



MZANTSI WAKHO RESEARCH PROTOCOL

Summary

Mzantsi Wakho is a mixed methods, longitudinal, community-traced study of ART adherence and sexual health practices among adolescents in South Africa's Eastern Cape. The study was established in mid-2013, and is currently beginning its third annual wave of quantitative data collection. Qualitative data collection has been ongoing since the study's inception.

This document summarises the background, objectives, methods and ethical considerations of the study. This is an updated protocol as of February 2017.

Existing Research Ethics Committee approvals and government approvals (Appendix 1):

- (1) Inter-Divisional Research Ethics Committee (IDREC) of the Social Sciences and Humanities Division, University of Oxford (Ref No: SSD/CUREC2/12-21, Amendments: 20 Nov 2014, R43892/RE003 – 29 September 2016).
- (2) Centre for Social Science Research, University of Cape Town (Ref No: UCT/CSSR/1/2014(ii))
- (3) Department of Health, Eastern Cape Province (29 August 2013)
- (4) Buffalo City Municipality Health sub-district approval (23 Jan 2014, 2 Oct 2015)
- (5) Department of Education, Eastern Cape Province (4 April 2014)
- (6) Frere Hospital (2013)

Overarching study timeline:

2013 – 2014: Qualitative and contextual analysis, participatory action research, quantitative methods piloting and adaptation

2014 – 2015: Wave 1 survey; qualitative interviews and focus group discussions, participatory research, clinic observations, design and adaptation of T2 questionnaire

2015 – 2016: Wave 2 survey and patient file data collection, clinics research team, qualitative interviews and focus group discussions, clinic observations

2017-2018: Wave 3 survey and patient file data collection, qualitative research.

2017 update of publications

Publications including information about the theory, design, ethics, methods, context and substantive findings from the Mzantsi Wakho study include:

Cooper, D., Harries, J., Moodley, J., Constant, D., Hodes, R., Mathews, C., & Hoffman, M. (2016). Coming of age? Women's sexual and reproductive health after twenty-one years of democracy in South Africa. *Reproductive Health Matters*, 24(48), 79–89 DOI: 10.1016/j.rhm.2016.11.010

Cluver, L. D., Toska, E., Orkin, F. M., Meinck, F., Hodes, R., Yakubovich, A. R., & Sherr, L. (2016). Achieving equity in HIV-treatment outcomes: can social protection improve adolescent ART-adherence in South Africa? *AIDS Care*, 28(sup2), 73-82. DOI: 10.1080/09540121.2016.1179008

Toska, E., Cluver, L. D., Boyes, M. E., Isaacsohn, M., Hodes, R., & Sherr, L. (2016). School, supervision and adolescent-sensitive clinic care: combination social protection and reduced unprotected sex among HIV-positive adolescents in South Africa. *AIDS and Behavior*, 1-14. DOI: 10.1007/s10461-016-1539-y.

Toska, E., Gittings, L., Hodes, R., Cluver, L. D., Govender, K., Chademana, K. E., & Gutiérrez, V. E. (2016). Resourcing resilience: social protection for HIV prevention amongst children and adolescents in Eastern and Southern Africa. *African Journal of AIDS Research*, 15(2), 123-140. DOI: 10.2989/16085906.2016.1194299

Hodes, R., Toska E., and Gittings, L 2016. Babies for bling: Are teenage girls having children to access grants?, *HIV Nursing Matters* 7 (2): 20-23.



Natrass, N., Hodes, R., & Cluver, L. (2016). Changing Donor Funding and the Challenges of Integrated HIV Treatment. *AMA Journal of Ethics*, 18(7), 681. DOI: 10.1001/journalofethics.2016.18.07.ecas3-1607

Hodes, R. (2016). The culture of illegal abortion in South Africa. *Journal of Southern African Studies*, 42(1), 79-93. DOI: 10.1080/03057070.2016.1133086

Vale, B. (2016). Negotiations of Blame and Care among HIV-positive Mothers and Daughters in South Africa's Eastern Cape. *Medical Anthropology Quarterly*. DOI: 10.1111/maq.12351

Pantelic, M., Boyes, M., Cluver, L., & Thabeng, M. (2016). 'They Say HIV is a Punishment from God or from Ancestors': Cross-Cultural Adaptation and Psychometric Assessment of an HIV Stigma Scale for South African Adolescents Living with HIV (ALHIV-SS). *Child Indicators Research*, 1-17. DOI: 10.1007/s12187-016-9428-5

Vale, B., & Thabeng, M. (2016). Redeeming Lost Mothers: Adolescent Antiretroviral Treatment and the Making of Home in South Africa. *Medical Anthropology*, 35(6), 489-502. DOI: 10.1080/01459740.2016.1145218

Cluver, L. D., Hodes, R. J., Sherr, L., Orkin, F. M., Meinck, F., Lim Ah Ken, P., & Vicari, M. (2015). Social protection: potential for improving HIV outcomes among adolescents. *J Int AIDS Soc*, 18(Suppl 6), 20299. DOI: 10.7448/IAS.18.7.20260

Toska, E., Cluver, L. D., Hodes, R., & Kidia, K. K. (2015). Sex and secrecy: How HIV-status disclosure affects safe sex among HIV-positive adolescents. *AIDS Care*, 27(sup1), 47-58. DOI: 10.1080/09540121.2015.1071775

Cluver, L. D., Hodes, R. J., Toska, E., Kidia, K. K., Orkin, F. M., Sherr, L., & Meinck, F. (2015). 'HIV is like a tsotsi. ARVs are your guns': associations between HIV-disclosure and adherence to antiretroviral treatment among adolescents in South Africa. *AIDS*. 29(Suppl 1), S57-65. DOI: 10.1097/QAD.0000000000000695

Vale, B., & Thabeng, M. (2015). Mobilising AID (S)? Contesting HIV as a Social and Economic Resource among Youth in South Africa's Eastern Cape. *Journal of Southern African Studies*, 41(4), 797-813. DOI: 10.1080/03057070.2015.1041811

1. Purpose of the Study

Southern Africa is home to 1.2 million HIV-infected adolescents (1), whose long-term health outcomes depend on strict adherence to antiretroviral therapy (ART). The limited research conducted with adolescent ART-users in Africa reflects low adherence rates (2) and poor access to sexual and reproductive health (SRH) services (3). As adolescence is a time of increased risk-taking and experimentation, HIV-positive teenagers represent an especially vulnerable and challenging group for HIV service providers. However, their retention in ART programmes and use of SRH services remain under-investigated, and HIV-positive adolescents have rarely been included as partners in the design and operationalization of their own HIV and SRH services.

This research applies innovative investigative strategies to study the health needs of HIV-positive young people growing up in contexts of extreme risk, investigating their potential for resilience, and exploring how to support their adherence to ART and uptake of SRH services. It fills a pressing research gap by investigating areas of intersection between adolescent ART adherence and SRH, while also offering methodological and programmatic innovation through the development of youth-driven tools to support ART adherence and SRH service uptake.

This study uses both qualitative and quantitative methods to achieve two aims:

- (1) To identify and investigate risk and resilience-promoting factors for ART adherence and access to SRH services amongst HIV-positive teenagers, through linked qualitative and quantitative studies.



- (2) To collaborate with HIV-positive adolescents, healthcare and social service providers using participatory research methods to evaluate adolescent ART adherence and SRH service access.

In line with these aims, this mixed-methods research project will have three components:

1. In-depth **qualitative** research with adolescents and key informants (caregivers, health and social workers) to explore: 1) how HIV-positive adolescents use, adopt and resist HIV care and treatment, and SRH services, including the factors and processes that influence these behaviours, and 2) how those caring for HIV-positive adolescents experience and perceive challenges and facilitators of ART adherence and SRH uptake.

2. Participatory **qualitative** workshops to involve adolescents as key stakeholders in:

- a) Exploring ART adherence and SRH service uptake,
- b) Assisting youth in negotiating the barriers and challenges that impede their desired retention in care.

3. A linked **3-year longitudinal quantitative** study of 1000 HIV-positive adolescents to assess risk and resilience-promoting factors for ART adherence, SRH utilization, and health outcomes in HIV care. This quantitative study is directly informed by the ongoing qualitative research.

The aims and methods for this study were developed through collaborative planning between HIV-positive adolescents, researchers from health and social sciences, UNICEF and South African National Departments of Health, Social Development, Basic Education and Women, Children and Disabilities, alongside clinical researchers at the Eastern Cape Department of Health, Frere and Cecilia Makiwane hospitals, NGO (Pediatric-Adolescent AIDS Treatment for Africa (PATA)), and CBOs (Kheth'Impilo, Raphael Centre, Small Projects Foundation and Keiskamma Trust). Ongoing consultations with these and other partners, including the Treatment Action Campaign and Kidzpositive, have underlined the importance of combining three information sources: in-depth qualitative research on the experiences of HIV-positive adolescents, particularly as these relate to ART and SRH; active collaboration with teens to develop relevant support tools; and quantitative survey methods.

The interdisciplinary and collaborative nature of this study, and its inclusion of a range of partners, aims to inform a broad-based, inclusive approach to HIV policy and programming. Since the study is planned in collaboration with HIV-positive adolescents, as well as state and non-state partners at local, national and global levels, it provides an opportunity to bring the experiences of youth into the policy arena. Policy and programming impact are integral aims of this research, and will be combined with ongoing results dissemination to NGOs, CBOs, government and health sectors, as well as to participating communities.

This study has a direct capacity-building aim, is led by two South African Principal Investigators (RH and LC) and includes several South Africa-based PhD, Masters and postdoctoral students. Conducted through partnerships at the Universities of Cape Town and Oxford, investigators recognise disparities in the production and dissemination of academic knowledge between the global north and south. In emerging publications, in presentations in a wide variety of fora, and in their teaching, training and supervision programmes, researchers grapple with the theoretical, methodological and practical implications of these discrepancies, including in the relationships between researchers and participants, and in the spheres of HIV research, policy and programming more broadly. Through close collaboration, including the design and adaptation of research tools, data analysis and writing, and presentation, the study aims to advance HIV social science in Southern Africa through training and support at all levels of project management. All staff take part in capacity-building programmes within the project (see section 13 for details).

2. Background

90% of adolescents living with HIV reside in Southern Africa, including those infected through mother-to-child transmission in childhood, and in youth (4). South Africa has the world's largest population of HIV-positive adolescents (1). ART provides an opportunity for long-term survival and wellbeing (5,6), but requires diligent lifetime adherence of 87-95% (7) to attain viral suppression and prevent viral resistance (8,9). Non-adherence is particularly hazardous in most low- and middle-income countries, where there are commonly only two drug regimens available in the public health sector (10). Non-adherence also presents a wider public health threat: transmission of drug-resistant HIV (11).



Adolescence is often a time of initiating sexual relationships, characterized by low levels of communication and openness (12). Many health programs use models of ‘therapeutic citizenship’ (13,14), proscribing disclosure of sero-status to romantic partners and others, the use of condoms during sex, and adherence to both ART and contraception. However, fear of rejection and internalized stigma result in low rates of disclosure to partners (15). In contrast, research has found low levels of adherence among HIV-positive youth (2), and demonstrated that AIDS-affected youth are more sexually vulnerable than other adolescents, with high levels of unprotected sex (2,3). Adherence and SRH service uptake are closely linked for HIV-positive adolescents, but their specific needs present challenges to resource-constrained health services (16). In order to develop effective interventions to support HIV-positive adolescents and improve their health outcomes, this research seeks to understand risk and resilience-promoting factors for adherence and SRH service utilization.

