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Methods

Identification of risk factors, complications and sequelae of OM was the starting point. (Figure S1, Table S1). Given the complexity of the causal pathways, the frequent overlapping of conditions, the lack of clear and consistent definitions and the fact that conditions included may have a mild and temporary nature or be rare, we focused in our review on AOM, CSOM, and on permanent Hearing Impairment (HI, both conductive and sensorineural) caused by OM (Figure S2). This simplification is consistent with that adopted in previous estimates of the OM GBD.[1]

We searched for all articles presenting original data on incidence or prevalence of AOM or CSOM, and linking HI data with CSOM (proportion of HI caused by CSOM, or proportion of CSOM cases causing HI). The systematic review covering AOM, CSOM, HI and related risk factors was carried out on Medline (PubMed, last search 11/08/2008), Embase (last search 23/07/2008), Lilacs (last search 11/08/2008), Wholis (last search 11/08/2008), without any language restriction (detailed search strategies in Table S2). We retrieved 9356 records that became 7168 after duplication removal. We carried out a two-step evaluation to identify relevant papers:

1) 1st step: by titles, abstract and keywords, aimed at identifying papers on epidemiology and risk factors of OM and reviews on OM (Figure S3). Papers on risk factors were used to review and complete the risk factors diagram (Figure S4).

2) 2nd step: by full text, when available, aimed at identifying papers on epidemiology of AOM, CSOM and HI. All articles with original data on AOM, CSOM or HI incidence or prevalence were included.

Information on mortality was collected through WHO vital registration databases, when available and reliable, or estimated for countries and areas where data were unavailable or unreliable.

Relevant data were extracted and transcribed into records and divided by country and WHO region. Records included a reference code and information on the condition (AOM, CSOM or HI), the year the data were collected, whether they related to incidence or prevalence, the age of the subjects covered by the study, and whether data were stratified by urban/rural or by socio-economic status. Records also comprised all age ranges and data were inserted accordingly. The last columns of the database included information on HI when such data were available: proportion of cases of CSOM with HI, dB (decibel), and whether the data were for unilateral or bilateral HI.

Both the selection of relevant papers and data extraction were carried out independently by two of the authors (respectively by LM and AB, and by LM and MM or LV). Any disagreement were resolved through discussion involving a third author (LR).

Estimation process: incidence of AOM and CSOM

When only prevalence data were available, prevalence was transformed into incidence based on the average duration of AOM and CSOM. Although studies show that clinically symptomatic AOM usually has a shorter duration [2,3] we assumed a duration of 21 days because when both prevalence and incidence data were available the actual duration, including the effusion was shown to be around 21 days.[4] This was the only real evidence on duration of AOM we could rely on. The average duration of CSOM in adults is 10 years.[5–10] For adolescents and young children, however, in the absence of data, and lacking in literature a method to convert prevalence to incidence when duration of illness is longer than age, we created an arbitrary duration scale for each age group: one year in the first year of life, two years in the 2-4 age group, three years in the 5-9, four years in the 10-14, five years in the 15-19 and six in the 20-24.

The estimation process was divided into two phases. In the first and second phase all estimations were done by country within a specific area, the only exception being Oceania, for which we extrapolated country specific data to the whole region.

Estimates were generated for all age groups.[11] We did not calculate estimates by gender, since evidence on gender differences is scanty and conflicting.

Estimation of AOM and CSOM incidence: first phase

The first phase was carried out by the following formula based on risk factors:

\[ N_{\text{est}} = (\text{Pop}_{\text{new}}) \times (\text{Inc}_{\text{Ref}}) \times \left(1 + \sum_{i=1}^{n}[(\text{Prev}_{\text{RF, new, i}} - \text{Prev}_{\text{RF, Ref, i}}) \times (\text{RR}_{\text{RF, i}} - 1)]\right) \]
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Were $N_{new}$ is the number of cases, $Pop_{new}$ is the population we want to estimate the cases for, $Inc_{Ref}$ is the incidence in the reference population, $Prev_{Ref,new,i}$ is the prevalence of a specific risk factor $i$ in the new population, $Prev_{Ref,Ref,i}$ is the prevalence of the $i$ risk factor in the reference population, $RR_{Ref,i}$ is the risk ratio for risk factor $i$.

