Reviewer's report

Title: Development of Quality Indicators for Antimicrobial Treatment in Adults with Sepsis

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Reviewer: dilip nathwani

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Review: Development of Quality Indicator for Antimicrobial Treatment in Adults with Sepsis

Bundles of care, applied through an all or nothing approach, have been devised for the management of sepsis to convert clinical practice guidelines into meaningful changes in behaviour and clinical outcomes. The evidence base to support this has most clearly been defined for the management of patients with severe sepsis or septic shock and to a much lesser extent inpatients with only sepsis. However, many systems around the world have extrapolated the benefits applied to severe sepsis/septic shock in to the sepsis setting and there is some emerging evidence to support this.

However, quality indicators specifically looking at the appropriateness of empiric antimicrobial therapy have been suggested but have not been formally developed as potential indicators through a systematic and structured approach. Therefore, this paper which attempts to develop quality indicators for antimicrobial treatment in adults with sepsis is welcome.

I have a significant number of reservations regarding this paper which I believe require attention: These are major compulsory revisions.

1. The title of the paper states that the Quality Indicators developed for antimicrobial treatment are for adults with sepsis. However, the second Quality Indicator in the final set is for adult patients with severe sepsis and septic shock. These are not the same patient population and there needs to be clarity around this.

2. The definition of appropriateness in measuring the impact of antimicrobial therapy on key outcomes is fundamental to this analysis. I do not accept that the authors have undertaken a full systematic review to understand how clinicians or investigators have defined appropriate antibiotic therapy. I would refer the authors to an excellent paper by McGregor JC et al in Clinical Infectious Diseases 2007; 45:329-337.

3. I cannot find in the manuscript the strength and quality of evidence to support the included and excluded indicators that were considered. As the authors will be aware that for clinical guidelines recommendations to be included as quality indicators the strength and the quality of the evidence base needs to be strong. This is particularly true when we are looking for an association of a process
indicator on key outcomes. Therefore, I would wish to know whether compliance with each of the indicators suggested has an impact on clinical outcome, length of stay, antibiotic resistance or cost. These were the indicators that the authors have included in their analysis.

4. The authors provide five final set of quality indicators as a means of monitoring antimicrobial use in hospital adult patients with sepsis. The authors do not allude to their utility as independent measures of quality process or whether they need to be applied through a bundle approach for impact on the various outcomes. I do think this needs to be clarified in more detail.

5. When one is attempting to assess the quality of care in sepsis management not only is the appropriateness of the treatment important but whether the first dose of antibiotic therapy is administered immediately. I would refer the authors to Marwick et al JAC 2007;60:694-697. The risk assessment approach here is relevant and of interest.

6. The modified Delphi procedure outlined in the development process is well validated and the authors clearly possess significant expertise in this area. I do have some concerns about the composition of the 6 panel members. Four of these are infectious disease specialist’s who have specialist interest in this area and are probably biased towards one specific view. Since the majority of sepsis is managed by internist or surgeons outside the ICU I would have thought inclusion of them within the expert panel would have been appropriate. Furthermore, whilst the high response rate to both questionnaires increases the validity of the results attendance of 43% by the expert panel I would not deem as satisfactory but rather disappointing. This may have an impact on the robustness of the developmental process.

7. My next series of comments are in relation to table 3 and the final set of quality indicators proposed.

a. Quality indicator 2 recommends that antimicrobial therapy should be started as soon as possible, preferably within the first hour. This is not clear and open to misinterpretation. Therefore I think it should have been antimicrobial therapy should be started within the first hour. This is measurable and are commonly used process indicator. The point I made in relation to severe sepsis and septic shock is applicable to this proposed indicator. Furthermore, documentation of the time of the clinical diagnosis is notoriously difficult to measure or elicit from case note review. This clearly would have an impact in defining the numerator. Have the authors considered testing these indicators in real world practice? Their ability to measure these in routine practice prospectively or retrospectively is key.

b. What is the evidence base to support that at least two sets of blood cultures should be taken and their impact on the range of outcomes suggested. For pragmatic purposes one blood culture may be all that is possible and recommending this would it make a difference? Furthermore, how essential is it that culture from suspected sites of infection should be taken, particularly when there is no availability of the specimen?

c. Quality indicator 4 (number 45) suggests that empiric antimicrobial therapy should be changed to pathogen directed therapy “as soon as culture results
become available”. How does one in the real world measure “as soon as culture results become available”? Once more for pragmatic purposes surely it may be easier to measure a change in pathogen directed therapy within 24 hours of the culture being available?

d. Quality indicator 5 (numbers 42 & 43) remain confusing as they rely on a combination of measures that look at compliance with national and local guidance. Most healthcare systems who adopt national guidance allow local flexibility for adaptation and adoption of national guidance in to local practice depending on resistance patterns and so on. I think that for this indicator to be valuable in measuring real world clinical practice for managing sepsis the sole indicator should be empiric antimicrobial therapy prescribed in relation to local guidance. I think this indicator reflects very much Dutch practice and I am not sure it is entirely consistent or adaptable to practice elsewhere. Furthermore, in terms of measuring accordance to local or national guidelines does this mean that the choice of therapy is consistent with this or does it also apply to dose, proposed duration, route etc. This needs clarification.

e. I think the data would benefit from validity in a range of health care settings as the authors point out.

f. For clinicians timely antibiotic, supportive therapy and optimising the quality of antibiotic use are all key. The utility of this bundle should be as part of the sepsis bundle. Therefore, further streamlining of indicators that have impact on outcomes and are supported by high quality evidence base only may be worth considering for inclusion in a sepsis/antibiotic bundle.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I do know two of the authors personally but do not regard this as a significant conflict of interest.