Author's response to reviews

Title: The incidence and health burden of earaches attributable to recreational swimming in natural waters

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Author's response to reviews: see over
July 24, 2013

Dear Editor:

We are pleased to submit the revised version of our manuscript. We thank the editors and reviewers for their comments. The changes we have made to address the concerns raised have improved the manuscript and clarified several important aspects of the results and their interpretation.

Sincerely,

Timothy J. Wade. Ph.D MPH
US EPA Human Studies Facility
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Editor’s comments:

After the Discussion section, insert the heading Conclusions stating clearly the main conclusions of the research and giving a clear explanation of their importance and relevance. Please format the List of abbreviations as abbreviation term and separating the pairs with semi-colons in sentence format. The heading after the Competing interests should read Authors' Contributions. In the References section please remove the issue numbers and use full page references e.g. 357-362. There appears to be a typo in the page reference for #11. For the tables, all horizontal lines should be visible.

1. The title would benefit from having a study design included and in the email addresses replace the hyphen with a colon.

*Changes made*

2. The Abstract should be moved to the next page. Please remove the lines between the heading Abstract and the text and the one between the Abstract and the Background section. The Abstract headings should be Background, Methods, Results, and Conclusions.

*Changes made, added Methods section to Abstract.*

3. After the Discussion section, insert the heading Conclusions stating clearly the main conclusions of the research and giving a clear explanation of their importance and relevance.

*Conclusion section added with emphasis on the main conclusions, importance and relevance.*

4. Please format the List of abbreviations as abbreviation:term and separating the pairs with semi-colons in sentence format.

*Changes made*

5. The heading after the Competing interests should read Authors' Contributions.

*Change made*

6. In the References section please remove the issue numbers and use full page references e.g. 357-362. There appears to be a typo in the page reference for #11.

*Formatting to references corrected; corrected page numbers (15-18 instead 15-8)*

7. For the tables, all horizontal lines should be visible.

*Horizontal lines added to all tables*
Reviewer 1 (Dr. Sam Dorevitch) Comments and Responses

Major Essential Revisions

1. First, no association between ear symptoms and either duration of exposure or water quality was observed. Reference 12 of the manuscript found that frequent swimming in surface waters was strongly associated with otitis externa. While frequency of swimming and duration of swimming are not the same, one would expect greater physical effects on the external auditory canal with longer duration of water recreation. Biological plausibility would have been supported by such an association. Study subjects in NEEAR and similar studies couldn’t be blinded/masked regarding water exposure status but were likely unaware of water quality. Confidence that exposure results in outcome would have been much greater if the exposure (water quality) were one about which study participants were unaware. This caveat should be expanded upon in the ‘discussion’ section.

We agree that over-reporting of earache among swimmers could account for some of the observed differences in earache among swimmers and non-swimmers. We also agree that associations among swimmers with some type measure to which participants are effectively blinded such as a water quality parameter or duration of swimming would have provided evidence against such a reporting bias. Although it is difficult to make detailed comparisons with the study cited reference 12 (van Asperen et. al.) which utilized a retrospective case-control design, and observed a strong relationship between otitis externa and swimming in freshwater lakes in the past two weeks, they did find the association increased with the number of days of swimming (frequency). We did not measure frequency of other swimming events directly, but we did observe an association between earache and “other swimming” (other head immersion swimming in the week prior to the beach visit -see elevated Odds Ratios in Table 3). Although we might also have expected an association between earache risk and duration in the water for reasons suggested by the reviewer, duration of exposure may not be as important as individual characteristics which pre-dispose individuals to susceptibility to otitis externa. For example Strauss (1987) cites several characteristics that make individuals more susceptible to ear infections following water exposures:

“There are several variables that influence the factors of moisture, warmth, and microorganisms and predispose an individual to ear canal infections... The presence or absence of these variables explains why some people develop ear canal infections while others do not, even though the exposures may be similar. Tortuous, narrow, or partially obstructed ear canals are prone to infection. Bony exostoses, plugs of cerumen, or retained foreign objects are causes of obstruction”

and

“...dermatoses that affect the canal...can compromise the protective factors of the canal lining and hence make it more susceptible to microorganism invasion. Dermatoses that may alter the external ear canal include allergic conditions, eczema, psoriasis, contact dermatitis, seborrheic dermatitis, neurodermatitis, or mechanical factors.”
Again, we did not measure these individual characteristics so cannot address directly the extent to which these factors affected the lack of observed association with duration in the water and earache. However, such individual susceptibilities may provide some explanation why no association with duration of swimming was observed on our data. Among those with a pre-disposition to outer ear infection it may be possible that duration of exposure is not a critical factor.

Regarding water quality, we did not test for microorganisms which would be likely causes of otitis externa infections such as Pseudomonas aeruginosa, and we have recognized this as a limitation of our study. Moreover, consistent associations between otitis externa and water quality have not been established from previous studies. So, the lack of association between these parameters and earaches was not necessarily surprising or unexpected. We have expanded our discussion of this issue and included additional reference citations in the Discussion section.

Despite the possibility for a reporting bias in this observational study, there are several reasons that the effect, if present, may not be strong. First, subjects reported on numerous symptoms as part of the NEEAR Water study and earaches were not particularly emphasized in relation to these other symptoms. Swimming and non-swimming respondents were therefore probably unlikely to be abnormally or specifically focused on their earache symptoms. Second, several of the other symptoms studied showed no association or inconsistent associations with swimming exposures after adjustment for covariates (respiratory illness; skin rash; eye irritations, published previously see Wade 2008; Wade 2010). It is unclear why a reporting bias, if present, would specifically affect earache and not other types of illness. Third, the association between earaches and swimming exposures was remarkably consistent across beach sites and age groups. One might expect reporting biases, if present, to vary by age group or other respondent characteristic (e.g., parents may be more likely to over-report earaches for their swimming children). Moreover this consistency in effect across age groups with regard to presumed otitis externa infections is consistent with reports that these infections affect age groups approximately equally. Finally, “earache” is a relatively non-subjective symptom with which most people are familiar with, and we anticipate it is easily, or at least equally, understood by swimmers and non-swimmers.

However, we agree there is the potential for a reporting bias which we cannot fully account for in our data. To address the reviewer’s concerns regarding the validity of self-reported earache and the potential for reporting bias, we have expanded on this limitation in the discussion section. We more strongly stated the possibility of recall bias affecting the results, and included the issues discussed above. We have also expanded on our discussions providing possible rationale why duration of exposure and water quality were not associated with earache incidence.


2. Second, in Table 1, participants under 1 year of age had incident ear symptoms at a frequency that was higher than or similar to other groups. Table 3 demonstrates the strongest association between head immersion and ear symptoms was observed in age 0-1 (vs. 20-59). On the other hand, Reference 14 suggests than the incidence of otitis externa is less than half that among people age 0-4 vs. 5-9 or 10-14 yrs. Otitis media extremely common in children less under 1 year of age (infants) – approximately 180 cases/1,000 children per month according a study conducted at 3 US sites (Venacchi, Lesko et al, 2004 in the Int. J Pediatric Otorhinolaryngology).

We thank the reviewer for the reference and agree that otitis media is a much more likely cause of earaches especially among infants and young children. As we have defined “earache”, symptoms associated with otitis media, otitis externa, trauma and ear pain associated with injury, allergy and other conditions would be captured. Therefore, the regression results in Table 3 and the significant coefficient for ages 0-1, cannot be interpreted that the association between head immersion swimming and ear symptoms is elevated among those age 0-1 (i.e., there is an interaction between age and swimming on earache incidence); rather they should be interpreted that those age 0-1 reported a higher frequency (approximately 2 times increased odds) of earache compared to those age 20-50 (controlling for covariates including swimming). This is consistent with what is generally well understood; that young children have more earaches, most likely attributable to otitis media, but not necessarily a higher susceptibility to swimming associated earache. In fact as we noted in the paper (under section “Regression models and excess risks”), we tested for an interaction between age-group and head immersion swimming with regard to earache and found no evidence of different effects of head immersion on earache across age-groups. We also note in the Discussion: “Although young children reported a higher overall incidence of earache, the excess risk attributable to head immersion swimming exposure was no higher than other age groups.” This is also shown in Figure 1, where the difference in earache between swimmers and non-swimmers is approximately constant across age-groups and certainly no higher in the 0-1 age group. We have changed “no higher” to “slightly lower” in this section of the Discussion based on the model results discussed below.

