

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	The quest for certainty regarding early discharge in paediatric low risk febrile neutropenia: a multi-centre qualitative focus group discussion study involving patients, parents and healthcare professionals in the UK
<b>AUTHORS</b>	Morgan, Jessica; Phillips, Bob; Stewart, Lesley; Atkin, Karl

### VERSION 1 – REVIEW

<b>REVIEWER</b>	wje tissing university medical center groningen, the netherlands
<b>REVIEW RETURNED</b>	10-Nov-2017

<b>GENERAL COMMENTS</b>	<p>The paper concerns an interesting topic: views and opinions on early discharge in febrile neutropenia patients. Earlier papers included mainly parents and children, but here also professionals are included. The method of using focus groups is a well-established and useful one. The paper is well written, although a bit lengthy, I think the message could be the same when using less words.</p> <p>The finding that the professionals let their own personal fear dominate existentiële guidelines / statistics is for me the most striking, and might be explored in a bit more in the discussion. Eg why? What was the age of the professionals, as I would expect that this would be more the case in the older professionals. But of course I might be wrong.</p>
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<b>REVIEWER</b>	Rochelle Maxwell Children's Hospital at Montefiore/Albert Einstein College of Medicine, USA
<b>REVIEW RETURNED</b>	20-Nov-2017

<b>GENERAL COMMENTS</b>	This is a well done study addressing an important topic. Since there are so few studies that have examined provider preferences, as the authors highlight, I would suggest adding in as a reference Sung et al. J Clin Oncol. 2004;22(19):3922-3929 which used slightly different methods to examine both provider and parental preferences with regard to outpatient vs inpatient FN therapy.
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<b>REVIEWER</b>	Aditi Vedi Cambridge University, United Kingdom
<b>REVIEW RETURNED</b>	21-Nov-2017

<b>GENERAL COMMENTS</b>	<p>This is a detailed and well executed study involving stakeholders from all areas involved in paediatric oncology care. It identifies barriers to change in the febrile neutropenia arena based on risk stratification. However, it does not address the major factor that a robust stratification tool still does not exist. The certainty that is sought in the risk stratification of paediatric febrile neutropenia has not been addressed and is an important question awaiting further investigation and study.</p> <p>Incentivised studies may lead to recruitment bias. Also qualitative studies involving interviews/focus groups conducted in English may also lead to recruitment bias, predominantly from participating patients and parents, as evidence by Table 2, whereby the vast majority of participants are White British.</p> <p>Some numbers and figures would help put the results into a more understandable format. For example, tabulate or group the responses into categories based on which group said what and in how many numbers. Although this is a qualitative study, an overall impression of where the answers/discussions were predominantly directed would be very useful.</p> <p>Page 5, line 15 - Were the involved healthcare professionals oncology used only or did they include emergency medicine staff? And/or infectious diseases specialists or intensive care specialists?</p> <p>Page 5 line 18 - Modified Alexander rule - not a commonly used stratification tool. Needs further explanation</p> <p>Page 7, line 41 - "poor statistical literacy" seems to be quite a broad sweeping statement</p> <p>Transcripts - The ermm quotes don't add much to the conversation</p>
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<b>REVIEWER</b>	Leticia A. Barajas Nava Hospital Infantil de México Federico Gómez, México
<b>REVIEW RETURNED</b>	22-Dec-2017

<b>GENERAL COMMENTS</b>	<p>It is an interesting study, provides information relevant to the management of pediatric cancer patients. The inclusion of populations from different centers offers an overview of the perception of both clinicians and caregivers. Including health professionals allows knowing the needs of scientific knowledge. Knowing that the parents of children with febrile neutropenia are unaware the risk of outpatient management, in addition to presenting some uncertainty, indicates the need for training of these populations.</p> <p>I consider that this study should be published since it provides information relevant to the care and attention of children with febrile neutropenia.</p>
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<b>REVIEWER</b>	Amita Trehan Pediatric Haematology Oncology Unit, Advanced Pediatric Centre, Postgraduate Institute of Medical Education and Research, Chandigarh 160012 India
<b>REVIEW RETURNED</b>	26-Dec-2017

