Author's response to reviews

Title: Measles transmission from an anthroposophic community to the general population, Germany 2008 - Effect of early intervention on size and duration of measles clusters in school and kindergarten settings

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Author's response to reviews: see over
From
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To
MD Melissa Norton
Editor-in-chief
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MS: 2124752057471830 - Measles transmission from an anthroposophic community to the general population, Germany 2008 - Effect of early intervention on size and duration of measles clusters in school and kindergarten settings

Dear Dr. Norton,

Thank you for your letter regarding our manuscript “Measles transmission from an anthroposophic community to the general population, Germany 2008 - Effect of early intervention on size and duration of measles clusters in school and kindergarten settings” (manuscript no. 2124752057471830). We appreciate the comments of the Reviewers and the Editorial Board very much. Please find our response to them in the following and the revised manuscript version below.

With kind regards,
on behalf of the authors,

Maria Wadl
Editorial comments:

- English: The manuscript was revised by a native English speaker, with particular attention to the abstract.

- Ethics: The manuscript is about an outbreak investigation. Local health authorities in Germany are the competent bodies obliged by law to collect specific data and to take measures (such as immunization). The only additional data collected in this outbreak investigation was information by a questionnaire.

The manuscript reads as follows (Page 7, last paragraph; Page 8, first paragraph):

"Additionally, the LHA collected data on reasons for non-immunization and complications from all notified cases through a questionnaire administered by telephone or post. If patients were under age 16, parents were queried. Study participation was voluntary. We assumed implicit informed consent when a completed questionnaire was returned."

We hope this finds your approval.

- Journal style: the authors ensured that the manuscript conforms to the journal style of BMC Public Health.
Reviewer 1

Major Compulsory Revision

1. “Results: Effect of differently applied control measures in schools and kindergartens, and Discussion”: you compared the median number of measles cases in the schools with intervention A (school exclusion of non immune persons immediately after the first reported case) to the median number of cases in schools with intervention B (school exclusion after the second reported case). Besides the different reactivity of each intervention, these numbers depend also on the size of schools, specifically on the number of pupils or students not immune for measles. As mentioned in the discussion, it would ideally be necessary to compare attack rates (with an odds ratio and CI). This analysis was not performed because the population at risk was not well known (end of discussion). Could we not assume that all non-immune individuals attending these schools are the population at risk (this information is known since it was necessary for intervention)? Even if we do not know the details of contacts between cases and non-immune individuals from each school, this seems a very reasonable approach given the high infectivity of measles (also by aerosols). In the worst case, it seems all the same useful to calculate an attack rate per school, and globally for schools A respectively B considering all pupils regardless of their immune status, with discussion of the limitations of this approach in the discussion section.”

The authors agree that it would be ideally to compare attack rates of institutions by implemented intervention (A or B); the population at risk should be persons who were non-immune to measles and exposed. We lack information about how many persons were regarded as non-immune and as exposed and were therefore excluded from school for 2 weeks. Following the suggestions of reviewer 1 and 2 we decided to compare overall attack rates of the institutions globally and by intervention (A or B) and to dispute the limitations of this approach in the discussion.

The manuscript reads now as follows:

Results (Page 13, Paragraph 4):

"The mean attack rate in institutions was 6%. Stratification by intervention led to a mean attack rate of 5% (range: 1-16%) if intervention A was used and 7% (range: 1-21%) if intervention B was applied. Average attack rate ratios in institutions where intervention A was implemented were 1.6 times lower (95% CI: 0.4-6.1) than those of institutes where intervention B was applied."

Discussion:

(Page 16, Paragraph 3)

“The compared attack rates should be interpreted with caution since the number of persons who were already immune against measles was not identified in the clusters. Therefore, we can assume that the calculated attack rates are rather underestimates.”

(Page 17, Paragraph 3)
“Third, information on the population at risk (number of susceptible contacts per school or kindergarten) was not sufficiently available. Therefore, attack rates were compared among all children and/or teenagers attending the affected schools and kindergartens.”