Despite the crucial role played by HIV-positive adolescents in their own retention in care and in preventing HIV transmission, few programming approaches have been led by youth themselves. Advocacy groups of people living with HIV (PLHIV) have repeatedly called for increased community participation in health service delivery and greater involvement of PLHIV in research (17). By leveraging the participation of HIV-positive adolescents in the design of youth-friendly support tools, the study will aim to further programmatic collaboration between service-users and service-providers and to enable adolescent-focused approaches to ART adherence and the uptake of SRH services.

2.1. State of the evidence at study inception in 2013

Limited research and interventions exist for adolescents living with HIV (ALHIV) outside of the United States (US) (18). The available, largely qualitative, work identifies challenges with romantic relationships, education, gender and family roles (often within homes disrupted by parental death), illness and depression (19,20). Preliminary reviews conducted prior to the field research beginning in 2014 have identified one published qualitative (21) and two quantitative studies (2,22) on adolescent ART adherence in sub-Saharan Africa. Nachege et al. reported adherence rates, but not risk or protective factors, in 154 adolescents in a private sector clinic programme in nine countries. Adolescent adherence was 21% at 6 months and 7% at two years, lower than that of adults. Evans et al. used clinic records in 7 NGO-supported clinics in Mpumalanga and Gauteng provinces. Older adolescents (15-19 years old) showed greater levels of unsuppressed viral load, virological failure and loss to follow-up. Two further adolescent studies in the region investigate linked outcomes: in a US-run specialist clinic in Botswana, psychological distress was associated with virologic failure amongst 692 adolescents (23); and in Uganda, 575 adolescents on publicly-funded treatment showed 2-year mortality of 8.5% (24).

The limited research on HIV-positive adolescents in sub-Saharan Africa reveals the complex challenges that arise from disclosure of HIV status, ART adherence and the uptake of SRH services. These challenges include individual-level (mental health, self-perception), family-level (parental death, parenting), community-level (norms about sexual activity, stigma), and structural ones (transition to care, poverty). ALHIV are confronted by difficulties associated with transition from paediatric to adult HIV care (25), HIV status disclosure to peers (26), the taboos associated with young people’s sexuality (27), parental AIDS illness and death (28,29), and the resultant poverty, stigma and bullying victimization (30). Longitudinal evidence also suggests that adolescents who have lost a parent due to AIDS are at heightened risk of psychological distress due to stigma-by-association (31). Teenagers must grapple with these challenges within caregiving arrangements that may include parental death and sickness (19,21). Beliefs regarding pollution and uncleanness – related to HIV and to medication side-effects – may create ambiguity in adolescents’ understandings of their own bodies and medical rituals, and this is complicated further by the experiential overlays of peer interactions, romantic relationships, the negotiation of gender and family roles, and the transition into and out of school.

Although research has been conducted on reproductive intentions and services for HIV-positive adult women in South Africa (32,33) there are significant evidence gaps on access to SRH and retention in HIV care for HIV-positive adolescents, both in relation to ART and SRH programmes. The available studies have found that access to ART has accelerated pubertal and sexual maturation (34), with 88% of HIV-positive 15-19 year old girls reporting sexual activity in Kenya (3). Research has also demonstrated inconsistent condom use, poor uptake of SRH services and repeated unintended



pregnancies and terminations among HIV-positive adolescents (3). While access to prevention of mother to child transmission (PMTCT) services has reduced rates of vertical transmission in South Africa (35), research on whether female HIV-positive adolescents are accessing these services and outcomes is limited (36).

Gender, age, environment (urban/rural) and route of transmission may all play a role in determining ART adherence and SRH service uptake, but further research is needed. HIV-positive adolescents differ in clinical and social markers, such as disease stage, neurological impact of ART, and disclosure to and by families. For example, vertically-infected adolescents have more resistant virus mutations, while those infected in adolescence are more likely to have been diagnosed through pregnancy, and almost nothing is known about those infected through South Africa's high rates of childhood sexual abuse¹.

This study of HIV-positive adolescents hypothesizes an interactive model of individual, family, school, structural and service-level factors influencing ART adherence and SRH service uptake as well as health outcomes in HIV care, potentially mediated by HIV-disclosure, stigma associated with ART and with adolescent sexual activity, and the potential side-effects of both ART and contraception. This model also presents an opportunity for research to inform policy and practice. Even when some risk factors may be unalterable (such as orphanhood), the identification of *modifiable* risk and resilience factors provides valuable evidence to inform interventions. This study will be the first to investigate risk and protective factors for ART adherence and its connections to SRH service uptake amongst HIV-positive adolescents in South Africa. Using both qualitative and quantitative methodologies, it aims to unpack the complex interplay between these health services and to use participatory and youth-driven methods to develop a tool to promote ART adherence and SRH service uptake.

3. Methodology

This study combines research and programmatic development, and asks the crucial questions: what are the lived experiences of HIV-positive adolescents in relation to ART and SRH, and what obstructs or promotes their ART adherence, uptake of SRH services, and positive health outcomes on ART? It uses participatory methods to ensure that adolescents are active agents in the conceptualization and design of a tool to facilitate ART adherence and SRH service utilisation.

This study uses mixed qualitative and quantitative methods to achieve two aims:

- (1) To identify and investigate risk and resilience-promoting factors for ART adherence, access to SRH services and positive health outcomes in HIV care amongst HIV-positive teenagers, through linked qualitative and quantitative studies.
- (2) To collaborate with HIV-positive adolescents, healthcare and social service providers to understand ways to improve adolescent ART adherence and SRH service uptake.

This study will use:

- i) Systematic reviews of risk and protective factors in ART adherence, SRH service uptake and internalised stigma for HIV-positive adolescents (completed); a systematic review of the effects of decentralising HIV care for health outcomes among youth in low- and middle-income countries (underway); and reviews of best practice in programmes for HIV-positive adolescents (based on the UNICEF Lessons Learned report on strengthening health services and outcomes for adolescents living with HIV, 2013);
- ii) Qualitative and participatory methods with adolescents and key informants (caregivers and service providers), followed by
- iii) Semi-structured interviews, ethnographic research and clinic observations with social and health service providers working in ART, SRH, PMTCT and Out Patient Department clinics. Methods iii) and iv) will be integrated with:
- iv) Quantitative longitudinal survey (n=1500, 3 years, with inclusion of HIV-negative community controls) to test risk and resilience-promoting factors for adherence, SRH

¹ Amongst those perinatally-infected, some have been on treatment from an early age, and new research suggests that around a third are 'slow progressors': surviving without diagnosis or care, but becoming ill around puberty (4).



service uptake, and positive health outcomes and to measure acceptability of the support tools developed in the participatory stage. Data collected during this survey will include: patient file data (i.e. viral load, CD4-cell count), clinic-level data (i.e. resources, such as counseling, staff/ patient ratio in the clinic) and individual-level panel survey data (i.e. potential individual, family, school and community-level factors) through tablet-administered questionnaires. Survey items were informed by extensive literature reviews as well as the qualitative component of Mzantsi Wakho. Where possible, standardized validated measurements were used. Cognitive interview methods ensured cultural relevance and understandability (37) of key measurements that had not been validated among teens in sub-Saharan Africa. Prior to data collection, the survey was translated, back translated and piloted with 17 HIV-positive teens. More than 20 leading academic and research experts on adolescent health research were consulted on approaches to interviewing HIV-positive adolescents, scales used in interviews and overall study design.

The three-year study combines qualitative, participatory and quantitative approaches. In 2013, research preparation comprised systematic literature reviews of risk and resilience-promoting factors for adolescent adherence and SRH use. It also included extensive consultation with government, NGOs, CBOs and our longstanding AIDS-affected Teen Advisory Group.

3.1. Preliminary consultations

The study design is based on both a literature review and extensive consultation with government and NGOs. Consultations have taken place with: UNICEF, UNAIDS, SA National Action Committee for Children Infected and Affected by AIDS, National Departments of Health, Social Development and Basic Education, SANAC, Health Systems Trust, Keiskamma Trust, Kheth'Impilo, Desmond Tutu HIV foundation, Kidzpositive, and the Treatment Action Campaign, as well as clinics and youth groups, and our Teen Advisory Group of AIDS-affected adolescents, who helped to guide previous qualitative and quantitative research on the previous Orphan Resilience study and Young Carers studies (www.youngcarers.org.za). The TAG group was established in 2008 and includes children and adolescents living in AIDS-affected families as well as HIV+ adolescents aged between 12 and 24, with whom we have conducted collaborative research since 2008 (approved by Oxford IDREC in 2008 and 2012 and included in UCT REC applications in 2009).

3.2. Avoiding stigma

A primary concern of this study is to avoid the potential for the research to stigmatise participants or their families. In light of high levels of HIV-related stigma in South Africa, the quantitative study will be presented within communities and organisations as investigating service access for teenagers who have had any extended contact with the health system. This ethically necessary methodological approach provides an opportunity to identify differences in risk and resilience factors between HIV-positive and HIV-negative adolescents, and to explore the need for targeted support. Recruitment processes and documentation will not mention HIV or AIDS, but will mention adolescent health and access to health services in general. This approach was emphasised as essential in community consultations prior to our past two research studies (Young Carers) in order to avoid unintentional disclosure and stigma, and has been approved for both studies by UCT's Health Sciences REC. In each community or location, both adolescents with HIV and those with other chronic illnesses or disabilities (such as asthma or epilepsy) or those accessing other types of health services such as home-based care will be included in the study, with purposive oversampling of HIV-positive adolescents. This will allow a non-stigmatising research process, as well as 'matching' of participants.

For the qualitative study, participants will be sampled in a range of ways, including through women's health clinics, trauma clinics, ART clinics, ART support groups and programmes for AIDS-affected and HIV-positive youth. While ART clinics and support groups will necessarily target HIV-positive youth, programmes for AIDS-affected teenagers may also include those not living with HIV. In these instances, all youth in the programme will be eligible to participate in the research, but engaging HIV-negative youth will only serve a comparative and ethical function – allowing researchers to observe similar and different experiences between HIV-positive and HIV-negative youth, and preventing participation-associated stigma.



3.3. Community partners: sampling beyond the clinic

All other known studies of HIV-positive adolescents to date have been based on ART clinic samples, which are necessarily biased towards participants more engaged in the HIV health system. If we are to effectively identify barriers to SRH uptake and ART retention, it is essential that sampling includes adolescents who have never accessed SRH or have ceased ART. Clinic-based samples will include a combination of state and NGO-run clinics (both primary health and antenatal facilities), as well as a variety of types of clinics: primary, ANC, OPD and women's health clinics. Key partners in accessing health facilities are facility managers and senior healthcare workers in 31 clinics, Keiskamma Trust (Hamburg, Eastern Cape), Small Projects Foundation (East London, Eastern Cape), Kheth'Impilo (King Williams Town, Eastern Cape), Raphael Centre (Grahamstown, Eastern Cape), Paediatric AIDS Treatment for Africa (PATA) and provincial government departments. Sampling will therefore take place in both clinic and community settings. Adolescents who have been lost to follow-up will be identified from clinic-specific defaulter lists, ensuring that the sample has an "intention to treat" approach to sampling by including all those that have initiated ART and then stopped. Non-clinic settings will include schools, children's homes, home-based care organisations and community-based sampling through youth programmes in villages or cities. Similar to qualitative research, the researchers will also be engaging (in a non-research capacity) with broader categories of youth in the community through programme facilitation and workshops. This is to ensure that the researcher team does not become associated only with HIV/AIDS, which could amount to participants incurring stigma through their association with the researchers. The CBO and NGO advisors, and healthcare workers (both clinic and community-based) participating in this research collaboration will guide researchers in selecting, approaching and accessing these community forums.

3.4. Qualitative methods

Why qualitative research?

Public health research and practice has cast the challenge of adolescent ART adherence and SRH service use in predominantly clinical terms, informed by a set of assumptions about youth, risk and compliance (5,18) with medical prescription. Yet the meaning and relevance of these constructs for adolescents on ART and using SRH services remains poorly understood and only superficially accounted for in many HIV treatment, care and support programmes. Exploring young people's practices of HIV treatment and SRH uptake as expressions of agency will deepen understandings of youth risk-behaviour, providing a potential opportunity to design, implement and integrate health programmes that are more responsive and ultimately more effective approaches to adolescent healthcare.

