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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 23770

Title: Comparison of pediatric and adult antibiotic-associated diarrhea and Clostridium difficile infections

Reviewer's code: 00068404

Reviewer's country: China

Science editor: Ze-Mao Gong

Date sent for review: 2015-12-17 14:53

Date reviewed: 2015-12-21 22:58

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This manuscript was conducted to compare AAD and CDI in pediatric and adult populations and determine significant differences and similarities that might impact clinical decisions. This is a carefully done systematic review, the topic is of considerable interest and has a good clinical significance, which can guide clinical work. The reference of this study is relatively sufficient and reasonable. The language of this article is relatively smooth and has readability. On the whole, this is a good article which deserves publication.



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 23770

Title: Comparison of pediatric and adult antibiotic-associated diarrhea and Clostridium difficile infections

Reviewer's code: 00504462

Reviewer's country: Mexico

Science editor: Ze-Mao Gong

Date sent for review: 2015-12-17 14:53

Date reviewed: 2015-12-22 06:22

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

I read your manuscript with great interest and your review has been a good effort to go through the bibliography and analyze it. However, your effort is lacking in some points that need some clarification: a) Your pediatric age group definition is a bit confusing as you wrote that "generally, the pediatric population is defined as aged one month to 18 years of age, but for pediatric CDI this age range has been shifted to 1-21 years old". However, you did not then proceed to state which age range you used for the rest of the analysis. It is a reality that there are many changes from birth through childhood and the adolescent years, and many authors divide the pediatric group into neonates (under 1 month in age), then for children from 1 month to 4 years, children 4 years to 10 years, and finally adolescence. (Your only reference is that "infants younger than one year old are typically excluded".) b) If I understood correctly you are arguing that cdi is different from aad, but the articles you cite do not support this directly because the cited studies show that a risk factor for cdi is the use of antibiotics. Can you clarify this argument and look for more appropriate supporting studies? c) From the lack of good definitions, some of your data and conclusions are confusing. d)



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The manuscript is also too long, maybe because of the precedent aspects, and I could suggest, maybe that you could rewrite it, and break it into 2 manuscripts. Alternatively, try to focus your definitions and objectives. Hope you can fix it and resubmit it soon Sincerely



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 23770

Title: Comparison of pediatric and adult antibiotic-associated diarrhea and Clostridium difficile infections

Reviewer's code: 02731212

Reviewer's country: United States

Science editor: Ze-Mao Gong

Date sent for review: 2015-12-17 14:53

Date reviewed: 2015-12-23 04:00

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

This review article compares pediatric and adult AAD, and also compares pediatric and adult CDI. This seems like a worthwhile comparison to make because (1) it has been suggested that these entities differ substantially in adults and children, and (2) gastroenterologists who practice at small hospitals may be called upon to serve both children and adults. Of course, it is challenging to make sensible comparisons across studies involving different populations (how, for example, can we draw conclusions by examining a study that tests the effectiveness of flagyl vs vancomycin for CDI in adults and then another similar study in children?). However, the authors take a sober approach and, for the most part, the manuscript is successful. MAJOR COMMENTS: 1. AAD is a diagnosis of exclusion and patients with AAD are heterogeneous: some have undiagnosed gastrointestinal infections, and others have non-infectious diarrhea which may be related to the loss of normal commensal bacteria. This is especially true for older studies of AAD, where the only testing may have been stool cultures. Because it is so hard to say much about AAD, I did not find these sections helpful. Why not focus exclusively on CDI, where the patients are more homogeneous? 2. A



