CRITICAL REVIEW FORM:
THERAPY ARTICLES

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Citation: Williams, D. MD, et al. Short- vs Standard-Course Outpatient Antibiotic Therapy for Community-Acquired Pneumonia in Children – The SCOUT-CAP Randomized Clinical Trial. *JAMA Pediatrics*. 2022; 176(3): 253-261.

Study Objective:

To assess clinical resolution of CAP in children with short course vs standard course of antibiotics and to assess antibiotic-associated adverse effects and antibiotic resistance genes (resistomes) in these patient populations.

Study Methodology:

Multi-center, double-blind, placebo-controlled clinical trial performed at 8 outpatient settings (20% ED patients 80% Urgent care or other outpatient settings)

Eligible children were approached on days 3 to 6 of their initial therapy and had to have Parental report of clinical improvement that included:

- No Subjective fever or documented temperature 38.3 °C or higher in preceding 24 hour
- No Tachypnea (50 breaths per min for < 2 years; 40 breaths per min ≥ 2 years old)
- No Severe cough

If enrolled patients were randomized to either continuing their current antibiotic or placebo for 5 additional days.

Primary Outcome: Response Adjusted for Duration of Antibiotic Risk (RADAR) measured at the first outcome assessment visit (OAV1 on days 6–10). Ranked overall experiences.

Secondary Outcome: RADAR at OAV 2 (days 19-25), adequate clinical response, adverse effects and resistome measures.

GUIDE	COMMENTS
I. Are the results valid?	
A. Did experimental and control groups begin the study with a similar prognosis	
1. Were patients randomized?	Probably. Authors mention randomization was 1:1 but do not go into detail regarding the randomization process (i.e., computer generated)

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?	Randomization and allocation concealment was not adequately described. The authors do not describe exactly how they were able to ensure that the study participants received their previously-prescribed antibiotic or how they were switched to the study drugs. There was a potential for some unblinding here.
3. Were patients analyzed in the groups to which they were randomized?	Yes. Authors described using ITT analysis.
4. Were patients in the treatment and control groups similar with respect to known prognostic factors?	Yes. (Table 1) Both groups were children who were matched regarding age, sex, race, antibiotic, etc. Caucasian children were over-represented (61.5%)
5. Were patients aware of group allocation?	Patients/families were blinded to their groupings. Same dosing was applied. Placebo had a matching taste and appearance to corresponding antibiotic.
6. Were clinicians aware of group allocation?	They do not describe blinding process clearly. This is my area of largest concern for this study. Over 90% were prescribed Amoxicillin unclear how they matched initial antibiotic/placebo with study drugs.
7. Were outcome assessors aware of group allocation?	They do not specifically describe how outcome assessors were blinded.
8. Was follow-up complete?	Of 385 patients included in randomization, 330 were included if final analysis and intention to treat including worst case analysis was used which should adjust for those lost to follow-up
What are the results ?	
1. How large was the treatment effect?	**More desirable DOOR for short-course strategy: 0.48 (95% CI, 0.42-0.53) at OAV1** **More desirable RADAR in short course strategy: 0.63 (95% CI, 0.57-0.69)** The following were **not** statistically significant (all 95% CIs): - Proportions of inadequate clinical response (0.5%; -2.4 to 3.7) - Participants with persistent symptoms at OAV1 (1%; -6.8 to 4.7) - Participants with persistent symptoms at OAV2 (0.1% -5.3 to 5.4) - Participants reporting adverse effects from antibiotics (3%; -7 to 13). - Adverse effect at OAV2 (2.6%; -7.7 to 12.9)

2. How precise was the estimate of the treatment effect? (CI's?)	**See above**
III **How can I apply the results to patient care?**	
1. Were the study patients similar to my patient?	Yes, similar aged children to those seen at CHKD however disproportionate white population.
2. Were all clinically important outcomes considered?	Yes. Using DOOR, they specified adequate clinical response, resolution of symptoms, and the presence of antibiotic-associated adverse effects as well as treatment failure, hospitalization, or death.
3. Are the likely treatment benefits worth the potential harm and costs?	Yes, a reduction in antibiotic time/exposure showed a similar clinical outcome and no harm to the children, while showing a reduction in resistance genes, which has long-term implications in each child's future response to antibiotics and personal resistisome.

Limitations:
- They don't specify their randomization or blinding technique
-Exclusion criteria were very broad. All very healthy children. Most may have had viral illness. No standardization of parameters for the clinical diagnosis of pneumonia.
May not be powered to adequately assess difference in harms.
- RADAR assumes that shorter course is better, which if fine/makes sense for antibiotic stewardship; however, does insert inherent bias
- DOOR is an ordinal ranking and not totally objective and therefore has room for bias.
- Few diagnostic tests were performed to compare hard data (blood cultures, CXR, etc.)
- Study was limited to "otherwise healthy" children younger than 6 diagnosed with "uncomplicated CAP" who demonstrated early clinical improvement during the first 5 days (at time of enrollment: no subjective fever, documented temperature above 38.3 C+ in preceding 24 hours, tachypnea (50+/min) in those 2 years or younger, and 40+/min in those 2 years or older, and severe cough), so cannot extend these conclusions to children with underlying conditions, those with severe pneumonia, and those did not show early improvement.

Clinical Bottom Line: A shorter course of antibiotic therapy may be considered in non-severe pediatric community acquired pneumonia.