Public health programmes often position HIV-positive youth both as 'vulnerable victims' and 'reckless risk-takers'. While the former suggests helplessness, positioning youth as ill-equipped for self-care and independence (12), the latter invokes a powerful public health threat. Both assumptions necessitate ongoing, but paternalistic, intervention with the aim of encouraging, even policing, youth compliance (14,38). Constructions of youth irresponsibility and recklessness are in stark contrast to ideals of 'therapeutic citizenship' (13,14), now prevalent in HIV and SRH programmes. Here, high demands are placed on teenagers to practice 'responsible lifestyles'. This includes strict adherence to complex treatment regimens, disclosing to intimate partners, negotiating safer sex and accessing and adhering to family planning (often shorthand for avoiding parenthood) - all of which are complicated by context. Public health constructions of the behaviours, needs and desires of young people have powerful effects on the design, implementation, and ultimate efficacy of interventions. Despite the crucial role played by HIV-positive adolescents in their own retention in care and in preventing transmission of HIV, very few of the programmatic responses to improve their health-seeking behaviours incorporate adolescent participation in their design.

In the field of HIV programming, a growing body of anthropological and sociological research has demonstrated that individuals and societies may have entirely different perceptions and priorities to those assumed by public health models (39-42). The standard public health framework often positions human beings as isolated decision-makers, unencumbered by social circumstances. Little attention has been given to the social structures, obligations or uncertainties that shape health behaviours in ways that thwart or contradict medical prescription.

For example, it is possible that considerations of enjoyment, peer acceptance and dignity may



supersede those of long-term survival for some adolescents. We need to consider that secrecy may be an ‘embodied practice’ (43) for these teens – in other words, tactically withholding information regarding sexual practices and HIV status may be integral to negotiating the social world, in which norms of culture, gender, authority and sexuality may mitigate against strict compliance with prescribed health-seeking behaviours such as adherence to ART and contraception. The lived realities of these adolescents may be strikingly different from the adult disclosures necessitated by HIV support groups and ART adherence programmes. This study will consider the hierarchies of power within which adolescents live – of culture, generation and the healthcare system. Without in-depth engagement with the deeply held beliefs and understanding of young people regarding the meanings of SRH, chronic illness and bodily integrity, and their relation to different conceptions of an adult future – including fertility desires – we risk developing ineffective or irrelevant interventions based on inaccurate assumptions that do not account for the centrality of agency and locality in health-seeking behaviours, and that thus have little effect on improving adolescents’ adherence to ART and SRH services.

While urgent, evidence-based solutions are required to support ART adherence and improve reproductive health outcomes among adolescents, this research also recognizes the experiential and cultural complexities of living as a teenager in South Africa. This research therefore aims to generate high-quality data on adolescent ART adherence and understandings of SRH through beginning the first phase of the study with in-depth, multi-methods qualitative research.

Qualitative Research Methodology

A multi-methods qualitative study will be conducted with approximately 50 adolescents and 70 caregivers, healthcare and social care workers. It will explore the web of contextual and interpersonal factors that inform adolescent ART-adherence and utilisation of SRH services. Data collection methods will include in-depth thematic and narrative interviews, clinic observations, and action participatory exercises.

Programmatic interventions that include adolescent participation in youth-friendly health promotion tools are starting to be explored in Southern Africa with promising results (44–46). This is in line with global policy trends, which advocate for increased community participation in health service delivery, shifting of health promotion tasks to lay workers in order to address human resource shortages (47), and greater involvement of people living with HIV (PLHIV) (17). By leveraging the participation of HIV-positive adolescents in the design of youth-friendly support tools, the study will aim to further programmatic collaboration between service users and service providers towards a more holistic approach to youth health-seeking behavior.

This qualitative research will inform the development and interpretation of the quantitative survey, and the qualitative and quantitative research team members have planned a set of integrated qualitative and quantitative dissemination activities.

3.5. Quantitative methods

The findings of the qualitative research, for instance relating to the nature and significance of socio-cultural barriers that potentially impede ART adherence and SRH service utilisation, have informed the content of the quantitative survey, which is underway in 2014. Data collection includes both participant self-report and assessment of clinic records. The quantitative study will take place in collaboration with providers and researchers with extensive experience in pediatric and HIV research in the Eastern Cape.

The first stage of the quantitative survey intended to interview 600 HIV-positive adolescents, but interviewed 1,060 in total. The second and third stages of the quantitative survey will include a one-year and two-year follow-up, complemented by patient file data extraction.

The annual quantitative surveys will include 1) biomarkers of adherence; 2) a self-report questionnaire that is completed in the supportive presence of an interviewer due to potential low levels of literacy. This questionnaire will collect information about socio-demographics, health service access and potential risk and resilience-promoting factors for ART adherence and SRH service uptake. Questionnaires will be administered using audio mobile-assisted self-interviewing, with language and structure suggested by the Teen Advisory Group and adolescents living with HIV. In addition, 3) clinic-level data on both patient clinic records and services provided by the healthcare facilities will be collected from hospitals and clinics.



The quantitative study will focus on identifying risk and resilience-promoting factors for ART adherence (in comparison to other long-term medication), improved or positive health outcomes on HIV care, and understandings and uses of SRH services among adolescents in South Africa. It hypothesises an interactive model of multiple interlinking influences on adolescent adherence, with potential risk and protective factors including neurocognitive, health service-related, financial, psychological, familial, cultural, nutritional and peer-related ones, but will also include factors arising from the qualitative stage. By identifying potentially modifiable intervening factors, this study will aim to inform evidence-based interventions to promote ART adherence, improved health outcomes, and SRH service uptake. Please contact the research team for copies of questionnaire items at mzantsiwakho@gmail.com.

3.6. Characteristics of the Study Population

Sampling

Sampling for both the qualitative and the quantitative study recruitment will use the WHO definition of adolescents: aged 10-19 (1,48).

Qualitative sampling

The qualitative sample will be comprised of adolescents on ART and HIV-positive adolescents who are using SRH services, recruited from sites that provide health and social support services for teenagers living with HIV. These include women's health clinics, trauma clinics, ART clinics, youth programmes for AIDS-affected and infected teens and ART support groups. These recruitment sites are likely to produce a biased sample given that all adolescents will be currently accessing services. However, engaging participants over a year-long period will allow for the inclusion of adolescents who are both retained and lost in systems of care.

While the study will be presented to youth as being about 'your life and your engagement with health services', recruitment that is based in ART clinics or programmes for HIV-positive youth implies that the researcher is aware of the HIV-status of prospective participants. Presenting the study as being about 'your life and health' will make room for those who are not particularly open about their HIV-status to participate. Whether or not participants choose to openly disclose their HIV status to the researcher will be left up to them. Presenting the study as being broadly about 'health' will also allow a non-stigmatizing way to present the research to youth groups that include both AIDS-affected and infected teens. To ensure that participants feel comfortable and safe at all times, they will choose the time and place for research-related activities and un-structured engagements.

Additional participants in the qualitative study include healthcare workers, social workers, doctors, counsellors, teachers and caregivers. Adult participants linked to adolescent participants (i.e. their caregivers, health workers or social workers) will only be interviewed with permission from the adolescent.

Quantitative sampling

Due to a lack of data on the population of HIV-positive adolescents and low disclosure rates, identifying the composition of a representative sample of HIV-positive teenagers presents numerous methodological challenges. Extensive review and consultations with the Department of Health and UNICEF have identified poor availability of data. National-level data either excludes under-15 year olds (Statistics South Africa, 2011) or groups by 0-14 and 15-49 years (HSRC, 2009), thus precluding identification of adolescents. The 2012 UNAIDS Country Report for South Africa, using clinic-level data, is unable to distinguish between adults and children – and certainly not adolescents – receiving ART. In addition, there is a lack of data on proportions of adolescents infected horizontally, during childhood or adolescence, and of vertically-infected adolescents who have been informed of their status (49).

In summary, the 3-stage sampling strategy is as follows: 1) Probability-proportional-to-size selection of ART sites using the Department of Health register and initial clinic mapping results; 2a) Sampling of all adolescents on clinic registers that have initiated treatment including adolescents on treatment and in care, and adolescents who have defaulted or been lost to follow-up; 2b) Sampling of all vertically-



infected adolescents on clinic registers including those lost to follow-up and 3) One-year follow-up interview and 2-year tracking of clinic records.

Stage 1: Selection of ART sites using the DoH register. Using a clinic list from online databases of clinics and the Tier.net system recently established by the National Department of Health, (e.g. DoH, 2012) we consulted with healthcare providers in 84 clinics on the numbers of adolescents on treatment in each clinic. Probability-proportional-to-size random sampling from this list, stratified by area, was applied to reach the intended 600 cases. 32 facilities with more than 5 adolescents on treatment each were stratified in four groups by size: 10 facilities with 5-9 adolescents on treatment, 10 facilities with 10-19 adolescents on treatment and 10 facilities with 20-60 adolescents on treatment. The remaining 2 facilities, Frere and Cecilia Makiwane Hospitals, provide treatment for more than 300 adolescents each and were thus included in a fourth group.

Stage 2a: Sampling of all adolescents on clinic registers that have initiated treatment in the past three years. Using clinic records, all adolescents who have ever initiated treatment will be approached for voluntary participation in the study. These adolescents will include primarily adolescents infected through sexual transmission. Female participants recruited at ANC clinics will be eligible for the study if they are currently on ART as part of a PMTCT programme or if they initiated lifelong ART at pregnancy (based on current protocols in which pregnant women with $CD4 < 350$ must initiate lifelong ART). *Stage 2b: Sampling of all vertically-infected adolescents on clinic registers.* Stage 2 sampling will include patients currently on treatment, as well as those who are lost to follow-up - no longer attending clinics – estimated 14% per year in a recent South African study (22). All other adolescent adherence studies include only clinic attendees (2,23,24), but equally important is the inclusion of adolescents who have started treatment but who are no longer or not currently accessing HIV services (often called ‘defaulters’ or ‘lost to follow-up’). To date, no known adherence studies have included this group, and our sampling approach aims to do so in order to minimise potential bias towards adolescents more engaged in the HIV health system.

Stage 3: Annual follow-up interviews and tracking of clinic records including HI-viral load, CD4 count, morbidity, loss to follow-up and mortality for two rounds. All adolescents will be re-interviewed at one year and adherence will be measured through self-reports. We are hoping for sufficient funding for a third year of interviews. In addition, our clinic-based research staff will work closely with health facilities over 3 years to record viral load measurement and pill counts, and will use clinic records to identify regularity of CD4 cell counts, morbidity, loss to follow-up and mortality. Quality of clinic records ranges from excellent to poor, and those clinics with poor record-keeping have requested assistance with building capacity from our research team to reach Department of Health standards. This capacity-building will have a dual benefit of ensuring adequate records for our research, and providing support to under-resourced health facilities. Refusal rates and socio-demographic characteristics of refusers will be recorded and analysed to estimate the extent of bias in the sample. We are also exploring possibilities of collaboration with the NHLS for long-term follow-up of clinical outcomes.

All of the very few other known studies to date of adherence amongst adolescents have used clinic-based samples. This approach has methodological drawbacks as, by default, it excludes key groups of non-adherent adolescents who do not attend their clinic appointments (similar to examining truancy by using a sample of school-attending children and adolescents) or adolescents who do not actively engage with the healthcare system, for example by sending their caregiver to pick up their medication. In order to access both clinic-attending and other at-risk groups within HIV-positive adolescents, a range of targeted sampling strategies will be used, with recruitment in a range of locations, including antenatal clinics, ART clinics, testing sites and STI clinics, schools, children’s homes, home-based care organisations and community-based sampling.

