Title: Promoting Viral Suppression Among Transgender Women Living With HIV in Santo Domingo
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C.5.8 Aim 1 Analysis: To estimate the initial effects of GAP, we will use survey, viral load, and monitoring data. We will **first examine if randomization succeeded** by conducting balance tests with baseline data, which will also inform the specification of the effects estimation model. **Second, we will examine loss-to-follow-up** (LTF) (expected not to be >10%) and determine if those LTF have different characteristics of those retained and if there is any variation between intervention and control groups. **Third, we will estimate initial effects of the intervention**. We will first estimate the intention-to-treat (ITT) effect using linear probability (or logistic) model with a GAP intervention indicator as the only explanatory variable and using endline data only. The ITT model will be $Y_i = \alpha_0 + \alpha_1 P_i + \varepsilon_i$, where Y_i is the outcome of individual i, P_i is a dummy indicator variable for being in the treatment group or not, and ε_i is the standard error term. The coefficient α_1 will be our ITT effect estimate. Although the GAP intervention will be randomly allocated across participants, it is possible that some differences in baseline characteristics and outcomes between the groups will be observed. To correct for those imbalances, **we will use difference-in-differences (DID) models** that include baseline covariates; the DID model estimates intervention effects by taking the difference between the changes observed in the outcome in the intervention group and the changes in the control group, adjusting for baseline differences. The DID model will be estimated using baseline, midline, and endline data and will be specified as: $Y_{it} = \alpha_0 + \alpha_1 P_i + \alpha_2 T1_t + \alpha_3 P_i * T1_t + \alpha_4 T2_t + \alpha_5 P_i * T2_t + \alpha_6 X_i + \varepsilon_{it}$, where Y_{it} is the outcome of individual i at time t, P_i is an indicator variable for being in the intervention group or not, $T1_t$ is an indicator variable for the observation from midline, $T2_t$ is an indicator variable for the observation from endline, X_i represents characteristics of the individual at baseline, and ε_{it} is the standard error term. The coefficient α_3 will be our DID intervention effect at midline, and α_5 at endline. This DID model allows us to examine the evolution of the intervention effects over time.

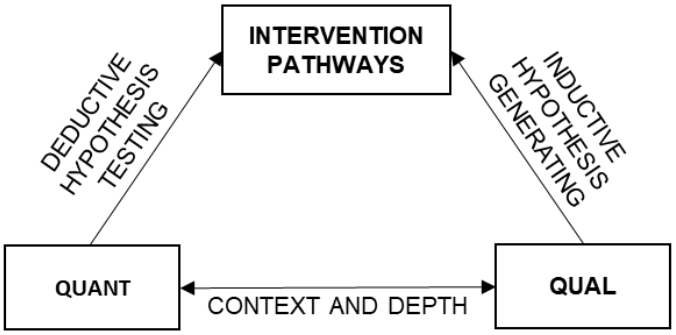
A second set of analyses will examine the effect of each component of the intervention on the main outcome at midline and endline. We will estimate the following model: $Y_i = \alpha_0 + \alpha_1 P1_i + \alpha_2 P2_i + \alpha_3 P3_i + \alpha_4 X_i + \varepsilon_i$ where $P1_i$ is a measure of individual counseling (e.g. # of counseling sessions individual i received); $P2_i$ is a measure of navigation (e.g. # of interactions with individual i); and $P3_i$ is a measure of community support building (e.g. # of group sessions attended by individual i). We will further extend this model to examine if different levels of intensity of exposure have different effects on the outcome. We will define three levels of intensity (low, medium, high) depending on the number of navigation interactions to estimate the following model: $Y_i = \alpha_0 + \alpha_1 P1_i + \alpha_{2Med} P2Med_i + \alpha_{2High} P2High_i + \alpha_3 P3_i + \alpha_4 X_i + \varepsilon_i$
where, $P2Med_i$ is a dummy variable indicating that individual i had medium exposure to navigation and $P2High_i$ is high intensity exposure to navigation sessions. In this model, α_{2Med} is the effect of medium exposure to navigation on the outcome, and α_{2High} is the effect of high exposure to navigation on the outcome. The reference category is low exposure.

