Pathways to survival

Identifying psychosocial, family and service mechanisms to improve anti-retroviral adherence amongst adolescents living with HIV in Southern Africa

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Front Cover: Posters created during Teen Advisory Group participatory research activity
“Helping Hands: Dream Clinics and Dream Schools”
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EXECUTIVE SUMMARY

This report summarises the study findings and impact of a research project implemented jointly by the Universities of Oxford and Cape Town: *Pathways to survival: identifying psychosocial, family and service mechanisms to improve anti-retroviral adherence amongst HIV-positive adolescents in Southern Africa* (hereafter: *Mzantsi Wakho* – *Your South Africa* - its locally used name). The core source of funding for this high-impact and successful study came from the Nuffield Foundation. This study was also supported by supplementary co-funding.

This study was the first to systematically examine potential causes of ART non-adherence and non-retention in HIV care amongst adolescents (10-19 years old) in Sub-Saharan Africa. Through additional funding awarded to the research team, additional research aims were also examined.

The research project was implemented by a team of more than 50 researchers, including capacity-building for early-career academics and students in South Africa and the UK. In July 2015 – March 2018, this multi-disciplinary, mixed-methods team engaged with over 1,600 adolescents, 100 caregivers, and 120 healthcare providers through participatory workshops, in-depth interviews, ethnographic research, and three waves of quantitative surveys. In parallel, a clinic team engaged with over 79 public health facilities collecting data from clinic managers, healthcare providers, and patient files (with appropriate consent).

With the essential support of the Nuffield Foundation, this study became the world’s largest longitudinal cohort of adolescents living with HIV. Mzantsi Wakho’s research team successfully followed up and maintained high retention rates across three time points, as research participants transitioned from early adolescence into youth. The study has already had major impact on policy, UN guidelines and programming for adolescents living with HIV.

**Study Aims**

The primary aim of the Mzantsi Wakho study was to identify ways to improve health outcomes for adolescents living with HIV, particularly their HIV-related outcomes: ART adherence, viral suppression, and retention in care. It investigated the psychosocial, family and health service factors that shape ART adherence among adolescents living with HIV South Africa. By combining longitudinal qualitative and quantitative data, this study was the first to systematically examine potential causes of non-adherence amongst adolescents in South Africa, and to unpack the complex interplay between these causes. Main research aims were to:

- Examine differences in rates of adolescent adherence amongst key subgroups
- Identify which risk and resilience-promoting factors predict adherence amongst adolescents, and investigate interactive pathways, interactions and cumulative effects
- Examine whether risk and resilience-promoting pathways differ amongst subgroups of adolescents living with HIV
Our research aims were adapted and supplemented by additional research questions which emerged during the study, and through iterative engagements with adolescents, policy-makers and implementers. Additional co-funding was awarded which allowed the following research aims:

- Investigate access to sexual and reproductive health services amongst adolescents living with HIV
- Investigate combinations of social protection interventions (‘cash plus care’) and healthcare interventions for HIV-transmission reduction in adolescents living with HIV
- Determine whether adolescents living with HIV have better or worse health outcomes when receiving HIV care at decentralised healthcare facilities, compared to routine care at centralised facilities
- Determine which service-related factors predict better health outcomes for adolescents living with HIV receiving care at decentralised healthcare facilities

Findings

Mzantsi Wakho’s research has translated into findings that are highly relevant to health and social policy and programming for young people. This report outlines major study findings and its impact. The study has to date resulted in 42 peer-reviewed publications in journals including the Lancet Child and Adolescent Health, AIDS, Journal of the International AIDS Society and PloS One.

State of the evidence: Several systematic and literature reviews conducted by the team found that the state of the evidence on adolescents living with HIV is very limited, with most of the existent research consisting of cross-sectional quantitative studies and qualitative research\(^3\),\(^4\),\(^5\),\(^6\),\(^7\). Reviews found very few studies from sub-Saharan Africa that investigated drivers of ART non-adherence and sexual risk-taking. One of the reviews focused on which social protection provisions may support children and adolescents living with HIV to have better health outcomes. It concluded that while social protection is widely recognised for its positive impact on HIV prevention among HIV-uninfected adolescents and youth, few policies and programmes directly acknowledged the needs of adolescents and youth living with HIV\(^3\).

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\(^3\) Carly Hudelson and Lucie Cluver, ‘Factors Associated with Adherence to Antiretroviral Therapy among Adolescents Living with HIV/AIDS in Low- and Middle-Income Countries: A Systematic Review’, *AIDS Care, 27.7* (2015), 805–16.


\(^7\) Marisa Casale, Lucie Cluver, and Anna Carlqvist, ‘Systematic Review: Evidence Update of Interventions to Improve Retention in HIV Care and Adherence to Antiretroviral Treatment among Adolescents and Youth’.
Youth and Stakeholder experiences:
Adolescents and stakeholders were engaged as active participants, but also as advisors to research methods. This involved participatory exercises such as Yummy or Crummy (with types of medication and pills), mapping of government social support grants expenditure, life narrative and social support visualisation exercises. Findings showed challenges that young people face when trying to access inflexible benefits and services that are meant to guide them through their transition from childhood to adulthood.

