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# Referrals for recurrent respiratory tract infections including otitis media in young children

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#### ABSTRACT

Objective: (a) To establish whether disease-related, child-related, and physician-related factors are independently associated with specialist referral in young children with recurrent RTI, and (b) to evaluate whether general practitioners (GPs) follow current guidelines regarding these referrals.

Methods: Electronic GP records of children under 24 month of age, born 2002–2008, were reviewed for RTI episodes using ICPC codes. Child-related factors were extracted from the prospective WHISTLER birth-cohort in which a considerable part of children had been enrolled. To evaluate guideline adherence, referral data were compared to national guideline recommendations.

Results: Consultations for 2532 RTI episodes (1041 children) were assessed. Seventy-eight children were referred for recurrent RTI (3.1% of RTI episodes; 7.5% of children). Disease factors were the main determinants of referral: number (OR 1.7 [CI 1.7–1.7]) and severity of previous RTI episodes (OR 2.2 [CI 1.6–2.8]), and duration of RTI episode (OR 1.7 [CI 1.7–1.8]). The non-disease factors daycare attendance (OR 1.3 [CI 1.0–1.7]) and 5–10 years working experience as a GP compared with <5 years (OR 0.37 [CI 0.27–0.50]) were also associated. Fifty-seven percent of referrals for recurrent RTI were made in accordance with national guidelines.

Conclusions: Referral of children for recurrent RTI was primarily determined by frequency, severity, and duration of RTIs; the influence of non-disease factors was limited. Just over half of referrals were made in accordance with guidelines.

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#### 1. Introduction

Recurrent respiratory tract infections including acute otitis media (RTIs) are among the leading reasons for primary care consultation and for referral to pediatricians and/or ear, nose and throat (ENT) specialists [1–3]. Otitis media may be considered as a respiratory tract infection since the middle ear is connected with the respiratory tract and is often preceded by a respiratory tract infection. Referral rates are highest in children under two years of age [3,4]. The rationale for referral and subsequent ENT surgery (e.g. adenotonsillectomy, ventilation tubes) is debated, and ENT surgical rates vary widely [5–7]. This indicates that referral might not depend solely on disease factors such as the frequency, severity

and duration of episodes, but that child and physician characteristics could play an additional role. This would be problematic, since overuse of referrals could increase surgical interventions without benefit.

According to the guidelines of the Dutch College of General Practitioners referral for recurrent RTI is indicated if acute otitis media (AOM) occurs more than 4 times per year, sore throat occurs more than 5 times per year, or if otitis media with effusion (OME) persists for more than 6 months [8–10]. Whether GPs follow these recommendations in daily practice is unknown. Little is known on appropriateness of specialist referral in general, and more evidence is needed to improve the specialty-referral process [11–13].

The aim of this study was to gain insight into determinants and appropriateness of recurrent RTI referral. We set out to (1) determine the independent association of disease factors (frequency, severity, and duration of RTIs), and non-disease factors (parental education level, both parents working outside the home, daycare attendance, and GP's working experience) for recurrent

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RTI specialist referral; and (2) to assess the degree of guideline adherence in children referred for recurrent RTI.

#### 2. Materials and methods

#### 2.1. Determinants of referral for recurrent RTI

Study population Children 0-24 month old born 2002 to 2008 enrolled in the Wheezing Illnesses Study Leidsche Riin (WHIS-TLER), and registered in one of the four Julius Health Centers (JHCs) serving Leidsche Rijn were included. The WHISTLER study is a large prospective birth cohort study on the determinants of lower respiratory illnesses. Patients were recruited from Leidsche Rijn, a new residential area in the city of Utrecht in the Netherlands. Study design details have been described elsewhere [14]. In short, healthy newborns were included in the cohort at the age of 2-3 weeks and child characteristics were recorded using standardized questionnaires. For the current study we used the following childrelated characteristics: (a) high parental education defined as higher vocational or university education; (b) both parents working defined as mother and father both having paid work outside the home at the time of birth, and (c) daycare attendance, assessed monthly and defined as  $\geq 2$  month attendance in the quartile of GP consultation. Since the latter characteristic was assessed only during the first year of life, attendance at the age of one year was assumed identical until the age of two years. All WHISTLER participants with a complete follow-up duration of 24 months were considered eligible for the current study. The WHISTLER study was approved by the Medical Ethics Committee of the University Medical Center Utrecht and parents of participants provided written informed consent.