Incidence in the reference population refers to the incidence for those countries for which data were available from the literature.

Risk estimates were extracted from the literature review and in particular from:

- Day-care centre attendance (RR) 2.45 (1.51-3.98) Meta-analysis [12]
- Exclusive bottle-feeding vs. exclusive breastfeeding up to six months (RR) 2.00 (1.43-2.78) Meta-analysis [13]
- Parental smoking (RR) 1.66 (1.33-2.06) Meta-analysis [12]
- Malnutrition (RR) 3.48 (1.63-7.42) Nigeria[14]

The choice of limiting the list of risk factors to the ones above was determined, among the more relevant, by two fundamental reasons. The first being that we needed good quality data on risk ratios and, thus, we focused on data from meta-analyses. The second reason is that we needed risk factors for which we could have reliable information for each country. Malnutrition was an exception but we considered it to be a key factor in developing countries. Malnutrition was included only for developing countries (no data on malnutrition is available for developed countries and malnutrition is certainly more important in developing countries), while day-care centre attendance was only included for developed countries (no data on day-care centre is available for developing countries and is certainly more important in developed countries).

We used two different sets of risk factors. For Western Europe, North America High Income, Asia Pacific High Income and Australasia we used the following risk factors and associated Relative Risks (RRs): adults smoking (RR 1.66), exclusive breastfeeding at six months (RR 2.00), day-care attendance (RR 2.45). Data for these risk factors, for the year 2005, were taken from WHO, UNICEF and OSCE reports and databases (www.oecd.org/els/social/family/database). [15–19] For all other areas, day-care was substituted with under five children underweight (RR 3.48).

For Western Europe, AOM incidence was estimated from data on incidence from Finland [20] and Spain [21] for ages up to 15 years. For older ages we used the Dutch College of General Practitioners (NGH) practice guideline from the Netherlands (note 2). [22] After plausibility checks, and extension of estimates to all age groups, “northern” countries were estimated with Finland while “southern” countries were estimated with Spain.

For CSOM we started with data from Israel,[23,24] Finland,[25] UK [26,27] and Greenland.[28–30]

Age distributions were not complete for the four countries, thus incidence estimates for the missing age groups were reciprocally estimated using available data. We then took the complete distribution of incidence for Finland and UK and build a combined average distribution. This combined distribution was used to estimate all other Western European Countries – with the exception of Israel and Greenland – with the RRs model. For the combined distribution we used average RRs from Finland and UK.

For North America High Income we extended the estimates we had for Western Europe after checking for coherence with data from literature which was, however, quite old for 2005 estimates.[4,31–34] For Asia Pacific High Income we used data from 1991 [35] and 1981 [36] with data on AOM and COM on all age groups from Rep of Korea and estimated 2005 with the risk formula and then all other countries in the area. Australasia was estimated with Western Europe with the risk formula but for Australia aboriginals were estimated separately. [37]

For the areas specified below, estimates were generated from original data from at least one country and then extended to the other countries with the risk factors formula. In case the age distribution of incidence of AOM and CSOM was not available, a hybrid distribution generated from data from Democratic Rep of Congo (90%),[38] South Africa (4%),[39,40] Korea (3%) [35,36] and Western Europe (3%). The age distribution is however irrelevant, considering that during phase two, two other age distributions were elaborated. It was relevant only when original data were not available for the 1–4 age group and incidence for this age group had to be estimated from other age groups.