Violence & non-adherence: Analyses examined associations between non-adherence and nine violence types. Of these, four violence types were independently associated with non-adherence: physical abuse by caregivers, witnessing domestic violence, teacher violence and verbal victimisation by healthcare staff. Violence exposures at home, school, and clinic are major and cumulating risks for adolescent ART non-adherence. Prevention, mitigation, and protection services may be essential for the health and survival of adolescents living with HIV. Risk of past-week non-adherence rose from 25% with no violence, to 73.5% with four types of violence exposure. Evidence-based programmes that address different types of violence include: parenting programmes, school violence prevention, and healthcare provider training programmes.

Cash + Care – combination social protection supports ART adherence and safe sexual practices:
Quantitative analyses focused on risk and resilience-promoting factors for ART non-adherence and sexual risk-taking. Resilience-promoting factors were conceptualised in two categories: cash factors and care factors. Cash factors included: having enough money to get the clinic, food security, and access to free school. Care factors included: parental/caregiver supervision and support to get to the clinic, support groups, appropriate medicine stocks, adolescent-sensitive staff, sufficient time during appointments. Additional care factors included: age-appropriate and support disclosure to adolescents of their own HIV status. Cumulative effects were found in combining both cash and care factors for supporting both ART adherence and safe sexual practices.

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12 Elona Toska, Lucie Cluver, Mark Boyes, Maya Isaacsohn, and others, ‘School, Supervision and Adolescent-Sensitive Clinic Care: Combination Social Protection and Reduced Unprotected Sex Among HIV-Positive Adolescents in South Africa’, AIDS and Behavior, 21.9 (2017), 2746–59.
Cash + Care provisions and ART adherence:
Three social protection provisions were associated with reduced non-adherence: food provision, HIV support group attendance and high parental/caregiver supervision. Combination social protection showed additive benefits. With no social protection, percentage probability of past-week non-adherence was 54%, with any one protection 39-41%, with any two social protections, 27-28% and with all three social protections, 18%. These results demonstrate that social protection provisions, particularly combinations of cash and care factors, may improve adolescent adherence.

Cash + Care provisions and safe sexual practices: Analyses examined whether cash and care social protection provisions were associated with reduced unprotected sex. Lower rates of unprotected sex were associated with access to school, parental supervision, and adolescent-sensitive clinic care. Combination social protection had additive effects amongst girls: without any provisions 49% reported unprotected sex; with 1-2 provisions 13-38%; and with all provisions 9%. Combination social protection has the potential to promote safer sex among HIV-positive adolescents, particularly girls.

Findings also contributed to the discourse of how the Sustainable Development Goals (SDGs) can be achieved for adolescents living with HIV as well as broader populations. Food security, access to clean water, healthy caregivers, and employment were strongly associated with adolescent well-being and increased chances of surviving and thriving.

STACKing the odds for retention in care: Analyses of clinic-level factors focused on two key outcomes: retention in care and internalised stigma. Retention in care was not significantly associated with the following clinic-related factors: healthcare staff able to answer adolescent questions, adolescent received information, confidentiality of information, flexible hours, waiting time and travel

13 Toska, Lucie Cluver, Boyes, Isaacsohn, and others.
time to clinic. However, a Stocked clinic, staff with sufficient Time to see adolescents, having someone to Attend the clinic with, enough Cash to get to the clinic, and Kind staff were strongly associated with improved retention in care. Combinations of these five interventions helped STACK the odds for HIV-positive adolescent retention in care, with likelihood of retention increasing exponentially with cumulatively more factors present. Similar factors were associated with internalised stigma: flexible clinic hours, kind staff, and a well-stocked clinic. Adolescents who accessed neither of the three (flexible clinic hours, kind staff and well-stocked clinics) were most likely to report internalised stigma compared to those who accessed all three.

**Adolescent transition out of paediatric care:**
Pathways in HIV care were identified by tracing movements across facility and care types. Associations between transition pathways and viral failure, mortality, loss to follow-up, and viral load change were tested. Only 20.4% of adolescents had transitioned out of paediatric HIV care. Two main pathways were identified: classical transition to adult HIV care (43.3%) and down-referral transition to primary healthcare clinics (56.7%). Across pathways, 27.3% experienced cyclical transition, or repeated movement between paediatric and non-paediatric care. Adolescents who experienced down-referral transition were less likely to demonstrate viral failure. Mortality and loss to follow-up were not associated with either pathway.

**Stigma and ART adherence**\(^\text{16}\): Findings suggest that, for Mzantsi Wakho participants, the public provision of ART in South Africa has not resulted in the social reconfiguration of HIV, from a heavily stigmatised, to a manageable and ‘normal’ chronic condition. While the rollout of ART has begun to reverse AIDS-related morbidity and mortality, impressions of HIV as a terminal illness persist – informing perceptions about the efficacy and safety of its treatment. Living with HIV remained strongly associated with a sense of contamination, with far-reaching impacts on health behaviours, particularly ART adherence. Participants feared that pill-taking exposed them to public censure and humiliation, revealing that living with HIV remains a marker of derogation. Moreover, their fears about the potential hazards of taking medicines – including the perceived threat of pharmaceutical adulteration, requires urgent attention in the form of improved treatment literacy and adherence counselling.