<b>GENERAL COMMENTS</b>	This is an interesting study.
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	<p>Management of febrile neutropenia (FN ) is not easy taking into consideration the unclear need for admission and the load on overburdened hospital beds. Also, a universally acceptable risk score for pediatric FN is a lacuna in the management of FN.</p> <p>The 2 main problems in this study are the small sample size and the exhaustive length of the manuscript.</p> <p>The small numbers of participants in the study hampers this research work. There are 3 teenagers and young adults in the patients group.  There are 11 parents in the group of children &lt; 13 years  There are 5 parents of group of children &gt; 13 years</p> <p>There are 6 doctors. Two consultants; 2 registrars; 1 SHO and the designation of the doctor in center 3 is not mentioned  There are 7 nurses, some being senior and 2 having an experience of less than a year.</p> <p>I do not think these numbers are sufficient to give a proper analysis, especially in a qualitative study. It is also to be noted that a couple of children/parents of children in the cohort never had FN. Possibly, it can be considered as a pilot study.  Amongst the medical personnel; I do not think having a group discussion with only 6 doctors can give a good perspective of what doctors think. One is a SHO. SHO's are undoubtedly excellent young doctors. Nevertheless, I doubt if a SHO can fully comprehend the risks/safety of a complicated versus an uncomplicated FN. Similarly with the nursing staff, a couple of nurses do not even have a years experience, whilst some have a decade's experience. We have to accept that in a 'subjective evaluation' experience of the person makes a difference.</p> <p>The background of the study can be made a single paragraph.</p> <p>The identification, recruitment and consent can be put point wise.</p> <p>Results  These are too long drawn out. I do not think there is a need to give so many anecdotal details on personal experiences. (pages 6 ,7 and 8)</p> <p>It is predictable that health care professionals and parents will have a different outlook.  It is anticipated that families would be emotional and not scientific in their approach towards the patient whilst medical personnel would be 'clinical'. 'Wellness' judged by a parent and physician is bound to differ.  With regards to risk stratification, parents and children would not know be expected to know or fully understand the risk stratification. Medical personnel also, would know regarding risk stratification only if they had learnt about it in a particular scenario. A one time statement where '0.1%' is being considered high does not really reflect statistical literacy.  Page 8, sentence 38/39 . Assessment of risk is not a purely technical act.....is an incorrect statement. There are risk scores for plenty of diseases including FN based on fixed criteria.</p> <p>Articulating and interpreting protocols ( page 8) : Again , it is the</p>
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	<p>seniority and experience of the healthcare professional who will understand that a protocol is not a rigid policy 'cast in stone'. Patients will look at a protocol as how they understand it. It is the healthcare professionals who explain these to a patient and possibly make FN appear to be the biggest monster while being treated for a malignancy.</p> <p>Page 9 and 10 Delays occur secondary to various reasons . These can just be stated. A root cause analysis would be required to further comment on the same and these points can be summarized in a paragraph. I do not think the other issues discussed here were part of the study. This includes travelling time; parking; impact on the family, out of pocket expenses etc. Psychological effects are also not part of the aims of the study. Am sure it will be appreciated that there are psychological elements to even a visit to the hospital. I think adding all this detracts from the nature of this study. Possibly, only the 6 points in the last paragraph, which goes onto page 11 are relevant. This may be given in a single paragraph. Again, giving too many anecdotes detracts from the original purpose of the study.(page 11) The 3 benefits from hospitalization as perceived by patients/families (page 11, line 42-57) may be given in a paragraph.</p> <p>Discussion Authors have written that the patients and the medical personnel had a different focus of the disease. I think this goes without saying. They are both stakeholders with essentially the same priority. It is the way of viewing that is different. This paragraph may be shortened (para 2) Possibly, it can be reworded to give the healthcare personnel's and patients perception of FN and combine it with paragraph 2 on page 13 ( lines 10-21) as they are similar . The negative consequences of care may be reworded. I do not think stress on 'horror stories ' is needed. Just from an outsider viewpoint, every health professional has horror stories, which is not the realm of the manuscript. Page 13, lines 22-47. What I understand is the authors want to say that when the therapy under discussion/being provided is not 'evidence based', we need to make a shared informed decision with the knowledge of all stakeholders. This paragraph needs rewording in simple prose. Strengths and weaknesses: I think the stress here should be that FN needs stratification and that families, nurses and physicians need to be aware of this. Page 14; paragraph 1: challenge that recruitment was less and how to get more people to participate.....again can be put in a few lines . One can also use a survey monkey for such purposes.</p> <p>Conclusions : As the number analyzed is too small, it is suggested that this may be called a 'pilot study' . The only point which is actually made is that families/patients need more involvement in decision making in children with FN.</p>
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### VERSION 1 – AUTHOR RESPONSE

#### Editorial Requests:

- Please revise your title to indicate the study design (i.e. qualitative study) and setting. This is the preferred format of the journal.