2. “Results: Effect of differently applied control measures in schools and kindergartens, and Discussion”: since the purpose of this article is to compare the outcome of two interventions, and in particular the advantage of strategy A compared to strategy B, it would be more specific to provide the number of measles cases in the clusters and their durations AFTER onset of intervention. Accordingly, the index cases of clusters A and the first two cases of cluster B should not be counted, and the calculation of the duration of the cluster should start with the intervention.”

The authors addressed this comment.

The manuscript reads now as follows:

Methods (Page 9, Paragraph 3):
“In order to analyse the effect of the respective intervention we excluded the case with the first disease onset from all clusters in which intervention A was applied and the two cases with the first disease onsets from all clusters where intervention B was used. The duration of clusters by intervention was calculated starting with the onset of the respective intervention.”

Results (Page 13, last Paragraph; Page 14, Paragraph 1):
“Clusters in kindergartens and schools had a median number of 3 (intervention A; range: 1-7) versus 13 (intervention B; range: 2-21) cases (P=0.05), and lasted a median of 3 (intervention A; range: 0-36) versus 26 (intervention B; range: 3-66) days (P=0.13).”

Discussion (Page 16, Paragraph 5):
“The compared attack rates should be interpreted with caution since the proportion of persons who were already immune against measles was not identified. Therefore, we can assume that the calculated attack rates are rather underestimates.”

Accordingly, the Poisson regression model was recalculated:

Methods (Page 10, Paragraph 1):
“Using a Poisson regression model we estimated the average decline of cases per 7-day interval. We categorized the days of disease onsets in 7-day intervals, starting with the onset of the second case in clusters with intervention A and of the third case in clusters with intervention B as day 1.”

Results (Page 14, Paragraph 2):
“The estimated mean decrease of cases per 7-day interval was 58% using intervention A and 29% intervention B, indicating that the average number of cases per 7-day interval decreased 1.7 times (95% confidence interval: 1.1-2.7; P=0.03) slower using intervention B compared to intervention A (Figure 4).”

Discussion (Page 16, Paragraph 4):
“The estimated mean attack rate ratio indicated that exclusion of susceptible persons from schools and kindergartens starting with the first incident measles case (intervention A) was more effective than exclusion of susceptible persons after the second case (intervention B).”
Minor Essential Revisions

1. “Outbreak background”: indicate immunization coverage for measles in the four counties most affected by the outbreak.

The authors addressed this comment.
The manuscript reads now as follows (Page 5, last Paragraph; Page 6, first Paragraph):
“The average vaccination coverage of first graders for two doses of measles vaccine in the four counties was 76% (range 70-80%) in 2007/2008.”

2. “Data collection and descriptive analysis”: specify what are the criteria and the official notification deadline for measles.

The authors addressed this comment.
The manuscript reads now as follows (Page 7, first Paragraph):
“Physicians must report any suspected case, clinical cases of and deaths from measles within 24 hours to the responsible local health authority. Heads of laboratories are obliged to report any direct or indirect evidence of measles virus – if the evidence suggests an acute infection - within 24 hours to the responsible local health authority.”

3. “Data collection and descriptive analysis”: specify which test was used to compare medians.

The test used for comparing medians has already been described; the authors used the Mann-Whitney-U-Test (Page 9, last Paragraph; Page 10, first Paragraph).

4. “Methods: Clusters”: describe here the definition of a cluster (and not in results).

The authors addressed this comment.
The manuscript reads now as follows (Page 8, first Paragraph 4):
“Cases with disease onset a maximum of 18 days apart and spatial contact (e.g. same household, same school) were grouped into clusters.”

5. “Methods: Control measures”: describe here the two interventions (and not in results).

