Selecting infants with OM that need referral and further assessment: Creating a case-finding instrument

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ABSTRACT

Objective: In the Netherlands, many children are surgically treated for OM. Recent publications question the need for surgical treatment in common uncomplicated OM, although there is certainly a subgroup of infants that do need further assessment and possible treatment. The present study explores the possibility of using known and presumed risk factors for OM as an instrument for selecting and routing an infant with OM to further care.

Methods: Two questionnaires were used. A questionnaire embracing a wide range of OM-related factors was sent to 6531 children aged nine months that were routinely invited for the hearing screen at nine months. In a second stage, a structured history questionnaire regarding ear and/or hearing problems, subsequent referral and/or treatment, was sent to all parents of children at age 21 months, responding to the first questionnaire. Univariate analysis was performed for identification of potential predictors for surgical treatment of OM for the whole sample as well as for 4 different subsets. Multivariable regression analysis with stepwise backward deletion was applied to arrive at a model for optimal prediction of tube insertion. A ROC (receiver operating characteristic) curve and the accompanying sensitivity and specificity values were analyzed to determine cut off values.

Results: Univariate analysis found 10 items predicting surgical treatment for OM. Multivariable regression analysis resulted in a model with a ROC curve having an area of 0.801 and estimated coefficients for risk factors which were used to calculate a OM-score for each case.

Conclusion: The developed scoring sheet, e.g., to be used in combination with physical examinations and/or tympanometry looks promising as a predictor for those children that might benefit from further assessment and eventually surgically treatment for OM.

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1. Introduction

Ear and/or hearing problems caused by otitis media (OM) are highly prevalent in infants [1–4], with almost 80–90% of all children experiencing at least a single episode before the age of 1 year. These ear and/or hearing problems represent about 20% of all general practitioner (GP) visits in children 0–2 years of age in the Netherlands [5]. About 53% of these infants whose parents consult the GP will be referred to a specialist, mostly to an ENT-specialist (78%), and about 83% of the children referred to the ENT-specialist will thereafter be treated surgically [6]. In spite of recent publications questioning the need for (surgical) treatment for uncomplicated OM [7,8], the numbers of children treated surgically in the Netherlands remain high [9]. Persistent OM can result in hearing loss [10,11] and subsequent developmental problems, such as speech and/or language delays. Furthermore, it can cause behaviour [12] and/or balance problems [13]. Most affected children will have uncomplicated OM. However, a subgroup of infants with OM, at risk for longer term OM-related problems, need further assessment and possibly treatment. The children in scope are very young, and for this reason it is intrinsically challenging to determine the individual need for referral and further assessment in this age group. Up to 2002, children in the Netherlands were screened for hearing loss at the age of nine months primarily to find congenital permanent impairments. Instead, the predominant majority of the children

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repeatedly failing the hearing screen at nine months had OM-related hearing loss [14–17] and of these, most then underwent surgical treatment. Therefore, the screen also functioned as a tool for identification and subsequent referral and treatment of persistent OM-related hearing loss. The screen at nine months has now been replaced by the neonatal screen and, unexpectedly, since then more children not less are treated surgically for OM [9]. Considering recent publications questioning the need for treatment in uncomplicated OM, there might be a need for a case-finding instrument for infants, selecting those at risk for hearing and developmental problems. Such case-finding would have to be inexpensive and feasible for a primary care setting; it should assist the GP in selecting those infants with OM that need further assessment by an ENT-specialist.

The present study examines whether known and presumed risk factor items for OM, combined in a questionnaire to be completed by parents of infants, can be used to predict which children will be treated with ventilation tubes. Treatment with tubes, i.e. ear and/or hearing problems sufficient to warrant treatment, is taken as outcome measure in statistical modelling, and we thus explore the possibility of using a combination of risk factor items as an instrument for selecting and routing an infant with diagnosed or suspected OM to further care. The study population consists of a large number of otherwise healthy infants from the general Dutch population that were invited for the routine hearing screen at age nine months.