GP consultation data Electronic charts of included children were reviewed for RTI episodes using the following International Classification of Primary Care (ICPC) codes: upper RTI/pharyngitis (R74); sore throat (R21); sinusitis (R75); tonsillitis/peritonsillar abscess (R76); laryngitis/tracheitis (R77); AOM (H71); OME (H72); pneumonia (R81); acute bronchitis/bronchiolitis (R78); cough (R05); dyspnea (R02); and wheezing (R03) [15]. New episodes of RTI were documented after an RTI free interval of at least 28 days [16]. From each RTI episode the following characteristics were abstracted: episode severity; antibiotic prescription; and any documentation of a previous visit to a pediatrician or ENT specialist not preceded by GP-referral for recurrent RTI (e.g. previous self-referral to the emergency department or previous referral by the GP for acute RTI). Severity of episode was scored as present if the child presented with one or more alarming symptoms and/or risk factors for adverse outcome, as described in the RTI guidelines [8-10,17,18] [webappendix 1]. Subsequently, specialist referrals for (a) recurrent RTI (the outcome of interest analyzed) or (b) other reason (i.e. acute referral) were recorded. Finally, we recorded graduation dates of the attending GPs, and used years since graduation as surrogate parameter for GP working experience (categories < 5 years, 5-10 years, >10 years or "substitute GP/trainee/assistant"). To check data-validity the authors EB en ACvdP double-entered data for 5% of all cases (agreement: 97%).

Data analysis The independent association of disease-, child-, and GP-related factors for the outcome "recurrent RTI referral" was estimated for each RTI episode, using generalized estimating equations (GEE) analysis with an exchangeable working correlation structure [19]. GEE models were used to account for the clustering of RTI episodes within children. The study outcome, "recurrent RTI referral", is likely to be correlated for episodes from the same child. While parameter estimates from ordinary logistic regression on correlated data will not be very different, the standard errors will be too small, resulting in *p*-values that are too

low or confidence intervals that are too narrow. GEE corrects the standard errors for the correlation of episodes within children. Due to the very low incidence of recurrent RTI referral, the number of explanatory variables to be used in the model was selected a priori. The following 11 variables were entered into the model: disease factors: number of previous RTI episodes, presence of previous severe RTI episode, severe course of current RTI episode, number of consultations in current RTI episode: child-related factors: parental education, both parents working outside the home, and day care attendance; GP-related factors: GP working experience; and other potential confounding factors: previous visit to a pediatrician or ENT specialist not preceded by GP-referral for recurrent RTI (e.g. after self-referral), time since last RTI episode, and antibiotic prescription during the course of the episode. After the GP had referred for recurrent RTI disease, subsequent consultations were excluded from the analysis.

Because child-related factors had missing values (3–24%), more than a third of the cases could not be used in the model to predict recurrent RTI referral based on the chosen predictors. To address this considerable loss of power and the potential bias incurred by using only complete cases, multiple imputation by chained equations was used to create complete datasets [20]. Missing data were imputed in two steps: first, child-level variables were multiply imputed, and complete datasets with child-level data were created; next, episode-level data were imputed five times for each of the complete child-level datasets, resulting in 25 complete datasets. Results from the GEE analyses on the imputed datasets were combined using Rubin's formulas in two steps: first to combine the results from the 25 episode-level datasets into five results corresponding to the child-level datasets, and then again to combine those five results into one [20,21]. Analyses were performed using the "mice" (multiple imputation) and "geepack" (GEE) packages in "R" version 2.10.0.

### 2.2. Guideline adherence

Study population Anonymous electronic chart data of all children from the IHC with RTI episodes during the study period were used (i.e. also for non-WHISTLER participants). Analogous to the above analysis, RTI episodes were identified using the predetermined ICPC codes and children referred for recurrent RTIs were identified. The number and duration of RTI episodes prior to referral was recorded and the specific reason for referral was abstracted from the GPs' notes (categories: referral for recurrent sore throat, AOM, OME, cough, and common cold, respectively). According to the Medical Ethics Committee of University Medical Center Utrecht approval was not needed for this anonymous retrospective patient record study. Data analysis Dutch general practice guideline criteria available for recurrent RTI referral were as follows: AOM more than 4 times per year/more than three times per 6 month, sore throat more than five times per year, or OME persisting for more than 6 months (8-10). No guideline criteria were available for recurrent cough and recurrent common cold referral, therefore adherence for these referrals could not be assessed. Since for research purposes an RTI episode had been strictly defined as starting only after an RTI free interval of at least 28 days we manually reviewed data from all children that were referred after fewer episodes than indicated in the guidelines, to determine whether the RTI episodes could have been regarded by the GP as in fact more than one separate episodes. We arbitrarily split episodes including more than one diagnoses (e.g. AOM and 1 week later pneumonia) or more than one antibiotic prescription (e.g. another course of antibiotics 2 weeks later) into multiple episodes to ensure that guideline adherence was not underestimated.

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