The research team is aware of the need for extreme sensitivity around disclosure – particularly time since disclosure, and context of disclosure – 20% of pregnant adolescents in South Africa are HIV-positive and most are diagnosed as part of a Prevention of Mother-to-Child Transmission (PMTCT) programme. There are also complexities around partial disclosure (for example adolescents told that they are taking medicine for an unspecified illness), and ‘unspoken’ disclosure (where adolescents have guessed that they are HIV-positive but have never been told). Some adolescents recruited through clinics will be unaware of their own status, and our research team has developed research protocols (see below) to negotiate this complex ethical issue.



3.7. Recruitment and Enrolment

Recruiting from health facilities: Qualitative and Quantitative Studies

Approval from the Eastern Cape provincial Department of Health has been given to access state clinics and hospitals, and health records (adolescents and their caregivers additionally give consent each year for accessing of health records). Healthcare workers at the facilities will be informed of the researchers' presence and purpose in the clinics and will be encouraged to ask questions or make recommendations. Access to potential adolescent participants will be negotiated with the help of doctors, nurses and community healthcare workers/expert patients. While there are clear power inequalities between community healthcare workers and their patients, qualitative research among community healthcare workers suggests that they are often more trusted by adolescent participants than nurses or doctors (50). Recruitment for the quantitative study in clinics will be conducted by research assistants who will be assigned to work in particular clinics, where they will build rapport with healthcare workers and clinic staff. In the first place, clinic cards and patient rosters, provided with the permission of site staff, the district, and the provincial Department of Health, will provide information about eligible participants, including the numbers of eligible adolescents on treatment and their status (active, transferred or lost-to-follow-up). Adolescents who present for treatment at the ART, women's health, OPD and trauma clinics of healthcare facilities will be approached with information about the study, and a request to participate should they wish to. The process of obtaining assent and consent is clarified in detail in below.

Because teens may not have disclosed their HIV-status or sexual activity to their family, negotiating initial access through caregivers or guardians may risk violating their privacy. It is notable that the consent of a legal guardian is not required in order for a child older than 12 to initiate ART or access a range of SRH services. However, legal guardians will need to provide consent about their child participating in a research project about young people's experience of health services. Community health workers, who interact with families regularly, may also assist in negotiating legal guardian consent.

The question of consent is complex, especially given that adolescents are situated within the power structures of the clinic or hospital, communities and homes. Access and consent will need to be negotiated and re-negotiated on an ongoing basis, with continual re-enforcement that participation is voluntary and may be withdrawn at any time without repercussions. Importantly, researchers will ensure that any sign of discomfort or non-consent (whether verbal or not) will be interpreted as non-consent, following British Psychological Society guidelines in working with children.

3.8. Inclusion and Exclusion Criteria

Qualitative study

Participants are eligible for one-on-one research engagements (individual interviews, unstructured participant observation, participatory group workshops) if:

- a) They were first enrolled between the ages of 10-19 years ,
- b) They are currently initiating/or have previously initiated ART or are accessing SRH services, or they are attending a youth programme for AIDS-affected teens, and
- c) If they are below 18 years of age, they, and their legal guardian, have given written, informed and voluntary consent

Participants are eligible for group research activities (focus groups and participatory exercises) if:

- a) They were between the ages of 10-19 years when first enrolled,
- b) If they are below 18, they, and their legal guardian, have given written, informed and voluntary consent,
- c) They are willing to discuss their experiences of HIV and sexual health with the researcher and fellow participants, and
- d) They sign a confidentiality agreement stipulating that they will not share what is discussed inside the group-space with others.

Quantitative study

Participants are eligible for the quantitative study if:

- a) They were between the ages of 10-19 years old at baseline (born between 01/01/1995-31/12/2004),



- b) They have accessed/are accessing treatment for HIV (antiretrovirals), and
- c) If they are below 18, they, and their legal guardian, have given written, informed and voluntary consent.

3.9. Qualitative Research Procedures

The qualitative study will engage adolescent participants over a 36 month period, using multiple methods to explore their treatment decisions and retention in HIV and SRH programmes. A range of participatory and more structured data collection methods will complement observation and un-structured research. Group-based activities will form part of ongoing programme facilitation with HIV-positive youth, which researchers will conduct in collaboration with local HIV/AIDS organisations. In addition to working with youth participants, interviews will be conducted with caregivers and healthcare workers, who may or may not be those caring for or providing services to the teenage participants.

This study design aims towards a minimally invasive, participatory research methodology (51) that will facilitate the collection of triangulated qualitative data. The research methodology, while systematized and well-substantiated, will also be adaptive and responsive to contextual, ethical or practical demands.

Existing qualitative research on adolescent adherence to ART has often been conducted with caregivers (52) producing research *about* children, but rarely *involving* children (53). The reasons for avoiding research with adolescents pertain to ethical considerations over their vulnerability and concerns that data obtained from children may be less reliable. However, there is a growing body of literature arguing that adults cannot serve as proxies of adolescent experience and that young people can be competent participants, as long as researchers facilitate their participation with caution and sensitivity (51).

In South Africa, seminal studies have facilitated focus groups with HIV-positive adolescents on ART (21,54) and conducted qualitative interviews with youth and their caregivers (54). Mixed methods approaches conducted within a more extensive time-frame will facilitate rapport between researchers and respondents, thereby improving the validity of data collected and allowing for triangulation of methods.

Qualitative data for this study will be collected through: ongoing participant observation, semi-structured in-depth interviews, clinic observation, body-mapping, and participatory group workshops. More detail on how, and at what stage, of the research process these methods will be implemented is provided below. The use of a variety of methods, both traditional and innovative, may help to address some of the ethical and methodological issues that arise in conducting research with adolescents (55). It may help sustain participants' interest, guard against the bias of using a single method, triangulate and crosscheck data, determine the efficacy of different methods (55), and negotiate a balance between non-invasive participation and guided interaction.

Rapport-building and participant observation

Identifying and recruiting participants for this study will require careful, creative and adaptive strategies, which give full consideration to the ethical and methodological challenges of working with teenagers, speaking about sensitive topics such as sex, gender, violence, health and illness, and entering the research setting as an outsider. The research team has established partnerships with local HIV/AIDS organisations, primary healthcare clinics, and hospitals, all of which will advise on the most appropriate way to approach potential participants. The research design will also be informed by ongoing consultations with AIDS-affected and HIV-positive teenagers, both through activities with the long-standing Teen Advisory Group and the research team's involvement in facilitating programmes for HIV-positive youth. These interactions will provide an opportunity to learn how young people prefer to be engaged, what their interests and concerns are, and what discursive strategies they use to understand and to describe sexuality and health.

Research will begin with an 8-week period of rapport-building, during which researchers will build relationships with HIV-positive adolescents through ongoing participation in NGO programme activities, observation in primary healthcare clinics, and shadowing community health workers. As researchers build relationships with adolescent patients, they may also participate in aspects of their daily life. Researchers will also be facilitating a range of extra-curricular programmes, including art-



making, health-related workshops and skills-building with HIV-positive young people over this period. The numerous interactions with HIV-positive youth, both inside and outside of health facilities, will allow opportunities for more structured research participation. During the rapport-building phase, both health-facility and programme-based youth will be aware of the researchers' position as a participant observer. Permission to access state health facilities was obtained from the South African government. Researchers will always introduce themselves as researchers to those who enter the 'scene' of study.

During the period of initial rapport-building and observation, adolescents will decide if they would like to participate in more ongoing (one-on-one un-structured time with the researcher) and/or structured (workshops, focus groups or interviews) components of the research, and offer suggestions of how, when and where they would like to engage with researchers. In cases in which participants indicate an interest in participating, the researcher will begin negotiating legal guardian and/or other forms of adult consent in consultation with the adolescent (as explained in the section on consent below). Another key aim of the rapport-building period will be to recruit Xhosa-speaking key informants to assist with access and translation. These may be teenagers or adults, depending on what is appropriate for the setting, and what participants are most comfortable with.

In light of low disclosure rates, the possibility that legal guardians may not know about adolescents' HIV-status or SRH service access, and the fact that some of the recruitment sites may also include HIV-negative teens, recruitment materials and consent forms will not make reference to HIV. One-on-one interviews, which will lead from initial rapport-building and group activities, will be guided by participants, and may include walks, visits to the family home or attending the clinic together.

During the period of rapport-building, participants will be informed of a range of upcoming, more structured research activities in which they could choose to participate. Participation will be voluntary and may be withdrawn at any time without consequence. The order in which activities take place will be negotiated in field and may occur simultaneously for participants who choose to take part in more than one activity. Research activities will be introduced as ways for young people to tell stories about their lives, their bodies and their health, and will not make explicit mention of HIV. The extent to which teenagers reveal their HIV-related experiences will be left up to them, and may depend on the nature and context of the research activity.

Research activity 1: In-depth interviews

Adolescent participants may volunteer to participate in a series of (largely informal) interviews, some more lengthy than others. These interviews will be interspersed and sometimes merged with ethnographic activities, such as visits to adolescents' homes, playing, cooking or visiting the clinic. The participant will choose the interview location and, with their consent, some of these interviews may be recorded, although it is more likely the researchers will take notes. Initial interviews will ask about the *life histories* (56) of respondents, beginning with an open-ended question like, 'Can you tell me the story of your life?' and probing where necessary. These initial interviews will elicit information about respondents' upbringing, when they were diagnosed with HIV, how they discovered their status, their experiences of SRH services, their past experiences of sexuality and intimate relationships, and the current members of their household. Life histories provide a vital context through which to understand respondents' behaviour.

Life history narratives involves the narration of one's life experience, including highlighting the most important aspects in the domain of inquiry (57). Such an approach provides interviewees with a degree of agency to discuss what they feel is important and interpret their life stories, and can capture nuanced and holistic perspectives of risk and agency (58,59). It is a way to gather data to improve understandings about how adolescents see themselves, to shed light on items that participants might not otherwise disclose, and for participants to answer questions that researchers might not think to ask (59–61).

Follow-up interviews will explore participants' daily lives, engagement with HIV and SRH services, treatment practices, and perceptions and experiences of HIV, particularly as they pertain to major health events such as an opportunistic infection or pregnancy, adherence struggles and successes. Where respondents have also taken part in body-mapping, interviews will be informed by the themes and ideas that emerge through these media.



All interviews will explore a list of themes, but will be minimally-structured. Using open-ended questions is more likely to evoke a genuine, spontaneous narrative as well as eliciting un-anticipated findings (62). Where necessary, gaps will be filled with more follow-up questions or prompts (63). Where feasible and consented to, researchers will also conduct interviews with respondents' guardians and healthcare workers to explore their perspectives on respondents' health-related practices. Separate interviews will also be conducted with 68 healthcare workers, social service providers and guardians about their experiences of caring for adolescents on ART.

Research activity 2: Focus group discussions and participatory action research

PIs and other researchers on this project have extensive experience facilitating workshops with children, adolescents and adults. A range of participatory research activities that use visual media to explore teenagers' experiences of ART and SRH will be conducted through day or weekend workshops or through two-hourly sessions connected to support group activities.

These activities may include a combination of HIV-positive, HIV-negative and 'status-unknown' participants. With participants who have not disclosed their HIV status, confidentiality will be maintained. In our past research, this has taken the form of framing questions about illness and medicines in the more general sense of chronic illness and treatment, rather than with specific reference to HIV and ART. A confidentiality contract is discussed and signed by the group in the first session of the workshop.

Given the effect of peer influence on adolescent behaviour, researchers will need to consider the extent to which focus group responses are shaped by peers in the group. Respondents may not be willing to share the intimacies of living with HIV with their peers, in which case participatory strategies will be adjusted to accommodate one-on-one as opposed to group reflections.

