Author's response to reviews

Title: The informed consent in southern Italy does not adequately inform parents about infant vaccination

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Author's response to reviews: see over
15 January 2014

Dear Dr. Silvestre,

Re: Manuscript reference No. 2695535761044527

Please find attached a revised version of our manuscript now titled “The informed consent in southern Italy does not adequately inform parents about infant vaccination”, which we would like to resubmit for publication in BMC Public Health

The following pages contain my responses to each of the comments of the reviewers. For clarity, I present the comments of the reviewers in full (in italics) and respond to each comment point-by-point. I also include the specific manuscript revision after the response to the reviewer. Revisions to the text are shown using yellow highlighting for additions.

Reply to Referee 1

1. Is the question posed by the authors well defined?

While the article does not pose a specific question, the authors state that they “explored the roles of informed consent and health care providers as sources of vaccine information for parents”. In my opinion, this statement needs further clarification. From reading the article, my understanding is that this is a study of the effectiveness of information giving and the informed consent process at vaccination centres in the Campania Region of Italy. Knowledge and comprehension of the information given, whether or not parents had read the information and whether or not they had signed the consent form appear to be the principle outcome measures used by the researchers.

As suggested, we have clarified the objectives of the study.

(Original version in abstract) We explored the roles of informed consent and health care providers as sources of vaccine information for parents.

(Revised version) We explored whether informed consent was delivered to the parents, whether they signed the consent form, and whether they read and acquired the information about the vaccination that their child would receive.

(Original version) We report on the roles of informed consent and of the health care providers on parents’ knowledge about infant vaccination policies. This issue is relevant because parents are the main decision-makers with respect to whether certain vaccinations are given to their children. Moreover, the information that should be provided by informed consent to parents are easy to explain and to understand.
We explored whether informed consent was delivered to the parents, whether they signed the consent form, and whether they read and acquired the information about the vaccination that their children would receive. This issue is relevant because informed consent plays an important role in parents’ knowledge about infant vaccination policies, and because parents are the main decision-makers with respect to whether certain vaccinations are given to their children.

The authors describe informed consent as a source of information, when in fact informed consent is a process. Did they actually mean to say that the consent form was a source of information?

We did not analyse the whole process of informed consent. Here, when we talk about it we mean a written document that meets the definition of informed consent as a source of information (see response to the second reviewer at point 19).

I also think the role of health care providers as a source of information needs further explanation: How did they provide the information to the parents? Was it presented orally, as a written document, or both?

We did not systematically explore the role of the health operators as a source of information, because it varies among different operators and among different centres. In general, they are not interested in providing information because it is delegated to the written informed consent process. However, we have clarified in the manuscript the difference between written informed consent and the informed consent process. We also added the following text:

(Revised version p. 4) The policy at each centre was to provide informed consent about vaccination as a written document that the parents were to be instructed to read and sign.

2. Are the methods appropriate and well described?

Randomisation: Which randomisation method was used to select the four vaccination centres? What steps did the researchers take to prevent bias?

I have specified the sampling method.

(Original version) We randomly selected one UOMI from each of the four cities with the largest populations in the Campania Region (Napoli, Salerno, Caserta, and Avellino).
We selected one vaccination centre from each of the four cities with the largest populations in the Campania Region (Napoli, Salerno, Caserta, and Avellino). We randomly selected one of the ten vaccination centres that are present in the city of Napoli. Only one vaccination centre is present in the cities of Salerno, Caserta, and Avellino.

3. Are the data sound?

Some of the data in Table 1 are not clear to me. The study population is 1039. However, the sum of mothers and fathers in the different age groups is 1036, and the sum of mothers and fathers by marital status is 1033. Likewise, the sum of mothers and fathers by level of education is 1036, while the sum of mothers and fathers by employment status is 1034. I’m also not sure how the percentages were calculated in each case. I recommend a revision of these data and more information to explain the discrepancies.

These sums are slightly lower than 1039 because there are missing data for each variable. We have corrected the table by adding the item “missing”, as you can see below:

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mother</th>
<th>Father</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>(%)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15-19</td>
<td>12</td>
<td>(1.3)</td>
</tr>
<tr>
<td>20-29</td>
<td>229</td>
<td>(24.7)</td>
</tr>
<tr>
<td>30-39</td>
<td>516</td>
<td>(55.7)</td>
</tr>
<tr>
<td>40-49</td>
<td>165</td>
<td>(17.8)</td>
</tr>
<tr>
<td>50-59</td>
<td>5</td>
<td>(0.5)</td>
</tr>
<tr>
<td>missing</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>807</td>
<td>(87.2)</td>
</tr>
<tr>
<td>Other</td>
<td>118</td>
<td>(12.8)</td>
</tr>
<tr>
<td>missing</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary school</td>
<td>30</td>
<td>(3.2)</td>
</tr>
<tr>
<td>Middle school</td>
<td>215</td>
<td>(23.2)</td>
</tr>
<tr>
<td>High school</td>
<td>370</td>
<td>(39.9)</td>
</tr>
<tr>
<td>College degree</td>
<td>312</td>
<td>(33.7)</td>
</tr>
<tr>
<td>missing</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>465</td>
<td>(50.2)</td>
</tr>
<tr>
<td>Unemployment</td>
<td>461</td>
<td>(49.8)</td>
</tr>
<tr>
<td>missing</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>930</td>
<td>(89.2)</td>
</tr>
</tbody>
</table>
In Table 3. There are errors in the following percentages.

This has been corrected (see table)

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?

5. Are the discussion and conclusions well balanced and adequately supported by the data?

The results raise a number of interesting questions which are not addressed in the discussion/conclusions:

• Is there any relationship between the demographics of the participants and their knowledge and understanding of the information given to them?
  For example, does age or level of education have any impact on comprehension?

In the text we have specified that: “With the exception of the difference between centres’ distribution of informed consent forms, there were no significant differences when the data were disaggregated according to sociodemographic characteristics.”

• 41.9% of respondents had not signed the consent form prior to vaccination. I would be interested to know why they had not done so. Was it because they had not understood the information given, because nobody had asked them to sign the consent form in the first place, or for other reasons?

We are sorry that the text was not clear. When we said “consent not signed”, we intended “not signed because not received”. No parent refused to sign the informed consent form (apart from the 5.3% that said “I don’t remember”). Therefore, we have modified the text to clarify this potential misunderstanding. See the reply to the second reviewer (point 4).

• All children received the hexavalent vaccine in spite of the fact that 41.9% of parents had not signed the consent form. The authors claim that at one centre none of the parents received the consent form. This suggests a lack of awareness the principles of informed consent amongst staff working at the vaccination centres. I think it would be beneficial for the authors to explore this further in their conclusions.
We have changed and updated the discussion including a comment on this item. See below and see the revised version of discussion in the revised manuscript.

(revised version p. 10) These data show that in our area, informed consent as a process and as a written document that requires a signature is not sufficiently implemented at the vaccination centres. This is in spite of the implementation of a European Directive in December 2009 that was approved in Italy, which made informed consent mandatory for all types of vaccination, for all citizens. Since each vaccination centre depends on the local health authority, the latter is responsible for this deficiency. In a broader sense, the weak consideration for informed consent implies little interest in the principle of autonomy and perhaps an insufficient knowledge of the law.

• The authors report that none of the parents was asked for consent to give the non-mandatory vaccines to their child, and yet 52.8% of respondents had signed a consent form before their children were vaccinated. It would be interesting to know exactly what it was they had consented to.

• What can we learn from these findings? Does the information about the vaccines need to be presented in a way which is clearer and easier for the parents to understand? Do the doctors and nurses working at the vaccination centres need better training in informed consent procedures?

• I think it would be helpful to include samples of the information leaflets used in the appendix, so that the reader can appraise the information given to parents at the vaccination centres.

• In their conclusion the authors report that “consent procedures did not allow parents to acquire correct information about vaccine options for their children”. I think would be useful to include a description of exactly what consent procedures are employed in the vaccination centres in question, and a consideration of why they failed to inform the parents.

These last four issues are now more clearly addressed in different parts of the text (above all in the discussion).

6. Are limitations of the work clearly stated?
The authors state that external validity is the main limitation of their study.

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?

The references need some minor essential revision. References 16 and 17 are not
cited in the text.

We have corrected, and added to, the references.

8. Do the title and abstract accurately convey what has been found?

The title indicates the general subject area of the study, but does not tell the reader much about this particular study.
The abstract summarises the article fairly well.

We have changed the title as follows: The informed consent in southern Italy does not adequately inform parents about infant vaccination

9. Is the writing acceptable?

The meaning of some sentences in the text was not clear to me: For example the following sentence is a little ambiguous:
“Moreover, the information that should be provided by informed consent to parents are easy to explain and to understand”

We have clarified this sentence:
(original version) . Moreover, the information that should be provided by informed consent to parents are easy to explain and to understand.

(revised version p. 4) Moreover, in general, most options available for medical interventions are very complex. It is difficult to explain the details of the therapeutic alternatives, the potential outcomes, and the balance between risk and benefits. However, for infant vaccinations, the information provided by informed consent is easy to explain and to understand.