The authors addressed this comment.
The manuscript reads now as follows (Pages 8-10):
“In Germany, the LHAs are responsible for the implementation of control measures. In order to assess the effectiveness of implemented control measures, the Robert Koch Institute interviewed the LHAs by telephone. Our interviews of the local health authorities revealed that they applied two different control measures in schools and kindergartens (preschool) during the outbreak: the trigger for exclusion of non-immune persons from the respective school or kindergarten for 14 days after the last contact to an infectious case was either the notification of at least one measles case (intervention A) or at least two measles cases (intervention B) in the
respective school or kindergarten. Immune persons were those with at least one documented vaccination against measles a minimum of three weeks before disease onset, immunity confirmed by serology or anamnestic measles. Intervention A and B were implemented compulsory. Compliance was not controlled for. Vaccination cards in schools and kindergartens were checked by staff from the LHAs in three of the affected counties, and by staff from the respective school or kindergarten in the fourth county.

Attack rates were calculated and negative binomial regression was used to estimate the average attack rate ratio with 95% confidence intervals (95% CI) according to the implemented measure. Teachers and staff of schools and kindergartens were not included in the denominators of the specific institutions.

In order to analyse the effect of the respective intervention we excluded the case with the first disease onset from all clusters in which intervention A was applied and the two cases with the first disease onsets from all clusters where intervention B was used. The duration of clusters by intervention was calculated starting with the onset of the respective intervention. The school cluster in the anthroposophic school in Salzburg city (since Austrian health authorities were responsible for the intervention) and clusters in kindergartens and schools with all cases occurring on the same day (0 days apart, mode of intervention did not differ) were excluded from analysis.

We compared the median number of cases per cluster and the median duration of clusters in days according to the implemented intervention using the Mann-Whitney-U-Test. Using a Poisson regression model we estimated the average decline of cases per 7-day interval. We categorized the days of disease onsets in 7-day intervals, starting with the onset of the second case in clusters with intervention A and of the third case in clusters with intervention B as day 1.”

6. "Methods: specify if the teachers and staff of schools and kindergartens were included in the study (as subjects to intervention, cases of measles, denominators).

The authors addressed this comment. The manuscript reads now as follows:

Methods (Page 9, Paragraph 2):

“Attack rates were calculated and negative binomial regression was used to estimate the average attack rate ratio with 95% confidence intervals (95% CI) according to the implemented measure. Teachers and staff of schools and kindergartens were not included in the denominators of the specific institutions.”

Results (Page 11, first Paragraph):

“We identified 217 measles cases in the four counties. No case was found in teachers or staff of schools and kindergartens.”
7. “Results: Outbreak description”: “25 cases were hospitalized”: precise 25 of 217 161 cases and give the corresponding percentage. If it is 25/161, reverse paragraphs 4 and 5.

The authors addressed this comment.  
The manuscript reads now as follows:  
Results (Page 11, Paragraph 4):  

“Overall, 25 of 217 (11%) cases were hospitalised for a median of four days (range: 1-13 days).”

8. “Results: Effect of differently applied control measures in schools and kindergartens”: a double overlaid figure showing the epidemic curve for the 6 A schools and the curve for the 4 B schools (in distinguishing each school / kindergarten in both cases) would be useful, permitting to assess the dynamics of the introduction of measles in each institution. Interacting with the intervention this dynamic can influence the final number of cases (for example in the strategy B, the final outcome would probably differ if the second case occurs two days after the index case (multiple introduction by almost concomitant cases of the same generation) or whether it occurs 12 days after (second generation)).

The authors added in Figure 1 the period of time, in which interventions A and B were implemented respectively. Regarding the dynamic of the outbreaks in the institutions by intervention (A or B) we refer to Figure 4.

9. “Discussion”: the duration of the school clusters may also depend on the number of cases and hence of pupils in each school. This also needs to be mentioned among limitations in the discussion.

The authors addressed this comment.  
The manuscript reads now as follows:  
Discussion (Page 17, Paragraph 4):  

“Last, the duration of the school and kindergarten clusters may also depend on the number of cases and hence of attendees in each institution.”

10. “Discussion” “Our study confirms that health professionals should use all opportunities...”: I agree, but reformulate (“confirm”) because this was not the topic of your study.