**Harnessing Sustainable Development Goals to reach viral suppression for adolescents living with HIV**\(^\text{17}\): The United Nations Development Programme (UNDP) has proposed the approach of development accelerators: provisions that lead to progress across multiple SDGs. A recently published article in the Lancet Child and Adolescent Health tests the model of development accelerators using data from the Mzantsi Wakho sample of adolescents living with HIV. Three provisions were found to

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16 Cluver, Pantelic, Orkin, and others.
be development accelerators for adolescents living with HIV: high parenting support, government cash transfers, and safe schools. Each was associated with positive outcomes across at least three SDGs. Parenting support was associated with good mental health, no high-risk sex, no violence perpetration, no community violence, and no emotional or physical abuse. Cash transfers were associated with HIV care retention, school progression, and no emotional or physical abuse. Safe schools were associated with good mental health, school progression, no violence perpetration, no community violence, and no abuse. For 5 of 11 SDG-aligned targets, a combination of two or more accelerators showed cumulative positive associations, suggesting ‘accelerator synergies’. For example, the percentage probability of adolescents living with HIV reporting no abuse (SDG 16.2) with none of safe school, cash transfer or parenting support was 0.25. The percentage probability cumulatively increased to 0.76 with the provision of cash transfers, safe school and parenting support. Services that simultaneously promote several SDG targets, or combine to support particular targets, may be essential to meeting HIV targets such as violence prevention, mental health and retention in care. These may also suggest flexible approaches in a context of reduced HIV-specific funding and a global focus on wider development goals.

Mental health & internalising and externalising symptoms: Analyses aimed to identify correlates of internalising and externalising symptoms. Better physical health was negatively associated with all measures of internalising symptoms. Negative clinic interactions were associated with higher depression scores. Access to clinic support groups appeared to be protective against symptoms of both anxiety and depression. Emotional abuse and bullying victimisation were associated with worse outcomes on all mental health measures. Parenting-related factors, positive parenting was associated with better mental health across all measures and poor parental monitoring was associated with more anxiety and conduct problems. Bullying victimisation, self-efficacy, and positive parenting may be crucial intervention targets as they were associated with better outcomes on most or all mental health measures. These factors can also be addressed without directly targeting adolescents living with HIV (reducing the chances of accidental exposure and stigma), and are associated with better adolescent mental health in South Africa more generally.

Suicidality and depression in adolescents living with HIV: Almost half of the adolescents living with HIV in our study has experienced some level of HIV-related stigma. HIV-related stigma is a risk factor for depression and suicide, especially in adolescents living with HIV. Higher perceived social support was directly associated with less depression, while being part of a clinic-based support group was not. However, the combination of having more available social support and participating in a clinic-based

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support group appeared to protect adolescents living with HIV who were experiencing HIV-related stigma from depression and suicidal thought and behaviours. Findings reinforce the potential of social support as an important protective general mental health and stress-buffering resource for adolescents living with HIV. Suicidality in adolescents living with HIV can be mitigated by strengthening multiple sources of social support, such as early clinic and community-based interventions.

**Impact of the research**

With the crucial support of the Nuffield Foundation, this study’s findings created unprecedented opportunity to achieve major policy and programming influence which directly impacts adolescents and youth affected by HIV/AIDS in South Africa and the region. Since inception, the team shared progress and research findings with policy-makers and implementers at local, national and international levels. The team has presented findings in nearly 60 presentations at over twenty-five conferences and workshops. Findings and research priorities have been shared with several hundred of stakeholders engaged in adolescent health and HIV/AIDS policy and programming.

Beyond the wide dissemination of research findings, tailored recommendations for policy adaptations and programming were made. First, Mzantsi Wakho has achieved major impact on South African implementation and policy. Eastern Cape healthcare workers have participated in sensitisation training on the importance of providing adolescent-friendly health facilities. In 2017, the Dr Hodes and Toska collaborated with South Africa’s National Department of Health and UNFPA to produce *South Africa’s National Adolescent and Youth Health Policy*. In June 2018, Prof Cluver and Dr Toska held dissemination and research prioritization meetings with Deputy Director General of Health, Dr Yogan Pillay, Deputy Direction General of Welfare Services, Mrs. Connie Nxumalo, and Deputy Director General of Education, Dr Granville Whittle in Pretoria, South Africa. These meetings highlighted future research gaps and how current Mzantsi Wakho findings can inform policy and programming. This will directly impact adolescents and youth in the Eastern Cape and South Africa.

and the UN Development Programme (2019). Study findings have informed UNAIDS’ and UNICEF programming (see page 25), and a series of policy briefs with UNICEF ESARO and Regional Inter-Agency Task Team on Children Affected by AIDS Eastern and Southern Africa (RIATT-ESA).

More information about our dissemination and impact activities can be found in the main report and further details on the Mzantsi Wakho and research team websites. A podcast series is also available on the Mzantsi Wakho website.
Background

Globally, AIDS-related mortality is on the rise among adolescent living with HIV while all other age groups experienced reductions. HIV/AIDS-related deaths amongst adolescents have tripled since 2000, with AIDS now the leading cause of death amongst adolescents in Sub-Saharan Africa. Adolescents are the age group with the highest rates of non-adherence to antiretroviral therapy (ART). Southern Africa is home to 1.7 million adolescents living with HIV, with the largest population of adolescents living with HIV living in South Africa. This is the result of a high rate of HIV infection among youth, coinciding with the survival of the first generation of perinatally infected infants into adolescence. The long-term health outcomes of this generation depend on strict lifetime ART adherence of 87-95%.