2. Methods

2.1. Questionnaires

2.1.1. PEPPER questionnaire for infants with an appointment for the hearing screen at age nine months

The PEPPER item pool (‘Persistent Ear Problems, Providing Evidence for Referral’), initially developed in the United Kingdom, embraces a wide range of OM-related factors in a single instrument for use in primary care, and can be completed by the child’s parent or guardian within 3 min. To facilitate use, the items were pooled into the PEPPER questionnaire. The English version of this questionnaire (Appendix A) was translated into Dutch. Although standardisation is not an issue here, it was also translated back into English by an English native speaker, resulting in only minor shades of difference in wording.

2.1.2. Follow-up questionnaire at the age of 21 months

A structured history questionnaire, named Q21, comprised 12 questions about attending the hearing screen, referral subsequent to this hearing screen, visits to the GP because of suspected ear- and/or hearing problems and subsequent referral to a specialist (ENT-specialist, paediatrician, or audiology department etc.) and treatment by an ENT-specialist. See Appendix B.

2.2. Study population

Parents of all children born between 1-6-2004 and 31-12-2004 in the province of Limburg, in the South East of the Netherlands, received the routine invitation for the hearing screen at age nine months by means of the distraction hearing test (CAPAS, Compact Amsterdam Paedo-Audiometrical Screening), along with information about this study, a consent form and the PEPPER questionnaire. The parents were asked to complete the questionnaire and the consent form, and to bring both to the well baby clinic at the screening visit. The results of the questionnaire were not shared with the well-baby clinic doctors in order to ensure that routine practice procedures were maintained.

All parents who returned the PEPPER questionnaire received the Q21 follow-up questionnaire at the child’s age of 21 months. The present sample consists therefore of those children for whom the data of the hearing screening data, a completed PEPPER questionnaire and a completed follow-up questionnaire form were all present.

Specific approval of an ethical commission was not needed, as the outcome of the questionnaire was unknown to the well baby clinic doctors and therefore it did not change practice at the well baby clinic. Written informed consent was obtained from all the parents of the children participating in the study.

The questionnaires were scanned and the responses entered into a SPSS file (version 15.0), and thereafter checked and merged with the CAPAS data. Excluded from the study database were children known to have a sensorineural hearing loss or permanent conductive hearing loss and children with Down syndrome and cleft palate or other craniofacial malformations. The latter provide sufficiently strong risk factors on their own to drive the management of the few cases involved.

2.3. Statistical analysis

The response rate to the Q21 questionnaire was investigated for potential selection bias.

Univariate logistic regression was performed on the cases which had data for both the PEPPER questionnaire and the Q21 questionnaire. To facilitate the identification of potential predictors, two strategies were followed. First, two equally sized disjunctive datasets were randomly created from the entire dataset and each of the potential risk factors was examined relative to the outcome variable ‘treatment with tubes’. Second, as both ‘being a boy’ and ‘having siblings’ predicted the outcome in the total dataset as well as in both at random chosen subsets and these items could therefore be considered as strong predictors, the total dataset was split into four subsets accordingly. Univariate logistic regression was then applied to each of the PEPPER items separately for each of the subsets to reduce the possibility of overlooking potential explanatory factors. Making a univariate association a prerequisite in this way, economies degrees-of-freedom and avoids unstable or un-intepretable entries with negative sign being used in the multivariate modelling.

Some responses were particularly thinly spread and their analysis would have been unreliable, so certain response categories were collapsed. ‘Having cold symptoms’ and ‘nasal congestion’ were applied in dichotomous form, where ‘yes’ comprises ‘often’ and ‘always’ responses, and ‘no’ comprises ‘never’, ‘seldom’, ‘only with a cold’ and ‘not applicable’. ‘Number of ear infections in the past three months’, ‘siblings with OM problems’ and ‘cre`che with 4 children’ were also shrunk to a dichotomous form.

