EXAMPLE ABSTRACT

PhD project abstract

HIV-associated [redacted] in virally suppressed people living with HIV: Challenges in adherence and management

Rationale

Despite viral suppression, people living with HIV (PLWH) are at a 2-fold higher risk of developing non-communicable diseases (NCDs) such as cardiovascular disease and metabolic disorders compared to their HIV-negative counterparts. Increased NCDs have been shown to be driven by underlying inflammation, leading to endothelial dysfunction and subsequent cardiovascular and metabolic disease. A major contributor to ongoing inflammation is [redacted] a persistence of viral replication below the detectable threshold of current viral load assays (currently < 20 copies/mL).
(ART) can lead to viral suppression with adherence rates as low as 80%, but imperfect adherence is known to cause residual viraemia, significantly contributing to HIV-associated NCD development. In clinical practice, imperfect (<100%) ART adherence is prevalent, occurring in 24%-57% of PLWH, and presents a significant modifiable factor to reduce residual viraemia and subsequent NCDs.

It is currently unclear if [redacted] directly associated with endothelial dysfunction and other HIV-associated NCDs. It is also unknown if metformin, a well-known diabetic drug with pleiotropic effects, can be repurposed for some non-diabetic NCDs. The overall aim of the PhD is therefore to determine specific challenges in ART adherence and address the management of select HIV-associated NCDs in virally suppres

Objectives

Adherence-as-prevention

To determine the association of:

1. Imperfect ART adherence and NCD development in virally suppressed PLWH.
2. Imperfect ART adherence and [redacted] using the point-of-care EndoPAT® device.

Management of HIV-associated NCDs

3. To determine the utility [redacted] for HIV-associated NCDs.
4. To explore the effects and mechanisms o[redacted] as an intervention for HIV-associated sensory [redacted] a common NCD without effective treatments.
5. To determine the validity and optimal dose of the [redacted] recommendation due to the drug-interaction with

