## **Meta-analysis**

# Systematic review and meta-analysis of the effectiveness of antibiotic prophylaxis in prevention of wound infection after mesh repair of abdominal wall hernia

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**Background:** The aim was to determine whether systemic antibiotic prophylaxis prevented wound infection after repair of abdominal wall hernia with mesh.

**Methods:** This was a systematic review of the available literature identified from multiple databases using the terms 'hernia' and 'antibiotic prophylaxis'. Randomized placebo-controlled trials of antibiotic prophylaxis in abdominal wall mesh hernia repair with explicitly defined wound infection criteria and a minimum follow-up of 1 month were included. After independent quality assessment and data extraction, data were pooled for meta-analysis using a random-effects model.

**Results:** The search process identified eight relevant trials. Two papers on umbilical, incisional or laparoscopic hernias, and six concerning inguinal and femoral (groin) hernias were suitable for metaanalysis. The incidence of infection after groin hernia repair was 38 (3.0 per cent) of 1277 in the placebo group and 18 (1.5 per cent) of 1230 in the antibiotic group. Antibiotic prophylaxis did not significantly reduce the incidence of infection: odds ratio 0.54 (95 per cent confidence interval 0.24 to 1.21); number needed to treat was 74. The number of deep infections was six (0.6 per cent) in the placebo group and three (0.3 per cent) in the antibiotic prophylaxis group: odds ratio 0.50 (95 per cent c.i. 0.12 to 2.09). **Conclusion:** Antibiotic prophylaxis did not prevent the occurrence of wound infection after groin hernia surgery. More trials are needed for complete evidence in other areas of abdominal wall hernia.

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#### Introduction

Mesh repair is rapidly becoming the most popular technique for repair of abdominal wall hernia<sup>1-7</sup>. More than 80 per cent of abdominal wall hernias occur in the groin and in the Western world most are repaired with prosthetic mesh. The most popular technique is the Lichtenstein hernia repair, with a flat mesh to reinforce the inguinal wall. In repair of incisional hernia (the second most frequent abdominal wall hernia) mesh repair results in a lower recurrence rate than suture repair<sup>3</sup>. Other hernias, such as umbilical and epigastric hernias, are also increasingly repaired with mesh techniques.

It remains uncertain whether antibiotic prophylaxis is indicated to prevent postoperative superficial and deep wound infection after mesh repair of abdominal wall hernia. The incidence of infection after inguinal hernia repair has been reported to vary from 0 to 9 per cent<sup>8</sup>. When a foreign body such as a polypropylene mesh is used, prevention of a deep infection is more important. A Cochrane review of inguinal hernia in 2004 concluded that antibiotic prophylaxis for elective inguinal hernia repair cannot be firmly recommended or discarded<sup>9</sup>. This was because the number of patients in randomized trials was limited. Recently, new information has become available.

Because meta-analysis has shown that mesh repair reduces the risk of hernia recurrence, it is accepted as the procedure of choice for abdominal wall hernia repair<sup>2,3,6,7,10-13</sup>. Both in the USA and Europe over 1.5 million abdominal wall hernia repairs are performed annually<sup>13</sup>, and so even minor improvements in treatment could have a large medical and economic impact. Reduction in the number of wound infections would impact on patient satisfaction, sick leave and wound care. Conversely, avoiding antibiotic prophylaxis could reduce the risks of toxic and allergic side-effects, the possible development of bacterial resistance<sup>14</sup> and minimize costs. A systematic review and, where possible, a meta-analysis of randomized controlled trials (RCTs) was carried out to determine whether antibiotic prophylaxis prevents wound infection after mesh hernia repair.

