**Critical Review Form**
**Therapy**

PGY-1

Chabok A, Påhlman L, Hjern F, Haapaniemi S, Smedh K; AVOD Study Group. Randomized clinical trial of antibiotics in acute uncomplicated diverticulitis. Br J Surg. 2012 Apr;99(4):532-9.

**Objectives:** **"to evaluate whether antibiotic treatment for acute uncomplicated left-sided diverticulitis is necessary for recovery without complications after a 12-month follow-up interval. " (p. 533)**

**Methods:** **This open-label, multicenter randomized controlled trial was conducted at 10 surgical departments in Sweden and 1 in Iceland between October 2003 and January 2010. Patients aged 18 years or over with uncomplicated left-sided diverticulitis verified by CT scan were eligible. Exclusion criteria included signs of abscess, fistula or free air on CT, immunosuppression, pregnancy, ongoing antibiotic therapy, high fever, peritonitis, or sepsis.**

**Patients were randomized in blocks of 4, stratified by center, and allocation was made by the use of sealed envelopes. Patients were assigned to receive either IV fluids alone, or IV fluids in conjunction with broad-spectrum antibiotics (chosen according to participating center's routines) given for a total duration of 7 days. The decision to switch to oral antibiotics, and the decision to discharge the patient, were made by the attending surgeon based on signs of clinical improvement.**

**Patients were contacted by telephone or letter at a minimum of 12 months after discharge, and asked to complete a questionnaire regarding abdominal pain, bowel symptoms, or recurrence of disease requiring hospital readmission. The measured outcomes included complications during hospital stay (bowel perforation with free air, abscess, fistula formation), and complications during follow-up (recurrence of disease, need for surgery).**

**A total of 669 patients were randomized, of whom 46 were excluded, leaving a cohort of 623 patients. There were 309 patients in the no antibiotic group and 314 in the antibiotic group. The median age was 58 years (range 23-88), and the median body mass index (BMI) was 27.7 kg/m$^2$.**

| Guide | | Comments |
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| **I.** | **Are the results valid?** | |
| **A.** | **Did experimental and control groups begin the study with a similar prognosis (answer the questions posed below)?** | |
| 1. | Were patients randomized? | Yes. "Randomization in blocks of four and stratified |

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| | | by centre was performed by opening a sealed envelope, distributed by the Centre for Clinical Research in Vasteras." (p. 533) |
| 2. | Was randomization concealed (blinded)? In other words, was it possible to subvert the randomization process to ensure that a patient would be "randomized" to a particular group? | Uncertain. While the envelopes were prepared off-site, there is no mention of them being opaque, and no information regarding storage and access. It is unlikely, but possible, that the randomization process could have been subverted (allocation concealment). |
| 3. | Were patients analyzed in the groups to which they were randomized? | Yes. An intention to treat analysis was used, despite 10 patients in the no antibiotic group receiving antibiotics and 3 patients in the antibiotic group not receiving antibiotics. |
| 4. | Were patients in the treatment and control groups similar with respect to known prognostic factors? | Yes. Patients were similar with respect to age, gender, comorbidities, BMI, initial WBC and CRP, temperature, degree of abdominal pain as measured by a visual analogue scale, and degree of abdominal tenderness as measures on a 4-point scale. A history of prior diverticulitis was more likely in the no antibiotic group (44.8 vs. 35.6, p = 0.02). |
| **B.** | **Did experimental and control groups retain a similar prognosis after the study started (answer the questions posed below)?** | |
| 1. | Were patients aware of group allocation? | Yes. This was an open-label study and patients were not blinded to treatment group. It is possible that significant performance bias and recall bias on the part of patients could have contributed to the outcomes. |
| 2. | Were clinicians aware of group allocation? | Yes. It is possible that significant performance bias on the part of clinicians could have affected the outcomes. |
| 3. | Were outcome assessors aware of group allocation? | Yes. The primary outcomes assessors were patients filling out the questionnaires and clinicians interpreting the answers. Since this was an open-label study, it is open to the possibility of recall bias and observer bias. |
| 4. | Was follow-up complete? | No. For the primary analysis, follow-up data was available for all patients. For follow-up analysis (involving contact at least 12 months after discharge), a total of 41 patients (6.6%) were lost to follow-up, with similar rates of attrition between the two groups. |