Adolescence is characterised as a transitional period of emotional and social development, accompanied by growing independence and changing relationships with families, peers and romantic partners. This transitional period is associated with increased risk-taking and experimentation. Research has found low levels of adherence among adolescents living with HIV, and documented high-risk sexual and reproductive health outcomes. Non-adherence can also lead to viral resistance and greater risk of onwards HIV-transmission through increased viral load. This concern is further compounded by HIV care services not responding to the particular needs of adolescents living with HIV. A recent situational analysis of 218 ART-providing health facilities across Sub-Saharan Africa found very low provider knowledge of the specific needs of adolescents in HIV care. There are increasing calls and efforts to create adolescent-responsive health systems (e.g. adolescent-friendly clinics, peer support programmes), particularly in Sub-Saharan Africa.

References:

27 Nachega and others.
29 Nachega and others.
represent an especially vulnerable and challenging group for HIV service providers. However, their retention in ART programmes and use of sexual reproductive health services remain under-investigated.

Adolescents living with HIV have rarely been included as partners in the design and operationalization of their own HIV and sexual reproductive health services. Much of the evidence on adherence in sub-Saharan Africa has focused on single biomedical predictors (e.g. complexity of different treatment regimens). This contrasts with the more established research field of child development, which suggests that it is not single factors, but rather multiple interlinking pathways that predict child outcomes in contexts of high risk. In order to develop effective interventions to support adolescents living with HIV and improve their health outcomes, this research sought to understand risk and resilience-promoting factors for adherence and sexual reproductive health service utilization.

**Research Questions**

The study aimed to elucidate risk and resilience-promoting factors for ART non-adherence and sexual risk-taking practices among adolescents living with HIV. The study’s primary research aims were:

- Research aim 1: To examine differences in rates of adolescent adherence amongst key subgroups i.e. female/male, younger/older, urban/rural, vertically/horizontally infected adolescents
- Research aim 2: To identify which risk and resilience-promoting factors predict adherence and retention in care amongst adolescents, investigate interactive pathways, interactions and cumulative effects
- Research aim 3: To examine whether risk and resilience-promoting factors and pathways differ among subgroups of adolescents living with HIV.

Our research aims were adapted and supplemented by additional research questions which emerged during the study, and through iterative engagements with adolescents, policy-makers and implementers. Additional co-funding was awarded investigate the following research aims:

- Investigate access to sexual and reproductive health services amongst adolescents living with HIV
- Investigate combinations of social protection interventions (‘cash plus care’) and healthcare interventions for HIV-risk behaviour reduction in adolescents living with HIV
- To determine whether adolescents living with HIV have better or worse health outcomes when receiving HIV care at decentralised healthcare facilities, compared to routine care at centralised facilities
- To determine which service-related factors predict better health outcomes for adolescents living with HIV receiving care at decentralised healthcare facilities

**Policy and Programming Influence**

The team conducted a community audit and stakeholder mapping which informed and expanded the study’s targeted dissemination networks. This enhanced the reach of the study’s impact activities. It also ensured findings were disseminated to stakeholders with major influence in adolescent health and HIV/AIDS policy and programming. Findings were disseminated in the form of presentations,
policy briefs, training and webinars. Evidence generated from this study supported programme implementers to develop and implement evidence-based interventions to improve ART adherence and survival for adolescents living with HIV. This is further expanded on in the “Evidence into Action” section below.

**Forecasted study impact**

The study’s impact is two-fold. First, Mzantsi Wakho has established a rigorous evidence base on pathways through which different factors shape ART adherence among adolescents living with HIV in Southern Africa. Second, the study has continued to actively share findings with programme implementers, policy-makers and other interested stakeholders at the local (Eastern Cape, South Africa), national (South Africa), regional (Eastern and Southern Africa), and international levels. The combination of these efforts has had short-term impact and potential long-term gains, including policy and programming changes in Southern Africa, conceptualising additional research on adolescent well-being, and bringing together stakeholders invested in the well-being of adolescents and young people affected by HIV.
METHODOLOGY

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. This research applied innovative investigative strategies to study the health needs of adolescents living with HIV who are growing up in contexts of extreme risk. Methods were developed to investigate adolescents’ potential for resilience, and explore how to support their adherence to ART and uptake of sexual and reproductive health services.

Quantitative methodology and sample: The quantitative sample aimed to include all adolescents who had initiated ART in a large urban, peri-urban and rural health district of the Eastern Cape in South Africa. Research assistants went to all 52 clinics providing ART to adolescents (10-19 years old), identified paper and computerized patient files of every adolescent who had ever initiated ART, and traced them to their homes in over 180 neighbourhoods. To avoid stigmatizing participants, neighbours and other adolescents in the household were also interviewed. At baseline (2014–2015), the study recruited a total of 1,519 10–19-year-old adolescents. The sample included 1,063 adolescents living with HIV and 456 neighbouring or co-habiting peers who were not HIV-infected. The study took place in 9 hospitals, 5 community health centres, and 38 primary health clinics, 35% of which were in rural communities. The survey has had exceptionally high retention rates (94% Year 1–Year 2, 94% Year 1–Year 3, 97% Year 2–Year 3) (Figure 8). This shows high levels of acceptability of recruitment processes and interviews developed by the research team.