## Methods

A Medline, Embase, CINAHL, DARE, ACP, LILACS and Cochrane register search using the terms 'hernia' and 'antibiotic prophylaxis' was carried out to identify RCTs published between 1966 and March 2005. All languages were considered. The search was performed independently by two reviewers who selected potentially relevant papers based on title and abstract. References from the selected papers were used to complete the search. Experts in the field were contacted for potential data, and abstract books of leading hernia meetings held during the past 5 years were checked manually for unpublished data. All randomized placebo-controlled trials with use of antibiotic prophylaxis in abdominal wall mesh hernia repair with explicitly defined wound infection criteria and a minimum follow-up of 1 month were included. Each paper was reviewed independently by three reviewers and a quality assessment was performed according to the scoring system of Jadad et al.<sup>15</sup>. Discrepancies between the reviewers were resolved by consensus. Only papers with a Jadad score of 3 or more were considered appropriate for further analysis. Data were extracted from the studies and pooled using Review Manager from the Cochrane collaboration<sup>16</sup>.

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A random-effects model was used to correct for clinical diversity and methodological variations between studies. The effectiveness of antibiotic prophylaxis in preventing wound infection was expressed as an odds ratios (OR) with 95 per cent confidence interval (c.i.) for dichotomous data. Numbers needed to treat (NNT) were calculated from the ORs and the background risk of wound infection in patients in placebo groups. No subgroup analysis was performed. If it remained unclear from a study whether data were presented for patients or hernias, a sensitivity analysis (worst-case scenario) was performed by varying the distribution of bilateral hernias between treated and placebo groups.

## **Results**

The search resulted in 26 potentially relevant studies, and identified eight papers that reported prospective randomized data on the use of antibiotic prophylaxis in abdominal wall surgery with prosthetic reinforcement. Eighteen papers were excluded, six because non-mesh techniques were employed, one compared different prophylactic regimens and 11 were not RCTs. *Table 1* summarizes the eight included randomized trials and the outcome of the assessment; the extracted results did not differ between the three reviewers.

The study of Abramov *et al.*<sup>17</sup> described 35 hernias, of which only 23 per cent were repaired with mesh. Despite several flaws in design, including lack of proper randomization, this was the only study that addressed antibiotic prophylaxis in umbilical and incisional repair, and so it was accepted for the systematic review. The only study concerning laparoscopic hernia<sup>18</sup> was considered

**Table 1** Quality of, and infection rates in, prospective randomized studies on the use of antibiotic prophylaxis in prevention of wound infection after abdominal wall mesh hernia repair

Reference	Jadad score	No. of patients	Infection (%)	Correct randomization	Double blind	Wound infection definition	Follow-up	Accepted in meta-analysis	
Incisional and umbilical hernia mesh repair									
Abramov et al. <sup>17</sup>	0	35	26	No, alternately	No	Yes	1 month	No, only 23 per cent mesh repair. Best evidence	
Laparoscopic inguinal	Laparoscopic inquinal hernia mesh repair (TAPP)								
Schwetling et al.18	0	80	0	No, alternately	No	No definition	n.a.	No. best evidence	
Open inguinal or femor	Open inquinal or femoral hernia mesh repair								
Morales et al.19	4	524	1.9	Yes	Yes	Yes	1 year	Yes	
Yerdel et al.20	5	269	4.8	Yes	Yes	CDC criteria <sup>25</sup>	1 year	Yes	
Celdran et al.21	4	91	4.4	Yes	Yes	CDC criteria <sup>25</sup>	2 years	Yes	
Oteiza et al.22	3	247	0.4	Yes	No	CDC criteria <sup>25</sup>	1 month	Yes	
Aufenacker et al.23	5	1008	1.7	Yes	Yes	CDC criteria <sup>25</sup>	3 months	Yes	
Perez et al. <sup>24</sup>	5	360	3.1	Yes	Yes	CDC criteria <sup>25</sup>	1 month	Yes	

CDC, Centers for Disease Control and Prevention; n.a., data not available.

