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Title: The development of the upper respiratory microbiome on infancy and the dysbiosis related with wheezing syndrome and health on children from the rural tropics of Ecuador

Dr. Paul 34043 Cardenas p.cardenas@imperial.ac.uk MD ¹, Prof. Dr Philip 34044 Cooper P.J.Cooper@liverpool.ac.uk MD ², Prof. Miriam 34045 Moffatt m.moffatt@imperial.ac.uk ¹ and Prof. Dr William 34046 Cookson w.cookson@imperial.ac.uk MD ¹. ¹ NHLI, Imperial College London, London, United Kingdom and ² FEPIS, USFQ, Quininde, Ecuador .

Body: The hygiene hypothesis has identified a relationship between living in rural areas and the acquisition of protective environmental factors against the development of asthma and atopy. In a previous pilot study carried out on a population living in the rural tropics of Ecuador, we found a correlation between particular bacterial species and early onset wheezing in infants (Cardenas et al. 2012). We extended this investigation and carried out a larger retrospective time series study. **Methods:** We performed pyrosequencing of bacterial 16S rRNA gene from oropharyngeal samples from 109 infants with episodic wheezing and 156 controls at different ages (7, 12 and 24 months). Bioinformatic analysis were conducted with QIIME. **Results:** Significant differences between cases and controls were found for the Fusobacteria, Proteobacteria and Actinobacteria. A significant increase in potential pathogenic bacteria (Neisseriaceae, Haemophilus, Staphylococcus) was found in cases whilst a higher prevalence of Veillonella spp. was seen in controls. When age was considered differences were found in the microbial flora present (alpha diversity Shannon index).

Conclusions: The respiratory microbiota is different at phyla, genera and OTUs levels when comparing between wheezing and healthy children. A progressive more complex respiratory microbial community develops with age.