

Peer Review File

Article information: <https://dx.doi.org/10.21037/ajo-23-45>

Reviewer A

Comment 1:

There is already a fair amount of literature published on this subject but this paper does represent the findings of a large tertiary referral centre in an Australian setting, which makes it appropriate for publication in this journal.

Reply 1:

Thank you for this opinion. No change to text required.

Changes in text: Nil.

Comment 2:

It is well-written and follows logical arguments and reasonable conclusions. However, the data presented is not in line with the final clinical algorithm. If they aim to offer an evidence-based approach, then why retest normal hearing patients again at 6 months and 12 months? I agree that this is a sensible approach but it does not strictly follow their own presented data. 95% of patients with meningitis will not have any hearing loss and of those, several studies including their own data show that if the first audiogram is normal then further SNHL is not seen so I am not sure why they have then decided to retest those patients twice more? Perhaps they could justify this? Is it simply that the consequences of missing a hearing loss are so large. This is fair but then why make guidelines evidence-based.

Reply 2:

Thank you for your response. We agree that our study did not identify any children with new SNHL if their first audiogram was normal. Based purely on this data it would be reasonable to suggest that if the first audiogram was normal these children could be discharged from audiology follow up. However, as referenced in the discussion (paragraph 3), some studies have identified children with normal hearing on first audiogram and progressive SNHL on subsequent tests. We acknowledge that these numbers are small, Jensen et al 2023 identified one patient with progressive SNHL and Woolley et al 1999 again only identified one patient. Brookhouser et al 1994 finds a larger number of children with progressive SNHL post meningitis but does not comment if these children had normal or abnormal audiograms initially. On discussion with our audiology colleagues at Queensland Children's Hospital and the Cochlear Implant MDT, it was felt that without large volume studies and a lack of research confirming no risk of progressive loss, that all children should be offered ongoing audiology review. As you state, the consequences of missed hearing loss are significant, and perhaps even more so in a post-meningitis child with learning and/or developmental delays secondary to their infection.

Changes in text (Discussion, line 260):

Whilst no children in this study were found to have new SNHL on subsequent audiology if their first test was normal, we have recommended repeat audiology at 6 and 12 months. The rationale for this is multifactorial. A small number of studies have identified new progressive SNHL after meningitis in children with initial normal audiology and these children are also considered at risk for developmental delays and cognitive impairment(9,21,23,24).

Comment 3:

Secondly, it would be simpler in the algorithm to state that any abnormal audiogram (of any severity) should be referred immediately to the ENT team as they can then direct intervention (further audiological testing, amplification or urgent CI) accordingly, rather than the treating team (eg ICU, Neurology, Paediatrics) re-testing the patient which could impart unnecessary delays in crucial intervention eg administration of steroid or urgent imaging for consideration of CI in cases of impending ossification.

Reply 3:

We acknowledge the reviewer's concern regarding further delay if repeat testing is performed. Please note that if the SNHL is severe or profound then this second test is not required and urgent referral should be made. On consideration of this suggestion however, we have now included a recommendation for concurrent ENT referral whilst also arranging for repeat testing.

Changes in text (discussion, line 256):

Should hearing loss of any degree be confirmed on initial testing, urgent referral should be made to an ENT surgeon and repeat audiology should occur at 2 weeks to qualify the loss and identify any rapidly progressive change. Importantly, if the initial audiogram suggests severe or profound SNHL, the audiologist should make immediate contact with the Cochlear Implant coordinator to expedite the child's care.

Comment 4:

Clearly the heterogenous nature of the international treatment algorithms is not ideal and is no doubt contributory to the variance in patient treatment. Having yet another guideline from another state is not ideal and stresses why Australia or Australia and New Zealand should look at forming an otological society that could produce uniform guidelines across the country/ countries to prevent confusion.

Reply 4:

We agree with this reviewer's concern regarding the lack of Australia wide or Aus-NZ wide guideline. The difficulty in creating such a guideline lies in the varied referral pathways, funding, and patterns of care among differing health services. Each state has differently funded newborn hearing screening programs which highlights the heterogeneity of audiological services around Australia and New Zealand. The addition of a State-wide Queensland guideline aims to at least streamline post meningitis audiological care in Queensland and perhaps, with time, can be used to contribute to the formation of an Australia wide guideline in conjunction with other guidelines from other states. Despite the lack of otological society in Australia and New Zealand, ANZSPO could be well positioned to facilitate such a guideline and the addition of Queensland data may help in doing so.