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	Morales <sup>19</sup> ( $n = 524$ )*	Yerdel <sup>20</sup> (n = 269)*	Celdran <sup>21</sup> ( $n = 99$ )†	Oteiza <sup>22</sup> (n = 247)*	Aufenacker <sup>23</sup> (n = 1008)*	Perez <sup>24</sup> (n = 360)*
Total infections (%)	1.9	4.8	4	0.4	1.7	3.1
Deep infection (%)	0.8	1.5	0	0	0.3	0.6
Mesh removal (%)	0.8	1.1	0	0	0.2	0.6
Body mass index (mean)	n.a.	25.0	26.2	n.a.	n.a.	n.a.
Diabetes	n.a.	Excluded	18 (18)	n.a.	Excluded	n.a.
Recurrent hernia	39 (7.4)	Excluded	13 (13)	Excluded	Excluded	Excluded
Duration of surgery (min)	34	63	65	40	40	53
Grade of surgeon						
Specialist	524 (100)	0 (0)	75 (76)	247 (100)	571 (56.6)	n.a
Trainee	0 (0)	269 (100)	24 (24)	0 (0)	437 (43.4)	n.a
Bilateral hernias	0 (0)	0 (0)	8 (8)	Excluded	56 (5.6)	Excluded
Femoral hernia	23 (4.4)	Excluded	Excluded	20 (8.1)	Excluded	Excluded
Use of drains	Excluded	60 (22.3)	n.a.	n.a.	15 (1.5)	0 (0)
Local anaesthesia	n.a.	111 (41.3)	99 (100)	226 (91.5)	17 (1.7)	0 (0)
Day surgery	51 (9.7)	n.a.	99 (100)	247 (100)	463 (45.9)	n.a.
Mesh type	Polypropylene	Polypropylene	Polypropylene	Polypropylene	Polypropylene	Polypropylene
Exclusion bias <sup>26</sup>	30 of 554 (5·4)	11 of 280 (3·9)	0 of 91 (0)	3 of 250 (1.2)	7 of 1015 (0·7)	0 of 360 (0)

Table 2 Data from six randomized controlled trials on antibiotic prophylaxis in inguinal and femoral mesh hernia repair

Values in parentheses are percentages. \*No. of patients; †no of hernias; n.a., data not available.

 Table 3 Results of studies in the systematic review of antibiotic prophylaxis in prevention of wound infection after abdominal wall mesh hernia repair

	Mean age			Type of	No. of patients with infection				
Reference	п	(years)	Men (%)	antibiotic	Placebo	Antibiotic	Р	NNT	
Incisional and umbilical	Incisional and umbilical hernia mesh repair								
Abramov et al.17	16 inc.	55	n.a.	Cefonicid 1 g	4 of 8 (50)	0 of 8 (0)	0.076	2	
	19 umb.	52	n.a.		4 of 10 (40)	1 of 9 (11)	0.303	3	
Laparoscopic inquinal I	nernia mesh i	repair (TAPP)							
Schwetling et al. <sup>18</sup>	80	55	86	Cefuroxime 1.5 g	0 of 40 (0)	0 of 40 (0)	1.0	$\infty$	
Open inguinal and femo	oral hernia m	esh repair							
Morales et al.19	524	54	90	Cefazolin 2 g	6 of 287 (2·1)	4 of 237 (1.7)	0.737	248	
Yerdel et al.20	269	56	93	Ampicillin + sulbactam 1.5 g	12 of 133 (9·0)	1 of 136 (0.7)	0.002	13	
Celdran et al.21	91	58	90	Cefazolin 1 g	4 of 49* (8)	0 of 50* (0)	0.059	13	
Oteiza et al.22	247	57	85	Amoxicillin + clavulanic acid	0 of 123 (0)	1 of 124 (0·8)	0.318	NNH 124	
				2 g					
Aufenacker et al.23	1008	58	96	Cefuroxime 1.5 g	9 of 505 (1·8)	8 of 503 (1.6)	0.813	520	
Perez et al. <sup>24</sup>	360	61	98	Cefazolin 1 g	7 of 180 (3·9)	4 of 180 (2·2)	0.540	59	

Values in parentheses are percentages. \*No. of hernias (91 patients). NNT, no. needed to treat; NNH, no. needed to harm; TAPP, transabdominal preperitoneal; inc., incisional; umb., umbilical; n.a., data not available.

weak (incorrect randomization and lack of definition of wound infection) but, in the absence of other studies, it was considered best evidence.