For Asia South, CSOM estimates for years 1–4 were elaborated from data from Bangladesh[41,42] adjusted for both low and high Socio Economic Status with the differential expressed in data from India.[43] AOM for years 1–4 was also estimated with data from Bangladesh.[44] For North Africa / Middle East, CSOM and AOM 1–4 years, CSOM estimates were calculated from data on Saudi Arabia,[45] Data on AOM were also calculated from data from Saudi Arabia.[46,47] Both for CSOM and AOM the data were adjusted to the age group 1–4 with the help of the distribution on incidence from Australasia which was quite similar for the ages for which we had data. For Asia South East, CSOM were estimated from prevalence data Malaysia, Philippines, Thailand and Vietnam.[48–52] AOM estimates were
derived from Thailand prevalence data on ages 5-13 [49] shaped on ages 1-4 with the help of the distribution from Asia South and Western Europe. For Sub-Saharan Africa East CSOM was calculated from Tanzania 1994 on ages 5-19 [53] and shaped on age 1-4 with the hybrid distribution by age. For Sub-Saharan Africa Central, CSOM 1-4 was estimated with data from Democratic Republic of the Congo.[38] AOM 1-4 estimate was calculated on the ratio between AOM and CSOM cases from Zambia. For Sub-Saharan Africa West, CSOM were based on data from Nigeria [54,55]. AOM estimates were based on data from Nigeria [54]. For Sub-Saharan Africa Southern, estimates for CSOM were based on data from South Africa [40] and Swaziland [56] on children from 5-15 years of age, and then shaped on 1-4 years using the hybrid distribution by age. For the Caribbean, CSOM 1-4 was estimated from Jamaican data on OME prevalence in 5-7 years old,[57] translating OME to CSOM and AOM with data from Saudi Arabia [47]. These data were shaped to years 1-4 with the hybrid distribution by age. For Latin America Tropical estimate for CSOM in 1-4 was generated from data from Brazil on COM prevalence in 6 to 18 years old. [58] CSOM and AOM incidence for all age groups were then estimated by comparing CSOM incidence on 6-18 years old from Brazil with the same incidence in Dem Pop Rep of Korea chosen for their similarities. For Latin America Central, AOM incidence was estimated on the basis of Mexican data on ages 0-14,[59,60]

**AOM and CSOM estimates: Second phase**

Areas for which we did not have any data were: Europe Central, Europe Eastern, Oceania, Asia East, Asia Central, Latin America Southern and Latin America Andean. To be able to cover these areas and to fine tune the estimates elaborated in phase one, we adopted a more robust strategy.

Phase two was based on exponential regression models. A model for AOM and a model for CSOM incidence rates were built for less industrialised areas. These models were based on the following factors:[15–17] prevalence of Acute Respiratory Infections (ARI) in children under five (ARI-U5), underweight prevalence in under five children (U5), under five mortality rate (MR-U5), proportion of children under six months exclusively breastfed (EBF), prevalence of adults smoking (AS).

These models were based on data and phase one estimates from 45 countries (Sub-Saharan Africa East: Kenya, Uganda, Mozambique, Zambia, Ethiopia, Tanzania, Malawi. Sub-Saharan Africa Central: Democratic Republic of the Congo. Sub-Saharan Africa West: Nigeria, Cameroon, The Gambia, Mali, Senegal, Côte D’Ivoire, Sao Tome and Principe, Mauritania, Ghana, Chad, Burkina Faso. Sub-Saharan Africa Southern: Namibia, South Africa, Zimbabwe. Asia South East: Cambodia, Myanmar, Indonesia, Laos, Maldives, Philippines, and Vietnam. Caribbean: Dominican Republic and Jamaica. Latin America Tropical: Paraguay. Latin America Central: Guatemala) and helped estimate AOM and CSOM incidence for the age group 1-4 years and validate the estimates of all countries. These models had an R² of 0.83 for AOM and 0.85 for CSOM:

- AOM = 35.1859 * (1.0235^{ARI-U5}) * (1.0060^{U5-U5}) * (0.9979^{AS}) * (1.0079^{MR-U5}) * (0.9846^{EBF})
- CSOM = 4.8451 * (1.0152^{ARI-U5}) * (1.0298^{U5-U5}) * (1.0055^{AS}) * (1.0021^{MR-U5}) * (0.9872^{EBF})

We should not be surprised to see that single risk factors have coefficients that vary from >1 to <1 in different models (i.e. AS in the models above and EBF in the ones below), if we take into account the possibility of different interrelations between risk factors considered simultaneously.