Research Activity 3: Clinic observation and shadowing of healthcare workers

Healthcare workers constitute a vital vanguard in the provision of HIV and SRH care and treatment services to HIV-positive adolescents. Through close and respectful observation of the experiences and practices of healthcare workers, this research will explore the challenges that they experience in their clinical encounters with HIV-positive teens. Permission to 'shadow' healthcare workers who encounter HIV-positive adolescents through their work at ART, Women's Health, OPD and Trauma clinics, was sought and obtained from both hospital management, nurse managers, and the healthcare workers themselves in each of the five facilities in which qualitative researchers have worked since 2013. If this permission is granted, researchers will shadow healthcare workers, with a particular focus on nurses, the front-line care providers in most of these clinical contexts. Through clinic observation, supplemented with in-depth interviews, researchers aim to learn about how nurses experience consulting, treating and supporting the teens in their patient cohorts. They explore understandings of the greatest facilitators of, and barriers to, ART adherence and the uptake of SRH services, as well as their intimate and direct knowledge of how the services which they provide may potentially be improved to support better health outcomes among teenagers.

Integrating and linking with quantitative methods

To date, research on ART adherence and SRH decision-making among HIV-positive children and adolescents has been minimal, and what is available has been characterized by a sharp divide between qualitative and quantitative studies. Clinic-based quantitative research has been unable to account for the subtlety and complexity of influences on adolescent ART adherence and SRH decision-making, nor has any known research included adolescent participation in the design of surveys and support tool.

This study has the further aim of directly informing the design of a linked quantitative study of barriers and facilitators for HIV-positive and -negative adolescents, and to utilize this larger sample to test for acceptability the adolescent-designed support tool described above. Sequencing of research has allowed data collected and analysed in the qualitative study to contribute directly to the quantitative study – not only in what questions are asked, but also in how they are asked and in what order. By exploring the cultural, generational and gendered structures of authority in which adolescents are embedded, and by eliciting important information about the way in which adolescents understand, live and speak about



key concepts such as HIV testing, ART medication, contraception and fertility desires, quantitative research has been guided by emerging qualitative findings.

By working collaboratively, qualitative and quantitative researchers have integrated the study design and adapted research tools. This cooperation will continue throughout data collection, analysis and dissemination.

3.10. Quantitative Research Procedures

The quantitative data collection process will include: (1) participant interviews, (2) secondary data from patient records, and (3) facility-level information.

Quantitative Measures – Adolescent Questionnaire

The questionnaires are drafted after consultations with over two dozens of experts in the field of adolescent health and piloted with HIV-positive youth in South Africa and the region. Measures use (where available) tools validated in Southern Africa (64–66). All measures have been piloted prior to use.

Digital devices – 7-inch tablets – will be provided to participants for completing the questionnaire. Trained research assistants will sit with adolescents to demonstrate how to use the tablet and to guide the participant where necessary. The participant will then be offered the opportunity to complete the questionnaire autonomously. The name or contact details of the participant will not be included in the questionnaire – each individual will only be identified through a unique participant ID. Data will later be collated, but the confidentiality of the participant will be upheld. The use of mobile devices – 7-inch tablets – will increase the accuracy of the answers given by participants. Adolescent participants of multiple studies using mobile devices have reported that this method allows for more truthful answers and greater confidentiality (67–70). A study among students in South Africa concluded that most students perceived the electronic questionnaire to be a more confidential method of answering questions about sex: 77% of those using electronic questionnaires and 51% of those using paper questionnaires (71). The cellphone number made available in recruiting material will only be accessible to the research team. If participants leave a ‘please call me’ message (a free text message), only members of the research team will contact them. Should participants share additional contact details with researchers (Facebook, Whatsapp, etc.), this information will be kept confidential.

(i) *Outcome measures: Adherence.* For adolescents who report having been prescribed any chronic medication, a triangulated approach to measuring ART adherence, found to be the most reliable method amongst youth (72,73) will be used. It is important to measure adherence across a sufficient but feasible time period. Our systematic reviews of ART adherence amongst adolescents, adults and children (in preparation) found either cross-sectional surveys using retrospective reporting of general adherence (74), or of past 3 days (75,76) with a small number of studies using pharmacy refills up to 24 months (2). Although pharmacy refills are only a moderately reliable indicator of ART adherence, it is important to measure adherence over a longer-term period by identifying change over time. This study therefore proposes the use of three methods for assessment of adherence. 1) each participating adolescent will receive visits, including a questionnaire completed with the help of an interviewer. These will collect information about ART adherence, socio-demographics, service access and potential risk and resilience-promoting factors, using standardised instruments and triangulating measures of adherence (77,78) and used in South Africa (79–81); 2) viral load and CD4 cell-count (where available) measures; 3) medication refill rates (82). Viral load, CD4 and medication refill rates will be recorded from patient files at each facility where they are receiving care.

Sexual and reproductive health outcomes will be measured using standardized tools from similar Southern African studies and studies among HIV-positive adolescents in the region and globally. Sexual health outcomes will include measures of: (i) sexual activity: debut, current levels, (ii) types and number of partners (83) condom use by partner type, (iv) forced sexual experiences/ sexual abuse, (v) transactional sex, and (vi) HIV knowledge and attitudes. Reproductive health outcomes will include (i) parenthood ideations and plans, (ii) pregnancy – past and current, and use of contraception (hormonal, condom, termination of pregnancy, etc.). Through open-ended questions, the survey will explore experiences of adolescents in accessing SRH services and potential reasons for dropping out or defaulting.



Health outcomes on HIV care will be recorded from patient files at each facility where participants have received care within the study area. In addition to viral load and CD4 cell counts, health outcomes for HIV care will include measures of WHO disease stage, presence of TB symptoms, any new medical diagnoses (morbidity), and mortality. Approval for accessing health records has been obtained from all healthcare facilities, from the Provincial Department of Health and from all adolescents and their primary caregivers in the survey.

Potential risk & resilience factors: (Figure 1) Individual factors include mental health issues (84), HIV-related neurocognitive impairment (23), physical and learning disability (85), level of treatment understanding, and beliefs in myths or fears around HIV or medication (86). *Gender, sexuality and sexual health factors* are highlighted as important by HIV-positive adolescents (87). Potential factors include transactional sexual relationships and challenges around disclosure to sexual partners, particularly unintended disclosure via taking medication (21). Teenage pregnancy and enrolment into a PMTCT programme may positively or negatively impact adherence. Studies of PMTCT programmes report low adherence, and a qualitative study of teenage mothers reported overwhelming fears of confidentiality breaches by obstetrics staff (88). In addition, contraceptive and sexual health services use may impact adherence, with reports of healthcare staff strongly critical of adolescents wishing to have sexual relationships and plan families.

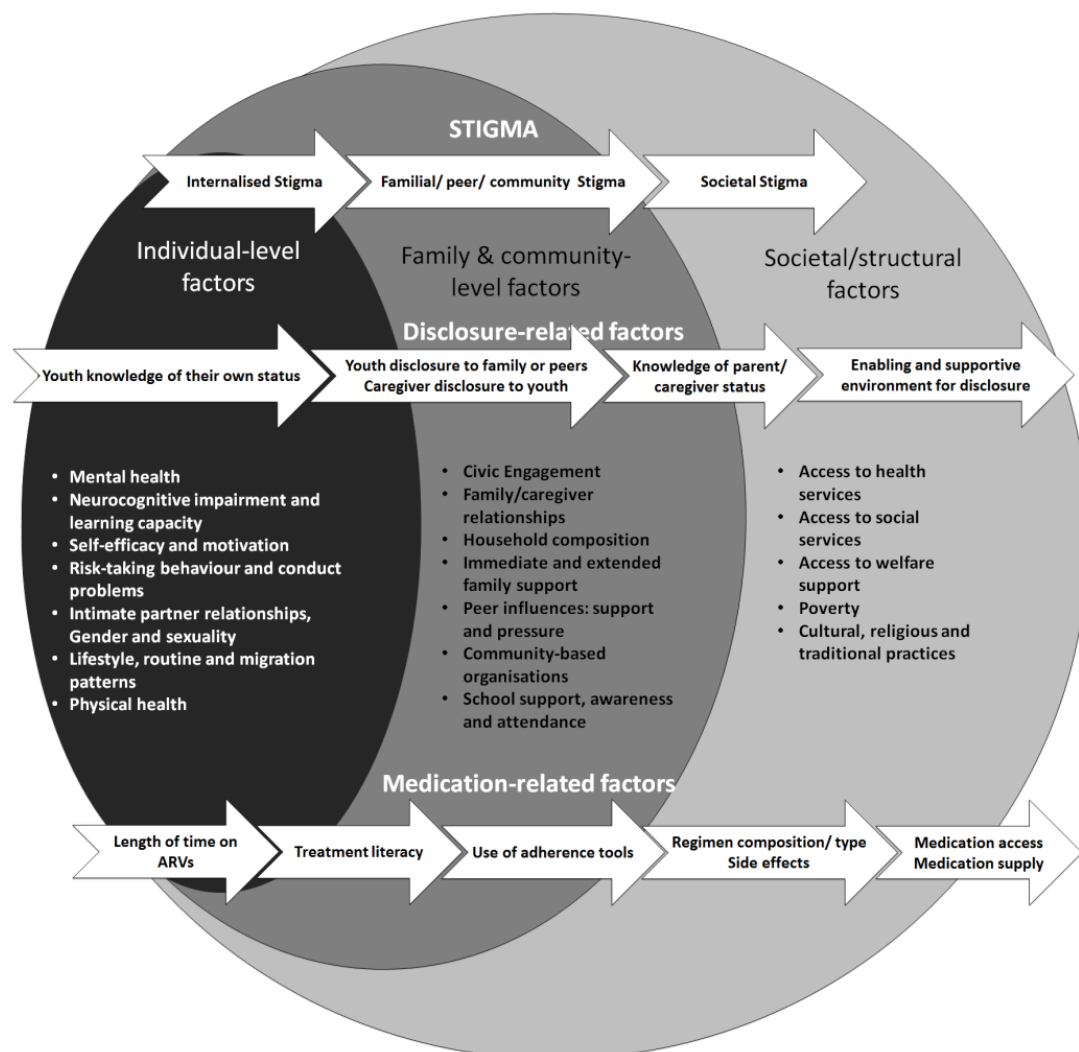
Family and community factors: Qualitative studies suggest that *family relationships* and extent and nature of primary caregiver involvement may be crucial (89). Potential factors will include HIV disclosure by and to families (and timing and nature of disclosure) (90), migration, changes of primary caregiver due to death and illness, physical, emotional and sexual abuse and domestic violence (91).

School, peer & community factors may be particularly important as adolescents develop social identities (92). Potential factors include bullying, stigma and support inside and outside school (93), school attendance and achievement, drug and alcohol use, gang membership and incarceration.

Structural factors: Social protection and economic factors include socio-economic status, food security (94) and access to services such as state grants and social services. Distance and transport to clinics have been shown to impact adult adherence (95), and may present even greater difficulties for adolescents with fewer financial resources. *Antiretroviral, HIV treatment, care and support service factors* include use of traditional healers, the social position of those who may recommend alternatives ART (96), complexity of regimens and palatability of medication. Side-effects of medication (such as fat redistribution – lipodystrophy) may be especially embarrassing for adolescents in their peer environment. Prior research indicates that experiencing lipodystrophy and other side effects of HIV medication can affect people's self-esteem, sense of control, social and sexual relations, and can contribute to demoralization, forced disclosure, and the decision to stop treatment (97,98). Access to HIV support services such as support groups, youth clubs and adherence monitors, may be an important predictive factor. In addition, adolescent experiences in health services may be relevant, as qualitative studies report adolescents treated with disapproval and contempt by healthcare staff (99).