The patient characteristics in six RCTs on open inguinal and femoral hernia mesh repair suitable for meta-analysis are documented in *Table 2*. These included 2464 open inguinal and 43 femoral hernia repairs (*Table 3*).

For groin hernia, the incidence of infection was 38 (3.0 per cent) of 1277 in the placebo group and 18 (1.5 per cent) of 1230 in the antibiotic group. The pooled

data for the six studies are presented in *Fig. 1*. There was no statistical heterogeneity (P = 0.18,  $\chi^2$  test). The OR for wound infection after antibiotic prophylaxis was 0.54 (95 per cent c.i. 0.24 to 1.21), resulting in a NNT of 74. The study by Celdran *et al.*<sup>21</sup> did not specify which group the eight bilateral hernias were included in, so a sensitivity analysis was performed; in the worst-case scenario the infection rate in Celdran's placebo group was four of 41, resulting in an OR of 0.53 (95 per cent c.i. 0.23 to 1.21).

	Proportion with	wound infection				
Reference	Antibiotic Placebo		Odds ratio (random)	Weight (%)	Odds ratio (random)	
Morales <i>et al.</i> <sup>19</sup>	4 of 237	6 of 287	<b>_</b> _	22.62	0.80 (0.22, 2.88)	
Yerdel et al. 20	1 of 136	12 of 133	<b>←</b>	11.96	0.07 (0.01, 0.58)	
Celdran et al. 21	0 of 50	4 of 49	<b>← □ ↓</b>	6.59	0.10 (0.01, 1.91)	
Oteiza et al. 22	1 of 124	0 of 123		5.68	3.00 (0.12, 74.36	
Aufenacker et al. 23	8 of 503	9 of 505		29.91	0.89 (0.34, 2.33)	
Perez et al. 24	4 of 180	7 of 180	<b>_</b> _	23.24	0.56 (0.16, 1.95)	
Total	18 of 1230	38 of 1277		100.00	0.54 (0.24, 1.21)	
			0.01 0.1 1 10 100			
			Favours Favours antibiotic placebo			

Fig. 1 Pooled data from six studies of antibiotic prophylaxis in prevention of wound infection after mesh inguinal hernia repair. Odds ratios are shown with 95 per cent confidence intervals. Test for heterogeneity:  $\chi^2 = 7.62$ , 5 d.f., P = 0.18,  $I^2 = 34.4$  per cent. Test for overall effect: Z = 1.49, P = 0.14

	Proportion with de	ep wound infection		Weight (%)	
Reference	Antibiotic	Placebo	Odds ratio (random)		Odds ratio (random)
Yerdel <i>et al.</i> 20	1 of 136	3 of 133		38.96	0.32 (0.03, 3.13)
Celdran <i>et al.</i> <sup>21</sup>	0 of 50	0 of 49			Not estimable
Oteiza <i>et al.</i> 22	0 of 124	0 of 123			Not estimable
Aufenacker <i>et al.</i> 23	1 of 503	2 of 505		34.93	0.50 (0.05, 5.54)
Perez <i>et al.</i> 24	1 of 180	1 of 180		26.12	1.00 (0.06, 16.11
Total	3 of 993	6 of 990		100.00	0.50 (0.12, 2.09)
			0.01 0.1 1 10 100		
			Favours Favours antibiotic placebo		

Fig. 2 Pooled data from five studies of antibiotic prophylaxis in prevention of deep wound infection after mesh inguinal hernia repair. Odds ratios are shown with 95 per cent confidence intervals. Test for heterogeneity:  $\chi^2 = 0.39$ , 2 d.f., P = 0.82,  $I^2 = 0$  per cent. Test for overall effect: Z = 0.94, P = 0.35

The number of deep infections after inguinal and femoral hernia repairs was six (0.6 per cent) in the placebo group and three (0.3 per cent) in the antibiotic prophylaxis group, with an OR of 0.50 (95 per cent c.i. 0.12 to 2.09) and NNT of 401 (*Fig. 2*).