We have amended the title as requested.

- Along with your revised manuscript, please provide a completed copy of the COREQ checklist (<http://www.equator-network.org/reporting-guidelines/coreq/>).

Please find this attached. This required significant adaptation to the manuscript which we trust you understand.

Reviewer: 1

Reviewer Name: wje tissing

Institution and Country: university medical center groningen, the netherlands

Competing Interests: none declared

The paper concerns an interesting topic: views and opinions on early discharge in febrile neutropenia patients. Earlier papers included mainly parents and children, but here also professionals are included. The method of using focus groups is a well-established and useful one. The paper is well written, although a bit lengthy, I think the message could be the same when using less words.

- Thank you Dr Tissing. We have attempted to reduce the length of the manuscript whilst simultaneously addressing all reviewers' concerns. We hope that the result is much improved.

The finding that the professionals let their own personal fear dominate existentiële guidelines / statistics is for me the most striking, and might be explored in a bit more in the discussion. Eg why? What was the age of the professionals, as I would expect that this would be more the case in the older professionals. But of course I might be wrong.

-We agree that this is a thought-provoking finding. The range of ages of the participants in each focus group is provided in table 2. We have explicitly not provided further detail so as to protect participant confidentiality. Our findings were not that age influenced the professionals' fear, but instead that centre culture played a greater role. We have added a sentence to this effect within the Discussion section of the manuscript.

Reviewer: 2

Reviewer Name: Rochelle Maxwell

Institution and Country: Children's Hospital at Montefiore/Albert Einstein College of Medicine, USA

Competing Interests: None declared.

This is a well done study addressing an important topic. Since there are so few studies that have examined provider preferences, as the authors highlight, I would suggest adding in as a reference Sung et al. J Clin Oncol. 2004;22(19):3922-3929 which used slightly different methods to examine both provider and parental preferences with regard to outpatient vs inpatient FN therapy.

-Thank you. We are happy to include a reference to this paper and have added this within the Background section of the manuscript.

Reviewer: 3

Reviewer Name: Aditi Vedi

Institution and Country: Cambridge University, United Kingdom

Competing Interests: None declared

This is a detailed and well executed study involving stakeholders from all areas involved in paediatric oncology care. It identifies barriers to change in the febrile neutropenia arena based on risk stratification. However, it does not address the major factor that a robust stratification tool still does not exist. The certainty that is sought in the risk stratification of paediatric febrile neutropenia has not been addressed and is an important question awaiting further investigation and study.

-Thank you for your kind review. We appreciate the challenges of risk stratification and have added a sentence to the Background with respect to this, as well as a more explicit recommendation about risk stratification within the Discussion.

Incentivised studies may lead to recruitment bias. Also qualitative studies involving interviews/focus groups conducted in English may also lead to recruitment bias, predominantly from participating patients and parents, as evidence by Table 2, whereby the vast majority of participants are White British.

-We recognise that highly incentivised studies may lead to recruitment bias. However, there is also a need to reimburse participants for travel costs and time in recognition of the sacrifices that they make to participate in research. Failing to do so may also lead to recruitment bias as some participants may not be able to afford to travel or take time from earning to participate. We were advised by the assessing ethics committee to include these incentives and have followed INVOLVE guidelines regarding the amount of remuneration. We also recognise the potential effects of using English language only focus groups, but for practical reasons, including numbers of potential participants for other language groups, we were not able to provide other options. We had already highlighted this difficulty within the discussion and have added further discussion to make this clearer.

Some numbers and figures would help put the results into a more understandable format. For example, tabulate or group the responses into categories based on which group said what and in how many numbers. Although this is a qualitative study, an overall impression of where the answers/discussions were predominantly directed would be very useful.