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

Adolescent self-report questionnaire: Adolescents and youth have been traced over three waves of data collection over a 4-year period (2014-2018). Throughout this period adolescents were invited to participate in three rounds of a quantitative interviews (i.e. adolescent health and well-being questionnaire). Quantitative interview materials were administered through tablets which included teen-friendly images and language designed to engage youth in a comfortable and open style. Paper versions of the questionnaires with magazine-style formatting were used in contexts where tablet-based interviewing was not possible due to power-shortages. Informed consent was sought at each stage of the data collection process in order to allow participants to decline to participate at any stage.
**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 were complemented with data recorded from patient files. Participant self-reports through the adolescent questionnaire and data extracted from patient files were linked through an anonymous unique identifier. Data was extracted from patient files over three waves of data collection.

**Clinic-level information:** Factors including type of facility, 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 sexual and reproductive health services. Based on literature reviews conducted\(^\text{32}\), the research team developed a clinic-level “profile” of literature-informed indicators, which were linked to each patient who receives care in that clinic during data analysis.

![Figure 9 Mzantsi Wakho Timeline](image)

**Qualitative methodology and sample:** The qualitative study engaged adolescent participants, using multiple methods to explore their treatment decisions and retention in HIV and sexual and reproductive health programmes. A range of participatory and structured data collection methods complemented observations and ethnographic research. Group-based activities formed part of ongoing programme facilitation with youth living with HIV. In addition to working with youth participants, interviews were conducted with caregivers and healthcare workers.

From the study baseline until the end of follow-up, qualitative research had included 24 months of home, school and clinic observations, body-mapping, and participatory group workshops (i.e. Teen Advisory Group workshops). 150 in-depth interviews were conducted with youth, healthcare providers and families, with over 1,000 hours of home and clinic observations. The use of a variety of methods, both traditional and innovative, helped to address ethical and methodological issues that

\(^{32}\) Hudelson and Cluver.
arose throughout conducting research with adolescents. Qualitative research activities aimed to explore: (i) how adolescents living with HIV use and adapt medicines and sexual and reproductive health services, and (ii) how their caregivers and healthcare workers understand the challenges that adolescents confront. These research aims were adapted in response to emerging themes and topics that were relevant to investigate.

**Advisory Panels:** The study benefitted from two advisory panels: a Policy Advisory panel and a Methods Advisory panel (Figure 10). To ensure most efficient use of member time, individual consultations were held with each member throughout the study. The study also benefitted from feedback from the Teen Advisory Group. The Teen Advisory Group is a group of AIDS-affected youth who provided feedback on various matters including the study design, topics to be included in the questionnaire, and methodologies to recruit young people. Outcomes of engagement with Teen Advisory Group are described in detail below.

**Research setting**
The study took place within a health sub-district of the Eastern Cape constituting urban, rural, and peri-urban settlements. The Eastern Cape is a province with the lowest per-capita GDP in South Africa, and has interrupted and poor service delivery and high-level of adversity\(^3^3\).

Ethics
Ethical approval was given by two Institutional Review Boards at the Universities of Cape Town (CSSR 2013/4) and Oxford (SSD/CUREC2/12-21). We obtained provincial approval from the Departments of Education and Health and participating health facilities to conduct this research, including accessing medical records. Additionally, facility level approval was arranged through facility specific approval processes. Facility specific protocols were followed, and ethics requests were reviewed by internal ethics review committees who provided clearance for the study to collect information from medical records. In addition to these formal procedures, research assistants also obtained verbal permission from head nurse and ward managers responsible throughout data collection. All participants and their primary caregivers provided written informed consent for interviews and accessing clinical records. Consent procedures were also read aloud in case of low literacy. There were no financial incentives for participation, although all adolescents (whether they agreed to participate or not) received a ‘snack pack’ containing a snack and cool drink during the interview, and a small ‘thank you pack’ with personal products such as toothpaste and a toothbrush. The items included in these packs were selected by the Teen Advisory Group as preferable and appropriate. At each point of data collection, the adolescents are asked whether they would be willing to be approached again in the future, and at each stage consent was obtained from both adolescent and their primary caregiver. Confidentiality was maintained except in cases of disclosure of risk of harm. Where participants reported on-going or prior abuse or violence, referrals were made to relevant child protection, health services, or police (n = 112 referrals). A registered child protection social worker oversaw referrals and subsequent follow-up.

Analysis
Quantitative analysis: Data analysis was undertaken in SPSS, STATA and MPlus where needed. Mixed-methods approaches were used to validate and contextualise research findings. All analyses controlled for socio-demographic co-factors and potential confounders.

Descriptive statistics, multivariate regression and ANCOVA were used – for example to examine differences in rates of adolescent adherence amongst key subgroups. Multivariate regressions were utilised to identify which risk and resilience-promoting factors predict ART adherence. Structural equation modelling was used – for example to test risk pathways from HIV-related disability to internalized HIV stigma, and in ongoing analyses to understand moderated pathways from bullying to non-adherence via heightened depression and anxiety. A set of statistical techniques previously utilised in our longitudinal studies of AIDS-orphaned children were applied to investigate interactive pathways, interactions and cumulative effects between factors. This includes log-linear modelling which was used to test interaction effects in regression models, mediator and moderator analyses in path analysis. Structural equation modelling allowed for simultaneous analysis of multiple predictors, intervening variables and outcomes.