Changes in text (Conclusion, line 297):

We acknowledge that guidelines exist in other states of Australia and internationally. The authors would support a comprehensive Australia wide review with a view to producing a national referral guideline for Australia and New Zealand.

Comment 5:

I feel the data presented is important to add to the published literature but I am less inclined to support the proposed guideline given it only muddies an already saturated set of guidelines on this subject and is not clearly evidence-based, even by their own data.

Reply 5:

We acknowledge the reviewer's opinion on our proposed guideline. As detailed in the comment above, the inclusion of repeat audiology at 6 and 12 months arises from concern that our subject group is not large enough to exclude this requirement entirely. The future development of a consensus statement or national referral guideline would improve clarity which we would entirely support.

Changes in text: As per Comment/Reply 4.

Reviewer B

Comment 1:

This paper presents a review of bacterial meningitis in Queensland and a retrospective review of the outcomes of children with regard to their hearing as well as the wide variability in referral patterns and practices. Overall, the manuscript is well written but there are a number of formatting / grammatical / past and present tense / sentence structure issues which need to be addressed prior to publication:

1. Abstract methods section – Line 55 – incomplete sentence
2. Abstract conclusion Line 69 – could the authors justify how they compared their series with other developed countries? Was their series compared to developing countries?
3. Line 83 – suggest “four” instead of 4
4. Line 87 – suggest “...the incidence...”
5. Line 94-95 – This sentence is confusing, consider rewording
6. Line 108 – Suggest “birth” instead of “O”
7. Line 113 – What is a “problem code”
8. Line 114 – Suggest “allowed”
9. Line 128 – How was a “possible diagnosis” searched for? What was the database search methods used?
10. Throughout the manuscript means, ranges, medians, and standard deviations are not consistently reported. In addition, numbers as being used without referring to what they signify. For instance
 - a. Line 129 – 20.7 days (5-42) – what does 4-52 refer to?
 - b. Line 143 – 47 (82.5%) – what does this number refer to?
 - c. Line 153 – 34 had repeat testing – what does 34 refer to and what were their results?

11. Line 158 – What does successful bilateral cochlear implantation mean?
12. Line 162 – What does suitability mean?
13. Line 188 – Spelling error in assessment
14. Line 188 – What is the increased risk of labyrinthitis?
15. Line 251 – Suggest remove “what we hope”

Reply 1: Thank you for your review and for noting the above errors. Each has been amended in the text as follows;

Changes in text:

1. Abstract methods section – Line 55 – incomplete sentence
 - a. Now reads (line 55): “A cross-sectional retrospective review was conducted of treatment and outcomes of all children aged 0-18 years diagnosed with bacterial meningitis at Queensland Children’s Hospital between November 2014 and December 2021 (7 years). Descriptive data analysis including...”
2. Abstract conclusion Line 69 – could the authors justify how they compared their series with other developed countries? Was their series compared to developing countries?
 - a. Apologies for the lack of references here, this has now been rectified. We did not compare the series to developing countries for a number of reasons. These being the difference in vaccination rates, the different aetiology of bacterial meningitis in developing countries and the difference in treatment paradigms, in particular, availability and use of corticosteroids.
 - b. Now reads (line 81): The incidence of SNHL post bacterial meningitis was 5.2% which remains comparable to that of other developed countries such as the UK and New Zealand (1,2)
3. Line 83 (now line 95) – suggest “four” instead of 4
 - a. Now reads “Fortunately, in the last four decades...”
4. Line 87 (now line 99)– suggest “...the incidence...”
 - a. Now reads: ...the incidence...”
5. Line 94-95 (now line 106) – This sentence is confusing, consider rewording
 - a. Now reads: Despite high rates of childhood vaccination and improved hospital care, meningitis related hearing loss is still reported in approximately 5% of cases overall, with *S. pneumoniae* meningitis recording rates of hearing loss up to 32%.
6. Line 108 (now line 128) – Suggest “birth” instead of “O”
 - a. Now reads: A retrospective cohort study of all children from birth to 18 years of age treated for...
7. Line 113 (now line 134) – What is a “problem code”
 - a. A “problem code” is a term used for medical coding which assists in data tracking and billing. This has been removed from the text to reduce confusion as it does not add to the description of the methodology
 - b. Now reads: Initially, a hospital database search was conducted to identify patients with a diagnosis of bacterial meningitis.
8. Line 114 (now line 135) – Suggest “allowed”
 - a. Now reads “allowed”
9. Line 128 – How was a “possible diagnosis” searched for? What was the database search methods used?