-Thank you for this comment. We appreciate the particular value that counting and tabulation provides in qualitative research, allowing a different overview and assessment to that performed within our analysis. This is certainly a potential future exploration of this dataset and may indeed provide further interesting analytical points. We will bear this in mind for later works with this large volume of data.

Page 5, line 15 - Were the involved healthcare professionals oncology based only or did they include emergency medicine staff? And/or infectious diseases specialists or intensive care specialists?

-For this study, paediatric haematology and oncology based professionals only were included. In the UK, few children with low risk febrile neutropenia are managed by EM or ID professionals. Additionally, ICU staff are likely to have minimal experience of low risk patients. We have clarified this within the Methods section.

Page 5 line 18 - Modified Alexander rule - not a commonly used stratification tool. Needs further explanation

-We chose to use the Modified Alexander rule as this is the risk stratification tool advised by the UK's NICE guidelines. We have added a sentence to this effect within the Methods section of the manuscript.

Page 7, line 41 - "poor statistical literacy" seems to be quite a broad sweeping statement

-Thank you. We have rephrased this sentence to read "these statistical misunderstandings".

Transcripts - The ermm quotes don't add much to the conversation

-There is much debate about the inclusion of verbal hesitations in quotations of qualitative work. Whilst certainly important in analytical approaches such as discourse analysis, their use in other analyses is debated. They can be informative, in allowing readers to see where participants are forming ideas, searching for phrases or seeking to express themselves more clearly. However, others may argue that they can take up precious space in word limited publications and can reduce reading fluency, bearing in mind that written language and spoken language are very different. As a team, we have chosen to leave these hesitations in this manuscript, but are willing to discuss this further if the editorial team feel strongly regarding this issue within the journal standards.

Reviewer: 4

Reviewer Name: Leticia A. Barajas Nava

Institution and Country: Hospital Infantil de México Federico Gómez, México

Competing Interests: 'None declared'

It is an interesting study, provides information relevant to the management of pediatric cancer patients. The inclusion of populations from different centers offers an overview of the perception of both clinicians and caregivers. Including health professionals allows knowing the needs of scientific knowledge. Knowing that the parents of children with febrile neutropenia are unaware the risk of outpatient management, in addition to presenting some uncertainty, indicates the need for training of these populations. I consider that this study should be published since it provides information relevant to the care and attention of children with febrile neutropenia.

-Thank you for this kind review. We hope the discussion section of the manuscript now more thoroughly addresses your concerns regarding education of families about febrile neutropenia.

Reviewer: 5

Reviewer Name: Amita Trehan

Institution and Country: Pediatric Haematology Oncology Unit, Advanced Pediatric Centre, Postgraduate Institute of Medical Education and Research, Chandigarh 160012, India

Competing Interests: None declared

This is an interesting study. Management of febrile neutropenia (FN) is not easy taking into consideration the unclear need for admission and the load on overburdened hospital beds. Also, a universally acceptable risk score for pediatric FN is a lacuna in the management of FN.

-Please see earlier response to Reviewer 3.

The 2 main problems in this study are the small sample size and the exhaustive length of the manuscript. The small numbers of participants in the study hampers this research work. There are 3 teenagers and young adults in the patients group. There are 11 parents in the group of children < 13 years. There are 5 parents of group of children > 13 years. There are 6 doctors. Two consultants; 2 registrars; 1 SHO and the designation of the doctor in center 3 is not mentioned. There are 7 nurses, some being senior and 2 having an experience of less than a year. I do not think these numbers are sufficient to give a proper analysis, especially in a qualitative study. It is also to be noted that a couple of children/parents of children in the cohort never had FN. Possibly, it can be considered as a pilot study.

-Respectfully, we disagree with this comment. Within qualitative research, the number of participants involved is not necessarily as important as in quantitative research, where "power" plays a vital role. Instead, "the quality of information obtained per sampling unit, as opposed to their number per se" (Sandelowski M, Research in Nursing & Health, 1995, 18, 179-183) is what is important. The focus is on the data obtained, the breadth and depth of information being of more value than the number of participants involved. To quote Barbour, "there is no magic number and more is not necessarily better". This study has considerable strengths in that it has multiple repeated groups – that is multiple groups in each centre and multiple groups of each participant type. This allows increased confidence in the findings. We do not agree that this is a pilot study, given these observations and the significant amount of data obtained during the research.

