PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Improving paediatric antimicrobial stewardship in remote and regional Queensland hospitals: development and qualitative evaluation of a tailored intervention for intravenous-to-oral antibiotic switching
AUTHORS	Sharman, Leah; Avent, Minyon L.; Lyall, Vivian; Fejzic, Jasmina; Clark, Julia; Irwin, Adam; Graham, Nicolette; van Driel, Mieke L

VERSION 1 – REVIEW

REVIEWER	Kern, Winfried Freiburg University
REVIEW RETURNED	10-Aug-2022

GENERAL COMMENTS	The aim of this qualitative study was to develop and evaluate a user-led creation and implementation of an intervention package for early IV-to-oral switching at pediatric divisions of seven regional hospitals. A combination of two conceptual theoretical frameworks, „decision sampling framework“ and „person-based approach“ was used. The authors describe four phases of their work. The first three were about the identification/development of multifaceted intervention materials, their review (by 20 healthcare workers and 8 parents/guardians), and their adaptation. The fourth phase was a qualitative evaluation of the intervention by 20 healthcare workers (6-months post-intervention). Phase 1, obviously, has already been published (but is not identified in the references section which states „blinded for review“). Phase 3 also seems to have been published previously („blinded for review“). Phase 4 was done using semi-structured interviews (lasting 5 min to 32 min) with 20 practitioners from the seven study sites, eight of them were physicians. The results section starts with phase 2 (but table 1 in the methods section shows the identified material from phase 1). The comments obtained from phase 2 are extensively reported/shown (table 3). The phase 4 results are outlined separately for what has been named overarching themes „application“, „education and support“, and „team dynamics“. Some of the results are interesting, others (such as the identified barriers) are not unexpected. The strength is the tailoring and adaptation of the materials by stakeholders. A weakness is the lack of quantitative data (such as e.g. estimates for „early“ switching before and after intervention). Another limitation is the lack of patient-guardian interviews in the evaluation. Comments: - Abstract: the authors state that their „offering of tailored

	interventions …. was able to successfully inform and adjust practice across hospital teams“ – what is meant by successful information and adjustment of practice ? Changed practice can be assumed based on the interviews but should not be taken as proven - Why has the evaluation (phase 4) not included parents/guardians ? - Page 13: „Factors of patients and their caregivers also influenced decisions to use (or not use) the material. For example, patient-guardian leaflets were utilized intermittently, with some finding them useful adjuncts to delivering face-to-face advice with patient-guardians, and for others, the materials were most useful with complex patients“. This is a very general statement, and it is not well understood (documented) how this is derived from the interview data, in particular since there were no interviews with guardians. - Page 18: „Similar to previous research, the major barriers to uptake and engagement with the intervention were structural [5,7]. Most hospital sites noted difficulties with the hierarchy of medical engagement. For some, there were difficulties with high turnover of consultants and senior medical staff, such that medical teams did not have consistent leadership and the support to utilize interventions“. Again, as is stated („major barriers“), it is not well explained how this was eventually scored as „major“ in comparison with other potential barriers. - In the post-interventional panel there were many pharmacists. How were they involved in the switching decision ? Did they have similar views as nurses or physicians regarding the intervention value ans obstacles ? - What were the differences between hospitals (if any) ? - Has there been any baseline evaluation regarding length of stay and duration of parenteral therapy in the hospitals ? Different baseline situations with their specific contexts might have a substantial impact on the preferred type, efficacy and the eventual evaluation of such interventions.