For more industrialised areas (Europe Western, North America High Income and Australasia) we built exponential models to estimate AOM and CSOM for 1-4 years old children based on breastfeeding, adults smoking, day-care attendance (DCA) and under five mortality rate. The models were based on 22 countries Europe Western countries (Austria, Belgium, Cyprus, Denmark, Finland, France, Germany, Greece, Greenland, Iceland, Ireland, Italy, Luxembourg, Malta, The Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, United Kingdom) and helped re-estimate the other countries and validate the estimates of all countries. The R² for these models were 0.61 for AOM and 0.79 for CSOM:

- AOM 1-4 = 20.9264 * (0.9882^{EBF}) * (1.0124^{DCA}) * (1.0008^{AS}) * (0.9998^{MR-U5})
- CSOM 1-4 = 0.8572 * (1.0010^{EBF}) * (1.0110^{DCA}) * (1.0123^{AS}) * (1.0023^{MR-U5})

The estimates of AOM and CSOM for Australia, Greenland and New Zealand were calculated as a weighted average of the estimates for aboriginals and non-aboriginals, with weight based on proportion of aboriginals to non-aboriginals by age group. For Asia Pacific High income we kept the estimates based on the first phase model.

To estimate the complete country distribution of incidence for all age groups, for AOM we selected two countries with extreme distributions (Chad, and an average between the Netherlands and Rep of Korea). The Netherlands and Republic of Korea had low incidence of AOM and robust age distribution data and estimates. The age distribution of AOM
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incidence in Chad was particularly high and had been estimated in phase one with data from Nigeria on 0 to 14 years of age [54] and extended to older age groups following the proportion between AOM and CSOM incidence. For each age group, the two extreme incidence distributions were connected with linear regression, thus each intermediate age distribution of incidence could be estimated.

For CSOM we selected three countries with extreme distributions in terms of incidence rates (Democratic Rep of the Congo, Netherlands, Rep. of Korea) having the Democratic Rep. of the Congo high incidence and the Netherlands and Rep. of Korea low incidence. In this case, however, the Netherlands and the Rep. of Korea were kept separated because we noticed a different pattern in the age distribution of CSOM that could be explained as a further evolution in the reduction of incidence from the Netherlands to the Rep. of Korea. Again, for the Netherlands and the Rep. of Korea we had solid age distribution estimates, while from the Democratic Republic of the Congo, we had original data on all age groups.[38] The three distributions were linked with linear regression two by two, i.e. Dem. Rep. of the Congo with the Netherlands and the Netherlands with Rep. of Korea.

Uncertainty bounds for AOM and CSOM estimates

Uncertainty bounds were calculated using the standard error (SE) of the second phase regression models. For Asia Pacific High Income, which were estimated by model from phase one, we assumed the SE to be the same as in the second phase regression models. Further sources of uncertainty derive from the data selected from original studies, from the estimates generated by the adoption of the model used in phase one, from the decision on how to estimate the age distributions, from the approach taken to convert prevalence to incidence. To account for all sources of uncertainty, which would be difficult to include in the model, we increased the confidence level to 99%. Thus, even if we kept the SE from the model developed in phase two, we calculated the uncertainty bounds for a confidence level of 99%. It is, however, important to emphasise that the increase from 95% to 99% should be considered as a way to include other sources of uncertainty and that by no means these bounds should be considered to express 99% confidence.

Estimation process: prevalence of Hearing Impairment

According to the WHO definitions [61,62] (Table S3), we estimated the prevalence of HI for all four degrees.

We used the following assumption to extend the estimates to the four degrees of HI or to estimate the WHO thresholds from other thresholds used (pg.6): “Where non-WHO thresholds used, the prevalence of hearing impairment at the WHO thresholds was interpolated assuming the log of the cumulative prevalence is linear with threshold. This relationship holds reasonably well in most studies.” [62]

If we only had data on HI in single ears, we considered 25% of HI in single ears to be HI in best ear: we calculated this proportion as an average of what we found in the data extracted from the literature.[47,63–65]

For Western Europe:

- In Finland 6.4% of CSOM has HI >35db in single ear;[66]
- Incidence of CSOM per 100 children per year = 0.077;
- Estimated 1.6% of CSOM has HI>35db in best ear (25% of 6.4%);
- This means 1.6% of 0.077% with CSOM = 0.001232%.

We estimated cases of HI due to otitis media on the basis of the Oman [67] age distribution of HI. The Oman study was the only one reporting a complete age distribution of HI due to OM. The Oman distribution included HI caused by presbyacusis and accidents, thus we corrected this distribution to only include HI due to CSOM, and on the basis of the 0.19% of the population affected by HI due to CSOM calculated from Oman but adjusted to Europe, using Finland (0.001232%).