Overall, I think the clarity and coherence of the article could be improved with guidance and input from a native English speaker.

The text has been edited by Edanz.

Rev 2
Discretionary Revisions
Abstract
(1) Suggest shorter sentence construction needs to be used here in the results section. Less semi colons could be used and more short sentences should be written.
Results
Most of the respondents (89.5%) were mothers between 20 and 39 years of age (80.4% vs 59.6% of the fathers), they were married (87.2% vs 93.5% of the fathers), and only one-half of them were employed (50.2% vs 92.6% of the fathers). The informed consent form was received from 58.1% of parents was signed by 52.8%, but read by 35.0% of them. Only 1.5% of parents knew which vaccines were mandatory, and 25.0% of them believed that the entire hexavalent vaccine was mandatory. When we asked the parents which non-mandatory vaccinations were administered to their children, only 0.5% indicated the Haemophilus influenzae type B and none indicated the pertussis vaccine. Thirty-six per cent of the parents replied that their child had not received any non-mandatory vaccines. No parents were informed by the operators that their children would receive non-mandatory vaccines.

Introduction
(2) Given the authors are wanting to publish in an international journal I would suggest a little more detail on what ‘mandatory vaccination’ exactly means in Italy.

In Italy there is a huge legislative confusion around the concept of mandatory vaccinations. In the past, apprehension about reduction in the coverage rate was the prevalent attitude. However, the chance to eliminate the obligatoriness has been affecting this attitude, and it also has been affected by some constitutional Court decisions that enhance the individual’s right to choose in health matters.

(Original version) Information about these optional vaccines should be communicated to the parents, and informed consent should be obtained from parents before vaccination.

(Revised version p. 3) Information about these optional vaccines should be communicated to the parents, and informed consent should be obtained from parents before vaccination. However, in Italy the differences between mandatory and recommended vaccinations are weaker than in the past, and the concept of a “mandatory” vaccine is now ambiguous. Before 2008, children were not allowed to attend school if they were not vaccinated, but this rule has now been abrogated. Administrative sanctions for an unvaccinated child are rarely applied. If a parent refuses to vaccinate his/her child, the parent will receive an informative talk at the local health authority in an attempt to gain compliance. Legislatively, each Italian region is relatively autonomous, so the laws regarding vaccination vary throughout the country (e.g., in the Veneto Region, laws mandate that vaccinations are not mandatory).

(3) It is suggested that a definition of “informed consent” needs to either be mentioned here or in the methods section. For example; are the authors
evaluating the doctor’s duty to inform the parent about the vaccine, the benefits, risks and possible complications?

See point 19

Results

(4) Suggest restructuring results section here with three key points after describing the demographics of respondents: (1) n#s receiving the form, (2) n#s reading the form, and (3) n#s signing the form.

As suggested, we have modified the text and the table (the new table is at the end of the document) to better clarify the sequence “received”, “read”, “signed”.

(original version) The informed consent form was signed by 52.8% of the respondents (Table 2). At one centre, none of the parents received the consent form. At the other centres, between 93.7% and 70.0% of the parents signed the form. Only 66.3% of the parents who signed the consent form read the document. Overall, only 35.0% (364/1039) of the parents completely read the informed consent form.

(revised version p. 7) The informed consent form was received from 58.1% of the respondents. At one centre, none of the parents received the consent form, while at the other three centres 93.7%, 71.6%, and 70.0% of the parents received the form (data not reported in table). Among those who received an informed consent, it was signed by 90.9% (9.1% did not remember to sign it), while in total it was signed by 52.8% of the parents. Only 66.3% of the parents who signed the consent form read the document, while overall only 35.0% of the parents read the informed consent form (Table 2).

Discussion

(5) Paragraph 2 – For example it might be helpful to expand on what exactly has been debated about regarding the role of informed consent in infant vaccination and discuss this in relation to the study results.

We have changed and updated the discussion including a comment on this item. Please see the revised version of discussion in the revised manuscript.

(6) Paragraph 2 – please could the authors clarify what they mean in the sentence “sometimes we allow parents to refuse”…by “we”..who is “we”? The sentence has been eliminated. However, an explanation of this sentence is found in point 2.

(7) Paragraph 3 – The study results demonstrate that parents may not be receiving the consent forms and that only half sign the consent forms etc. I
suggest the authors quote their data here and have sentence summarising the implications of your results.

We have changed and updated the discussion including a comment on this item. See the revised version of discussion.

