Author's response to reviews

Title: Effect of Ascaris Lumbricoides specific IgE on tuberculin skin test responses in children in a high-burden setting: a cross-sectional community-based study

Authors:
Nelda van Soelen (neldavs@sun.ac.za)
Anna M Mandalakas (mandalak@bcm.edu)
H.Lester Kirchner (hlkirchner@geisinger.edu)
Gerhard Walzl (gwalzl@sun.ac.za)
Harleen M.S Grewal (Harleen.Grewal@Gades.uib.no)
Anneke C Hesseling (annekeh@sun.ac.za)

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TO WHOM IT MAY CONCERN

Manuscript submission for review: ‘Effect of Ascaris Lumbricoïdes specific IgE on tuberculin skin test responses in children in a high-burden setting: a cross-sectional community-based study’

We would like to submit the revised manuscript ‘Effect of Ascaris Lumbricoïdes specific IgE on tuberculin skin test responses in children in a high-burden setting: a cross-sectional community-based study’ for review and consideration for publication in the Journal *BMC Infectious Diseases*.

Infectious diseases are a continuous source of morbidity and mortality in paediatric populations from the developing world. Tuberculosis remains a major threat and paediatric tuberculosis constitutes up to 20% of the overall global caseload. Poor socio-economic circumstances, prevalent in many settings with a high burden of tuberculosis, predispose to poor living conditions, overcrowding and an increased risk of helminth exposure and infection.

The data reported on in this manuscript originated from a community-based tuberculosis household contact tracing study conducted in a poor urban setting in Cape Town, South Africa that are known to have a high burden of both tuberculosis and helminth infection. Immune responses to M.tuberculosis (*M.tb*) are known to be associated with enhanced Th1 cell mediated responses which may be down regulated by Th2 immune responses that are typically associated with helminth infection. The *M.tb* and helminth co-infection model has not yet been fully explored and available data are both limited and contradictory. Co-infection and the underlying immune responses potentially have important clinically measureable implications in widely used immune diagnostic tests that measures *M.tb* infection. We therefore investigated the effect of an *Ascaris* specific-IgE positive status on a commonly used marker of *M.tb* infection (TST) in children.
We explored the primary hypothesis that helminth infection in children, while controlling for \( M.tb \) exposure and other relevant covariates, would decrease the ability to generate an appropriate Th1 immune response characterized by a positive TST in children and a secondary hypothesis that the presence of \( Ascaris \) IgE will be associated with a modulation of the effect of well-known risk factors like age and the \( M.tb \) contact score on TST responses. The results demonstrated a high prevalence of both \( M.tb \) and \( Ascaris lumbricoides \) infection in children from households with and without documented tuberculosis exposure and our analyses suggested an inverse relationship between \( Ascaris \) IgE and TST positivity which is consistent with our hypothesis.

We chose to submit to *BMC Infectious Diseases* based on the open access policy and the manuscript content that is in line with the journal’s focus on aspects of the prevention, diagnosis, epidemiology and management of infectious diseases in humans. No potential competing interests have been declared by any of the authors of this manuscript.

As per your communication this revised version includes a statement to confirm that the research was carried out in compliance with the Helsinki Declaration and the Ethics Committee approval details were added. The revised first paragraph of the methods section now reads as follows:

“This prospective cross-sectional community-based study was nested in larger ongoing paediatric tuberculosis household contact tracing studies conducted in three communities in the Western Cape province, Cape Town, South Africa, with high burden of tuberculosis; Ravensmead, Uitsig (R/U) and Site C, Khayelitsha (Site C). The study was conducted in compliance with the Helsinki Declaration and was approved by the Health Research Ethics Committee of the Stellenbosch University (reference number N05/07/129 and N08/08/207).”

We will appreciate your review and consideration of this manuscript for publication.

Kind Regards
Nelda van Soelen

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Dr Nelda van Soelen  
Research Clinician  
MBChB, MPH  
*Desmond Tutu TB Centre*  
Department of Paediatrics and Child Health  
Faculty of Health Sciences  
Stellenbosch University  
South Africa  
Phone (27) 83 443 1439  
Fax (27) 86 684 0751  
Email: neldavs@sun.ac.za