- Prevalence of HI>35dB in best ear was extrapolated to countries on the basis of cases of CSOM per age group.
- Prevalence was cumulated to calculate cumulated cases and then cases by age group.
- Total for Western Europe were then calculated adding all cases per country and age group.

This was done for all regions for which we had countries with data: Brazil,[10] China,[68] India,[69,70] Malaysia,[50] Nigeria,[55] Oman [67] and South Africa.[40]

Once again, regression models were used in the second phase: one model was used to estimate the prevalence of slight HI (25dB to 40dB), and another to estimate moderate HI (40dB to 60dB), using estimates from respectively 11 and 10 countries (China, India, Japan, Malaysia, Australia, Oman, Finland, Brazil, United States of America, South Africa, Nigeria) for which we had more reliable data and/or estimates. In the 40dB model we used estimates from the same countries but excluding Malaysia, which did not have a good fit in the model compared with the other countries. The
two were exponential regression models using transformations of total incidence of AOM (ln(AOM)) and CSOM (ln(CSOM)) and the relation between otitis media (HI(Mort)) as regressors:

- HI-25dB = 1.5130 * (0.2382(ln(AOM)) * (0.7873(ln(CSOM)) * (3.6676(ln(MORT)) * (1.4317(ln(U5-MR)) * (1.0002(ln(CSOM)))/3) + (3.1712(ln(CSOM)))/3)
- HI-40dB = 440.51 * (1.1202(ln(AOM)) * (0.0078(ln(CSOM)) * (14.2427(ln(MORT)) * (1.4525(ln(U5-MR)) * (1.0002(ln(CSOM)))/3) + (66.1908(ln(CSOM)))/3)

Both models had a R² of 0.99. The other WHO thresholds were estimated using WHO assumptions on the relation between different degrees of HI.[62]

Unfortunately, we could only count on one complete age distribution of prevalence of HI [67] and we used this distribution to estimate the specific HI for all age groups from the general HI estimates with the regression models.

**Uncertainty bounds for HI**

Uncertainty bounds were calculated using the SE (SE=0.216823 for the 25dB model and SE=0.238823 for the 40dB model) of the second phase regression models for all areas. Other sources of uncertainty were the use of previously estimated AOM and CSOM incidence, the adoption formulas to transpose estimations (the WHO model to transpose 25, 40, 60 and 80dB) and decisions on how to transpose original data on worst to best year, the data selected from original studies (including the heterogeneity in methods used to establish HI in different studies and the uncertainty of survey data) and finally the adoption of the Oman distribution by age. Considering these other sources of uncertainty, as previously done with AOM and CSOM uncertainty bounds, we decided to increase the confidence level to 99%. Thus, even if we kept the SE from the estimation model, we calculated the uncertainty bounds for a confidence level of 99%. It is, however, important to emphasise that the increase from 95% to 99% should be considered as a way to include other sources of uncertainty and that by no means these bounds should be considered to express 99% confidence.

**Mortality estimates**

We selected a number of countries for which we had reliable WHO 2005 Vital Registration data (Argentina, Australia, Brazil, Colombia, Cuba, France, Hungary, Japan, Mexico, Netherlands, Rep. of Korea, Rep. of Moldova, South Africa, United Kingdom, United States of America, Venezuela), plus mortality estimates for China and India for the year 1990.[52] Using these data and regressors such as incidence of AOM, CSOM, AOM in 1-4, CSOM in 1-4 and under five mortality rate, we developed and evaluated three different regression models.

The 1st model was based on overall otitis mortality rate x 10million from 12 countries (Argentina, Brazil, China, Colombia, Cuba, Hungary, India, Mexico, Rep. of Moldova, South Africa, Venezuela) and four regressors (U5 mortality, overall CSOMx1000, CSOM 1-4, AOM 1-4) had a R² of 0.954 and a Standard Error (SE) of 8.09:

- MORT₁ = −107.3699 + 0.0804*U5-MR + 34.0711*CSOM − 0.3516*CSOM1-4 − 0.4326*AOM1-4

The 2nd was based on nine countries (Japan, Netherlands, USA, Venezuela, Mexico, Brazil, India, China and Western Europe) and two regressors (U5 Mortality rate and adult mortality): had a R² of 0.996 and an SE of 2.60:

- MORT₂ = 8.4023 + 0.5101*U5-MR − 0.1222*Adult-MR + 0.0168*(U5-MR)²

The 3rd model was based on seven countries (Japan, Rep. of Korea, USA, Australia, Western Europe, Hungary and Rep. of Moldova) and the same four regressors as model one: had a R² of 0.997 and an SE of 0.32:

- MORT₃ = −7.8715 + 0.5709*U5-MR + 2.3664*CSOM + 0.0776*CSOM1-4 − 0.0382*AOM1-4

For all areas but five we selected the average of two models (1st and 3rd). For Asia Pacific High Income we selected an average between the 2nd and the 3rd models. For Latin America Andean we used the 3rd model. Australasia used the 2nd model. The choice of the models to adopt for each area were made on the basis of models fitting vital registration data when available – even if less reliable than the ones used for the generation of the models – or on the basis of unreliable or negative estimates generated by the other models.

These estimates were for the overall mortality. We then had to divide this mortality in all of the age groups. For Western Europe the age distribution of deaths was estimated on the basis of the proportion between deaths and AOM+CSOM cases in the following countries: France, the Netherlands and the U.K. For Latin America Central, the
deaths reported for Mexico were used to generate the distribution by age for the region. For Latin America Tropical, the same was done with Brazil. For North America High Income the distribution by age was shaped on an average of actual death registered between 1990 and 2005. For Sub-Saharan Africa Southern the age distribution was shaped on the actual deaths reported for South Africa for 2005.

For all other regions where data were unavailable or unreliable we followed a different approach. The age distribution was shaped according to the proportion between mortality and AOM+CSOM cases in Western Europe for the following regions: Europe Central, Europe Eastern, Asia Pacific High Income and Australasia. It was done following the proportion between mortality and AOM+CSOM cases in Latin America Central for the following regions: Caribbean, Latin America Southern, Asia East, Asia Central, Oceania, Asia South East, Asia South, Latin America Andean, North Africa Middle East, Sub-Saharan Africa Central, East and West. The choice of the areas to be estimated by using as reference Western Europe or Latin America Central was made on the basis of similarities in AOM and CSOM incidence distribution.

Uncertainty bounds for mortality estimates

Uncertainty bounds were calculated using the SE of the regression models. Further uncertainty derives from the methodology used to estimate the age distribution, and from the fact we used as regressors the estimates of AOM and CSOM, which for their nature are subject to imprecision due to estimation models and arbitrary decisions on how to perform them. Considering these other sources of uncertainty, as previously done with AOM, CSOM and HI uncertainty bounds, we decided to increase the confidence level and we calculated the uncertainty bounds for a confidence level of 99%. As previously mentioned, however, by no means these bounds should be considered to express 99% confidence. For North America High Income, the lowest limit was considered the actual data reported and the highest was calculated proportionally.
Figure S1. Sequelae of OM (complete scheme) with ICD-10-CM diagnosis codes

* the weight of risk factors and complications is particularly related with recurrent episodes of AOM

1) intracranial supplicative complications
   - Brain abscess G06.6
   - Epidural abscess G06.0
   - Meningitis G00.0
   - Hydrocephalus G91.9
   - Lateral sinus thrombosis G08
   - Sinus cavernous thrombosis G08
   - Subdural abscess/empyema G06.0
   - Cerebellum G06.0
   - Labyrinthitis H83.2

2) extracranial supplicative complications
   - Facial nerve paresis H51.0
   - Mastoiditis H70
   - Petrositis H70.2
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Figure S2. Sequelae of OM, simplified scheme
Figure S3. 1st screening by titles, abstract and keywords
Figure S4. Risk factors diagram

- no breast feeding
- pacifier
- Age < 3 years
- Allergic rhinitis
- nutritional status
- bottle feeding
- frequent colds and upper respiratory tract infections
- Otitis Media
  - smoke and exposure to other air irritants
  - seasonality (winter, autumn)
  - overcrowding
  - day-care centre attendance
  - older siblings
  - genetic / immunodeficiency
  - Down syndrome, cleft palate and other genetic skull malformations
  - congenital cholesteatoma
Table S1. Definitions of main conditions involved in the sequelae of otitis media

- **Otitis media** is the generic term for all types of inflammation of the middle ear [71,72].