The authors addressed this comment.  
The manuscript reads now as follows:  
Discussion (Page 15, Paragraph 2):  

“Health professionals should use all opportunities (e.g. contact with patients), both to inform about the highly protective effect of measles vaccinations and to offer measles vaccination to persons, who are not yet immunized.”
Discretionary Revisions

1. “Results: Outbreak description”: consider also providing the average incidence of measles for the four most affected counties and for the whole of Bavaria.

The authors addressed this comment.
The manuscript reads now as follows (Page 11, Paragraph 1):
"In the outbreak period, the four counties had an average measles incidence rate of 32 cases per 100,000 person-time (range: 12-71) which was the highest among all Bavarian counties (overall: 2 cases per 100,000 person-time, Figure 1). Six weeks before and after the outbreak period, no other measles case was reported within the four counties."

2. “Results: Outbreak description”: “Vaccination of two of the five persons were laboratory confirmed”: unclear for me; do you mean that measles of 3/5 vaccinated persons was laboratory confirmed?

The authors addressed this comment.
The manuscript reads now as follows (Page 12, Paragraph 5):
"In total, 54 (25%) of 217 cases were laboratory confirmed. Among the confirmed cases were two of the five vaccinated persons including the patient vaccinated twice."

3. “Results: Outbreak description”: give in brackets the percentage of the main reasons for not being vaccinated.

The authors addressed this comment.
The manuscript reads now as follows (Page 12, Paragraph 4):
"The main reasons for not being vaccinated against measles were “fear of vaccine-related adverse events” (33%), “opposing measles vaccination in general” (30%) and the opinion “measles is not a severe disease” (18%) (Table 2)."

4. “Results: Clusters”: Add a note in the table 4 indicating the three schools where the same school bus played a role in transmission of measles.

Since Table 4 was removed, this comment is only addressed in the text.
(See Page 13, Paragraph 1):
"A total of 32 cases were linked to the use of a school bus which carried children and teenagers to and from three of the affected schools. However, all cases linked with the school bus were included in the respective school clusters."
5. “Discussion” “Our results are not statistically significant... This may be explained by the low number of cases”: in your results, the median number of cases was significantly lower with intervention A. Moreover, should you not rather speak of a low number of clusters (instead of cases)?

The authors addressed this comment.

The manuscript reads now as follows (Page 16, last Paragraph):

“Comparing the median number of cases per cluster our results was borderline statistically significant, if accepting an alpha-error-level of 0.05. This may be explained by the low number of clusters.”

6. “Discussion” “with low to moderate vaccination coverage”: consider to delete “low to” because school exclusion is difficult to implement and unfruitful where vaccination coverage is low.

The authors addressed this comment.

**Comments in the pdf Document**

The authors addressed these comments as possible.
Reviewer 2

General comments

1. For comparison of the two interventions A and B preferably relative numbers should be used. TABLE 4: *note + DISCUSSION: Last sentence: Authors mention, that attack rates couldn’t be calculated, since number of susceptible contacts was not sufficiently available. Attack rates could be calculated, but exposed persons should be determined (class or school.... ?), therefore a definition of a contact should be established. Attack rate is defined as number of exposed persons infected with the disease divided by the total number of exposed persons.

   The authors addressed this comment: please see point 1 of the Major Compulsory Revision from Reviewer 1.

2. Additionally, number and proportion of the susceptible population could be compared for each cluster. An insufficient information on susceptible population at risk is mentioned, however number of non-immune persons excluded in each cluster (according to intervention A or B) might be available. It would be useful to know, if all non-immune contacts fulfilled the requirement of the intervention A or B in sense of 14 days isolation, (and if it was based on recommendation or as a kind of mandatory command).

   We are afraid that the number and proportion of the susceptible population is not known in this outbreak investigation. Following the reviewers suggestions, we compared attack rates (see point 1 of the Major Compulsory Revision from Reviewer 1).

   The authors added (Page 9, first Paragraph) "Intervention A and B were implemented compulsory. Compliance was not controlled for."