Based on the initial findings of the qualitative research and participatory workshops on tool development, the final step of quantitative research will involve testing the feasibility of a tool for young people developed by adolescent participants. A quantitative appraisal of the tool's accessibility, potential for reach and exposure will be conducted with a sub-sample of the expected sample. Based on the main content of the tool, short-term outcome measures shall be selected and measured during the initial data collection and feasibility step. These outcomes will most likely include adherence to ART (past-month recall) and utilization of SRH services (primarily pregnancy, contraceptive use and TOP services).

Figure 1: Hypothesised risk and protective factors for adolescent ART and SRH use



Quantitative Measures – Retrospective and Prospective Patient Records

In light of potential poor treatment and health literacy rates among patients on ART, the questionnaire information on CD4, viral loads and medication refills (2) will be complemented with data recorded from patient files. This data will be recorded using a protocol previously applied in other studies among adolescents on ART (93) adapted to patient files in the facilities that participate in the study. Participant self-reports through the questionnaire and data extracted from patient files will be linked through an anonymous unique identifier. Data will be extracted from patient files at baseline and on an annual basis for two years (2015-2017).

Quantitative Measures – Clinic-level information

An extensive literature review on factors affecting adherence and access to SRH points to a series of clinic-level factors that affect both. Factors including type of facility (decentralised, i.e. primary clinic or community health centre vs. centralised, i.e. hospital), level of training for healthcare workers, clinics-based nutrition programmes, staff/patient ratio, distance of healthcare facility to patient home, provision of counselling, and ease of access to patient records are associated with improved adherence or access to SRH services (literature review is in process). To that end, the research team will develop a clinic-level “profile” of literature-informed indicators, which will be linked to each patient who receives care in that clinic during data analysis. Clinics will not be uniquely identified, but dummy variables will be computed based on the clinic-level factors for participants who receive care in that facility.



3.11. Data entry, safety, monitoring and storage

Data quality will be ensured through rigorous training, spot-checking during data collection and during data entry, which will happen in parallel with data collection.

All data collected will be automatically uploaded into a secure server through an open-source software platform – Open Data Kit (www.opendatakit.org), which will be anonymized prior to data analysis to ensure confidentiality of participants. Regular backups of all data will ensure that the database is safe.

Every effort will be made to maintain participants' confidentiality. All data will be identified by a unique participant number and kept in confidential files. Identifiers will be removed from interview transcripts, questionnaires and original recordings, and coded so that only the researchers can access identifiable information. No individual identifying information will be collected or disclosed in reports, publications, or presentations.

Participants will be notified, both verbally and in consent forms, that confidentiality may be breached if the participant is considered to be at significant risk of harm. This includes abuse, neglect or family violence (further details below).

Electronic versions of transcripts, recordings, questionnaires and field notes will be kept in a password-controlled electronic file, accessible only to the researchers. All study documentation including questionnaires and informed consents will be kept in locked cupboards or password protected hard-drives/ computers. Consent documents will be kept separately from questionnaires. Hard-copy data (transcripts, field notes and questionnaires) will be coded – removing identifiers so that only the researchers are able to link it to individuals using a study master list available only to the project investigators and fieldwork project managers.

Paper-based data will be stored within the secure offices of the AIDS and Society Research Unit at UCT once completed. Additional secure storage for data will be set up in the study location – Eastern Cape – for anonymised paper-based data such as patient file data extraction forms. Electronic data from tablet-based data collection will be stored in a secure, password-protected encrypted server at the University of Oxford.

3.12. Data Analysis

Qualitative Study

Qualitative data analysis will adopt key procedural principles from grounded theory (100). Data collection and analysis will occur simultaneously, 2.) Analytic codes and categories will be developed from the data and not from preconceived hypotheses, 3.) The analysis will use constant comparison to compare similarities and differences across and within themes, thereby limiting bias, 4) Theoretical memo-making will occur alongside analysis and during the write-up, and 5) The sample will be selected for the purpose of theory construction as opposed to the representativeness of the given population, following theoretical sampling, common to grounded theory (101). Multiple researchers will review the coded data in order to verify findings. The characteristics of the sample recruited will be thoroughly and clearly presented to ensure that others may assess the credibility and transferability of findings (102). Although safeguarding the confidentiality and anonymity of the participants is paramount, analysis will document the overall pool of available teenagers, caregivers and healthcare and social support workers that were deemed eligible for participation, how many refused to participate and their reasons for refusal.

Quantitative Study

Data analysis will be undertaken in SPSS, AMOS, R, STATA and MPlus where needed. Where relevant, mixed-method data will be used. All analyses will control for socio-demographic co-factors and potential confounders. The following research aims are indicative of analyses and questions, but further questions will of course be examined, and are responsive to policy issues and needs.

Research aim 1: To examine differences in rates of adolescent adherence and access to SRH amongst key subgroups will use descriptive statistics, multivariate regression and ANCOVA.

Research aim 2: to identify which risk and resilience factors predict ART adherence and SRH uptake



amongst adolescents, to investigate interactive pathways, interactions and cumulative effects between factors will use multivariate regression, and a set of statistical techniques previously utilised in our longitudinal studies of AIDS-orphaned children. These include log-linear modelling (103), testing of interaction effects in regression models, mediator and moderator analyses in path analysis, and structural equation modelling – which allows simultaneous analysis of multiple predictors, intervening variables and outcomes(104).

Research Aim 3: To examine whether risk and resilience factors and pathways differ among subgroups of HIV-positive adolescents will use ANOVA, SEM and log-linear modelling to compare subgroups;

Research Aim 4: To determine whether HIV-positive and HIV-negative adolescents have different exposure to risk and resilience-promoting factors, and to health services will use multivariate regression and ANCOVA.

Research Aim 5: To determine whether HIV-positive adolescents have better or worse health outcomes when receiving HIV care at decentralised healthcare facilities, compared to routine care at centralised facilities will use survival analysis and multivariate regression.

Research Aim 6: To determine which service-related factors predict better health outcomes for HIV-positive adolescents receiving care at decentralised healthcare facilities will use SEM and hierarchical linear modeling.

Finally, the quantitative study will analyze the feasibility of the tool developed through participatory workshops, focusing on participant satisfaction and potential for adherence/exposure to the tool by HIV-positive adolescents. Descriptive statistics and regression will be used to identify which tool features are most appropriate for HIV-positive adolescents.

4. Risks and Benefits for Participants

This study aims to investigate risk and protective factors for ART adherence, SRH service uptake, and HIV care outcomes among adolescents in South Africa. We will be interviewing adolescents as young as 10 years old, and because the interviewers are adults, this presents a significant power inequality. This power differential is further complicated by class and language distinctions between researchers and study participants. These inequalities will be sensitively and carefully considered. Building trust and rapport with participants, and explicit reflexivity during data collection, data analysis and reporting of the study will all be essential in generating high-quality data and research findings in a non-coercive setting. When fieldworkers are employed and trained for the study, training will focus on building social sensitivity towards unequal power relations. By explicitly encouraging social sensitivity and awareness of our team's roles as researchers and social positions, we will reduce feelings of inequality and prevent coercive work with participants. It is also important to recognise that in a positive and youth-centred research environment, adolescents may benefit from the opportunity to interact with adult facilitators. Adolescents may appreciate a trusted adult to confide in and an opportunity to access information in a confidential setting. We do not anticipate that the interviews will cause any additional distress either to adolescent participants or their caregivers. However, in order to reduce any risk of respondents becoming distressed, guidelines have been developed (see below).

We note that – in all our previous studies – a range of complex cases of children and youth in extreme need have arisen from our research (partly because this is often the first opportunity a child has to discuss in detail their lives, we have very high levels of disclosure regarding rape, abuse and other traumatic life events and conditions). All cases where a child or adolescent may be at risk or is experiencing significant harm are discussed in detail with the qualified South African child protection social worker on the team. Given the very low availability and variable quality of social services in some low-income areas of South Africa, close supervision by the social worker is provided of all cases, referrals and any supportive action taken by the team.

- 1) Qualitative data collection tools will be participant-driven and youth-oriented. Quantitative interview materials administered through tablets include teen-friendly images and language designed to engage youth in a comfortable and open style.



2) Many of the adolescents in this study who are HIV-positive will have disclosed their HIV-status to the researcher in confidence. This study recognises the duty of researchers to uphold participants' constitutional right to privacy and dignity, particularly in a context where HIV remains highly stigmatised.

Therefore, in line with the National Health Act (2004) and legal guidelines released by the Open Society Foundation (105) as well as the former AIDS Law Project (2003), researchers will not disclose the status of adolescent participants without their explicit consent. All researchers involved in the project have been trained on strict confidentiality and disclosure guidelines and have signed a fieldwork agreement that includes this information. In cases where HIV-positive participants report having unprotected sex with their partners, resulting in a tension between the participant's right to confidentiality and the public health impetus to protect at-risk partners, researchers will adopt the following procedure as per recent guidelines: 1) advise the adolescent about the risks of unprotected sex for both their own health and the health of their partner, 2) encourage voluntary disclosure and safer sex and provide support to the participant, 3) suggest a joint session with a trained HIV/AIDS counsellor who can assist the adolescent in disclosing or negotiating safer sex, 4) if these approaches are not successful, the researcher will inform the participant that they will be informing a doctor or healthcare worker familiar with the adolescent, explaining the ethical obligation to do so. This is in line with section 14 (79) of the National Health Act, which makes provisions for disclosure if non-disclosure amounts to a serious threat to public health. When consent for participation is sought, participants will be made aware that their confidentiality will be breached only to prevent grave harm and never before consulting with them. If researchers have to resort to informing a healthcare worker of a participant's unsafe sex practices and non-disclosure, it will be recommended that the relevant healthcare worker follow established best practice for HIV disclosure outlined in published legal guidelines (105).

- 3) Given the complex nature of adhering to long-term medication, this study will identify a number of adolescents who have defaulted or not yet initiated life-saving medication, including ART or TB medication. In cases when participants report non-adherence, the researchers will highlight the importance of adherence to medication and encourage the participant to consult their healthcare workers and adherence buddies. Specific information obtained on the dosage, adherence patterns and other influencing factors for each individual will not be shared with their healthcare worker or legal guardian in order to maintain participant confidentiality. However, adolescents experiencing symptoms of TB, pneumonia or any other opportunistic infection will be referred to a healthcare professional. Given the risk of significant harm, this constitutes a legitimate breach of confidentiality. Participants will be told at the consent stage and in information forms that there are limits to confidentiality when someone is deemed to be at risk of significant harm.
- 4) In order to protect confidentiality of the participants and protect them from the stigma associated with HIV/AIDS, each interview will be conducted with as much privacy as possible in a space chosen by the participant. In addition the study will be presented within communities as investigating health and social services experiences generally, rather than being an HIV-specific study.
- 5) As in all research with children and adolescents, there is a possibility that participants will take the opportunity to disclose difficult living circumstances or abuse. This study recognises that researchers have a responsibility towards children who may disclose information showing them to be at risk of severe harm. Recent research in South Africa has carefully considered these issues. Guidelines are set out by the HSRC/UNICEF study on children's psychological adjustment in South Africa (106) and in the South African Children's Institute/ACCESS Child Participatory Poverty Research (107). These promise confidentiality except when a child is shown through the research to be at risk. In cases of risk, and with the consent of the child, they will either be referred to organisations that can provide assistance (ACCESS study), or their caregivers will be told (UNICEF study). The choice of these options will be made in consultation with the social worker and psychologist on the research team, and on the basis of best outcomes for the child. Most research with vulnerable children in South Africa considers it an ethical principle to provide help for children whom the research identifies as in need. For example, research undertaken by the Medical Research Council Unit for Anxiety and Stress Disorders routinely refers children to child psychiatric services or to the University of the



Western Cape Child Psychology clinic in cases in which there is need for these services (108,109). A University of Cape Town study on child mental health referred children in need to social services, as does research in the Africa Centre on HIV-positive caregivers and infants (110). Researchers on this team have been investigators on three previous studies with AIDS-affected children in South Africa. Based on these studies and on protocols devised from research studies with similarly vulnerable groups (111), the following protocol is proposed:

- a) Informing all participants at the consent stage that everything said will be confidential unless it becomes clear that they are at risk of significant harm.
 - b) If information is disclosed that suggests that the participant, their sexual partner, or a member of the household is at risk of significant harm, the researcher will discuss concerns with the child at the end of the interview before any further action is taken.
 - c) If the participant or a member of their close network is at risk of severe harm, the researcher will discuss the possibilities for referral with the child participant. If the child does not consent to sharing of information, and the harm is not considered to be significant, the child will be given information about self-referral agencies such as ChildLine SA.
 - d) However, if the harm is considered to be significant the researcher, assisted by employed fieldwork volunteers, will consult with social services or other organisations. If the decision is made to take action, the participant(s) will be informed (*Please see attached draft referral form*). If referral requires disclosing the child's HIV-status, then the procedure described in 2) above should be followed.
- 6) This study has an obligation to plan for the possibility of participants, child or adult caregiver, becoming distressed. All interviews will be trained and experienced in working with affected children and families. The research team includes a social worker, a psychologist and HIV counsellors who will be available to supervise researchers and help them to discuss issues with the families and children following the interviews. As discussed above, if there is a need for a participant to access more extensive support (such as consulting a counsellor or attending a clinic) referrals will be made (Please see sample referral letters in the appendices).