C.5.9 Aim 1 Power Considerations: One of the goals of the proposed study is to estimate rates of viral suppression in each arm of study to inform the effect size of the intervention for future studies. We calculated the minimum detectable effect of the intervention considering a feasible recruitment target of 120 individuals who will be randomly assigned to treatment and control arms, and an expected LTF of 10%; this level is consistent with our past intervention research in the DR.[1,2] In the original AP study, we achieved 90% retention.[1] In the adaptation study, we achieved 87% (26/30) retention over 12 months, but we did not include a 6-month survey, which both serves to provide mid-point data as well as support retention.[2] We expect the baseline prevalence of viral suppression to be 64% based on our recent study of trans women sex workers living with HIV.[3] The minimum detectable effect for a power of 80%, a significant level of 5%, and a 50/50 split of the 120 individuals in the sample between the treatment and control group is of +13.3 percentage points.

C.5.11 Aim 2 Analysis: Aim 2 analysis will integrate quantitative and qualitative data to examine experiences with the intervention and pathways of influence. We will triangulate survey, interview, focus group and monitoring data for each component to identify the most parsimonious intervention package with the most relevant content. We will engage in an integrated analysis process whereby each data source will be used to inform the analysis and interpretation of the other.[4] For example, we will analyze survey data to *test our hypothesized pathways* of influence that we will then *contextualize* and *deepen* with analysis of the longitudinal qualitative data. We will also use analysis of the qualitative data to *inductively identify pathways* to explore quantitatively that we may not have hypothesized a priori (Fig 4).

Our approach to qualitative analysis is informed by Maxwell and Miller's theory of qualitative analysis, which distinguishes between thematic analysis based on comparisons across participants and narrative analysis based on trajectories and connections within participants.[5] We will integrate narrative and thematic analysis through a series of 3 overlapping analytic steps: 1) ***Summarizing***: We will read transcripts multiple times to prepare a narrative summary of the interview or focus group. The purpose of the summary is to reduce data while keeping the overall participant story(ies) intact and maintaining context. In the case of longitudinal interviews, the narrative summary will integrate all 3 interviews. From these summaries, we will establish a "narrative of change"[6,7] for each participant, which will include a description of the intervention experience, outcomes, or lack thereof, and pathways of influence and barriers; 2) ***Coding****:* Drawing on recurring themes identified in the summaries, we will develop a codebook, including descriptive and interpretive codes, to systematically code interview and focus group transcripts. Codes will address: intervention processes, outcomes, and recommendations, and emergent topics. The PI and two research assistants (one in the US and one in the DR) will apply the codebook to 2-3 transcripts, reconcile use of codes, and revise the codebook as needed until there is shared understanding of code application. All data will then be coded by the two RAs using the qualitative data analysis software ATLAS.ti. 3) ***Displaying***: After coding, we will summarize key patterns and merge codes into larger themes. We will visually display data through matrices to facilitate comparison, for example between suppressed and unsuppressed women.

Figure 4. Mixed Methods Analysis of Pathways



An ongoing step in the analysis will be to integrate insights from the qualitative interviews with insights from the survey data. We hypothesize that GAP will improve viral suppression through reduced stigma and increased social cohesion. To explore these pathways, we will estimate reduced-form models (see C.5.8). We will then conduct mediation analysis using a structural-equation model (SEM) relating the GAP intervention to the mechanisms (stigma, cohesion), and then relating the mechanisms to the main outcome (viral suppression). The SEM will be estimated by appropriate maximum likelihood procedures. We are cautiously optimistic that our sample size will allow us to estimate this model, but we recognize that precision of estimates could be limited. Estimates from the SEM will be informative of the pathways through which GAP components affect outcomes. Alternatively, we will assess the pathway from, for example, internalized stigma to viral suppression using a DID fixed-effects model to control for the endogeneity of internalized stigma. We acknowledge the limitations of the fixed-effects DID approach, namely, that it leads to larger standard errors and imprecise estimates. However, it could provide suggestive evidence of the effect of stigma and cohesion on HIV outcomes. Based on these models, we will use the qualitative analysis to

contextualize and add depth to quantitative findings and advance understanding of processes of stigma and social cohesion (Fig 4).

Findings from mixed methods analysis for Aims 1 and 2, integrating the perspectives of participants, providers, and intervention staff, will be used to determine impact and define pathways and refine the GAP model as needed in preparation for a larger efficacy trial. We will make an important contribution to the science of sequential implementation of multilevel interventions. We will engage in collaborative dissemination with local partners to determine an acceptable model to test at scale in the DR while also generating transferable findings for other settings where trans women experience sub-optimal HIV treatment outcomes.

References

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