3. Moreover, an important information about postexposure vaccination (or application of immunoglobulin) of susceptible contacts would be needed. We know, from RESULTS: Effect of differently applied control measures in schools and kindergartens: 2 paragraph, that ,"The county using intervention B informed as early as the occurence of the first incident measles in a kindergarden or school all contact persons about......and the necessity of protection by vaccination." Early vaccination or application of immunoglobulin is a specific and basic control measure, which could influence results of this study. Therefore it should be taken into consideration.

   Post exposure prophylaxis (PEP) was recommended by all four German local health authorities involved in this outbreak. However, PEP was not performed by the local health authorities but by general physicians. Information on the total number of persons receiving PEP is not available. As this proceeding was the same for all four local health authorities we assume the influence of post exposure prophylaxes on the size and duration of clusters as minor.
4. CONCLUSIONS: 2 paragraph: “Moreover, health professional have to be convinced that immediate notification of suspected measles cases to the health authorities is important for timely infection control measures.” This is very important information and it is also mentioned in discussion. Anyhow, was there some evidence of late reporting during the outbreak?

The authors calculated the reporting delay in days.

The manuscript now reads as follows (Page 11, first Paragraph):
“For the 215 measles cases with available information on date of onset and date of reporting the mean reporting delay was 6 days (range: 0-28 days); the reporting delay did not differ among the four counties.”

Minor Essential Revisions

5. METHODS: Data collection and descriptive analysis: 2 paragraph: “……………… resident of the four affected Bavarian counties.” In order to specify place, the names of the four counties should be written.

The authors addressed this comment.

The manuscript now reads as follows (Page 7, Paragraph 3):
“In this outbreak investigation, we defined a case as any resident of the four affected Bavarian counties (Berchtesgadener Land, Rosenheim, Traunstein, Mühldorf am Inn), diagnosed with clinical measles and disease onset between February 1 and August 30, 2008.”

6. METHODS: Laboratory analysis: “Laboratory confirmation using serology…..”…..the serological test could be specified.

The authors addressed this comment.

The manuscript now reads as follows (Page 8, Paragraph 3):
“The National Reference Centre for Measles, Mumps and Rubella in Berlin (NRC) used the Enzygnost Anti-Measles Virus IgM ELISA (Siemens, Germany) for the detection of anti-measles IgM in serum.”

7. METHODS: Clusters: Please, write concrete incubation period, which you used in your definition (...1-18 days)

The authors addressed this comment.

The manuscript now reads as follows (Page 8, Paragraph 4):
“Cases with disease onset a maximum of 18 days apart and spatial contact (e.g. same household, same school) were grouped into clusters.”

8. RESULTS: Outbreak description: 1 paragraph, 3 sentence: ………………………. Use incidence rate....... instead of incidence

The authors addressed this comment.

The manuscript now reads as follows (Page 11, Paragraph 1):
“In the outbreak period, the four counties had an average measles incidence rate of 32 cases per 100,000 person-time (range: 12-71) which was the
highest among all Bavarian counties (overall: 2 cases per 100,000 person-time, Figure 1)."

9. RESULTS: Outbreak description: 3 paragraph, 2 sentence: ....... In case of incidence rate ........use (170 cases/ 100,000 person years) ......................................................or in case of age specific incidence use (170 cases/ 100,000 population)

The authors addressed this comment.

10. RESULTS: Laboratory analysis: ...."In total, 54 (25%) cases were lab confirmed." ... by which lab method ?

The authors addressed this comment.

The manuscript now reads as follows (Page 11, Paragraph 1): "In total, 54 (25%) of 217 cases were laboratory confirmed by serology. "

11. RESULTS: Effect of differently applied control measures in schools and kindergartens: The content of the 1st and 3rd paragraphs describes more methods than results. However, current sequence of these paragraphs is easy to follow.

The authors addressed this comment and transferred the content of the first and the third paragraph in the methods section.

12. TABLE 3: A column “number of cases per cluster- ranged” could be added.

The authors addressed this comment (see Table 3).