## **Discussion**

In this systematic review of the effectiveness of antibiotic prophylaxis in abdominal wall mesh hernia repair, the analysis of six RCTs concerning groin hernia led to valid conclusions whereas the yield for other abdominal wall hernias was disappointing.

The reported rate of wound infection (2.2 per cent) after groin mesh repair in RCTs was no higher than that after conventional sutured repair  $(4.3 \text{ per cent})^9$ . As the use of antibiotics is not likely to increase the rate of wound infection, the net effect of randomized studies will almost always be zero, or in favour of the patients receiving prophylaxis. The present meta-analysis of six studies on the use of antibiotic prophylaxis in prevention of wound infection after mesh groin hernia repair did not favour the routine use of antibiotic prophylaxis.

The infection rate in low-risk patients undergoing clean inguinal or femoral hernia surgery should be below 2 per cent<sup>27</sup>. Superficial infection requires relatively simple treatment comprising wound drainage combined with antibiotics. As the rare deep infection results in a low risk of mesh removal (between 0.09 per cent<sup>28</sup> and 1.1 per cent<sup>20</sup>), and a remarkably low rate of hernia recurrence, there remains no indication for routine antibiotic prophylaxis in low-risk patients<sup>29</sup>. Avoiding

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antibiotic prophylaxis could reduce the risk of toxic and allergic side-effects, the possible development of bacterial resistance<sup>14</sup> and reduces costs.

If there are patients at higher risk of wound infection, the use of antibiotic prophylaxis could be re-evaluated<sup>27</sup>. In the trials with higher wound infection rates two differences could be seen: the duration of surgery was 1.5 times longer (64 min) and wound drains were used more often (22 per cent), both known risk factors for infection<sup>27,30</sup>.

This review uncovered the lack of RCTs examining wound infection in laparoscopic, incisional and other abdominal wall hernia repairs. The only laparoscopic inguinal hernia (transabdominal preperitoneal) repair study enrolled 80 patients without formal randomization, and demonstrated no infections<sup>18</sup>. This study virtually excluded a high risk of wound infection after laparoscopic repair, which has some logic as the incisions are small, although the operations take an average of 18 min longer than open repair<sup>31</sup>. Although hard evidence is lacking, it is probably acceptable to conclude that antibiotic prophylaxis is unnecessary for laparoscopic inguinal hernia repair.

The infection rate was significantly higher after incisional than inguinal hernia repair. The larger wounds require more dissection and frequently demand entry into the peritoneal cavity, thereby leading to a higher risk of bacterial contamination. Furthermore, the higher risk of seroma and haematoma formation dictates the need for drains, augmenting the chance of contamination of the prosthetic material30. The few trials on this subject are all biased because of inadequate (or no) randomization. The study of Abramov et al.<sup>17</sup> demonstrated a reduction in wound infection after umbilical and incisional repair with antibiotic prophylaxis, although only 23 per cent involved mesh. A non-randomized study by Rios et al.<sup>32</sup> reported a reduction in wound infection rate in 216 patients with incisional hernia from 18.1 to 13.6 per cent with the use of antibiotic prophylaxis. It has to be concluded that there is currently no evidence to support the use of antibiotic prophylaxis in incisional hernia repair and further RCTs are recommended.

It is difficult to assess the possibility of publication bias, resulting in omission of studies that showed no effect of antibiotic prophylaxis. However, if this existed, the effect of antibiotic prophylaxis would be even more modest than noted in the present meta-analysis, as failure to include the grey literature has been reported to overestimate a treatment effect by 15 per cent<sup>33</sup>.

There remains no indication for routine antibiotic prophylaxis (especially in low-risk patients) in groin mesh hernia repair. For other abdominal wall hernias recommendations await the results of further studies.

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