**Minor Essential Revisions**

(8) The writing requires some revision in terms of English language and grammar. The reviewer appreciates that writing a journal article in a language other than your first language spoken at home, may be difficult. However to publish this article in an English language journal, further work is required.

The revision includes editing by Edanz.

**Introduction**

(9) Paragraph 2 - please clarify the aim and outputs of the study, clearly stating whether you are evaluating health care providers role in the process of informed consent, or whether you are evaluating parent’s knowledge of vaccines or both.

As suggested, we have clarified this item.

(Original version) We report on the roles of informed consent and of the health care providers on parents’ knowledge about infant vaccination policies. This issue is relevant because parents are the main decision-makers with respect to whether certain vaccinations are given to their children. Moreover, the information that should be provided by informed consent to parents are easy to explain and to understand.

(revised version p. 4) We explored whether informed consent was delivered to the parents, whether they signed the consent form, and whether they read and acquired the information about the vaccination that their children would receive. This issue is relevant because informed consent plays an important role in parents’ knowledge about infant vaccination policies, and because parents are the main decision-makers with respect to whether certain vaccinations are given to their children.

(10) Paragraph 2/last sentence – Please rewrite and correct the English in this sentence.

This sentence was revised.

(Original version) Moreover, the information that should be provided by informed consent to parents are easy to explain and to understand.
Moreover, in general, most options available for medical interventions are very complex. It is difficult to explain the details of the therapeutic alternatives, the potential outcomes, and the balance between risk and benefits. However, for infant vaccinations, the information provided by informed consent is easy to explain and to understand.

Methods

(11) Last sentence - please could the authors clarify whether they refer to written informed consent in regards to consent to participate in the study or something else?

We have clarified the sentence. (See reply to point 19)

Results

(12) When referring to data in either Table 1 or 2 please reference it at the end of the sentence.

Corrected

(13) Please consistently use percentages when quoting data and/or total numbers i.e. (numerator/denominator) in this section.

The reporting of the results has been changed to consistent use of percentages in this section.

Discussion

(14) Paragraph 1 - I think it is misleading to start the overall summary of the results of this study by mentioning “other potential sources” of information i.e. media. These were not evaluated in the study and no conclusions can be drawn about the impact of these sources of information.

Although the media have not been evaluated in this study, according to our results they did not provide information to our sample. We think that this is an important indirect result of our study. So, we have partially modified the first paragraph. (However, if you want, you may to consider deleting the first two paragraphs of the Discussion)

(Original version) Health information from the media is not always correct, complete, and transparent (4,5); the media is, however, considered to be an important source of this information. In our study, the media alone was not sufficient to provide correct information about vaccination.
Health information from the media is not always correct, complete, and transparent [4,5]; the media is, however, considered to be an important source of this information. According to our results, the media was not sufficient to provide correct information to our sample about infant vaccination.

(15) Paragraph 2 – Vaccination has both individual (i.e. protection against infection and severe disease) and collective benefits (i.e. herd immunity may provide additional benefit through reduced transmission in the population). Have the authors taken these into consideration in your discussion of the difference in biomedical ethics in this paragraph?

We have changed and updated the discussion, and included a comment on this item. Please see the revised version of discussion in the revised manuscript.

(16) The last sentence in the conclusion section does not make sense. Are the authors saying that the informed consent process is not adequate enough to help provide parents the information they need to make an informed decision? “informed consent” does not “inform parents” itself.

As suggested, we have clarified this sentence. It is now the second to the last sentence.

(17) The aim of the study needs to be reworded so that it is clear exactly what the study is evaluating e.g. is it the process of obtaining informed consent from parents for vaccination of their children in vaccination centres in Italy? Clarification of the outcome measures for this study is needed.

As suggested, we have clarified the aim of the study.

We explored the roles of informed consent and health care providers as sources of vaccine information for parents.
(revised version) We explored whether informed consent was delivered to the parents, whether they signed the consent form, and whether they read and acquired the information about the vaccination that their child would receive.

Methods

(18) Methods are appropriate, but require some further clarity. Sample size – further explanation of the authors derived at the sample size would be helpful here. For example; what level of power and significance was assumed?

We used, and added to the text, the standard criteria for power (80%), confidence level (95%) and \( p \) value (< 0.05).

(19) Informed consent – The authors have provided no detail here on how they evaluated the “clarity and completeness” of the informed consent forms. Completeness can potentially be evaluated by checking against government recommendations as you list in the results section, but “clarity” is something that would require evaluation from the parent’s point of view on whether they understood the information in the consent form. Could the authors please update this section and the results section accordingly to demonstrate clearly the outcomes they were evaluating?