- a. A “possible diagnosis” refers to the possibility of an incorrect diagnosis being recorded by the medical coders. Queensland Children’s Hospital maintains a database using the REDCap translational research program which allows clinicians to generate large searches for particular terms such as “meningitis”. As this generates some confusion, the sentence has now been reworded.
 - b. Now reads (line 159): A hospital database search identified 75 patients with a recorded diagnosis of bacterial meningitis.
- 10. Throughout the manuscript means, ranges, medians, and standard deviations are not consistently reported. In addition, numbers as being used without referring to what they signify. For instance
 - a. Line 129 (now line 170) – 20.7 days (5-42) – what does 4-52 refer to?
 - i. This refers to the range of days: “20.7 days (range 5-42 days)”
 - b. Line 143 (now line 174) – 47 (82.5%) – what does this number refer to?
 - i. This refers to the number of patients: 47 patients (82.5%)
 - c. Line 153 (now line 184) – 34 had repeat testing – what does 34 refer to and what were their results?
 - i. This refers to the number of patients: “34 patients (89.5%) underwent repeat testing”
 - ii. The result of this repeat testing is displayed in Figure 1. No additional SNHL was identified with repeat audiology. This is now also reflected in the text: “There were no additional cases of SNHL identified on subsequent audiograms.”
- 11. Line 158 (now line 190) – What does successful bilateral cochlear implantation mean?
 - a. Successful bilateral cochlear implantation refers to complete placement of the implant within the cochlea. It does not refer to mapping or hours of use.
- 12. Line 162 (now line 193) – What does suitability mean?
 - a. Suitability refers to surgical anatomy and lack of radiological evidence of labyrinthitis ossificans.
 - b. This has now been reflected in the text: “radiological assessment to ensure absence of ossification and subsequent...”
- 13. Line 188 – Spelling error in assessment
 - a. Now corrected.
- 14. Line 188 – What is the increased risk of labyrinthitis?
 - a. Apologies that this was not discussed earlier in the paper. The introduction has now been amended to include further background on labyrinthitis ossificans and line 188 also amended.
 - b. Now reads (Introduction, line 110): In the cochlea, this may lead to labyrinthitis ossificans which can occur in up to 80% of post *S. pneumoniae* meningitis induced SNHL. The timing of onset of labyrinthitis ossificans is poorly defined in humans but has been demonstrated to occur within 3 weeks of meningitis(6,7). In the setting of ossificans, the new bone formation within the cochlear can make cochlear implantation challenging or even impossible. As cochlear implantation is the gold standard of care for severe to profound SNHL, early implantation in this setting becomes critical.
 - c. Discussion (line 223): Those children waiting such extended time for audiology assessment had increased risk of missing the cochlear implant window should they have had SNHL and subsequent early development of labyrinthitis ossificans.
- 15. Line 251 (now line 295) – Suggest remove “what we hope”
 - a. Thank you, “what we hope” has now been removed from the text

Editorial Comments

This manuscript summarizes the results of audiological follow-up and analyses of 57 children treated for bacterial meningitis at a tertiary hospital in Queensland. Overall, the topic is not new but represents important data in Australia. The main strength of this manuscript is that the authors create a new referral and review guideline for bacterial meningitis at QCH based the 7 years' review and existing literature/guidelines review. Below are some key concerns for further improvement.

Comment 1: Title.

Please kindly consider a more intriguing title that highlights the key issue addressed and key findings of this study. Just for your reference:

Referral and review recommendations for post paediatric bacterial meningitis based on a seven years' review of audiometric follow up in Australia: a cross sectional study

Reply 1:

Thank you for the suggestion. The title has been adjusted.

Changes in text:

Recommendations for audiometric follow up post paediatric bacterial meningitis based on an Australian experience: a retrospective cross sectional study

Comment 2. Abstract.

2A: I failed to find the knowledge gap/uniqueness/rationale in the current Abstract-background. The authors are suggested to clarify this clearly and thereafter, clearly state the aim of this study (to address this gap).

Reply 2A:

Thank you for your comment, we apologise for not clearly addressing the aims of the study early and this has now been amended.