The paper by Vernacchio et. al. (2004) reports a high incidence of otitis media. However, this study relied on parental reporting of infants’ ear infection diagnoses, and otitis media was not confirmed clinically. As a result these findings may also have been subject to over or under reporting. Other studies have reported a lower incidence of otitis media, ranging from 30-62% in the first year of life (Infant-Rivard et. al. 1993), which would be generally more consistent with what we observed for earache (30-62% per year, or, assuming constant incidence, about 2.5%-5.2% per month or about 1-2% in an 11 day follow up period).

To address the concerns raised by the reviewer, namely the potential impact of non-swimming associated otitis media infections on our results and conclusions; and related concerns, we have
conducted the following additional multivariate regression models: 1) a model with children 1 and under excluded; 2) a model with children 5 and under excluded; and 3) a model with only children 5 and under. We discuss these results further below and in the revised manuscript and provide the results from the models as Supplemental Information.


3. Third, it seems quite surprising that swimming (head immersion) is so commonly reported on behalf of NEEAR participants under the age of 1 year. That data available may not be able to distinguish between brief, limited head exposure versus full or repeated head immersion. Nevertheless, it seems unlikely that such a high percent of infants actually experience frequent or complete immersion of their head.

The specific question which was asked was: “Did {PERSON} put their face in water or submerge head in water today?”. While we agree it may be unlikely for young infants to immerse their head, it seems reasonable that at least 50% would put their face in the water but we are unaware of available other data that would support or refute the validity of this observation. The reviewer is correct, we do not have the data to distinguish repeated head immersion and limited head exposure. We agree that for young infants frequent head submersion is likely to be limited especially in comparison with older ages. We have clarified how we asked the question to more accurately reflect that the response includes head and face submersion in the water (see revised manuscript, “Swimming exposure”).

4. Fourth, the association between asthma/allergies and ear symptoms also argues for the conditions reported as being otitis media, as these are known risk factors for otitis media but are not established as risk factors for “swimmers ear.” Given these concerns that among very small children that 1) reported frequency of head immersion is remarkably high, 2) the “noise” of otitis media would be expected to overwhelm any “signal” of otitis externa, and 3) the observed pattern of more frequent ear symptoms among those the youngest age category relative to the age categories that prior studies have demonstrated are at higher risk, sensitivity analyses of swimming-associated ear symptoms should be repeated, excluding children under the age 1 and again, excluding those under the age 2, since the demographics of otitis media and otitis externa, and the frequency of “swimming” are likely similar in the <1 year and <2 year old groups.

We have conducted the additional analyses as suggested. They are now included as a Supplemental Table to the main manuscript and shown below. The results show a slightly stronger association for head immersion swimming and earache when children 5 years and under are excluded (OR=1.80; 1.69 and
1.67 for those over 5; those over 1 and all subjects, respectively). This may indicate some dilution of the effect as the reviewer suggested, by including very young children who are more likely to be afflicted with otitis media. However, since the number of children is few, especially in the 0-1 age group, the overall difference is not substantial and it is difficult to make a quantitative conclusion or assessment. We now discuss these results and this sensitivity analysis in the Results and again in the Discussion section. In addition, we included a separate model for children 5 and under only, and the association between head immersion swimming and earache is somewhat attenuated in this group, (OR=1.52, 95% CI=0.80-2.88).