- **Acute otitis media (AOM)** is usually a short-term inflammation of the middle ear, characterised by the rapid onset of one or more signs or symptoms of acute inflammation in the middle ear such as earache, tugging at the ear, fever, or irritability in the presence of a middle-ear effusion. It is often preceded by upper respiratory symptoms, including a cough and rhinorrhoea [71–73].

- **Otitis media with effusion (OME)**, also called glue ear, can be defined as a middle-ear effusion without signs of acute inflammation or infection. It is often asymptomatic, and in particular earache is relatively uncommon. OME can arise *de novo* or following AOM [71–73].

- **Chronic OME (COME)** is diagnosed when middle-ear effusion (MEE) fails to resolve within 3 months. The chance of spontaneous resolution decreases the longer the effusion persists [74].

- **Recurrent AOM** refers to frequent episodes of the illness within a period of 6 or 12 months. The National Institute for Health and Clinical Excellence (NICE) has previously defined this as more than four episodes in 6 months [75]. An American guideline defines it as three or more episodes in 6 months, or four or more episodes in a year [76].

- **Chronic suppurative otitis media (CSOM)** is defined as a persistent inflammatory process associated with a perforated tympanic membrane draining exudate for more than 6 weeks [76]. It is often associated with a cholesteatoma.

- **Hearing impairment (HI)**: is the total or partial inability to hear sound in one or both ears [77]. WHO defines disabling hearing impairment as having permanent unaided hearing threshold in the better ear of more than 30 dB in children aged up to 15 years, or more than 40 dB in adults at frequencies of 0.5, 1, 2, and 4 kHz [78].
  - **Conductive hearing loss** (CHL) is the total or partial inability to hear sound in one or both ears because of some mechanical problem in the external or middle ear. The three tiny bones of the ear (ossicles) may fail to conduct sound to the cochlea, or the eardrum may fail to vibrate in response to sound. Fluid in the middle ear can cause CHL [77].
  - **Sensorineural hearing loss** (SNHL) is the total or partial inability to hear sound in one or both ears resulting from a dysfunction of the inner ear. It most often occurs when the tiny hair cells (called cilia) that transmit sound through the ear are injured. This type of hearing loss is sometimes called "nerve damage," although this is not accurate [77].
### Table S2. Search strategies and results

<table>
<thead>
<tr>
<th>Engine</th>
<th>Strategy</th>
<th>Cites</th>
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</table>


Limits: 01/01/1980 to 11/08/2008 | 5736 |
| Embase | 


Limits: 01/01/1980 to 23/07/2008 | 3455 |
| Lilacs | Otitis AND epidemiology (Results 74)  

Otitis AND mortality (Results 11)  

Otitis AND morbidity (Results 7)  

Otitis AND prevalence (Results 19)  

Otitis AND incidence (Results 15)  

Otitis AND sequela$ (Results 9)  

Otitis AND fatality (Results 0)  

Otitis AND risk factor$ (Results 21) | 156 |
| WHOLIS | Otitis media OR otitis | 9 |
Table S3. WHO grades of hearing impairment

<table>
<thead>
<tr>
<th>Grade of Impairment (better ear)</th>
<th>Audiometric ISO value (average of 0.5, 1, 2, 4 kHz)</th>
<th>Impairment description</th>
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</thead>
<tbody>
<tr>
<td>No impairment</td>
<td>≤25 dBHL</td>
<td>No or very slight hearing problems. Able to hear whispers</td>
</tr>
<tr>
<td>Slight impairment</td>
<td>26-40 dBHL</td>
<td>Able to hear and repeat words spoken in normal voice at 1 metre</td>
</tr>
<tr>
<td>Moderate impairment</td>
<td>41-60 dBHL</td>
<td>Able to hear and repeat words using raised voice at 1 metre</td>
</tr>
<tr>
<td>Severe impairment</td>
<td>61-80 dBHL</td>
<td>Able to hear some words when shouted into better ear</td>
</tr>
<tr>
<td>Profound impairment</td>
<td>&gt;80 dBHL</td>
<td>Unable to hear and understand even including a shouted voice</td>
</tr>
</tbody>
</table>

Source: [61,62]
Reference List


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