‘Smoking’ was used as a dichotomised variable where ‘yes’ means more than one person smoking around the child or ≥20 cigarettes being smoked in the household.

Results from the univariate analyses led to various further constraints on the multivariate analysis as follows. Breastfeeding appeared to be a risk for surgical treatment with tubes: this ‘finding’ is counterintuitive and could reflect a shared socio-cultural bias in both referral and breastfeeding. As we did not want any resulting procedure to be socially discriminatory, we excluded breastfeeding from the modelling procedure. However, being exclusively bottle fed, did appear to be a risk factor and was included in the modelling procedure. Father working part time, was also a significant predictor in the univariate analysis. But, as working status of the parents was also likely to be more a socio-cultural factor than a marker of social economic status, it too was left out of the modelling stage. Those children that failed the hearing screen in winter had increased odds for treatment with
tubes, which was expected as OM is a seasonal fluctuating disease with a higher prevalence in autumn and winter. However, as the item ‘season in which the child was screened for hearing loss’ cannot be used as a predictor for tube insertion in the current absence of the hearing screen at nine months of age, it was excluded in the further analysis.

Any item having an at least marginally significant Odds Ratio (OR), defined as \( p < 0.20 \), and an expected direction in the univariate analyses in the different subsets was then considered as a candidate predictor for the multivariate model. The low threshold of \( p < 0.20 \) was used to increase the possibility of finding a predictive model, as some items could be non-significant predictors in isolation (\( p > 0.05 \)) but could, when combined with other items, enhance the prediction from the model. Logistic regression with one by one stepwise backwards deletion of the weakest predictor, was applied to each subset (by sex and siblings) to determine which reduced combination of variables together would best predict the outcome. The regression thus obtained offers a scoring formula to calculate the probability of the pathological value of the outcome measure, that can predict probability of this outcome for individual cases. These case probability values were saved and used as input values for the construction of ROC (receiver operating characteristic) curves, which represent the relation between sensitivity and specificity of the model or tool in discriminating the outcome. To determine the optimal cut-off point for prediction, the Youden index \( (J) \) was calculated as a measure of overall diagnostic effectiveness to enable the selection of an optimal cut-off point value. \( J \) occurs where the distance or difference between the ROC curve and the diagonal or chance line is maximal, i.e., at the cut-point that optimizes the instrument’s differentiating ability: \( J = \max (\text{Sensitivity} + \text{Specificity} - 1) \).

Initially, we were also interested in those children who on failing the hearing screen three times, were referred, did not consult their GP with ear and/or hearing problems at any time other than for failing the hearing screen, yet in the end were treated with tubes; as these children could be defined as having OM-related hearing loss without other parent reported ear problems. Only 45 children met all these criteria, too few to analyse.

The statistical software package SPSS 15.0 was used.

3. Results

A flow chart was constructed to present questionnaire response, referral and treatment with tubes (Fig. 1). A total of 10803 children were born from 1-1-2004 to 31-12-2004 in the Limburg, and the PEPPER questionnaire was sent to those 6573 children born from 1-6-2004 to 31-12-2004.

Only 39% of the children failing the screen repeatedly and with no other complaints were eventually recorded as treated with tubes. However, for those failing and with other complaints, this rose to 57%. Looking backwards, of all children treated with tubes 60% had had ear and/or hearing complaints but had not failed the hearing screen; 21% had failed the hearing screen but with no complaints, whilst 11% had failed the screen with complaints.

Univariate analyses performed on the total dataset and the two at random chosen subsets found statistically significant \( (p < 0.05) \) in prediction of the outcome ‘treatment with tubes’ for 10 items, all in the anticipated direction. These items, found in at least one of the analyses, were ‘male gender’, ‘slow-to-feed’, ‘ear infection in the last three months’, ‘ear infection in the last month’, ‘nasal congestion’, ‘having cold symptoms’, ‘attending day care’, ‘attending day care with >4 children’ and ‘having siblings’ and ‘being exclusively bottle fed’.