We modified the text in both the Methods and the Results sections:

(original version in Methods) Informed consent. The informed consents from the four vaccination centres were collected and analysed with respect to clarity and completeness.

(revised version p. 6) Informed consent forms. The infant vaccination informed consent forms that were presented by the health operators at the four vaccination centres were analysed with respect to completeness and clarity. Completeness was evaluated according to a definition that conformed with government recommendations: “Informed consent is a procedure to ensure that a patient, client, and research participants are aware of all the potential risks and costs involved in a treatment or procedure. The elements of informed consent include informing the client of the nature of the treatment, possible alternative treatments, and the potential risks and benefits of the treatment”.

Clarity was evaluated by the achievement of an agreement between all of the authors. However, all informed consent forms were also previously validated for clarity and completeness, by the ethics committees of the respective local health authorities.

(original version in Results) Informed consent. According to Italian law, parents should read and sign an informed consent form before their infant receives any vaccinations. The document should include information about which vaccines are mandatory, which are
recommended, the content of the hexavalent vaccine, and information about safety, effectiveness, contraindications, and how to respond to an adverse reaction. The informed consents from the four centres were similar and were sufficiently clear and complete with respect to the aims of the questionnaire.

(revised version p.6) Informed consent. The informed consent forms from the four centres were similar and were sufficiently clear and complete with respect to the aims of the questionnaire. They included information about which vaccines are mandatory, which are recommended, which vaccines were to be administered, the content of the hexavalent vaccine, and information about safety, effectiveness, contraindications, and how to respond to an adverse reaction.

Results

(20) Last sentence – “only 35% (364/1039) of parents” this data is not in Table 2. Please add this data to Table 2 or better explain how you arrived at recording this result.

We have modified and included these data in table 2.

(21) Table 3 – please update the response set headings for the question “Do you know which vaccines are mandatory?” – the response sets “Not correct” “Hexavalent” etc either need to be changed completely or require further explanation in the methods section.

The original question was: “Do you know which vaccines are mandatory?” and the answers were open-ended, so we summarized the responses into categories. We have clarified the meaning of the headings.

(original version) The following questions were used to investigate the parents’ knowledge and the vaccine information that they were provided: “Did you sign an informed consent before vaccination?” (main outcome); “Did you read the informed consent?”; “Have your children received other vaccinations in addition to the mandatory ones?”; “Do you know which vaccinations are mandatory?”; “Did anyone ask you for consent to give your child the two non-mandatory vaccinations that are included in the hexavalent vaccine?”.

(revised version p. 5) The following questions were used to investigate the parents’ knowledge and the vaccine information that they were provided: “Did you received a written informed consent before vaccination?” (yes/no) (main outcome); “Did you sign the informed consent” [yes/no/I don’t remember]; “Did you read the informed consent?”(yes/no/partially); “Have your children received other vaccinations in addition to the mandatory ones?” (yes/no); “if yes, which one?” (open); “Did anyone ask you for consent to give your child the two non-mandatory vaccinations that are included in the
hexavalent vaccine?” (yes/no); “Do you know which vaccinations are mandatory?” (open/I don’t know). The answers to this question were coded as: “correct” when only the four mandatory vaccinations were indicated, and “not correct” for all other responses, except that the response “hexavalent” (also not correct) was calculated separately.

(22) Last paragraph – “with the exception of the difference between centres’ distribution of informed consent” – the authors did not mention this measurement in the methods section. Either add the method for this evaluation or omit these results altogether. Also the authors should mention the methods you used to examine any significant differences in the data according to demographics.

We have reported in the methods section the criteria we used to examine any significant differences in the data according to demographics and vaccination centres.

(revised version p. 5) Using a univariate analysis and chi-square test, we analysed the parents’ responses according to demographic characteristics and to vaccination centre. A value of \( p<0.05 \) was considered to be statistically significant.

Discussion

(23) Further rewriting is needed before the discussion section demonstrates an adequate balance between reporting data and discussing the results in light of other relevant studies or work. For example do parents need to be better educated about the consent process, what it means and how they can become informed about vaccines? Or do health care workers need to be trained in how to provide informed consent procedures and information to parents? Or both?

We have changed and updated the discussion, have added references, and have included a comment on this item. Please see the revised version of discussion, and the references.

Level of interest:
An article whose findings are important to those with closely related research interests

Quality of written English:
Needs some language corrections before being published

The revision includes editing by Edanz.

Statistical review:
No, the manuscript does not need to be seen by a statistician.
I hope that the revisions to the manuscript and the accompanying responses are acceptable, and that the manuscript is suitable for publication.

I look forward to hearing from you.
Yours sincerely,

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