REVIEWER	Kirby, Emma University of New South Wales
REVIEW RETURNED	10-Oct-2022

GENERAL COMMENTS	Thank you for the opportunity to review this article, which focuses on the implementation and evaluation of an intervention package to improve timely and safe IV to oral antibiotic switch in pediatrics. The authors discuss their four phased approach, including orientation toward user-led design and evaluation. The article includes a thorough review of their range of resources/approaches, and highlights flexibility through their iterative approach to adjustment and improvement. The study includes parents/guardians as end-users in the earlier stages, but goes on to focus on input from health professionals (this is not a criticism – rather, I was interested to hear more about why parents were not included throughout the stages). Following a number of minor revisions, which I outline below, I would support this article's publication, and see the contribution of this article to ongoing research on AMS. P7: The authors state that post-intervention evaluation interviews were not able to include parents/guardians – some commentary on why this was, and what might be gained/missed from this would be useful (particularly in terms of future research). P8: A reference is needed to support/specify the working definition of data saturation here. P8: Has a copy of the interview questions been made available as a supplementary file? Can it be? It would be useful for a reader to see the list of questions provided to participants before the interview.

	P10: “Analysis used an essentialist approach that was reflexive and iterative to identify themes within the data [16,17].” More explanation of an ‘essentialist approach’ is needed here (and indeed clarification of the use of an essentialist approach) – reflexive and iterative identification of themes are processes present in the articles cited at the end of this sentence, but not an essentialist approach (in fact, a constructivist approach). Alternative references to support this should be used to cite as essentialist approach. P8: Phase 2 interviews were audio-recorded and transcribed verbatim – is there a reason these data are not shown in any quotations in the Findings section? It would be particularly interesting to hear about the data from parents/guardians, given they were not involved in later stages. Discussion: Certain points within the discussion require a little more explanation to ground them in the data presented. For example p17: “Providing decision-making support to junior doctors, nurses, and pharmacists increased their individual capacity to influence antibiotic decision-making…” – is there evidence to show that their capacity to influence was increased, or is this self-reported that they felt that their capacity was increased? Please clarify. The discussion paragraphs that follow (top of page 18) are much clearer in this regard. Moreover, the discussion about strengths and limitations is especially strong, and does a very nice job of highlighting the contribution of the study and method.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1: Dr. Winfried Kern, Freiburg University:
Comments:

1. Abstract: the authors state that their “offering of tailored interventions …. was able to successfully inform and adjust practice across hospital teams“ – what is meant by successful information and adjustment of practice ? Changed practice can be assumed based on the interviews but should not be taken as proven

Thank you to Dr Kern, we have adjusted the phrasing of the conclusions section of the abstract so that it is more clearly grounded in the data. See page 2:

> Despite structural barriers to AMS for switching from IV-to-oral antibiotics in paediatric patients, offering a tailored multifaceted intervention was reported to provide support and confidence to adjust practice across a diverse set of health workers in regional areas.

2. Why has the evaluation (phase 4) not included parents/guardians ?

The description of phase 4 now includes why patient-guardians were not included. See page 8:

> Unfortunately, these interviews were not able to include parents/guardians because access to this population was not feasible at the end of the 6-month intervention and after the completed treatment period for patients. Further we were not able to know who received the material to contact them for this phase of the research.

3. Factors of patients and their caregivers also influenced decisions to use (or not use) the material. For example, patient-guardian leaflets were utilized intermittently, with some finding them useful adjuncts to delivering face-to-face advice with patient-guardians, and for others, the materials were most useful with complex patients“. This is a very general statement, and it is not well understood (documented) how this is derived from the interview data, in particular since there were no interviews with guardians.

Thank you for making this point. We have included a different quote from a health practitioner that helps to illustrate this point further. We have also clarified that this sub-theme is based on providing explanations to parent/guardians and not whether parent/guardians found them useful, which as you point out, we can't know from our data. See Page 15:

> Factors of patients and their caregivers also influenced decisions to use (or not use) the materials. For example, patient-guardian leaflets were offered intermittently, with some health practitioners finding them useful adjuncts to delivering face-to-face advice with patient-guardians regarding why they were switching from IV to oral antibiotics. Alternately, others only offered leaflets with complex patients as they felt patient-guardians would be most receptive to the information.

Additional Quote included in Table 4:

> "...when we give patients information or their parents info I think if it's like a long-term chronic condition they are likely to read it and are more receptive." (Registrar, rural)

4. Page 18: Similar to previous research, the major barriers to uptake and engagement with the intervention were structural [5,7]. Most hospital sites noted difficulties with the hierarchy of medical engagement. For some, there were difficulties with high turnover of consultants and senior medical staff, such that medical teams did not have consistent leadership and the support to utilize interventions". Again, as is stated („major barriers"), it is not well explained how this was eventually scored as „major" in comparison with other potential barriers.