Multivariate modelling was first applied to the total dataset. Gender and ‘having siblings’ were then used to create the four subsets. Table 1 shows the items that significantly predicted

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**Fig. 1.** Flow chart of stages in inclusion plus number of children invited for the hearing screen and response rates for the PEPPER questionnaire, hearing screen and Q21 questionnaire.
4. Discussion

4.1. Main findings

In this study we explored the possibility of using risk factor items for OM to create an instrument aiding the GP in selecting those children (aged 0–3 years) with OM that need referral and further assessment. Multivariate modelling was applied to the total dataset and the four subsets. One model was created for the total dataset. Estimation of this model for each of the subsets separately resulted in negligible differences in the coefficients for the risk factors and therefore one scoring sheet was derived. The scoring sheet (Fig. 2) was obtained by multiplying each coefficient by 10 to obtain scores ranging from 0 to 61. Examination of the Youden index (Fig. 3) suggested an optimum cut-off probability of 0.05 or 0.06. A score of 20 corresponded with a cut off probability of 0.05 while a score of 22 corresponded with a cut off probability of 0.06.

A ROC curve was calculated (Fig. 4) for how well the scoring sheet predicted the outcome ‘treatment with tubes’ in the whole dataset. The area under the curve was 0.801 (CI: 0.76–0.84).

Tables 3 and 4 show the classification tables according to the cut-off point (predicted versus observed) with a Youden index of 0.05 (sensitivity = 0.72 and specificity = 0.73). Opting for fewer false positives would suggest taking the second best Youden index with a cut-off point of 0.06 (sensitivity = 0.69 and specificity = 0.76).

**Table 1**
Statistically significant items, for the total dataset and for four different subsets based on gender and having siblings, predicting ‘treatment with tubes’ (regardless of referral). The OR is given, with the significance level.

<table>
<thead>
<tr>
<th>Treatment with tubes</th>
<th>OR</th>
<th>OR</th>
<th>OR</th>
<th>OR</th>
<th>Total dataset</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4.62</td>
<td>4.62</td>
<td>4.62</td>
<td>4.62</td>
<td></td>
</tr>
</tbody>
</table>

**Table 2**
Logistic regression model for ‘treatment with tubes’.

<table>
<thead>
<tr>
<th>Treatment with tubes</th>
<th>Coefficient</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male)</td>
<td>0.57</td>
<td>1.78 (1.3–2.3)</td>
<td>0.001</td>
</tr>
<tr>
<td>Having siblings</td>
<td>0.69</td>
<td>1.98 (1.2–3.1)</td>
<td>0.0004</td>
</tr>
<tr>
<td>Siblings with OM</td>
<td>0.45</td>
<td>1.56 (0.9–2.2)</td>
<td>0.104</td>
</tr>
<tr>
<td>Day care &gt;4 children</td>
<td>1.29</td>
<td>3.22 (2.2–4.7)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Being exclusively bottle fed</td>
<td>0.31</td>
<td>1.40 (0.9–2.0)</td>
<td>0.112</td>
</tr>
<tr>
<td>Having cold symptoms</td>
<td>0.49</td>
<td>1.63 (1.0–2.3)</td>
<td>0.066</td>
</tr>
<tr>
<td>Nasal congestion</td>
<td>0.95</td>
<td>2.61 (1.5–3.8)</td>
<td>0.000</td>
</tr>
<tr>
<td>Ear infection last three months</td>
<td>0.83</td>
<td>2.31 (1.6–3.5)</td>
<td>0.000</td>
</tr>
<tr>
<td>Sucking was weak</td>
<td>0.71</td>
<td>2.11 (1.0–4.2)</td>
<td>0.045</td>
</tr>
<tr>
<td>Smoking</td>
<td>0.73</td>
<td>2.05 (0.9–4.6)</td>
<td>0.121</td>
</tr>
</tbody>
</table>