We note that – due to the time needed for data cleaning, merging across longitudinal timepoints and between individual questionnaires, clinical data and facility-level data, we are only beginning now to intensively analyse the Year 1 – Year 2 longitudinal data, whilst adding in the Year 3 data. We are preparing analytical techniques which will allow for time-varying adherence, including multinomial
regression models and fixed effects models. We will also be exploring opportunities for analytical models that allow natural experiments – for example we want to test the impact of adolescents becoming non-eligible for child social cash transfers at age 18, using regression discontinuity designs.

We also note that all percentages given in the papers and policy briefs are modelled percentage probabilities (using marginal effects, and controlling for a range of co-factors, as well as controlling for baseline outcomes). We choose this method because we find that odds ratios are poorly understood but that ‘flat’ percentages can overestimate effects by not allowing for co-factors.

**Qualitative analysis:** Qualitative data analysis adopted key procedural principles from grounded theory. Data collection and analysis occurred simultaneously. Analytic codes and categories were developed from the data and not from preconceived hypotheses. Analysis continuously compared similarities and differences across and within themes to limit bias. Theoretical memo-making occurred alongside analysis and during the write-up. Multiple researchers coded the data in order to verify findings.
KEY FINDINGS

This section summarizes overall Mzantsi Wakho findings. Individual publications are summarised in one-page policy briefs posted on the study website.

State of The Evidence

The research team reviewed our existing knowledge on health outcomes for adolescents living with HIV, with a focus on HIV social science. This resulted in four published systematic reviews summarised below.

1) Factors associated with adherence to ART among adolescents living with HIV in low- and middle-income countries (2015)\(^\text{34}\): This systematic review summarized the literature on quantitative observational studies examining correlates, including risk and resilience-promoting factors, of ART adherence among adolescents living with HIV/AIDS in low- and middle-income countries. A systematic search of major electronic databases, conference-specific databases, grey literature, and reference lists of relevant reviews and documents was conducted in May 2014. This included studies examining relationships between at least one factor and ART adherence as an outcome and were conducted in primarily an adolescent population (age 10-19) in low- and middle-income countries. The search identified 15 studies out of 7949 unique citations which identified 35 factors significantly associated with ART adherence representing a total of 4363 participants across nine different low- and middle-income countries. Relevant studies revealed few consistent relationships between measured factors and adherence while highlighting potentially important themes for ART adherence including the impact of (1) adolescent factors such as gender and knowledge of serostatus, (2) family structure, (3) the burdensome ART regimens, route of administration, and attitudes about medication, and (4) health care and environmental factors, such as rural versus urban location and missed clinic appointments. This review identified unique factors significantly related to ART adherence among adolescents living with HIV in low- and middle-income countries. This systematic review highlighted that more research using longitudinal designs and rigorous measures of adherence are required to identify the range of factors influencing ART adherence among adolescents living with HIV.

2) Predictors of HIV-related stigma in sub-Saharan Africa (2015)\(^\text{35}\): This systematic review aimed to synthesise evidence on predictors of internalised HIV stigma amongst people living with HIV in sub-Saharan Africa. Studies were identified through electronic databases, grey literature, reference harvesting and contacts with key researchers. Seventeen peer-reviewed articles and one draft book chapter were included out of 590 potentially relevant titles. Studies investigated socio-demographic, HIV-related, intra-personal and interpersonal correlates of internalised stigma. Eleven articles used cross-sectional data, six articles used prospective cohort data and one used both prospective cohort and cross-sectional data to assess correlates of internalised stigma. Poor HIV-related health weakly predicted increases in internalised HIV stigma in three longitudinal studies. Lower depression scores and improvements in overall mental health predicted reductions in internalised HIV stigma in two longitudinal studies, with moderate and weak effects, respectively. No other consistent predictors were found. This review found that studies utilising analysis of change and accounting for confounding factors are scarce. This necessary to guide policy and programming.

\(^{34}\) Hudelson and Cluver.
\(^{35}\) Pantelic and others.
3) Prevalence, Risk Factors, and Interventions to Reduce Sexual Risk-Taking among adolescents and youth living with HIV in Sub-Saharan Africa: A systematic review (2017)\(^{36}\): This systematic review was conducted in 2015-2016 on prevalence, predictors and programmes to reduce sexual risk-taking among adolescents living with HIV. Studies were located through electronic databases, grey literature, reference harvesting, and contact with researchers. Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines were followed. Quantitative studies that reported on HIV-positive participants (10–24 year olds), included data on at least one of eight outcomes (early sexual debut, inconsistent condom use, older partner, transactional sex, multiple sexual partners, sex while intoxicated, sexually transmitted infections, and pregnancy), and were conducted in sub-Saharan Africa were included. This review included 42 records (n = 35 studies) on at least one multiple sexual practice for 13,536 adolescents and youth living with HIV in 13 countries in sub-Saharan Africa. The majority of the findings were inconsistent across studies, and most studies scored <50% in the quality checklist. Living with a partner, living alone, gender-based violence, food insecurity, and employment were correlated with increased sexual risk-taking, while knowledge of own HIV-positive status and accessing HIV support groups were associated with reduced sexual risk-taking. Of the four intervention studies (three RCTs), three evaluated group-based interventions, and one evaluated an individual-focused combination intervention. Three of the interventions were effective at reducing sexual risk-taking, with one reporting no difference between the intervention and control groups. The review concluded that sexual risk-taking among adolescents and youth living with HIV is high, with inconclusive evidence on potential determinants. Included studies informed the analyses conducted to address the other research questions.