The research team is obligated to any participant who may feel distressed following the study or who may reports behaviours that require follow-up counselling. All interviewers are trained and experienced in working with affected children and their families. If a participant becomes distressed, interviewers will be available to discuss any issues he or she may have, and make referrals if required. Interviewers will also contact the project manager by cell phone when they have a particular concern, or when a participant requires more information or their case requires further discussion. Furthermore, in cases laid out in question 13.a (i), additional sessions might be needed to ensure that risks identified are addressed by participants.

Risks to Researchers

There are general risks in doing fieldwork and we ensure that all research assistants and fieldwork staff are trained in awareness and safety measures. Staff will not undertake interviews in any situation in which they feel uncomfortable or unsafe. Where there is concern about safety of an area, staff travel in pairs. Where needed, a 'community guide' with strong knowledge of risks will be hired to assist with staff safety. Consulting community organisations about the methods and purpose of the research in each area will also help to ensure that researchers do not face suspicion and mistrust from non-participants in the community. University counselling services will be made available to researchers should they need psychological support. All staff cars are properly equipped and regularly serviced.

Benefits to participants

Participants will have an opportunity to share their experiences and concerns with trusted and sympathetic adults and access referrals where necessary. Fieldworkers and volunteers on the project will assist adolescents in accessing health and social services. Given the network of partners and collaborators and the objectives of this study, the intention is for participants' responses to be used to inform health policy and programming for youth at local, national and regional levels. Health facilities and organisations participating in the study will receive feedback about the experiences of youth



patients, the aim of which is to have a positive impact on service provision. Finally, this project hopes to develop and test for acceptability an adolescent-driven support tool to benefit youth accessing ART and SRH.

5. Process of Obtaining Informed Consent and Consent

General Principles

All information sheets and consent forms will be given to potential participants and their legal guardians by the researcher or members of the fieldwork team. All information sheets and consent forms will be read to participants in their preferred language to prevent illiteracy from hindering a participant's understanding of the methods and purpose of the study. All participants will be told they have the right to decline to participate, drop out at any time, and that all the results will remain confidential. Any avoidance of study participation will be understood as a lack or withdrawal of consent.

Participants may consent to participate only after having the information sheet been read to them and been given an opportunity for questions.

Participants will have the opportunity to consider consent for up to a week before interviewers return. However, when we have previously offered participants periods of 24 hours to 1 week to consider consent, the vast majority have requested to participate immediately. In light of this, we propose that participants are offered the choice of whether to consent or refuse immediately, or to have 1-7 days to consider whether they choose to consent.

All participants should be capable of giving their own consent, and we will not interview any adolescent or adults deemed incompetent. Special care will be taken to ensure that all participants are fully aware of and understand the research.

We will obtain written informed consent from each participant in this study.

1) Consent for adolescents to participate

In order to ensure fully informed, voluntary consent for adolescent participants, all adolescents will be provided with information sheets describing the study in their first chosen language, which interviewers will read aloud. If participants are illiterate, they will be able to give verbal consent and indicate with a cross on the signature line. Particular attention will be given to issues surrounding statutory requirements to break confidentiality (i.e. if the adolescent or a member of their household is at significant risk). Only after the purpose of the study and the format of the interview have been explained will the adolescent be asked for their consent to participate.

All attempts will be made to ensure that the research is a positive and participatory experience for all participants, and that consent is both voluntary and informed. All interviewers will have experience in working with vulnerable children affected or infected by HIV/AIDS. If the participants have sensory difficulties, the research team will ensure they can access the questions, for example, a signer will sign the questions to deaf adolescents. Reading the questions out loud will ensure that blind adolescents can participate.

To ensure that children and adolescents do not feel obliged to participate in the research, emphasis will be placed on their ability to refuse to participate, or to cease participation at any point during the research (*See attached Consent and Information Sheets*). Following British Psychological Society Guidelines (112), any avoidance by adolescents of the interview situation will be taken as evidence of failure to consent. Adolescents who refuse to participate, or who stop the interview, will still receive snacks and certificates. All research materials will be provided in English and Xhosa. Interviewers will explain all aspects of the project to adolescents and answer any questions they may have in adolescent's preferred language.

Vertical HIV-infection can bring with it cognitive delays for children. These can be reflected in a wide range of difficulties, for example a lowered reading age or a lowered cognitive age. The effects and impacts of this for adolescents are still under-researched (48,113), and there are no clear guidelines on how to account for these difficulties in conducting research with children and adolescents who are vertically-infected with HIV. Many vertically-infected children look younger than their real age, may have developmental and educational delays (114) but feel and understand themselves to be teenagers.



There is also an ethical imperative not to exclude adolescents based on an inappropriate understanding of their potential developmental delays. This study hopes to address this by careful training of research assistants to assess cases in which adolescents do not seem to understand the process or meaning of participation in research, and in these cases will refer to expert partners working within this research collaboration for guidance. We understand that this is a complex issue, and would welcome the advice of ethics committees in addressing this.

2) Legal guardian consent for adolescent participation*

(*The following process and procedure is applicable to adolescents who have not yet turned 18. Adolescents who are 18-19 years old will be treated as adults with regards to informed consent issues.)

Each adolescent's legal caregiver will also provide consent for participation in this study, and will be provided with information describing the study in their first chosen language. Particular attention will be given to issues surrounding statutory requirements to break confidentiality (i.e. where the adolescent or a member of their household is at significant risk).

In some exceptional circumstances related to HIV/AIDS vulnerability, the adolescent may wish to participate but the legal guardian is unavailable (through death, living elsewhere and being uncontactable, or being too sick to give consent). In these cases, the adolescents will be excluded from the study.

In prior work with Young Carers and in our orphan resilience study, we identified a small but worrying group of orphaned children who wanted to participate in the study but who explained to us that they lived with a foster carer who was forcing them to undertake large amounts of domestic work against their will, and that the carer would not consent to their participation in the study because of the fear that this abuse would be revealed. When consent was requested from the caregiver, they did refuse. In cases in which children and adolescents experience abuse from caregivers or guardians, consent for the study would be difficult to obtain, as these caregivers would not want to be reported. In light of prior research findings regarding abuse experienced by HIV-affected children in the Young Carers project (115), we expect that similar difficult cases may arise in this study. These cases will be immediately reported to the appropriate authorities. Protocol about reporting the abuse and getting support for the participant will follow legal requirements and include reporting of the case to the social worker for the ward or local administrative unit. The team's co-PI is a trained South African social worker and will provide additional guidance on managing each specific case.

Research team members consulted colleagues at the University of Cape Town Health Sciences REC, the University of Witwatersrand, and Social Workers at Cape Town Child Welfare about this issue. We also consulted South African legislation, particularly the Department of Health Research Ethics Guidelines (2004). The ethics processes and procedures proposed in this research project were reviewed and approved by the following ethics committees and institutions:

- (7) I-DREC of the Social Sciences and Humanities Division, University of Oxford for the study protocol hereby presented (Ref No: SSD/CUREC2/12-21, amendments 20 November 2014, R43892/RE003 – 29 September 2016).
- (8) Centre for Social Science Research, University of Cape Town (Ref No: UCT/CSSR/1/2014(ii))
- (9) Department of Health, Eastern Cape Province (29 August 2013)
- (10) Buffalo City Municipality Health sub-district approval (23 Jan 2014, 2 Oct 2015)
- (11) Department of Education, Eastern Cape Province (4 April 2014)

A growing South African literature (116–119) argues that Section 71 of South Africa's National Health Act, which requires active written consent from a legal guardian where research subjects are under 18, runs the risk of compromising adolescents' constitutional right to privacy, confidentiality and dignity. This is particularly the case regarding research on stigmatised subjects such as HIV, ART and SRH (119). It also produces a recruitment bias in favour of respondents who communicate about sexual health with their guardians. Disclosing an HIV-positive status to family members may result in discrimination, violence and social ostracism (120). Hence additional parental or guardian consent may a) be logistically impossible, b) necessitate breaching of confidentiality, and c) place the participant at risk of harm (119)



This presents an ethical dilemma for research with HIV+ adolescents. On the one hand, it is essential that no unintended disclosure is made of an adolescent's HIV-status where they have not chosen to share this with their guardians. On the other hand, it is an ethical responsibility of a research project not to exclude those who are potentially the most vulnerable to non-adherence and other negative outcomes, because they lack family support and knowledge.

In order to ensure that these adolescents can participate in this important study, should they choose to, the research team has consulted with the National Pediatric Technical Working Group based at the National Department of Health and Dr. Luntu Galo at Cecilia Makiwane Hospital in East London, Eastern Cape to develop the following solution for such ethically complex, yet crucial participants.

In cases when the research team is aware that an eligible adolescent participant knows their HIV-positive status but the parent/guardian does not, the adolescent or family will not be approached for recruitment through health facilities. Instead, the research team will follow our 'broad community interviewing' approach, whereby we would interview a proximate home including an adolescent within the same road or area, using a non-HIV specific questionnaire and using the approach of a general health and social services survey for adolescents.

The study will follow the ethical guidelines for conducting research among adolescents as outlined in the Child Care Act (2005) and the Department of Health Ethics in Health Research (2004). Where the adolescent states that their caregiver will not consent to their participation in the study due to the fear that their abuse of the adolescent will be revealed, or in exceptional cases where the adolescent is unwilling to disclose their HIV-status to their caregiver (and is concerned that the research – whilst not focused only on HIV, will reveal this to the caregiver), the participant will be excluded from the study, but researchers will subsequently make social services referrals for all children and adolescents in abusive situations. Those eligible participants who have not disclosed to their legal guardian, parent or caregiver will be linked with disclosure counselling and support, where available at the local clinic.

Any adolescent who declines to participate before or after the interviewer has explained the project will not be interviewed, even if the legal guardian or nominated adult agrees to or encourages participation.

3) Informed consent for adult caregivers (qualitative study only)

For the qualitative study only, where adolescent participants assent, their caregivers will also be approached as potential interview respondents. This study will obtain informed consent for each adult caregiver. All adults will fill in 'opt-in' consent forms if they agree to participate. All information sheets, consent forms, and interview materials will be translated into participants' first language.