Thank you for highlighting this. We have revised this sentence for clarity to note that these were the most frequently discussed type of barriers. See Page 19:

> Similar to previous research, the most frequently highlighted barriers to uptake and engagement with the intervention were structural [5,7].

5. In the post-interventional panel there were many pharmacists. How were they involved in the switching decision ? Did they have similar views as nurses or physicians regarding the intervention value and obstacles ?

The obstacles for pharmacists were similar to other health workers. They were also burdened by turn-over and a lack of presence on the ward at times to be able to engage effectively with the materials. However, the main difference between each of the health practitioner groups was how they engaged with the materials and applied it to practice. We have updated parts of the Results and Discussion to reflect this and included in the demographics Table 2 the most preferred materials by each group – for pharmacists this was the ?STOP poster and the yellow reminder stickers that they were able to place in medication charts for review.

An example of changes on page 19:

> For some, mainly registrars, there were difficulties with high turnover of consultants and senior medical staff, such that medical teams did not have consistent leadership and the support to utilize interventions. This was also often recognized concerning pharmacy support, including from pharmacists themselves, with similar issues regarding lack of support stemming from high turnover or smaller wards at regional hospitals [7,18].

6. What were the differences between hospitals (if any) ?

We have included further discussion in the strengths and limitations section about the consistency of responses across sites as part of the discussion on transition to digital systems. See Page 21:

> Further, while we found consistent cross-site utilisation and acceptance of the materials, we are yet to grapple with the global change to digital medication charts and systems where prompt fatigue may render interventions like 'chart stickers' and visual reminders difficult to implement. Only one site included in this study had transitioned to a digital chart system. Although they were able to implement the materials flexibly, through posters near computers and links to guidelines, we need further research to understand the impact of digital systems in the implementation of future interventions [23].

We have highlighted in the results and discussion where the primary difference between sites occurred – staff turnover. This difficulty was discussed in more depth and higher frequency among rural and remote hospital sites. See page 15:

> Lack of support and engagement from some sites, particularly in rural and remote areas created difficulties in appropriate use of the materials.

And page 20:

> While staff retention was still identified as a problem at all sites, though particularly in rural and remote areas, the impact of staff turnover was lessened by broad training and support to health practitioners at multiple levels, including registered nurses, junior resident medical officers, pharmacists, and registrars.

7. Has there been any baseline evaluation regarding length of stay and duration of parenteral therapy in the hospitals ? Different baseline situations with their specific contexts might have a substantial impact on the preferred type, efficacy and the eventual evaluation of such interventions.

Thank you for this comment. We have addressed this in a previous publication by the authors and we have added a statement to the introduction summarising the main findings on page 4-5:

> In a recent publication we utilised a package of intervention materials for IV-to-oral switching in paediatric patients. This intervention allowed healthcare workers to tailor materials to their practice setting and patients' requirements, demonstrating that a tailored programme increased the percentage of patients whose IV therapy was appropriately stopped or switched to oral therapy as well as decreased the duration of IV antibiotics requirements.

Reference to this article is now included:
Avent ML, Lee XJ, Irwin AD, Graham N, Brain D, Fejzic J, van Driel M, Clark JE. An innovative antimicrobial stewardship programme for children in remote and regional areas in Queensland, Australia: optimising antibiotic use through timely intravenous-to-oral switch. J Glob Antimicrob Resist. 2022 Mar;28:53-58. doi: 10.1016/j.jgar.2021.11.014. Epub 2021 Dec 13. PMID: 34915202

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Reviewer 2: Dr. Emma Kirby, University of New South Wales
Comments:

1. P7: The authors state that post-intervention evaluation interviews were not able to include parents/guardians – some commentary on why this was, and what might be gained/missed from this would be useful (particularly in terms of future research).

