Author’s response to reviews

Title: Antibacterial resistance in ophthalmic infections: a multi-centre analysis across UK care settings

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Version: 1 Date: 20 Jul 2019

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(A FULL COPY OF THE RESPONSE TO THE REVIEWERS COMMENTS HAS BEEN UPLOADED AS SUPPLEMENTARY MATERIAL)

20 July 2019

Dear BMC Infectious Diseases,

Our thanks indeed for your comments and those from the reviewers, and for the opportunity to revise the manuscript accordingly.

We have submitted a marked up (changes highlighted in yellow) version of the revised manuscript. We have also compiled a response to each reviewer comment (table below).

Please do not hesitate to contact us if any further information is required.

Yours sincerely,

Dr Luke Moore

and on behalf of the co-authors.

Editorial comments
Please also clarify whether the infections/isolates reviewed were community- or healthcare associated as that may explain differences in pathogen and resistance patterns.

We agree that this data would be useful, but we had no access to clinical records relating to these patients as we noted in our limitations section. We can presume that by far the majority were community associated, and that healthcare associated/post ocular surgery infections were a small minority. We have added a sentence to that effect in our limitations section (row 304-306).

Reviewer 1 comments

Due to the study design and risk of ascertainment bias for the collection of this type of microbiology data (as highlighted by the authors), where specimens are more likely to be collected if there is empiric treatment failure or more severe disease, inferences should be taken with caution.

We agree. We have added additional emphasis to this point in our limitations section (row 311-312).

Any recommendation to changing the empiric prescribing guidelines would be premature without greater understanding of the numbers of patients presenting with ophthalmic infections that do not progress to having a specimen sent to the microbiology laboratory. These data are particular important for the primary and secondary care settings where there may be a high proportion of patients presenting who are treated successfully without microbiological sampling. Can the authors provide any insights to the prevalence of ophthalmic infection presentations to these various settings over this study period.

Whilst we agree that denominator data would be particularly useful in establishing the extent of any ascertainment bias from sampling only of treatment failure or more clinically severe patients, this data is not available from currently collected healthcare records as the clinical systems are still predominantly paper based, and pharmacy dispensing records are many, varied, and do not currently feed into any central repositories. This is why we advocate in our manuscript the need to consider sentinel surveillance for ophthalmic infections to determine the true burden of causative organisms and resistance. We have added an additional comment to note the issue raised by this reviewer (row 319-321).

These data from the tertiary care setting may be more complete, as there may be a higher proportion of specimens sent upon presentation with an ophthalmic infection. As Pseudomonas was isolated in such a high proportion of specimens from these tertiary care facilities, not recommending an antimicrobial with anti-Pseudomonal activity for treatment guidelines in this setting is unusual. Can the authors explain why there was no discussion regarding this recommendation.
We agree anti-pseudomonal agents should be considered in tertiary care and do make note of this in our discussion. We have added a sentence to strengthen this given the reviewers comments (row 291-294).

The recommendation of removing fusidic acid from the empirical prescribing guidelines for children, due to the high proportion of haemophilus detected in this population, would also of more likely value from this study and highlights the need for further investigation into this.

We have added a sentence to this effect in our recommendations section (row 279-281).

Reviewer 2 comments

Since the study was on a retrospective analysis of bacterial agents of ophthalmic infections, the more appropriate term would have been 'antibacterial resistance', although 'antimicrobial resistance' which is broader, is most times generally but inappropriately used. The title should therefore be modified as "Antibacterial resistance in ophthalmic infections: a multi-centre retrospective analysis across UK care settings"

Changed. Row 1.

Abstract: There was no description in the methodology or result section that supports the concluding statement "We find significant antimicrobial susceptibility-policy mismatches…." This statement should be modified or deleted.

We have recast the concluding statement in the abstract to better fit the research question. Row 61-62.

Line 39-41: The statement "Table 1 describes national and local secondary care guidance for the pharmacological management of bacterial conjunctivitis" should be re-cast. It is not appropriate to be reporting table in introduction (although table may be cited).

We have moved our signposting to this table on national and local prescribing guidelines to the methods section in the “study setting and design” section. Row 105-107.

The subtitle "Study setting" should appropriately read "Study setting and design"

Changed. Row 100.

The specimens from which those organisms were recovered should reflect under the methodology (although this appeared in the result section under patient demographics, which is inappropriate). Authors cannot describe in the result section what they have not stated in the methodology
We have expanded the methods section relating to what data was being collected. This now details specifically: patient characteristics, location of patients’ care (primary/secondary/tertiary), specimen type, and organism characteristics (identification, antimicrobial susceptibility pattern). Rows 109-111.

The following statement "Eye cultures were obtained from various sources including eye swabs (2358/2681, 88.0%), conjunctival swabs (98/2681, 3.7%), contact lens swabs (54/2681, 2.0%), corneal scrapes (148/2681, 5.5%), and invasive samples (23/2681, 0.8%)" should not be part of patient demographics. This is better put under pathogen distribution, which should now be renamed "Specimen and pathogen distribution"

Results subsection renamed “Specimen and pathogen distribution” and the section noted by the reviewer has been moved to rows 155-158.