Changes in text 2A: line 48

The aim of this study was to review the current referral and audiological follow up time of children suffering bacterial meningitis including identifying the incidence of SNHL and subsequent treatment outcomes. From this we aimed to offer a standardised referral guideline to be implemented across Queensland hospitals which also contributes to the available published literature on the topic.

2B: The present methods in the abstract could show more detailed information. For instance, for "descriptive data", clearly state they're "patient demographics, age at diagnosis, causative organism, length of hospital stay, audiological referral timeline and outcomes". For instance, also describe the literature/guideline review work (databases and timeframe searched) in the methods.

Reply 2B:

Again, thank you for this feedback. We have considered the above and edited the methods section accordingly.

Changes in text 2B: line 55

A cross-sectional retrospective review was conducted of treatment and outcomes of all children from birth to 18

years diagnosed with bacterial meningitis at Queensland Children's Hospital between November 2014 and December 2021 (7 years). Descriptive data including patient demographics, age, causative organism, length of hospital stay, audiological referral times and outcomes were collected. A review of recent literature was also conducted using PubMed with search terms "meningitis", "hearing loss" and "paediatric" to identify other published series on the topic and published guidelines from other health services. A review of our results plus published literature was then utilised to develop a post diagnosis audiology referral guideline for these children.

2C: Please clearly state in the methods that this is a cross-sectional study.

Changes in text 2C: line 55

A cross-sectional retrospective review was conducted of treatment and outcomes of all children from birth to 18 years diagnosed with bacterial meningitis

2D: One key information is missing in the present results in the abstract: the new referral and review recommendations the authors have proposed. This is essential and should be given.

Reply 2D:

Thank you for the feedback. The abstract has been adjusted accordingly.

Changes in text 2D: line 73

The wide variability in time to audiology review highlighted a lack of awareness and standardised pathway for audiology referral post bacterial meningitis. On review of the above and available local and international guidelines, the authors suggest audiology review within 2-4 weeks of meningitis diagnosis and if abnormal, either immediate referral to a cochlear implant team (if severe-profound SNHL) or repeat testing within 2 weeks plus otolaryngology referral if abnormal result but not severe.

2E: "Incidence of SNHL post bacterial meningitis remained within that of other developed countries", we may hardly make such a conclusion based on the given data/information in the abstract as there is no clear incidence data in the results.

Reply 2E:

Apologies for the lack of references here, this has now been rectified with the addition of NZ and UK references. The study identified the incidence of SNHL to be 5.2% in those that underwent audiology post meningitis. This has also now been included in the abstract for clarity.

Changes in text 2E: line 81

The incidence of SNHL post bacterial meningitis was 5.2% which remains comparable to that of other developed countries such as the UK and New Zealand(1)

2F: Similarly, these conclusions are abrupt as no results data is given before these conclusions: "The review highlighted wide variation in time to audiology referral and review, including a lack of referral guideline and awareness among non-ENT specialist medical professionals regarding risk of SNHL and urgency of assessment. Development and promotion of an evidence-based guideline aims to address this variation and improve patient outcomes for the future."

Reply 2F:

Thank you for your feedback. The results section of the abstract has now been reviewed to include these figures prior to the conclusion.

Changes in text 2F (Abstract, line 68):

80.7% of children were reviewed by audiology post treatment with wide variance in both referral time (0 to 97 days) and time to audiology review (8 to 304 days, median 36 days). Three children were diagnosed with sensorineural hearing loss (SNHL) post meningitis and all cultured *Streptococcus sp.* on CSF culture. One patient underwent successful cochlear implantation for their hearing loss. The wide variability in time to audiology review highlighted a lack of awareness and standardised pathway for audiology referral post bacterial meningitis.

Comment 3. Introduction

3A: Lines 80-84

“Nadol published a review of 578 cases of paediatric meningitis of which 236 were bacterial in nature. Twenty six (11%) children suffering bacterial meningitis died and of those whom survived, 28 (13%) were diagnosed with sensorineural hearing loss.”

The data mentioned is inconsistent with the original article: <https://pubmed.ncbi.nlm.nih.gov/642669/>

Reply 3A:

Apologies, thank you for noting this error. The number “578” has been corrected

Changes to text 3A: (line 92)

Almost 50 years ago, Nadol published a review of 547 cases of paediatric meningitis of which 236 were bacterial in nature. Twenty six (11.0%) children suffering bacterial meningitis died and of those whom survived, 28 (11.9%) were diagnosed with sensorineural hearing loss

3B: Lines 83-84: “Fortunately, in the last 4 decades our understanding of meningitis has progressed and death rates in developed countries are now below 5%.”

