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Title: Association between rhinovirus C infection and respiratory symptom severity in an unselected pediatric population, the EUROPA-study

M.P. 7659 van der Schee m.p.vanderschee@amc.uva.nl^{1,2}, J.G. 8286 Wildenbeest j.g.wildenbeest@amc.uva.nl³, S. 8287 Hashimoto s.hashimoto@amc.uva.nl MD¹, K.S.M. 8288 Benschop k.s.benschop@amc.uva.nl³, A.C. 8289 Schuurman a.c.schuurman@amc.uva.nl¹, N. 8290 Adriaens n.adriaens@amc.uva.nl¹, K.C. 8291 Wolthers k.c.wolthers@amc.uva.nl MD³, A.B. 8292 Sprikkelman a.b.sprikkelman@amc.uva.nl MD², E.G. 8293 Haarman eg.haarman@vumc.nl MD⁴, W.M.C. 8294 van Aalderen w.m.vanaalderen@amc.uva.nl MD² and Peter J. 8295 Sterk p.j.sterk@amc.uva.nl MD¹.¹ Respiratory Medicine, Academic Medical Centre University of Amsterdam, Netherlands ;² Paediatric Pulmonology and Immunology, Academic Medical Centre University of Amsterdam, Netherlands ;³ Medical Microbiology, Academic Medical Centre University of Amsterdam, Netherlands and⁴ Paediatric Pulmonology, VU University Medical Centre, Amsterdam, Netherlands .

Body: Rationale-In a paediatric population hospitalized for bronchiolitis rhinovirus (RV) type C is associated with more severe respiratory symptoms as compared to other RV genotypes (Bizzintino,ERJ,'11). RV infections in infants are linked to the development of asthma but specific clinical features of RV-C infection in the general population are unknown. We therefore aim to study the occurrence and respiratory symptom severity associated with RV-C in an unselected paediatric population. Methods-This is a cross-sectional study from the prospective EUROPA birth cohort, aimed at early prediction of asthma (N=1207;0-3 years). Nose and throat swabs were collected in both asymptomatic infants and infants whose parents consulted the GP for wheeze or dyspnea. RV presence was tested using a 5'UTR rtPCR with genotyping based on the VP4/VP2 region. Symptom severity was assessed by parents scoring the presence and severity of 10 symptoms (range 0-50) and by clinicians using the validated PRAM-score (range 0-12). Results-102 infants (13.3±5.5 months) presented with an infection of whom 53% had a positive RV PCR. RV-A, B & C were found in 35%, 4% and 24% of cases, respectively. 2/17 asymptomatic infants tested positive for RV-A. RV genotypes did not differ significantly regarding symptom severity as scored by parents ($\mu \pm SD = 14 \pm 6.4$; $p = 0.75$) and clinicians (1.5 ± 1.9 ; 0.33). Conclusion-Rhinovirus-C infection occurred in 24% of the infants and is associated with similar symptom severity as other RV-genotypes. Since RV-C appears to be commonly involved in wheezy episodes not requiring hospitalization, it's association with future development of asthma needs to be examined.