4) Social protection for HIV prevention amongst children and adolescents in Eastern and Southern Africa (2016)\(^{37}\): This research combined two research methodologies to summarise and assess the existing evidence on child- and adolescent-sensitive social protection for HIV prevention in Eastern and Southern Africa: (1) a rigorous review of academic, policy and grey literature on social protection, children and adolescents in Eastern and Southern Africa; and (2) consultations with 25 experts from a variety of national, regional and international institutions and research bodies. This was investigated through three objectives: (i) assess the evidence on the effectiveness of social protection for HIV prevention, (ii) consider key challenges to implementing social protection programmes that promote HIV prevention, and (iii) identify critical research gaps in social protection and HIV prevention, in Eastern and Southern Africa. Results from this research confirmed that HIV-inclusive child-and adolescent-sensitive social protection have the potential to interrupt risk pathways to HIV infection and foster resilience. In particular, evidence detailed the effectiveness of combination social protection particularly cash/in-kind components combined with "care" and "capability" factors among children and adolescents. This research highlights that social protection programmes should be dynamic and flexible, and consider age, gender, HIV-related stigma, and context, including cultural norms, to offer opportunities to improve programmatic coverage, reach and uptake. This research recommended that future research should explore which combinations of social protection work for sub-groups of children and adolescents, particularly those living with HIV.

In addition to the main findings of the systematic review, this research highlighted the potential of combination social protection to improve health outcomes for adolescents living with HIV and

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36 Toska, Marija Pantelic, Meinck, Keck, and others.
37 Toska, Lesley Gittings, Hodes, Cluver, and others.
reiterated the importance of care social protection, alone and in combination. It also identified challenges in implementing social protection provisions to support adolescent HIV-outcomes in the region. Such challenges were also identified at a structural level at a regional webinar hosted by the Regional Inter-Agency Task Team on Children Affected by AIDS Eastern and Southern Africa (RIATT-ESA) and a UNAIDS meeting.

Adherence
This study investigated factors associated with ART non-adherence among adolescent living with HIV in South Africa\textsuperscript{38}. Linear and logistic regressions tested associations of self-reported non-adherence, number of opportunistic infections and detectable viral load, controlling for all potential covariates. ART adherence was measured using responses from adolescent self-report\textsuperscript{39} questionnaire, using the standardised Patient Medication Adherence Questionnaire\textsuperscript{40}, combined with adolescent adherence measures developed in Botswana\textsuperscript{41}. Vignettes were included in the adolescent self-report questionnaire to reduce social desirability bias (Figure 11). Past-week and past-year non-adherence was defined using a 95% adherence cut-off, based on the number of prescribed daily doses\textsuperscript{42}. Analyses used past-week adherence due to evidence of increased reliability for more recent recall. Two validation measures of self-reported adherence were included. Opportunistic infections were measured as sores on the body or face, tuberculosis symptoms, shingles and mouth ulcers in the past six months, using a verbal symptom checklist\textsuperscript{43}. Additionally, for a 25% subset of adolescents from randomly selected clinics, viral load measures were collected from clinic files.

Potential covariates were included: socio-economic factors (age, gender, language, formal/informal housing, urban/rural location and education level), maternal and paternal death, perinatal/horizontal infection, co-habitation with caregiver who was AIDS-symptomatic or on ART, adolescent awareness of HIV status and duration of time on treatment and healthcare factors (past-month self-reported

\textsuperscript{38} Cluver, Toska, Orkin, and others.
\textsuperscript{40} Michel Duong and others, ‘Evaluation of the Patient Medication Adherence Questionnaire As a Tool for Self-Reported Adherence Assessment in HIV-Infected Patients on Antiretroviral Regimens’, \textit{HIV Clinical Trials}, 2.2 (2001), 128–35.
\textsuperscript{42} Duong and others.
health and time of travel to clinic, and whether the participant had received care in hospital for illness in the past year).

Self-reported non-adherence was 36% in the past week. Within the subset of adolescents where we collected viral load measures (n = 266), 45.1% had a detectable viral load (>75 copies/ml).

The sample had a mean age of 13.8 (median 13.0, SD 2.8, range 10–19), was 55% female, and 97% first-language Xhosa; 19% lived in informal housing, with 21% in rural areas and the remainder in peri-urban or urban locations. On average, adolescents reported completing nearly 6 grades of school (mean 5.77, SD 2.6, median 6.0, range 0–12); 44% were maternally and 30% paternally orphaned, with a further 3% of mothers and 16% of fathers were non-resident; 67% were perinatally infected. Adolescents had been on ART for an average of 5.9 years (median 5.0, SD 4.5, range 0–19 years), and 59.9% reported poor/not good health in the past 6 months. Mean travel time to healthcare facilities was three quarters of an hour (median 30 minutes, SD 95 minutes, range 1 minute to 3 hours).

Adolescents living with HIV are at high risk of ART non-adherence, with no associations of socio-demographic factors such as age, gender and mode of infection. Self-reported data show that more than a third of adolescents were non-adherent in the past week, and half were non-adherent in the past year. Associations of non-adherence with more opportunistic infections and higher viral loads have direct clinical implications for adolescent survival.