How did this data source from? Could the authors cite references to back up this statement?

Reply 3B:

Apologies, the references have missed being added. This data comes from US and European studies which are now cited in the article.

Changes in text 3B: (line 95)

Fortunately, in the last four decades our understanding of meningitis has progressed and death rates in developed countries are now below 5% (5,6).

3C: Lines 90-92:

“In Australia, the high vaccination rate against H. influenzae has significantly reduced the prevalence of associated meningitis, however S. pneumoniae meningitis remains of concern.”

This statement should be based on data and reference.

Reply 3C:

Again, apologies. The references to published literature have now been added.

Changes in text 3C: line 102

In Australia, the high vaccination rate against *H. influenzae* has significantly reduced the prevalence of associated meningitis, however *S. pneumoniae* meningitis remains of concern(8–10).

3D: Lines 101-104:

“We identified a paucity of clinical guidelines for non-ENT specialists in Queensland regarding audiological assessment, referral pathways and ideal time to implantation. This study aims to review the audiological follow up and hearing outcome of children treated for bacterial meningitis in a tertiary Queensland hospital.”

The logic of this statement does not seem to make sense. The current knowledge gap is not very relevant to AIM. Because Logical should at the very least look like either of the following, e.g. Because a lack of guidelines for hearing assessment, referral pathways, and ideal implantation times for non-Ear, Nose, and Throat (ENT) specialists was identified, the purpose of this article is to provide recommendations for guidelines for hearing assessment, referral pathways, and ideal implantation times for non-Ear, Nose, and Throat (ENT) specialists. Or for example, we do not currently know the hearing follow-up, hearing outcomes, referral pathways, and cochlear implantation of children diagnosed with bacterial meningitis in Australia by non-Ear, Nose and Throat (ENT) specialists, so this article aims to provide guidance on hearing assessment, referral pathways, and ideal implantation times for non-Ear, Nose and Throat (ENT) specialists by reviewing hearing follow-up, hearing outcomes, referral pathways, and cochlear implantation of children diagnosed with bacterial meningitis in a tertiary care hospital in Queensland.

Reply 3D:

Thank you for your feedback on the above section of the introduction. We have considered this and adjusted the introduction to better state the aims of the study.

Changes in text 3D: Line 116

Currently, there is a lack of Australian data on audiology follow up and hearing outcomes of children diagnosed with bacterial meningitis by non-Otolaryngology specialists. Thus the aim of the study was to review the current referral and audiological follow up time of these children, including their hearing outcomes and offer a standardised referral guideline for audiological surveillance post bacterial meningitis.

3E: Kindly indicate that this manuscript is written following the STROBE checklist.

Reply 3E: This is now including in the final line of the introduction.

Changes in text 3E: Line 112

We present this article in accordance with the STROBE reporting checklist (available at <https://www.theajournal.com/article/view/10.21037/ajo-23-45/rc>).

Comment 4: Methods and Results

4A: It is recommended that the authors include a description of the methods of the literature review and the results of the review (the methods and results of the abstract should be revised accordingly). This is because the article

mentions in the conclusion that "On review of the current literature, local and international guidelines, we have developed what we hope is a relevant and achievable referral On review of the current literature, local and international guidelines, we have developed what we hope is a relevant and achievable referral pathway for clinicians to follow for children with bacterial meningitis."

In this way, the core figure 3 guideline of the text will be more confident as it is clear that a comprehensive review of which literature, with established guidelines, has been carried out.

Reply 4A:

Thank you for noting this omission. We have since reviewed this and including additional text in the abstract and the main article.

Changes in text 4A:

In abstract, methods (line 59):

A review of recent literature was also conducted using PubMed with search terms including "meningitis", "hearing loss" and "paediatric" to identify other published series on the topic and published guidelines from other health services. A review of our results plus published literature was then utilised to develop a post diagnosis audiology referral guideline for these children.

In main text, methods (line 146):

Pubmed database searches were conducted using the terms "meningitis", "hearing loss", "paediatric", "guidelines", and "audiology" in varying combinations of some and all terms. Articles not published in English language were excluded. A search of each Australian state health service website and of the New Zealand Health website was conducted to identify locally available referral guidelines.

In main text, results (line 198):

Publicly available guidelines were identified from Royal Children's Hospital, Melbourne(13), New Zealand Department of Health(14), and the United Kingdom(15).

