Author's response to reviews

Title: Testicular cancer in men with Down syndrome

Authors:

Shaista Hafeez (Shaista.hafeez@rmh.nhs.uk)
Mausam Singhera (mausam.singhera@rmh.nhs.uk)
Robert Huddart (robert.huddart@icr.ac.uk)

Version: 2 Date: 27 May 2015

Author's response to reviews: see over
Dear Claire,

RE: MS 6198692391635139

Thank you for your E-mail dated 7th April 2015. We accept the reviewers’ and editor’s comments and have amended the manuscript accordingly. We enclose the revised manuscript with highlighted changes. Changes made to the manuscript in response to each comment are detailed below.

On behalf of all authors,
Yours sincerely,

Dr Shaista Hafeez
Recommended structural revisions:

I agree with the second reviewer that this is, overall, a well-written and informative review, and I agree with both reviewers that some clarification is important. I think the easiest way to address this would be to open each section with a brief introduction to the relevant issues for the general population, followed by how these issues may differ for the population with Down syndrome. For example, in the section on psychological impact a cancer diagnosis is a significant challenge for anyone and I feel sure there must be studies that could be cited showing what impacts testicular cancer has on affected individuals in the general population.

Agree. This has now been added p11 para 3 (highlighted).

The intellectual disabilities of those with Down syndrome no doubt presents challenges in managing psychological impacts, and the reduced fertility presumably also changes the psychological impact. The summaries of issues for the general population should be brief; they serve to set the scene for discussing issues that are particular to the treatment of men with Down syndrome.

Agree. This has been added throughout the text (highlighted).

I would also like to see a bit more detail, with suitable referencing. For example, you say ‘most testicular tumours in Down syndrome are seminomas’; what other types are there? What is the frequency of each? Another example would be the reference to the different ‘natural history’ of tumours in those with Down syndrome. What suggests they have a different aetiology? Do they respond differently to treatment?

Agree. This has been added p4 para 3 (highlighted).

This is not my area of expertise, but I assume from this article that men with Down syndrome must be more sensitive to radiation than the general population? More detail on this would also be good. What is the evidence? How is this best managed?

Partially agree. This would be good but the small sample size of most reported series in Down syndrome and testicular cancer has precluded definitive conclusions to made. However outcomes of ALL in those with Down syndrome has been described to support the hypothesis that the cytogenetic aberrations in Down syndrome could also lead to altered biological features in germ cell tumours p4 para 3 (highlighted).

Additional minor structural suggestions:

The headings could be made longer and more informative. For example, rather than ‘Incidence and aetiology’ something like ‘Incidence and aetiology of testicular cancer in Down Syndrome relative to the general population’ or, better still, ‘Increased incidence and distinct aetiology of testicular cancer in Down Syndrome’ would give the reader more cues as to what is to follow.

Agree. Changes to the heading have been made throughout (highlighted).
Copyediting issues to keep in mind:

There are many places where a comma is required or where one would be extremely helpful to the reader.

Some passages are difficult to understand due to awkward or unconventional wording. The reviewers have mentioned a few examples of this. Another one is:

‘In those with Down syndrome and stage II disease, treated with 4 cycles of carboplatin, more than 30% of patients fail’

Fail at what?

Agree. Sentence structure simplification throughout and clarification in terminology provided (highlighted).
Reviewer's report
Title: Testicular cancer in men with Down syndrome
Version: 1 Date: 21 March 2015
Reviewer: Alan Bittles

Reviewer's report:
Major Compulsory Revisions
1. This Opinion article appears to originally have been prepared for oral presentation. In its present form the specific intention and target readership is somewhat unclear since despite the title, ‘Testicular cancer in men with Down syndrome’, the actual manuscript ranges much more widely in content, e.g. encompassing extensive general opinions regarding the care and treatment of people with an intellectual or learning disability (Communication, informed consent and patient centred decision-making). Either greater content focus or a more adequately descriptive title would be appropriate.

Agree. Change made to title (highlighted). Title now reads Exploration of the treatment challenges in men with intellectual difficulties and testicular cancer as seen in Down syndrome: single centre experience

2. In other places it is difficult to know whether the text refers to males with Down syndrome, or to the general male population, or to both. For example, the section Non-seminomatous germ cell tumours (NSCCTs) commences by stating that ‘These tumours are less common in those with Down syndrome than the general testicular cancer patient population.’ Do the treatment protocols and estimates cited in the following three paragraphs (paras 2-4) therefore refer to the general population or to males with Down syndrome?
Agree. Clarification made (highlighted).

3. With regard to the comment (NSCCTs para 5) that ‘..learning difficulty in itself does not and should not preclude radical therapy’, does this statement specifically refer to or include individuals with Down syndrome? Likewise, ‘..lack of co-operation should not be assumed to be necessarily associated with lack of consent’ (para 5). To whom does this claim refer, and under what circumstances would intervention be justified?
Agree. Clarification made. Use of general anaesthetic to aid compliance should only be considered in circumstances where it is not possible to complete investigation and treatment safely p11 para 2.