We have added several additional points of clarification and discussion in both the Results and Discussion sections of the points raised above by the reviewer.

Table 1: Adjusted odds ratios for earache for selected age groups. Estimates from a logistic regression model with a random intercept for beach.

<table>
<thead>
<tr>
<th></th>
<th>5 years and under</th>
<th>Over 1 year</th>
<th>Over 5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AOR</td>
<td>95% CI</td>
<td>AOR</td>
</tr>
<tr>
<td>Head immersion swimming</td>
<td>1.52</td>
<td>0.80-2.88</td>
<td>1.69***</td>
</tr>
<tr>
<td>Age (ref. 20-50)**</td>
<td>1.53</td>
<td>0.88-2.66</td>
<td></td>
</tr>
<tr>
<td>Age 0-1</td>
<td></td>
<td></td>
<td>1.27*</td>
</tr>
<tr>
<td>Age 6-10</td>
<td>0.88</td>
<td>0.70-1.11</td>
<td>0.87</td>
</tr>
<tr>
<td>Age 11-19</td>
<td>0.76+</td>
<td>0.57-1.01</td>
<td>0.76+</td>
</tr>
<tr>
<td>Over 60</td>
<td>1.24</td>
<td>0.94-1.64</td>
<td>1.23</td>
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<td>Non-white race</td>
<td>1.33***</td>
<td>1.13-1.56</td>
<td>1.35***</td>
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<tr>
<td>Female</td>
<td>1.61***</td>
<td>1.26-2.05</td>
<td>1.58***</td>
</tr>
<tr>
<td>Unfamiliar animal contact</td>
<td>1.59****</td>
<td>1.35-1.88</td>
<td>1.56****</td>
</tr>
<tr>
<td>Other swimming2</td>
<td>1.42**</td>
<td>1.10-1.83</td>
<td>1.53**</td>
</tr>
<tr>
<td>Used insect repellant</td>
<td>1.62****</td>
<td>1.34-1.97</td>
<td>1.69****</td>
</tr>
<tr>
<td>Allergies</td>
<td>1.48**</td>
<td>1.15-1.90</td>
<td>1.43*</td>
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<td></td>
<td></td>
<td>0.92+</td>
</tr>
<tr>
<td>Miles travelled3</td>
<td>1.92</td>
<td>0.95-1.86</td>
<td></td>
</tr>
<tr>
<td>Rain (inches)4</td>
<td></td>
<td></td>
<td>0.80+</td>
</tr>
</tbody>
</table>

AOR=Adjusted Odds Ratio, 95% CI=95% Confidence Interval
1: For Under Age 5 model reference group is Age 2-5
2: Other head immersion swimming in the 1-week prior to the beach visit
3: Miles travelled to the beach (0-20; 21-60; 61-100; > 100 miles)
4: Inches of precipitation in previous 17 hours
5. Another sensitivity analysis that should be performed is to compare the adjusted incidence of ear symptoms in waders and non-swimmers. If waders have a higher incidence than non-swimmers, it would argue that factors off the causal pathway between water exposure and the establishment of ear symptoms are present, and may be present among swimmers as well.

Crude rates comparing non-swimmers, waders, and swimmers are shown in Table 1 (1.0; 1.3 and 2.0 percent, respectively). We have done the additional models and sensitivity analyses as suggested. “Waders”, i.e., those who entered the water but did not immerse their head, did not have a statistically elevated incidence of earache compared to non-swimmers (AOR=1.19; 95% CI=0.95-1.49; p=0.13). This slightly elevated incidence of earache among waders compared to non-swimmers may be at least partially explained by some moisture and humidity in the ear for those classified was waders. Head immersion swimmers also reported a higher incidence of earache compared to waders (AOR=1.44; 95% CI=1.20-1.74; p<0.0005).

We now discuss these findings in the results section.