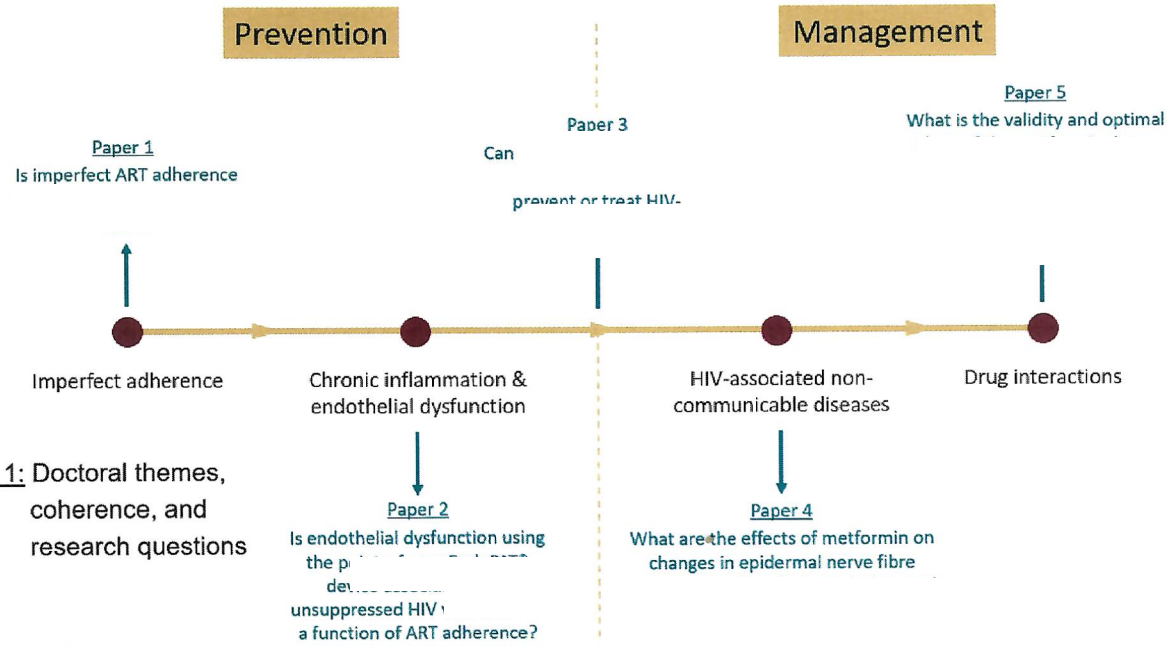

Figure 1: Doctoral themes, coherence, and research questions

Methods & design

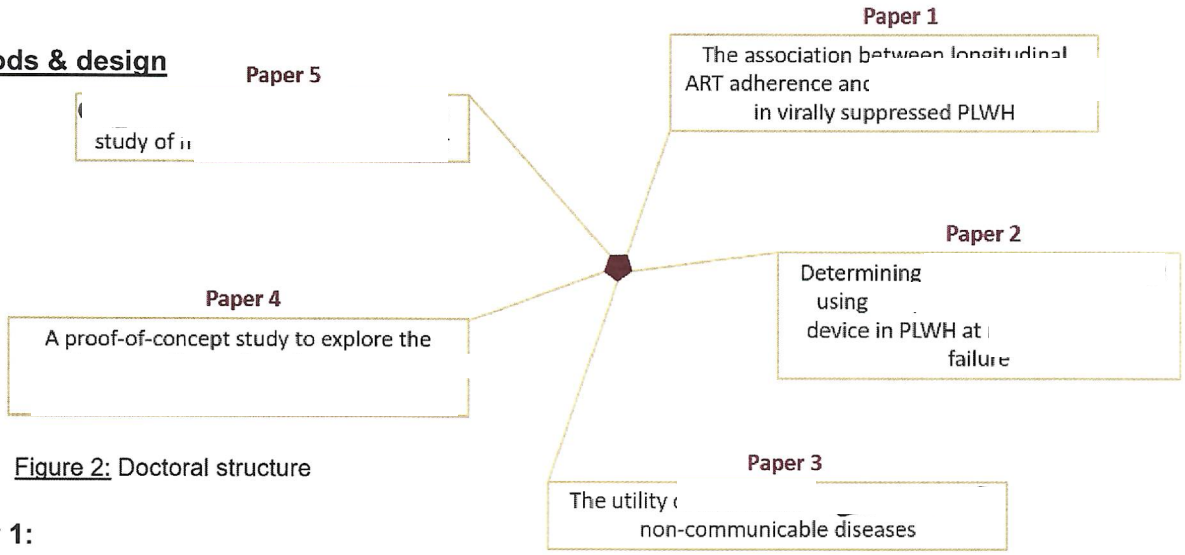

Figure 2: Doctoral structure

Paper 1:

Retrospective, longitudinal cohort study, using existing data from the longitudinal AIDS Clinical Trials Group (ACTG) research cohorts I

Paper 2:

Case-control sub-study of the active testing a care ART adherence device.

Paper 3:

Scoping review using a predefined search strategy in multiple electronic databases.

Paper 4:

Exploratory, pilot cohort sub-study of the active that is assessing PLWH with metabolic syndrome.

Paper 5:

Pharmacokinetic drug-interaction study using directly-observed metformin and dolutegravir administration with intensive metformin pharmacokinetic blood sampling and genetic drug transporter analysis.

Feasibility

All the studies of the PhD project have high feasibility of successful completion within the allocated time. The feasibility of all the PhD studies is ensured by the study designs and secured funding:

- Paper 1 is conducted as a longitudinal study of existing data after study completion has already occurred, and Paper 2 as a retrospective case-control design at the last visit of the parent study, with low anticipated drop-out. Additionally, Paper 2 will only seek to enrol approximately 80% of the parent study population, significantly improving the likelihood of successful completion.
- Paper 2, 4, and 5 are linked to existing parent studies that are active and recruiting, with the PIs having strong track records of successful previous study completions.
- Paper 1, 2, 4, and 5 have good probability of reaching their respective sample sizes, due to the experienced teams conducting the parent studies and successful environments of these studies.
- At the time of this application, the prospective data collection studies (Papers 2, 4, and 5) have already reached between 20% – 50% of their sample sizes.
- Funding for all the PhD studies has been secured for all objectives and for the duration of the studies and overall PhD project.

Research translation & dissemination plan

The research will be translated into non-scientific language and shared with the communities from where it was obtained, to include participants and communities throughout the research process. Research findings will be disseminated through presentations at local and international scientific meetings, accredited journal publications, institutional media releases, and by placing raw data in a protected data repository for potential future use.

Potential impact

The research findings will add valuable data on NCD associations in virally suppressed PLWH, the potential of the versatile drug metformin to be used in HIV care, and of PLWH. This has significant immediate and future implications for HIV-associated NCDs in South Africa and globally.