4. In the section on Survivorship (para 1), the rather sweeping statements on rising life expectancy in people with Down syndrome and the influence of improved management of congenital cardiac abnormalities merit supporting, contemporary references.
Agree. The appropriate reference has been provided. Irving at al., 2012 describe management and outcome of cardiovascular anomalies in a defined Down syndrome population over 22 year period.

5. It also is difficult to see the connection with Down syndrome in the Survivorship section para 2. ‘The young age at presentation and high cure rates of testicular cancer in the general population..’. The more so since at
several points in the text, including the Abstract and Conclusion, the authors have indicated that, in Down syndrome males with testicular cancer, there is ‘.suggestion of altered tumour biology and outcome compared to the general population.’.

Agree. We have expanded on this in response to earlier comment (p3 para 4, highlighted)

Minor issues not for publication
The text needs to be substantially revised and corrected for punctuation errors, inappropriate use or absence of the definite and indefinite article, occasional mis-spellings, inconsistent use of hyphenation, and some very odd phrases e.g.’..an altered natural history that in may turn effects cure’ (Introduction para 3).
Correction made (highlighted changes).

Use of the term ‘recent’ to describe a 2007 publication (ref. 21) is somewhat misleading.
Agree. Amended accordingly.

Updating of many of the references cited on more general aspects of Down syndrome would be appropriate.
Agree. Where available and appropriate updated references have been added.

Quality of written English: Needs some language corrections before being published
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:
I declare that I have no competing interests.
Reviewer's report
Title: Testicular cancer in men with Down syndrome
Version: 1 Date: 27 March 2015
Reviewer: Irene Tuffrey-Wijne

Reviewer's report:
First of all, I would like to congratulate the authors on a well-written paper covering an important topic. I found the manuscript interesting and informative.

The issues that arise when people with Down syndrome develop cancer need attention and focus. In my view, this paper contributes to this. However, there are a few issues that need to be addressed by the authors, as follows.

1. MAJOR COMPULSORY REVISIONS
(a) My main problem with this manuscript is the lack of clarity about its aim, focus and methods. The only indication is the sentence at the end of the introduction: "We review the clinical challenges in treating this group of patients and how individual needs can be supported in order to deliver the best care."

This is clearly not an original research paper; nor is it a systematic review of the literature. The authors need to be much clearer about the aim and scope of the paper. HOW did they review the issues? Is this a discussion paper based on the available literature (albeit not systematically reviewed), or on their own clinical experience? (they do refer to their own experience throughout the paper, so it would help to have a brief description of the authors' expertise). How were the topic areas within the paper selected? ("Incidence and aetiology"; "presentation"; "communication..." etc). They all seem relevant to me, but some description of what the reader is to expect would be important, perhaps along the lines of "We describe the incidence/presentation/etc, followed by some common issues reported in the literature (communication/psychological distress/survivorship/etc); we also address the specific treatment considerations for testicular cancer in men with Down syndrome." The latter ("Treatment", "Seminoma", NSGCTs") forms a significant part of the paper, and may even be the main part of it. The authors need to be clear about this, and perhaps the different sections more distinctly.

Agree. Clarification now provided with 1) title amendment, 2) justification/indication of experience p3 para 2, 3) summary of topics to be covered within the article added to introduction p3 para 2.

(b) It is also important that the authors include the aim, scope and methods of the paper in the title and abstract. Currently, on assessing the title and abstract, it wasn't clear to me whether this was a research paper, a discussion paper, a literature review or otherwise.

Agree. This has been amended. Clarification of the nature of article made p3 para 3. Methodology of literature search now made

NB I lack the clinical expertise to assess the "treatment" sections of the
2. MINOR ESSENTIAL REVISIONS
(a) Consistency needed in terminology. The authors use "learning disability" and "learning difficulty", seemingly interchangeably. I suggest that the current acceptable terminology in the context of a paper like this in the UK is "learning disability"; for an international audience, it is better to use the term "intellectual disabilities", as in some countries the term "learning disability" causes confusion.
Agree. On reviewer advice this has now be changed throughout for an international audience to intellectual disability (highlighted).

(b) Last paragraph of "Communication, informed consent and patient centred decision-making" section: "...central to almost all failings is often the lack of value placed on someone's life with learning disability." This is, in my view, too sweeping a statement that is difficult to back up with hard evidence. There have been a number of other contributing factors identified in recent studies, including, for example, a lack of staff understanding of learning disability and of the Mental Capacity Act in the UK, and the ‘invisibility’ of people with learning disabilities within healthcare systems and subsequent lack of reasonable adjustments (see for example our own report on patient safety of people with learning disabilities in hospitals:
http://www.journalslibrary.nihr.ac.uk/hsdr/volume-1/issue-13#abstract;
and the CIPOLD report:
http://www.bristol.ac.uk/medialibrary/sites/cipold/migrated/documents/fullfinalreport.pdf)
Agree. Although references 21-27 include the mental health act, DOH guidance and commissioned reports etc, in accordance with the reviewer comments we have expanded on the contributing factors to ‘invisibility’ (p8 para 2). Expansion on the specifics CIPOLD findings has also now been added.

(c) In the conclusion, please clarify the sentence "Guidelines are in place to ensure best practice is maintained" as these guidelines have not been described in the text.
Agree. Amended

Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:
I declare I have no competing interests