4) Informed consent for professional and community health and social workers (qualitative study only)

Healthcare workers will provide crucial information that will allow the research team to triangulate findings on factors affecting access to treatment (55) during the qualitative part of research. This study will obtain informed consent for each healthcare worker included. They will be given information sheets, consent forms, and interview materials in the participants' first language. Professional and lay health workers will be reminded not to mention their adolescent patients by name or to give any details that might identify patients. No real names (either of healthcare workers or patients they may accidentally mention) will be recorded in interview transcripts. Copies of all information sheets, consent forms and interview materials are attached in the Appendices.

6. Privacy and Confidentiality

Participants will choose the time, location and nature of their engagement with the research team. In the case of focus groups and other group-based research activities, participants will sign a confidentiality agreement, but will be warned that confidentiality cannot be guaranteed as group members may discuss what was said outside of the group despite having signed this contract. The cell phone number made available in recruiting material will only be accessible to the research team. If participants leave a 'please call me' message, only the research team will contact them. Should participants share their contact details with researchers, this information will be kept confidential.

7. Reimbursement for Participation



No financial incentives will be provided to participants, however all participants will be given snacks and thank-you packs with small gifts while participating in structured research activities. Participants will choose the site of their interviews to avoid unnecessary transport or child-minding costs, but if the participant chooses to travel for the purpose of maintaining privacy, they will be reimbursed for travel costs and, if necessary, a volunteer made available to assist with child minding. Participants involved in more ongoing research activities (particularly in the qualitative study) may also be offered assistance with homework, or other forms of non-monetary help based on the nature of the engagement. Following participation all participants will receive a Certificate of Participation regardless of completion. As in previous research conducted by members of this research team with HIV-affected communities, financial rewards will not be used. This is for two primary reasons: firstly, as financial incentives can in some cases lead to conflicts within the community or household, and secondly, in order to prevent adolescents agreeing to participate in the study in order to access money – which would reduce the voluntary nature of consent.

8. Emergency Care and Insurance for Research-related Injuries

Salaries for field staff who are not covered by university insurance include an additional sum to be paid towards medical insurance. In addition, the projects have extensive staff safety protocols, addressing issues from hazardous animals at research sites to road safety risks. All staff are trained in these protocols, which are available and attached.

9. What Happens at the End of the Study?

The study design, in partnership with government, NGOs and HIV-positive adolescents, has the specific aim of informing policy and programming. This collaborative approach to identifying the research focus and in designing the study is central in ensuring that findings will have direct relevance for HIV programming in South Africa's public health sector and beyond.

Specific policy impacts will include direct input into USAID, UNICEF, UNAIDS and PATA programming (through our regular meetings with these organisations), and national policy commitments such as sub-Saharan African governmental 'National Strategic Plans', National Action Plans for AIDS-affected children and the Department for Social Development's Strategy for Adolescent Sexual and Reproductive Health Services. Research team members have experience in the dissemination of research findings for inclusion in national HIV policies for both academic and advocacy purposes.

Dissemination and outputs will take place throughout the study and will include both peer-reviewed publications and dissemination strategies targeted at policy-makers and programmers. With the research partners PATA, UNICEF, UNAIDS, USAID-PEPFAR and the South African government, dissemination will include one-page policy briefs (see for example www.youngcarers.org.za/publications), presentations at key policy meetings such as the International AIDS Conference, the International Conference for AIDS and STI's in Africa, as well as smaller, high-level policy forms with government ministers in the Southern African region, funders such as UNAIDS/PEPFAR and the Global Fund. Dissemination of research findings will also take place at study sites, with health services, community meetings, and with local leaders.

Feedback to participants is a key part of a youth-focused research design (121). Researchers will also report back verbally to adolescent participants, encouraging their thoughts and feedback on emerging findings. For example, the later stages of the qualitative research will ask participants to respond to some of the quantitative findings, which will serve as a form of feedback. Presentations will be made to local NGOs, health services and community groups. No identifiable details will be given in any dissemination or feedback.

10. Research team

The UK and South Africa-based team builds on established strong working relationships between academics, government and civil society. Professor Cluver (Oxford University & University of Cape Town) has led two longitudinal surveys of 8500 AIDS-affected adolescents in South Africa and acts as



an adviser to the SA Government, WHO, USAID, UNICEF and Save the Children; Dr Hodes (University of Cape Town) has over 16 years of experience in HIV research and advocacy in South Africa, and has led qualitative research on HIV treatment and sexual and reproductive health since 2010, both within university research positions, and with leading HIV advocacy organisations (including the Treatment Action Campaign and *Médecins Sans Frontières* (MSF)); Dr. E. Toska (University of Oxford, University of Cape Town) has nearly 12 years of experience working on HIV-related programming and research, focusing on adolescent sexual and reproductive health in South Africa since 2012. Professor Lorraine Sherr (University College London) is a co-lead on the planned forthcoming HEY BABY addition.

The research also benefits from a large team of collaborators, students, volunteers and staff in Oxford, Cape Town and the Eastern Cape. Key members include: Dr Daniella Mark is Executive Director of Pediatric AIDS Treatment for Africa, an NGO working with 235 HIV clinics in 23 Sub-Saharan African countries, Dr Boyes (Curtin University) is a psychologist specialising in stress and coping;), Professor Orkin (University of Witwatersrand) is the former Chief Statistician of South Africa and is an expert on community survey analysis. Marija Pantelic, Craig Carty and Roxanna Haghighat are PhD students at the University of Oxford, and in addition, a University of Cape Town PhD student supported by ASRU and South Africa's National Research Foundation (Lesley Gittings). Additional support and supervision are provided to a cohort of graduate students working within the University of Cape Town's Public Health and Humanities Faculties (Samantha Malunga, Namhla Sicwebu), and to a Boston College undergraduate student (Sinazo Mwellie, studying project management in East London). The research team includes a senior HIV nurse, Mrs. Nontuthuzelo Bungane, two local assistant project managers: Mrs. Philiswa Mjo and Mavis Mpulmwana, and nearly 30 researchers.

For the EHPSA-funded portion of the study, Professor Rajen Govender (UCT's CSSR, Department of Sociology and the South African Medicines Research Council) and Dr. Nompumelelo Zungu (Director, Operations Research, South Africa's Human Sciences Research Council) are study advisors. They have thus far reviewed the ethical framework and methods used in the research component that focuses on social protection.

At inception, the study had a 'Methods Advisory Panel' of international experts in adherence research who helped to develop the questionnaire and methods: (Dr E Lowenthal, Children's Hospital of Philadelphia, Dr C Luo, Senior HIV Program Adviser, UNICEF and the UN Technical Advisory Group for Adolescents Living with HIV: Dr S Kassedde, Dr C Suzuki, Dr D Chamla, Ms P Lim Ah Ken). And a 'Policy Advisory Panel' (Dr R Yates, Senior Adviser, HIV/AIDS, UNICEF HQ,) UNAIDS (Dr R Jackson, UNAIDS Secretariat), UNICEF South Africa (Dr S Bhardwaj, Senior HIV/AIDS specialist, Dr S Crowley, Chief of Health), The South African Department of Social Development (Dr M Kganakga, Chief Director, HIV/AIDS), Department of Health (Dr L Madisha, Division of Pediatric HIV), Department of Basic Education (G Ndebele, Deputy Director-General of Social Inclusion).

In addition, the Teen Advisory Group of AIDS-affected adolescents – with whom we have worked since 2008 – are actively involved throughout the research in ensuring applicability and teen-friendly approaches.

11. Stakeholder Participation

Teenagers living with and affected by HIV/AIDS have been key contributors in designing, implementing and reviewing this study. The research team has a longstanding working relationship with a Teen Advisory Group (comprised of AIDS-affected teens and teens on ART, from the Western Cape and Eastern Cape). We will also be facilitating and working within existing programmes for a group of AIDS-affected teenagers linked to the Raphael Centre, Grahamstown, and a group of teenagers on ART linked to the Keiskamma Trust, Hamburg. Questionnaires and data collection tools will be piloted with these groups of young people who will be asked to give suggestions on how the design may be adapted to ensure it is teen-friendly. These groups will also highlight key issues and themes for exploration, suggest sensitive and exciting ways for engaging youth, and provide advice about the appropriate language and terminology to use in relation to sex, illness, medicine-taking and health. Where appropriate, some of these young people may be recruited as key informants or translators for the qualitative research.



The following stakeholders have been involved in ongoing consultations with the research team, focusing our attention on the most relevant and useful questions for practitioners in the field: UNICEF, the South African government, Paediatric AIDS Treatment for Africa, Kidzpositive, the Treatment Action Campaign, Kheth'Impilo, Keiskamma Trust and Raphael Centre. These organisations have contributed to our research design and will be key partners in disseminating findings.

Finally, participants in both the qualitative and quantitative study will be briefed on emerging findings and asked to provide feedback.

12. Conflicts of Interest

No member of the research staff will receive incentives for recruiting participants or for any other purpose directly related to the study.

13. Capacity-building and authorship

All research staff participate in quarterly capacity-building workshops as part of their paid work time. In the past year, workshops have included training on public speaking and presentations, the politics of knowledge production in South Africa, and conducting ethical research with 'disabled' participants.

In terms of publications, use of data and distribution of results, our approach emphasises providing opportunities for the whole team, including the capacity-building students, local staff, NGOs and government bodies involved to publish from and distribute findings. In our experience, even the most detailed advance-planning of who will first-author publications can require changes (as the study progresses and people's interests and expertise develop) but perhaps more important is the *ethos* of the research team regarding this important area. We believe that publications should be multiple-authored, to reflect both the collaborative nature of the study but also the collaborative approach we have to the analysis and writing of publications. We also believe that all study members should be encouraged and supported to write first-authored publications using data from the study. Beyond the core research team, other research members only have access to the anonymised version of the dataset, and only then after signing confidentiality agreements with the project investigators.

14. Ethical and Regulatory Compliance

There is an extensive body of local and international literature on ethical concerns in conducting research with children and young people. The ethical guidelines for this study are informed by a number of sources. These include the ongoing academic debate on informed consent and confidentiality (122), the ethical requirements of the universities and research institutions involved in research design, and ethical guidelines from psychological research bodies such as the British Psychological Society (112).

In planning study design and ethical protocols, key research guidelines and legislation in South Africa have been considered, including the Department of Health's Ethics in Health Research Guidelines (2004), the Department of Health, Guidelines for Good Clinical Practice in South Africa (2nd Edition 2006), the Open Society Foundation for South Africa's 'Best Practice Guide to HIV Disclosure' (2009), the AIDS Law Projects' 'HIV and the Law: A Resource Manual' (2003), 'Selected ethical-legal norms in child and adolescent HIV prevention research: Consent, confidentiality and mandatory reporting' (EDCTP 2011), the National Health Act 61 of 2003 (enforced starting 2012), the Children's Act (38 of 2005), the Children's Amendment Act (41 of 2007) and the Sexual Offences Act (32 of 2007). These South Africa specific documents have been supplemented by international guidelines, such as the WHO's Guidelines on HIV Disclosure and Counselling for Children up to 12 Years of Age (123), and the Helsinki Declaration (2008).



15. Additional documents – please contact the study team for these

1. Community and Schools information sheet (quantitative)
2. Information and consent form for adolescent participants
(qualitative)
3. Information and consent form for adolescent quantitative questionnaire (quantitative)
4. Information and consent form for participatory workshop on support tools design
(qualitative)
5. Guardian consent form for adolescent participation (qualitative)
6. Information and consent forms for caregiver participation (qualitative)
7. Information and consent forms for healthcare and social worker participation
(qualitative)
8. Interview guides: adolescent, caregiver, healthcare and social worker participation
(qualitative)
9. Adolescent screening sheet
10. Example referral forms for adolescents
11. Adolescent certificate of participation
12. Letter of support: UNICEF
13. Letter of support: PATA

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