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| **II.** | **What are the results (answer the questions posed below)?** | |
| 1. | How large was the treatment effect? | • In the no antibiotics group, 6 (1.9%)patients had complications: 3 perforations and 3 abscesses.<br>• In the antibiotics group, 3 (1.0%) patients had complications, all perforations.<br>• The relative risk of a complication in patients receiving no antibiotics, compared to those receiving antibiotics, was 2.0 (95% CI 0.51-8.0).<br>• Ten patients (3.2%) in the no antibiotics group were started on antibiotics during hospitalization. There were no complications in these patients.<br>• Hospital length of stay was similar between the groups, with a mean of 2.9 days in both groups.<br>• There were 6 (1.9%) patients in the no antibiotics group who required surgery during follow-up, compared to 2 (0.6%) in the antibiotics group: RR 3.0 (95% CI 0.62-15).<br>• Recurrent diverticulitis occurred in 47 of 290 (16.2%) patients in the no antibiotics group with follow-up data compared to 46 of 292 (15.8%) in the antibiotics group (p = 0.881). |
| 2. | How precise was the estimate of the treatment effect? | See above. Give the rarity of complications, the 95% confidence interval for the RR was quite wide and did cross 1. |
| **III.** | **How can I apply the results to patient care (answer the questions posed below)?** | |
| 1. | Were the study patients similar to my patient? | No. This study included only patients admitted to a surgical service with a diagnosis of diverticulitis. Many of our patients with mild diverticulitis are discharged home on oral antibiotics. Additionally, this study was conducted in Sweden and Iceland, with a relatively homogenous Caucasian population, which may have different rates of obesity and medical comorbidities that could affect outcomes. |
| 2. | Were all clinically important outcomes considered? | No. The authors considered immediate complications (perforation, abscess, fistula) and delayed complications (need for surgery, recurrence of diverticulitis). They did not consider complications of antibiotic therapy, complications of surgery, cost, patient satisfaction, or quality of life. |
| 3. | Are the likely treatment benefits worth the potential harm and | Uncertain. This is a very interesting open-label, randomized controlled trial which demonstrates low |

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| | costs? | complication rates (1.4%) in all patients with diverticulitis. The complication rate was nearly twice as high in the no antibiotics group compared to the antibiotics group (1.9% vs. 1.0%). This difference did not achieve statistical significance owing in large part to the relative paucity of complications in both groups. Further randomized trials will need to be conducted in more diverse populations with an emphasis on determining a clinically acceptable difference in complication rates. |

**Limitations:**

1. **While the study was randomized, there is no mention as to whether or not the envelopes were opaque (allocation concealment).**
2. **The authors do not explicitly state if a primary outcome was defined *a priori*.**
3. **It is likely that the racial make-up and prevalence of comorbidities is different in these Swedish and Icelandic populations than we see in the US (external validity).**
4. **The study was not blinded, potentially subjecting the results to performance bias and observer bias.**
5. **Follow-up by telephone/letter is subjective (recall bias).**

**Bottom Line:**

**This non-blinded randomized controlled trial conducted in Sweden and Iceland demonstrated low complications rates in patients with uncomplicated diverticulitis treated both with and without antibiotics, with no statistically significant difference between the groups: RR 2.0 (95% CI 0.51-8.0). There was also no statistically significant difference in hospital length of stay, need for surgery during follow-up, or recurrence of diverticulitis between the groups. Further randomized controlled trials will need to validate these results in different, preferably more heterogeneous populations before implementation in our institution. Researchers will also need to clearly define a clinically acceptable difference in complication rates.**