Thank you for highlighting this information was not included. It has now been included to reflect that it was not feasible to collect data from patients that may have utilised the parent/guardian leaflet. See page 8:

> Unfortunately, these interviews were not able to include parents/guardians because access to this population was not feasible at the end of the 6-month intervention and after the completed treatment period for patients. Further we were not able to know who received the material to contact them for this phase of the research.

We have also included further discussion of what may have been gained from including them in Phase 4 on page 20:

> A lack of patient-guardians included in this phase means we do not know the extent to which the patient-guardian leaflet was useful in informing their understanding of the switching process. This should be a priority in future research to ensure patient-guardian materials continue to be adapted to suit their needs.

2. P8: A reference is needed to support/specify the working definition of data saturation here.

A reference has been included and we have included more detail in this section regarding our approach. See page 8-9.

A minimum sample size of 15 participants was specified and recruitment stopped when interviews appeared to have reached data saturation (information redundancy), identified by a lack of variation in the richness of answers across participants [16].

16. Charmaz K. Theoretical Sampling, Saturation and Sorting. In: *Constructing grounded theory / Kathy Charmaz.* London: Sage 2014.

3. P8: Has a copy of the interview questions been made available as a supplementary file? Can it be? It would be useful for a reader to see the list of questions provided to participants before the interview.

Thank you for the suggestion. Supplementary file 2 has been included with the questions for phases 2 and 4.

4. P10: "Analysis used an essentialist approach that was reflexive and iterative to identify themes within the data [16,17]." More explanation of an 'essentialist approach' is needed here (and indeed clarification of the use of an essentialist approach) – reflexive and iterative identification of themes are processes present in the articles cited at the end of this sentence, but not an essentialist approach (in fact, a constructivist approach). Alternative references to support this should be used to cite as essentialist approach.

Apologies for the oversight. Thank you for pointing out the missing reference. We have now included an additional appropriate reference and provided more clarity regarding our approach. See page 11:

Analysis used an essentialist approach, reflecting the reality and experiences of participants, that was reflexive and iterative to identify themes within the data [17–18].

18. Byrne D. A worked example of Braun and Clarke's approach to reflexive thematic analysis. *Quality & Quantity* 2022;**56**:1391–412. doi:10.1007/s11135-021-01182-y

5. P8: Phase 2 interviews were audio-recorded and transcribed verbatim – is there a reason these data are not shown in any quotations in the Findings section? It would be particularly interesting to hear about the data from parents/guardians, given they were not involved in later stages.

We did not include quotes for this section for brevity. However, we have included supplementary material 3 that has detailed quotes for phase 2 of the design in a report format.

6. Discussion: Certain points within the discussion require a little more explanation to ground them in the data presented. For example p17: "Providing decision-making support to junior doctors, nurses, and pharmacists increased their individual capacity to influence antibiotic decision-making…" – is there evidence to show that their capacity to influence was increased, or is this self-reported that they felt that their capacity was increased? Please clarify.

Thank you for highlighting this. We have clarified this point as per your suggestion and alongside suggestions from Reviewer 1 we have provided more detail regarding differences between sites and practitioners in the discussion and within the results. See page 19:

The materials were used differently by each practitioner group to influence or support their own or others' decisions. Those who discussed using them in their own practice were most frequently junior doctors, nurses, and pharmacists, who felt they increased their individual capacity to influence antibiotic decision-making.

7. The discussion paragraphs that follow (top of page 18) are much clearer in this regard. Moreover, the discussion about strengths and limitations is especially strong, and does a very nice job of highlighting the contribution of the study and method.

Thank you for your kind feedback.

VERSION 2 – REVIEW

REVIEWER	Kern, Winfried Freiburg University
REVIEW RETURNED	04-Dec-2022

GENERAL COMMENTS	In my view all points raised have now been adequately addressed in the revision

REVIEWER	Kirby, Emma University of New South Wales
REVIEW RETURNED	18-Nov-2022

GENERAL COMMENTS	The authors have made sufficient improvements in their revisions, which as well-considered.