Amongst the medical personnel; I do not think having a group discussion with only 6 doctors can give a good perspective of what doctors think. One is a SHO. SHO's are undoubtedly excellent young doctors. Nevertheless, I doubt if a SHO can fully comprehend the risks/safety of a complicated versus an uncomplicated FN. Similarly with the nursing staff, a couple of nurses do not even have a years experience, whilst some have a decade's experience. We have to accept that in a 'subjective evaluation' experience of the person makes a difference.

-We felt that it was important to include professionals of all levels of experience within this study. Particularly given that SHOs and junior nurses are often the main professionals involved in the early management of low risk febrile neutropenia, they form a vital part of this study sample. If our junior colleagues do not understand febrile neutropenia, then this impacts on the service provided and the experiences of patients. Data related to their experiences should be collected so that we understand

perceptions of all professionals, and how they may respond to future changes. Whilst the ideal situation might be consultant decision making for all febrile neutropenia, this is not realistic and our research should instead reflect the real world.

The background of the study can be made a single paragraph.

-We have worked hard to edit this section, whilst also addressing other reviewers' points. We have therefore reduced to three paragraphs.

The identification, recruitment and consent can be put point wise.

-Thank you for this suggestion. We feel this would impact on the flow of the writing and therefore would prefer to leave this section as prose. We are happy to discuss further if the editorial team would prefer a different approach.

## Results

These are too long drawn out. I do not think there is a need to give so many anecdotal details on personal experiences. (pages 6,7 and 8)

-As we understand it, the quotations referred to as "anecdotal" are illustrations of the research data, similar to the provision of graphs or tables in quantitative research – they demonstrate the information on which the analysis is performed. The presentation of longer excerpts allows the reader to see the links between data and reported findings, as well as to view the benefits of stimulating focus group discussions. We have reduced the length of some of these quotations, though many remain included in their original form.

It is predictable that health care professionals and parents will have a different outlook. It is anticipated that families would be emotional and not scientific in their approach towards the patient whilst medical personnel would be 'clinical'. 'Wellness' judged by a parent and physician is bound to differ. With regards to risk stratification, parents and children would not know be expected to know or full understand the risk stratification. Medical personnel also, would know regarding risk stratification only if they had learnt about it in a particular scenario.

-We appreciate this engagement with the data. It may indeed be anticipated that professionals would be 'clinical' – however this is not the finding of our research, where professionals demonstrated emotional responses to risk and risk stratification. Again, whilst families might not know about formal risk stratification, we found that they clearly understood the principles and were deeply engaged in risk stratification of their children. Professionals in the UK, should know and understand risk stratification as this forms part of our national guidance on the management of febrile neutropenia. As they did not demonstrate this, it is important to state.

A one time statement where '0.1%' is being considered high does not really reflect statistical literacy.

-That is correct. This data is given as an example of the challenges that professionals experienced in interpreting statistics and links with the previous quote.

Page 8, sentence 38/39 . Assessment of risk is not a purely technical act.....is an incorrect statement. There are risk scores for plenty of diseases including FN based on fixed criteria.

-Though we agree that the performance of a risk score is a technical act, the overall assessment of risk involves the use of many underlying normative values and assumptions, as provided in the remainder of the sentence to which the reviewer refers. We trust that readers will be able to appreciate the nuances described.

Articulating and interpreting protocols (page 8) : Again , it is the seniority and experience of the healthcare professional who will understand that a protocol is not a rigid policy 'cast in stone'. Patients will look at a protocol as how they understand it. It is the healthcare professionals who explain these



to a patient and possibly make FN appear to be the biggest monster while being treated for a malignancy.

-Thank you again for engaging with this research. As our findings state, it did not appear to be the seniority of the professionals that influenced the understanding of protocols, but instead the centre culture in which they work. You are correct in asserting that professionals play a significant role in influencing patient perceptions – hence our examination of centre culture within this study.

Page 9 and 10

Delays occur secondary to various reasons. These can just be stated. A root cause analysis would be required to further comment on the same and these points can be summarized in a paragraph. I do not think the other issues discussed here were part of the study. This includes travelling time; parking; impact on the family, out of pocket expenses etc. Psychological effects are also not part of the aims of the study. Am sure it will be appreciated that there are psychological elements to even a visit to the hospital. I think adding all this detracts from the nature of this study.