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Minor Essential Revisions

6. The term “head immersion swimming” is cumbersome and the definition of categories of exposure could be clearer. Three mutually-exclusive categories of exposure have been created: no water contact (“non-swimmer”), water contact without head immersion (“wader”), and water contact with head immersion (“head immersion swimmer”). On page 4 under “Swimming exposure,” mention is made of “those who swam but did not immerse their body” – presumably another way of referring to the wader category. To determine risks of swimming-associated risks of ear symptoms, analyses include data from two of these categories (non-swimmers and head immersion swimmers) while descriptive statistics include data from waders as well. It would be simpler to refer to “head immersion swimmers” as swimmers throughout the manuscript. Waders (a better term than ‘non-immersion swimmers’) should be excluded from the descriptive statistics, since they are not included in the subsequent analyses.

We have clarified the discussion of the exposure categories as suggested by the reviewer. The sentence on page 4 noted by the reviewer is an error (“body” should be replaced with “head”) and we have corrected this. Although the term “head immersion swimming” may be cumbersome, we believed it was important to clearly distinguish our definition of swimming exposure from previous papers where swimming exposure was defined as a minimum of body immersion. We modified this definition for this report to account for moisture and water in the ears which is likely a critical risk factor for swimming-associated ear infections. We have replaced “head immersion swimming” with “swimming” throughout much of the paper, but retain the description in some places for clarity.

Waders are presented included in Table 1 for several reasons. First, to provide the demographic characteristics of the entire sampled population. Second, in addressing the reviewer’s concern raised above in comment 5, crude rates of earache for waders, swimmers and non-swimmers are provided in
We have noted this assumption now in the Methods section as well as the Discussion section.

8. The “Discussion” section notes that the cost estimate included the use of systemic antimicrobials in 1/3 of cases. Wouldn’t that have already been included in the estimated cost of $200/case cited in reference 14? Incidentally, the cost of a commonly used topical treatment for otitis externa (e.g., Cortisporin Otic) can be substantially greater than the cost of generic systemic antimicrobials.

The costs estimates are from two sources: one self-reported from participants which can be applied directly to the swimming-associated earache estimates, the second is from the cited references which estimated $200 per doctor’s visit, which includes out-of-pocket and insurer costs for the visit and prescription medication, which we did not measure directly, and would only apply to the fraction of swimming associated earache that resulted in a doctor or ER visit. Though the reviewer raises a valid point regarding costs of topical antimicrobials, the 1/3 in this section is concerned with the numbers of cases being prescribed potentially unnecessary systemic microbes instead of the recommended topical antimicrobials.

9. Page 9: “In summary, in a survey of over 50,000 participants...” Since those with pre-existing ear symptoms and the waders were not included in the analyses of risk, this number should be reduced to reflect the 39,418 that were included.

Change made
Reviewer 2

Major Compulsory Revisions
I found no significant flaws with this manuscript. The only potential shortcoming I recognize is the lack of a clinical diagnosis of reported earaches as otitis externa. Authors recognize this concern and address it head on. However this was not practical within the scope of the study. Self-reporting bias could have led to over reporting, but authors also recognize and address this concern.

See responses to Reviewer 1, we have expanded our discussion of this limitation

Minor Essential Revisions
The manuscript is well written and formatted well, with attention to detail. My one comment is that with the font used the y-axis label for figures 1 and 2 make ill difficult to read when capitalized.

We modified the figure legend so “I” in “ill” in the y-axis legend is lower case “i”

Reviewer 3

Minor Essential Revisions: Define the variables E and S after presenting equation 1, and in the List of Abbreviations

Change made and names for equation parameters have been clarified

Discretionary Revisions: Speculate on whether ear infections may be more frequent when a more energetic wave climate exists?

We did not observe this in our dataset as Surfside beach, which had the most energetic wave environment had a swimming-associated fraction of earache similar to the other beaches. Wave action could induce trauma or increase water exposure that might influence the development of ear infection but we felt we did not have enough data to discuss this in detail. Including wave height in the models did not improve the fit or modify the association.