Discretionary revisions

13. ABSTRACT: Background: 3 sentence – “In spring 2008, four...”….. change to “From March to mid-April 2008, four.....”

The authors addressed this comment.

The manuscript now reads as follows (Page 2, Paragraph 1): "From March to mid-April 2008, four neighbouring Bavarian counties reported 55 measles-cases mostly linked to an ongoing measles outbreak in an anthroposophic school in Austria."

14. ABSTRACT: Results: 3 sentence – please add number of cases who suffered complications

The authors addressed this comment.

The manuscript now reads as follows (Page 2, last Paragraph): "Twenty-nine (18%) of 161 cases suffered complications."

15. ABSTRACT: Results: I recommend to change the order of sentences. Concretely the two sentences regarding vaccination should straight follow each other. "In total, 156 (97%) of 161 cases with known vaccination status were not vaccinated. The main reason
The sentence about complications shouldn’t be between these two describing vaccination.

The authors addressed this comment.

The manuscript now reads as follows (Page 2, last Paragraph):
“In total, vaccination status was known in 161 (74%) cases and 156 (97%) of them were not vaccinated. The main factor for non-vaccination was "fear of vaccine-related adverse events” (33%). Twenty-nine (18%) of 161 cases suffered complications.”

16. BACKGROUND: Outbreak background: 2 paragraph: “Until mid-April…..” I recommend to add year “Until mid-April 2008…..”.

The authors addressed this comment.

The manuscript now reads as follows (Page 5, Paragraph 4):
“Until mid-April 2008, the number of measles cases possibly related to the outbreak in the Austrian school increased to 55, affecting the population of four neighbouring Bavarian counties.”

17. RESULTS: Outbreak description: 6 paragraph, 1 sentence: “Twenty-nine cases (18%)…….” add “Twenty-nine cases (18%) of 161 …...”

The authors addressed this comment.

The manuscript now reads as follows (Page 12, Paragraph 2):
“Twenty-nine cases (18%) of 161 developed complications; most frequently, otitis media was reported (n=14). A 13-year-old girl, who was hospitalised for five days, suffered from seizures (Table 1).”

18. RESULTS: Outbreak description: 7 paragraph, 4 sentence: How was the vaccination of two cases laboratory confirmed?

The authors addressed this comment: the vaccination was not confirmed but the measles infection.

The manuscript reads now as follows (Page 12, Paragraph 5):
“In total, 54 (25%) of 217 cases were laboratory confirmed. Among the confirmed cases were two of the five vaccinated persons including the patient vaccinated twice.”

19. RESULTS: Outbreak description: 8 paragraph: All reasons for not being vaccinated against measles are in the table 2. However, reasons “doctor advised against vaccination” and “vaccination not offered” might be mentioned in text, because they are very important and reflect failure of health care.

The authors agree that the reasons “doctor advised against vaccination” and “vaccination not offered” are important. For reasons of readability the authors prefer to refer for this information to Table 2.

20. RESULTS: Laboratory analysis: Complete ....“In total, 54 (25%) of 217 cases were lab confirmed.”
The authors addressed this comment.

**The manuscript reads now as follows (Page 12, Paragraph 5):**

“In total, 54 (25%) of 217 cases were laboratory confirmed.”

21. **TABLE 3: Add in heading % (of clusters)**

The authors addressed this comment (see Table 3).

22. **FIGURE 2: Title of the axis x could be “Week of disease onset”**

The authors addressed this comment (see Figure 2).

23. **FIGURE 1 and FIGURE 3: Consider, if “Measles incidence rate (cases per 100,000 person-time)...” would be more suitable in a given time period.**

The authors addressed this comment (see Figures 1 and 3).

Minor issues not for publication

24. **BACKGROUND: 1 paragraph: The period of infectiousness (contagiousness) could be mentioned too.**

The authors addressed this comment.