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style point. The frequent section breaks make the manuscript very choppy to read. Could the authors combine some of these sections? 3. One of the interesting things about this comparison is that it may help to shed light on pathophysiological differences between children and adults for AAD/CDI. The authors touch on this (p. 15) but there is no section explicitly focused on pathophysiology. MINOR: p. 4: "The burden and costs..." Actually, there are some studies and the authors cite some of them on page 8. p. 5, Definitions: I don't find this helpful and would incorporate the definitions into the manuscript. I don't think that "time to onset" requires such a long definition. p. 8: "Rates may also range..." This sentence is confusing. Rephrase. p. 11, Risk Factors: Modifiable risk factors are the most interesting and also the most useful. Can the authors be more specific than "broad spectrum" antibiotics? p. 11-13, CDI Risk Factors: What about acid suppression medications? These are a potentially modifiable risk factor and have been studied extensively in adults and studied at least somewhat in children. p. 14: "Adults with CDI have a more complex risk factor profile." I think the authors mean that adults with CDI tend to have more comorbidities than children with CDI. But don't adults always have more comorbidities than children? p. 25, higher doses of vancomycin: Can the authors cite specific evidence supporting high dose vancomycin? My impression is that there is little evidence that doses higher than 125 mg qid result in substantial benefit. The authors make a similar statement elsewhere in the manuscript. p. 24-26, CDI treatment: The authors breeze past FMT, which has strong evidence vs recurrence in adults. What about children? Tables. These contain useful information but are almost impossible to read—one can't easily tell which piece of information goes with which reference. I would restructure these.



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 23770

Title: Comparison of pediatric and adult antibiotic-associated diarrhea and Clostridium difficile infections

Reviewer's code: 00159305

Reviewer's country: Romania

Science editor: Ze-Mao Gong

Date sent for review: 2015-12-17 14:53

Date reviewed: 2015-12-19 02:57

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

To the authors, Good piece of work, well written. I have no concern about your manuscript. P.S. However, I have one concern: the core-tip is lacking! (please, write it) In addition, please see page 4 line 8: to pediatric..., and page 19, last paragraph line 2: delete one increased!



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 23770

Title: Comparison of pediatric and adult antibiotic-associated diarrhea and Clostridium difficile infections

Reviewer's code: 00033739

Reviewer's country: United States

Science editor: Ze-Mao Gong

Date sent for review: 2015-12-17 14:53

Date reviewed: 2015-12-26 04:21

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input checked="" type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

Dear authors: Thank you for allowing me to review your manuscript entitled "A Comparison of pediatric and adult antibiotic-associated diarrhea and Clostridium difficile infections." I found your review article very well written covering several important topics including antibiotic-associated diarrhea in both children and adults as well as C. difficile infection in the pediatric and adult population. Your presentation was balanced and provided one of the more comprehensive groupings of data for these topics that I have seen to date. I felt that you should be commended for writing on important topics and covering all relevant sub-topics associated with these disease states. Including the pediatric population side by side with the adults differentiates your manuscript as unique and exposes a shortage of data in the pediatric population for CDI and a true shortage of publications for antibiotic-associated diarrhea in both populations. I only had a couple of conceptual questions for you to consider and several minor changes to the document listed below. Major: 1. Adult CDI Severity: Consider adding information regarding white blood cell count, creatinine and albumin as commonly used indicators of disease severity for this population.



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These criteria should be initially described as a way of triaging disease severity (Cohen et al. 2010 and Surawicz et al. 2013). Once that has been described, then consider contextualizing that information into the discussion that already exists regarding how the various studies rated the disease severity so the reader has a better idea of how each study classified their patients. 2. Table 4: The crude mortality and colectomy rates are a bit confusing since no time frame is provided for these. Are these all 30-day rates? If so, please label. If not, please consider adding the time frame for the rates for each of these studies to allow the reader a better understanding of the data presented. Minor: Introduction 1. Page 4, Paragraph 1, Line 8: Please add a space between "to" and "pediatric." Epidemiology: 1. Pediatric CDI outbreaks: Page 10, Paragraph 2, Line 5: The sentence that starts with "While most studies..." reads strangely. Consider adding the word "in" between "While" and "most." 2. Adult CDI outbreaks: Page 10, Paragraph 3, Line 4: Please consider changing the sentence to read "the 1980s, with as few as..." 3. Page 18, Paragraph 2, Line 5: The sentence that starts with "Most AAD cases are mild-moderate..." reads strangely. Consider removing "AAD cases" at the end of the sentence and pluralizing the word adult. Consequences of Infection: 1. Page 19, Adult CDI Consequences, Paragraph 1, Line 2: The word increased is duplicated. Please consider removing one. 2. Page 39, Table 4, Cost, Pediatric CDI: Please consider adding a hyphen between the two dollar sums. Treatment: 1. Page 24, Treatment of pediatric CDI, Line 7: Consider removing the word "cases" to improve the flow of the sentence.