4B: It's great that the authors present the inclusion criteria, could you please also present the exclusion criteria in the Methods section?

Reply 4B:

Thank you for this comment. We have now included the exclusion criteria as well.

Changes in text 4B: line 141

Patients with a diagnosis of viral meningitis were excluded as were those with CSF features not in keeping with bacterial meningitis (white cell count, glucose and protein levels) despite the growth of an organism (deemed likely a contaminant).

4C: Line 108: "A retrospective cohort study of ..."

I noticed that the authors defined this study as a cross-sectional study in the STROBE Checklist. Please refine and keep consistent.

Reply 4C:

Thank you for bringing this to our attention. It has now been amended.

Changes in text 4C: line 128

“A retrospective cross-sectional study...”

4D: Lines 131-132: “Mean age at admission was 378 days (median 33 days, range 0 days to 17 years)”

The data is inconsistent/not mentioned with/in that in table 1.

Reply 4D:

Thank you for bringing this to our attention, the range has been corrected.

Changes in text 4D: line 163

Mean age at admission was 378 days (median 33 days, range 2 days to 17 years) and 45 patients (78.9%) were fully immunised as per the Australian National Immunisation Program Schedule.

4E: Table 1: the two categories “31 days-1 year” and “1-5 years” overlapped.

Reply 4E:

Apologies, this has now been clarified.

Changes in text (Table 1):

Now reads 0-30 days, 31 days to <1 year, 1-5 years, > 5 years

4F: Figure 1: Above the existing figure 1, the flow diagram would be improved by adding the initial 75 screened potential targets, then 18 ruled out incorrect recordings, and number of viral meningitis.

Figure 1: There are some discrepancies (inconsistencies or flowcharts of textual descriptions that are not clearly presented) or puzzles between the numerical changes in figure 1 and the description of figure 1 in the main text. For example, if you just look at figure 1, suddenly 33 becomes 41, an extra 8 for no apparent reason. Then 38 becomes 34, and 4 more are not described. 3 becomes 1, and 2 more are not described. Suggest to improve figure 1, so that it can stand alone.

Reply 4F:

Thank you for bringing this to our attention. Whilst it is explained in the text it is not well described in the Figure which we appreciate is confusing. We have since re-created Figure 1 to include the total number of 75 with exclusion of 18 and bacterial meningitis number of 38.

The number of 33 and 13 have been combined for the purposes of Figure 1 and then the 13 patients of whom were referred to audiology but the time of referral was not able to be determined were removed for statistical analysis of “time to referral”.

Changes in text 4F:

See Figure 1.

4G: Figure 1: Also, the time ranges interspersed in figure 1 seem unnecessary and distracting to the reader. Suggest putting it in a separate table:

“Referred for Audiology
median time to
referral: 8.5 days
(range: 0-97 days)

Attended audiology
median time to review.
31 days (range: 9-304 days)
(range: 9-304 days)”

Reply 4G:

Thank you for this suggestion, we have considered it at now added another table.

Changes in text 4G:

See Table 2.

Comment 5. Discussion

5A: Lines 135-136: “The most commonly isolated organism was *E. coli* (31) followed by *Streptococcus* species (5).” That statement is debatable. Because just out of those 57 diagnosed children, 31 were *E. coli* positive and 5 were *Streptococcus* species positive. It does not follow that *E. coli* is the most commonly isolated organism, followed by *Streptococcus* species statement. Because, as the authors state, there are still patients who do not IDENTIFY the organism, there is no way to ensure that *E. coli* must be THE MOST COMMON. A more rigorous wording would be that *E. coli* and *Streptococcus* species were positive in 31(54.4%) and 5(8.8%) of these patients, respectively.

Reply 5A:

Thank you for this suggestion, it has been re-worded as suggested.

Changes in text 5A: line 224

E. coli and *Streptococcus species* were positive in 31 (54.4% and 5 (8.8%) of these patients respectively.

5B: Lines 138: “Twelve patients (21.1%) failed to identify an organism on CSF culture but were deemed likely to have bacterial meningitis based on clinical features and other laboratory findings. Other bacteria identified included *Klebsiella*, *Serratia* and *Pasteurella*. Mean duration of IV antibiotic therapy was 20.7 days (5-42) with cefotaxime being the most common primary antibiotic used and mean duration of hospital stay was 25.2 days. Fourteen of 57 children (24.6%) were treated in paediatric intensive care.”