-We feel that highlighting the frustration caused to families by perceived delays in blood cultures is an important finding of the study. It describes their experiences and clearly informed their perceptions of length of stay in febrile neutropenia. Furthermore, the other issues described, including psychological effects of admission, also informed the participants' choices regarding outpatient care. We have made the reasons for including this data clearer in the results section.

Possibly, only the 6 points in the last paragraph, which goes onto page 11 are relevant. This may be given in a single paragraph.

-We have combined these into a couple of paragraphs and shortened the information where possible.

Again, giving too many anecdotes detracts from the original purpose of the study.(page 11)

-Again, see our earlier comments, these 'anecdotes' are in fact a key foundation in the presentation of qualitative data.

The 3 benefits from hospitalization as perceived by patients/families (page 11, line 42-57) may be given in a paragraph.

-Thank you. We have amended the manuscript accordingly.

Discussion

Authors have written that the patients and the medical personnel had a different focus of the disease. I think this goes without saying. They are both stakeholders with essentially the same priority. It is the way of viewing that is different. This paragraph may be shortened (para 2) Possibly, it can be reworded to give the healthcare personnel's and patients perception of FN and combine it with paragraph 2 on page 13 ( lines 10-21) as they are similar .

-We have worked to make the flow of the discussion more clear – stressing the original findings of this study, the interpretation in terms of differences in focus, how this impacts on negative experiences of care, its application to future research, relevant clinical theories and then the application of the work to clinical practice. We hope the reviewer can now see the justification for each paragraph within the discussion.

The negative consequences of care may be reworded. I do not think stress on 'horror stories ' is needed. Just from an outsider viewpoint, every health professional has horror stories, which is not the realm of the manuscript.

-This paragraph was intended to illustrate the differences in opinions regarding negative consequences of care. We have rephrased the paragraph accordingly.

Page 13, lines 22-47. What I understand is the authors want to say that when the therapy under discussion/being provided is not 'evidence based', we need to make a shared informed decision with the knowledge of all stakeholders. This paragraph needs rewording in simple prose.

-We apologise if there has been a misunderstanding. The paragraph intends to communicate that where there is equipoise regarding the right choice, even if evidence is available, then an evidence based discussion with patients and families can allow a shared decision. Indeed, we hope we have now stressed that evidence based decisions are vital and it is evidence that shows a lack of difference between options that allows shared decision making in the setting of low risk febrile neutropenia. We trust that this paragraph is now clearer.

Strengths and weaknesses: I think the stress here should be that FN needs stratification and that families, nurses and physicians need to be aware of this.

-We are not quite sure that this comment is a strength or weakness and thus have responded to this by adding a couple of sentences within the discussion.

Page 14; paragraph 1: challenge that recruitment was less and how to get more people to participate.....again can be put in a few lines . One can also use a survey monkey for such purposes.

-We have attempted to shorten this paragraph, taking into account advice for additional information given by other reviewers. We are not quite sure what the reviewer means by using a survey monkey for such purposes, but indeed there are other ways to collect data on stakeholder preferences and a survey may be an appropriate quantitative approach to this research question.

Conclusions : As the number analyzed is too small, it is suggested that this may be called a 'pilot study' . The only point which is actually made is that families/patients need more involvement in decision making in children with FN.

-Please see our previous response as to why we strongly feel that this is not a pilot study. There are many points made through the manuscript, but the reviewer is correct that the key "take-home" message should be that families need more involvement in decision making about febrile neutropenia and this data provides the scientific justification for this assertion.

#### VERSION 2 – REVIEW

<b>REVIEWER</b>	Amita Trehan Pediatric Hematology Oncology Unit Advanced Pediatric Centre, Postgraduate Institute of Medical Education & Research Chandigarh, India 160012
<b>REVIEW RETURNED</b>	21-Feb-2018
<b>GENERAL COMMENTS</b>	I have 2 major reservations in this manuscript 1. It is still extremely lengthy. The first draft was 5222 words and it is now 5240 words. 2. Its nice to have anecdotes from patients and health personnel , but I do feel that the number of such anecdotes provided is not really necessary for a scientific paper. The message gets lost in prose