**The manuscript reads now as follows (Page 4, Paragraph 1):**

“The period of contagiousness is usually 4 days before and after onset of rash.”
Reviewer 3

Minor Essential Revisions

- REFERENCES
  References 3 and 11 seem to be identical. Please check the use of capital letters in abbreviations of journal names; “Epidemiology and infection” should read “Epidemiology and Infection”, “The Pediatric infectious disease journal” should read “The Pediatric Infectious Disease Journal”, ...

  The authors addressed this comment. We used EndNote as soft ware tool for managing the references and “BMC public health” as citation style. However, capital letters for journals like “Epidemiology and Infection” seem not to be the default.

- FIGURE LEGENDS
  The legend in FIGURE 2 lists “February-August 2008 (N=217), while the legend of FIGURE 3 lists “March-July 2008 (N=217)”. I guess the legend in FIGURE 3 should read February-August too, as Table I lists “March-July (N=161).”

  The authors addressed this comment.

- DISCUSSION
  The last sentence in the third paragraph presently reads: “A considerable percentage of cases in our studies reported complications, indicating that measles is not a mild disease”. Here I disagree, as the fact that 8.7% experienced otitis media, 5.6% diarrhoea or 5.9% mood shifts does not indicate proof of a severe course. In fact, if I were an vaccination opponent, for me this data would underline that in developed countries measles is no longer a problem. I recommend to add an paragraph addressing the risk of late sequelae like SSPE in 1 in 100.000 cases, or mentioning the single patient who experienced seizures. The manuscript should also explain which etiology underlies the terms used in TABLE 1, like “Disturbance of consciousness” and “Mood shifts”; what are these terms supposed to mean in medical nomenclature (transitory ischaemic attacks? Encephalitis?).

  The authors added the patient reporting seizures in the discussion. Complications were queried without use of medical terminology. To the best knowledge of our native speaker the German words “Bewusstseinsstörungen” and “Persönlichkeitsveränderung” were translated with “disturbance of consciousness” and “mood shifts”, respectively.

  The manuscript reads now as follows (Page 15, last Paragraph; Page 16 first Paragraph):
  “A considerable percentage of cases (18%) in our study reported complications, including one case that had seizures. This indicates that measles is not a mild disease.”
Discretionary Revisions

- **ABSTRACT** The first sentence of the second to the last paragraphe should be rephrased avoiding the term “linked into”, e.g. to “Overall, 184 cases could be epidemiologically grouped into 59 cluster.” In the next sentence it could read “Of those, 41 clusters could be linked to households and 13 to schools or kindergartens.“, avoiding the term “could be allocated to”. In the last paragraph (Conclusions), please delete “or sceptics)” and rephrase the last sentence, as it is not clear who has to report to whom immediately.

The authors addressed this comment unless the proposal to delete “or sceptics”. In our point of view vaccination opponents refuse to receive vaccinations generally while vaccination sceptics may accept specific vaccinations for specific populations but other vaccinations for specific other populations not. Therefore we would prefer to make this differentiation.

- **METHODS** In the first sentence of the paragraph “Clusters”: instead of “were linked into clusters.”: “were grouped into clusters”.

The authors addressed this comment.

The manuscript reads now as follows (Page 8, first Paragraph 4): "Cases with disease onset a maximum of 18 days apart and spatial contact (e.g. same household, same school) were grouped into clusters."

- **RESULTS** In the first sentence of the paragraph “Laboratory analysis please use the term “laboratory confirmed” instead of “lab confirmed”, as the term “lab” is slang. In the last sentence of the paragraph “Clusters”, a closing bracket at the very end can be deleted. Last paragraph: the “p” in “poisson” in “poisson regression model” should be capital (“Poisson”). The authors use the term “Kindergarten”. Maybe they can state once what Kindergarten means in Germany, e.g. “Kindergarten (voluntary, children age 4-5)”. In some countries, e.g. Iowa, the term “Kindergarten” equals fist class of elementary school (mandatory, children age 6), in contrast to “preschool”, which equals Kindergarten in Germany.

The authors addressed these comments.