---

**Fig. 2.** Scoring sheet predicting ‘treatment with tubes’.
4.2. Strengths and limitations

We used the data of a large group of otherwise healthy children who were routinely invited for the hearing screen at nine months. Combining the results of this hearing screen together with the data from the two questionnaires resulted in a very large dataset of high statistical power. The original aim was to analyse the data from those children that only had OM related hearing loss. Unfortunately, the number of children that failed the hearing screen, were referred and in the end were treated with tubes was too low to permit analysis. Therefore, we focussed on creating an instrument predicting treatment with tubes.

OM is a fluctuating disease and we do not know which children from the entire dataset were treated for wise clinical reasons, nor which such children were missed and not treated at all, yet could have benefited from treatment. Many children in the Netherlands are referred by their GP to the ENT-department due to reluctance to prescribe antibiotics and this can in part explain the high number of surgical procedures for OM in the Netherlands, an aspect providing statistical power to the present study. It may perhaps not be representative for other healthcare systems. Extrapolating the results from this study to other countries raises two issues: external validity of the particular risk factors used, and appropriate cut-off values. Risk factors can differ between countries [19] with grossly different standards of living, or health and social care arrangements or health practices and belief systems (e.g., background levels of smoking). However, where the model in Table 2 and Fig. 2 does not suffer limited applicability from such differences, they provide strong a priori suggestions for efficient combinations of risk factors elsewhere. The local placement of a cut-off will be related to local intervention rates, thus reflecting policy and practice, so any extrapolation of the cut-offs should be done with awareness of this.

The response rate to the PEPPER questionnaire was 56.4%. To determine any participation bias, we compared the responders to the non-responders. Fewer children of responders did not attend the first hearing screen compared to non-responders (3.6% versus 14.8%). This follows from the PEPPER questionnaire being completed and brought to the well baby clinic at first test. Furthermore, the non-responders lived in areas with relatively higher percentage migrant population, more unemployment, and lower incomes which indicate a lower SES and this could explain the non-responding [20]. However, there appeared to be no bias in respect of referral. Slightly fewer children from responders were referred compared to non-responders (3.1% versus 3.6%, not statistically significant different). Thus we appear to be reporting on a sub-population with a high participation rate both in research and routine service, but without a difference in the average outcomes considered. The response rate to the Q21 questionnaire was higher (72.9%). This second questionnaire was only sent to those parents who had already replied to the first questionnaire, and a higher response rate was therefore to be expected.

4.3. Future research

The created instrument looks promising as predictor for which children (should) receive tube treatment. The next step could be a prospective evaluation in selected GP practices to further study the possibility of using the instrument to select children with OM that might benefit from referral to ENT.

5. Conclusion

The present study is a first attempt to create a case-finding instrument for the subgroup of children with OM needing referral and further assessment. A reasonably strong risk factor model for predicting tube insertion was found. The developed scoring sheet with 10 items, e.g. to be used in combination with physical examinations and tympanometry looks promising, although the practical problems of routine implementation remain to be evaluated.
Appendix A. PEPPER questionnaire

