HIV and Schistosoma spp. interactions: epidemiology and consequences for detection and prevention in the lake region of Tanzania

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ADDENDUM:

ENGLISH SUMMARY
SAMENVATTING
ACKNOWLEDGEMENTS
CURRICULUM VITAE
LIST OF PUBLICATIONS

ENGLISH SUMMARY

Approximately 36.7 million people are infected with HIV around the world while 218 million are infected with *Schistosoma* spp.. These infections overlap and an estimated 6 million individuals are HIV/*Schistosoma* spp. co-infected. The majority of co-infections occur in Africa.

In the context of the HIV/AIDS epidemic, co-infections typically exacerbate morbidity and mortality. The immunodeficiency caused by chronic HIV infection increases the risk of co-infection with many pathogens. Moreover, administration of antiretroviral therapy (ART) does not always restore the pathogen-specific immune response to co-infections to normal levels. We might thus expect HIV infection to increase morbidity associated with endemicity of *Schistosoma* spp., and likely *vice versa*.

Several studies have showed a clear association between infection with *Schistosoma* spp. and HIV, and being infected with *Schistosoma* spp. increases a woman's risk of HIV acquisition. However, a lot is still unknown or poorly understood about HIV/*Schistosoma* spp. co-infections, both epidemiologically and immunologically. Longitudinal studies, controlling for sex, age, and duration of HIV infection are missing. The impact of *Schistosoma* spp. co-infection on HIV/AIDS outcomes is poorly described and the impact of *Schistosoma* spp. co-infection on HIV transmission is also not fully understood.
This thesis seeks to add to the current epidemiological knowledge on HIV and *Schistosoma* spp. co-infections, with the hope to understand the discrepancy in the data to date, and to generate new hypotheses and new questions for immunological studies. All studies presented in this thesis were conducted in the Lake Zone of Tanzania.

Chapter 1 reviews the literature to date when the work of this thesis started and the gaps in knowledge that this thesis tried to fill in.

Chapter 2 evaluated Tanzania's achievements regarding the 90-90-90 targets, which are a target for ART programs worldwide defined by the Joint United Nations Programme on HIV and AIDS (UNAIDS). It aims to achieve 90% of people living with HIV diagnosed (knowing their status), 90% of those diagnosed initiated on ART, and 90% of individuals on ART being virologically suppressed. Reaching the UNAIDS targets requires early diagnosis and effective linkage to and retention in care. Evaluating Tanzania's progress regarding HIV care allowed us to define our study population better, and to understand additional challenges in the fight against co-infections. Our Tanzanian study population demonstrated some moderate successes. The major gaps to optimizing linkage to care included a prolonged time from seroconversion to awareness of HIV status, as well as a low percentage of enrollment in care for ART treatment. Our results highlighted the importance of access and better integration of HIV services within the general healthcare system and to on-going serosurveys.

Chapter 3 indicated that people who had *Schistosoma* spp. infection at the time of HIV-seroconversion developed adverse HIV outcomes more slowly than those without *Schistosoma* spp. infection. Our study was unique in its use of banked dried blood spots to determine the impact of *Schistosoma* spp. infection on HIV disease progression, approximately 2-5 years after HIV-seroconversion. The findings suggested that the effect of co-infections on long-term outcomes might be milder than previously thought. They also highlighted an urgent need for longer-term clinical and immunological studies to confirm these outcomes.

Chapter 4 gave a first estimate of the hazard ratio of HIV-transmission from *Schistosoma* spp. co-infected transmitting partners compared to non-co-infected transmitting partners. It showed a trend towards an increased transmission of HIV, though suggested that the clinical impact may be small. Surprisingly, the *Schistosoma* spp. infection status of the receiving partner seemed not to be a risk factor for HIV acquisition. This may have occurred because sex of the receiving partner was so strongly associated with HIV seroconversion that any other risk factor for transmission became relatively inconsequential in our analysis. We were unable to investigate the effect of sex on the relationship between *Schistosoma* spp. and HIV transmission because 13 of 14 HIV-seroconversions occurred in women. This study also demonstrated a risk of HIV acquisition 19 times higher in serodiscordant couples than in the general population, highlighting the need for couples' targeted HIV counseling and testing as a strategic way to address the continuing incident HIV infections in Tanzania.

Chapter 5 signified that individuals with HIV and *Schistosoma* spp. co-infections have lower viral loads than those with HIV alone, when accounting for time infected with HIV. The difference in viral load was clinically significant and suggested a protective effect of *Schistosoma* spp. infection against long-term HIV outcomes and HIV transmission, which is in line with the results of **Chapter 3**. This study indicated that duration of HIV infection may be a critical explanatory factor in the disparate findings of studies on HIV viral load and *Schistosoma* spp. infections. Studies that examined viral loads earlier in the course of HIV infection may report increased viral load in the setting of *Schistosoma* spp. co-infections, and studies over the longer term may report lower viral loads. Studies that did not take into account duration of HIV infection also may have compared individuals at different stages of their HIV infection.

Finally, **Chapter 6** showed that both, women and HIV-infected individuals (males as well as females), were significantly less likely to excrete *Schistosoma* spp. eggs when hosting the parasite, even after controlling for a given worm antigen level. Our findings clarified reasons for divergent results of past studies on the relationship between HIV and egg excretion. This work suggested that current guidelines for the use of microscopy to diagnose *Schistosoma* spp. infections in HIV-infected individuals and in women merit reconsideration.