It is recommended that this information also be organized in table 1.

Reply 5B:

Thank you for this suggestion. Table 1 has been updated accordingly to include additional data

Changes in text 5B:

	Age bracket			
	0-30 days	31 days - <1 year	1 – 5 years	>5 years
Total (57)	27	25	1	4
Male	18 (66.7%)	16 (64.0%)	0 (0%)	4 (100%)
Median age (range)	15 days (2-30 days)	76 days (32-205 days)	2 years	11 years (10-17 years)
Immunised*	19 (70.4%) (unknown 1)	21 (84.0%) (unknown 0)	1 (100%)	4 (100%)
Passed NBHS	22 (81.5%) (Unknown 2 pts)	21 (84.0%) (Unknown 4)	1 (100%)	3 (75%) (unknown 1)
Streptococcus sp.	1	2 (8.0%)	0 (0%)	2
E. coli	17 (63.0%)	13 (52%)	0 (0%)	1
Unknown organism	5	5	2	0
PICU Admission	8	2	1	3
Mean duration of IV antibiotic therapy (range)	21.7 days (5-44 days)	21.1 days (10-42 days)	7 days (no range)	20.8 days (14-34 days)
Mean duration of hospital admission	37.4 days (4-386 days)	13.5 days (3-52 days)	9 days (no range)	23.3 days (4-48 days)

5C: Lines 149-150: “Mean duration from ... was 63.4 days (median 36.0 days, range 8-304 days).”

But in Figure 1, it is median 31 days, range: 9-304 days.

Reply 5C:

Thank you for noting this error, it has been reviewed and corrected with the correct numbers.

5D: Figure 2 seems unnecessary. Consider just going directly to the discussion by adding references and mentioning this NICE management principle, i.e. this way: The UK NICE Guidelines for audiometric follow up post bacterial meningitis recommends “1. Offer formal audiological testing as soon as possible- Prior to discharge or within 4 weeks of being “fit to test”. 2. All children should be reviewed by a paediatrician, including their hearing test result, within 4-6 weeks of discharge; and 3. If severe or profound deafness, urgent assessment for cochlear implant candidacy”(10). Based on this, we further create figure 3, our suggested new referral and review guideline, for bacterial meningitis at QCH.

Reply 5D:

Thank you for this opinion. We have considered it and thus removed figure 2.

Changes in text: line 228

On review of local and international guidelines for audiology assessment post bacterial meningitis, the UK NICE guidelines provide a simple evidence-based guide to review. The guidelines recommend offering formal audiological testing as soon as possible (prior to discharge or within 4 weeks of being “fit to test”. Secondly, all

children should be reviewed by a paediatrician, including their hearing test result, within 4-6 weeks of discharge. And finally, if severe or profound hearing loss is identified, urgent assessment for cochlear implant candidacy should occur(16) .

5E Lines 153-154: “and 31 (81.6%) had audiology performed on at least 3 occasions.”
But in Figure 1, it is “>2 audiograms n=30”.

Reply 5E

Again, thank you for noticing this transcription error. It has now been checked and updated.

Changes in text: see Figure 1

5F: Lines 169-170: “Similar to current literature, this was most prevalent in those less than 1 year of age, with the median age in this subgroup being 30 days.”

Reference is lacking. Also, data in the results (line 132) is 33, not 30 days.

Reply 5F:

Thank you for the above comment. The difference in numbers comes from a subgroup analysis. Whilst the results refers to a median age of 33 days overall, the abovementioned section of the discussion refers to the subgroup of patients from birth to age 1 year. Regarding the lack of references, these have now been included.

Comment 6. Other minor concerns

“The wide variability in time to audiology review highlighted the need for an updated and well publicised audiology referral guideline.”

Typo--“Publicised”

Reply 6:

Thank you, this sentence has since been altered and the word “publicized removed”

Changes in text 6:

The wide variability in time to audiology review highlighted a lack of awareness and standardised pathway for audiology referral post bacterial meningitis.

Comment 7:

The number of keywords has exceeded the requirements of our journal (3-5), please consider keeping the core five keywords to ensure that the number is within a reasonable range.

Reply 7:

Apolgies, this has now been reduced to 5 keywords,

Comment 8:

Please provide the full name of the abbreviations in the Table footnotes and Figure legends, e.g., NBHS, PICU, CI, SNHL, QCH, etc.

Reply 8:

Apologies, abbreviations have now been added.