1. Is your child healthy or has (s)he a special condition? Yes/No.
2. Does your child have special condition? Yes/No.
   Special condition: Down syndrome, Cleft syndrome, other.
3. Were there special events during the pregnancy? Yes/No.
   Special events: infection during pregnancy, growth retardation, early birth, other.
4. Were there special events during delivery? Yes/No.
   Special events: meconium stained birth water, slow start, other.
5. Please give your best estimate of how old your child was when (s)he first had an ear infection?
   Answers: Younger than 3 months, 3-5 months, 6-7 months, 8-9 months, not applicable.
6. Please give your best estimate of how old your child was when (s)he first had a hearing problem?
   Answers: Younger than 3 months, 3-5 months, 6-7 months, 8-9 months, not applicable.
7. In the last three months including today, how many ear infections has your child had?
   Answers: None, 1, 2, 3, more than 3.
8. How many of these ear infections occurred just in the last month?
   Answers: None, 1, more than 1.
9a. ‘having had at least one ear infection in the last three months’? Yes/No.
9b. In the last three months, has your child breathed mainly through the mouth?
   Answers: Yes/No.
10. In the last three months, has your child snored?
    Answers: Yes/No.
11. In the last three months, has your child suffered from any of coughs, colds or sore throats?
    Answers 9a-9d: never, rarely, only during a cold, often, always, not sure.
    9a-9d*: Answer ‘yes’: ‘often’ and ‘always’.
    9a-9d**: Answer ‘no’: ‘never’, ‘seldom’, ‘only with a cold’ and ‘not applicable’.
10. Which members of the household currently smoke in the same room as the child?
    Answers: none, mother, father, childminder, other.
14. At a baby, does your child usually sleep on his/her…?
    Answers: front, side, back.
15a. Would you describe your baby (up to the age of 6 months) as having a weak suck? Yes/No.
15b. Would you describe your baby (up to the age of 6 months) as being slow to feed? Yes/No.
16 extra: ‘attending day care with > 4 children’. Yes/No.
17. How many children live at home (not counting this child) attend school, nursery or playgroup?
   Answers: one or more older children, other child at home, but does not attend, no other child at home.
17*: ‘having at least one sibling’. Yes/No.
18. This question refers to family members other than this child and only to blood relatives. Has either parent, or any brother/sister of this child, has similar ear or hearing problems?
   Answers: yes, needed operation, yes, but no operation, not sure, not had a problem.
18*: ‘having at least one family member with ear of hearing problems’ (father, mother or sibling). Yes/No.
19. Does father work: part time/full time/not applicable.
20. Does mother work: part time/full time/not applicable.

Response categories of some PEPPER items were combined when category counts were extremely small, noted above with *.

Appendix B. Q21

1. How often was your child tested for hearing loss at the well-baby clinic?
   0 times (your child hasn’t been tested at the well-baby clinic, but somewhere else): 1 times; 2 times; 3 times; More than 3 times
2. Was your child as a result of this hearing test referred by your well-baby clinic doctor to your general practitioner (GP)? Yes/No
3. If yes, did your GP refer your child to an ENT-specialist or audiology centre? Yes/No
4. If yes, how long did your GP wait before referring your child as was recommended by your well-baby clinic doctor (because of the result of the hearing screen)?
   Direct referral; 1 month waiting period; 2 months waiting period; 3 months waiting period; More than 3 months waiting period
5. Did you go to the GP with your child because of ear/hearing problems, without being referred by the health centre doctor? Yes/No
6. If yes, at what age for the first time?
   <3 months; 3 to 6 months; 6 to 9 months; 9 to 12 months; 12 to 15 months; More than 15 months
7. Did your GP refer your child (in the end) to a specialist? Yes/No
8. If yes, to which specialist (tick the box of the appropriate specialist)?
   ENT-specialist; Audiology centre; Paediatrician; Other doctor, being …
9. Has your child been treated by an ENT-doctor? Yes/No
10. If yes, what kind of treatment was given?
    Medication (eardrops, antibiotics)
    Operation: Adenoidectomy; Grommets; Adenoidectomy and grommets;
    Adenoidectomy and tonsilllectomy; Adenoidectomy and tonsilllectomy and grommets;
    Other surgery, being …
11. Did you have the impression that your child, if he/she underwent surgery, benefited of the procedure? Yes/No
12. If yes, could you tell us what has improved?
    My child’s hearing has improved; My child hasn’t got earaches anymore; My child doesn’t snore anymore; My child hasn’t got throat aches anymore; My child has more energy during the day; Other: …

References

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