ANODE trial (secondary analysis) showed greater protective effect with earlier administration of the intervention.[23] Prescribing prophylactic antibiotics requires caution because of potential side effects, increasing use of antibiotics, and risk of resistance. We observed no group differences in side effects and the timing of administration likely minimises infant exposure to the antibiotics used. One study found no increased risk of asthma/eczema in children exposed to antibiotics in utero when given before cord clamping during caesarean sections.[24] Postpartum antibiotic use was lower in the treatment group, consistent with the reduced overall use of antibiotics within six months post partum shown in the ANODE trial. While minimising antibiotic use is important, childbirth is a rare event, and the recommended regimen of three tablets constitutes only a small fraction of lifetime exposure.

## Conclusion

Using the primary outcome definition of healing complications, we found no significant effect of prophylactic antibiotics. However, when considering the secondary outcome clinically relevant wound complication, antibiotics significantly reduced the risk from 17% to 9%. This finding supports the use of prophylactic antibiotics in routine clinical practice after a second degree tear or episiotomy.

We thank the Department of Gynaecology and Obstetrics at Herlev Hospital for its financial and logistical support, and the Research Unit at Herlev Hospital for its financial contribution; the staff members on the delivery ward, maternity ward, and urogynaecological department for their enthusiasm and help with inclusions and consultations; expertenglish.dk for editing the language in the manuscript; and the five women interviewed before the study began and who contributed to adjusting and improving the study. Lastly, we offer our sincere appreciation to all the women who participated in our study, whose contribution was invaluable and deeply appreciated.

Contributors: All authors of this paper meet the ICMJE criteria for authorship and contributed to the design and planning of the study. KP and HJ were responsible for data collection and analysis. KP drafted the manuscript, which was reviewed and edited by the other three authors. During the revision process, we used ChatGPT to assist with the formulation of individual sentences, because none of the authors is a native English speaker and the reviewers had commented on language issues. However, we later decided to have the entire manuscript professionally proofread. The proofreader reviewed and revised the language throughout, including parts previously edited with the help of ChatGPT. KP and HJ are guarantors of the study. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Funding: The study was funded by the Research Unit and the Department of Gynaecology and Obstetrics at Herlev Hospital. None of the funders had any influence on the study design, data collection, analysis, interpretation of results, manuscript preparation, or the decision to publish. All authors had full access to all data, including statistical reports and tables, and take full responsibility for the integrity of the data and the accuracy of the analysis.

Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/disclosure-of-interest/ and declare: no support from any organisation for the submitted work, aside from their regular monthly salaries from Herlev Hospital and a six month research salary for KP provided by the Research Unit at Herlev Hospital; no financial relationship with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Ethical approval: The trial was approved in Denmark through the EU Clinical Trials Information System (CTIS; EU No 2022-501930-49-00) by the Danish Medicines Agency and the Danish National Committee on Health Research Ethics. All participants provided written informed consent.

Data sharing: The code used to analyse the data in the paper can be found in the supplemental files. The data underlying the findings in this paper are openly and publicly available and can be found here: https://dataverse.deic.dk/dataset.xhtml?persistentId=doi:10.60612/DATADK/WTK5BD. If you encounter problems accessing the data, please contact the corresponding author.

Transparency: This manuscript provides an honest, accurate, and transparent account of the reported study. No important aspects have been omitted, and all discrepancies from the originally planned study have been fully explained and appropriately registered.

Dissemination to participants and related patient and public communities: All included women, unless they have refused, will receive information about the treatment group to which they were allocated, along with the main conclusions of the study. This information will be sent to their secure digital mailbox on publication.

Provenance and peer review: Not commissioned; externally peer reviewed.



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**Web appendix:** Supplementary materials