**Risk and Resilience-Promoting Factors for Art Non-Adherence Among Adolescents Living With HIV**

Identifying the potential importance of combination social protection factors, the research team developed additional research aims to investigate combinations of social protection interventions (‘cash plus care’) to improve health outcomes for adolescents living with HIV. Responding to identified evidence-gap, the team examined quantitative and qualitative research findings as well as participatory research to identify risk and resilience-promoting factors for ART non-adherence among adolescents living with HIV in South Africa.

**Combination social protection for adolescents living with HIV:** Following a mixed-methods community audit with lead stakeholders, youth consultations and a systematic review, analyses explored which cash and care social protection provisions are associated with lower ART non-adherence and reduced sexual risk-taking. Analyses used multivariate regression, interaction and marginal effects models in SPSS and STATA, controlling for socio-demographic, HIV and healthcare-related covariates. Access to

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**Figure 12** Social protection associated with ART adherence among adolescents living with HIV (left) and Cash + Clinic + Care associated with ART safe sexual practices among adolescents living with HIV (right)
support groups, food security, and strong parental supervision were associated with improved ART adherence\(^\text{44}\) (Figure 12 - left). Access to free school, adolescent-sensitive clinic care, and strong parental supervision were associated with safe sexual practices\(^\text{45}\) (Figure 12 - right). Combinations of these interventions had considerable additive effects, especially in reducing sexual risk-taking among adolescent girls living with HIV.

**Relevance of HIV disclosure:** Two mixed-methods papers\(^\text{46, 47}\) contributed to the relevance and applicability of HIV disclosure guidelines for adolescents living with HIV. Quantitative analysis used logistic regressions, controlling for socio-demographic factors (sex, age, language, location, formal/informal housing and access to necessities) and multivariate hierarchical logistic regressions, using Hosmer and Lemeshow methods. Qualitative interviews were recorded and transcribed in full or (where participants preferred not to be recorded) written notes were taken. Thematic codes were developed from the data, based on the principles of grounded theory, and were triangulated through cross-checking with both study participants and researchers on both methodological components of the study.

First, cross-sectional analyses concluded that knowing one’s own HIV status was strongly linked to improved ART adherence among all adolescents living with HIV. Among perinatally infected adolescents who knew their status (n=362/540), disclosure prior to age 12 was associated with higher adherence. Qualitative findings suggested that disclosure was undertaken sensitively in clinical and family settings, but that adolescents' understandings of their HIV-status was partial, and at times transient with doubts that HIV was a ‘permanent’ illness and that ART was the most effective means of maintaining health\(^\text{48, 49}\).

The second set of analyses investigated associations between safe sex and three types of HIV-status disclosure: (1) knowledge of own HIV status, (2) knowledge of partner status, and (3) disclosure of HIV-positive status to partner\(^\text{50, 51}\). Analyses of the full Mzantsi Wakho sample including adolescents living with HIV and those uninfected, suggests that knowledge of own HIV status is strongly associated with safer sexual practices, while knowledge of partner status is associated with reduced safe sex. The relationship between disclosing to a partner and safe sexual practices was not significant – potentially due to very low levels of disclosure in this young sample. Qualitative research suggested that adolescents living with HIV feared rejection, stigma and public exposure if disclosing to sexual and romantic partners. Counselling by healthcare workers for adolescents living with HIV focused on benefits of disclosure but did not address the fears and risks associated with disclosure. These findings challenge assumptions that disclosure is automatically protective in sexual and romantic relationships for adolescents living with HIV, who may be ill-equipped to negotiate safer sex.

\(^{44}\) Cluver, Toska, Orkin, and others.

\(^{45}\) Toska, Lucie Cluver, Boyes, Isaacsohn, and others.


\(^{47}\) Toska, Lucie Cluver, Boyes, Isaacsohn, and others.

\(^{48}\) Cluver, Hodes, Toska, and others.


\(^{50}\) Toska, Lucie Cluver, Hodes, and Kidia.

\(^{51}\) Toska, Lucie Cluver, Boyes, Isaacsohn, and others.
Adolescent boys’ engagement with traditional and biomedical health services: Mzantsi Wakho was located in a district in which the practice of traditional circumcision has a long history. Ezobudoda (isiXhosa for ‘manhood things’) was a qualitative sub-study of Mzantsi Wakho that focused on the engagement of adolescent boys living with HIV, with traditional and biomedical health services and was conceptualized and managed by doctoral-candidate Lesley Gittings, under the supervision of Dr Rebecca Hodes and Assistant Professor Christopher Colvin. In recent years, medical male circumcision has been introduced in South Africa’s public health sector as a means of HIV-prevention. The Ezobudoda sub-study explored the biosocial lives of adolescent boys and young men living with HIV (n=36) within the Mzantsi Wakho sample. It engaged various qualitative methods, including health-focused life history narratives (n=36), focus groups (n=2) and semi-structured interviews (n=38).

Emerging findings indicate that traditional initiation/ circumcision presents a challenge to adolescent boys taking ART because pill-taking is forbidden during initiation. Participants reported feeling stressed and conflicted during this time and reported a range of strategies including (i) hiding medicines (ii) disclosing to a trusted person at initiation school or (iii) ceasing medicines-taking without telling anyone – including biomedical health providers. The 3 months post initiation also represented a challenge for health service access, as boys did not want to be seen in the clinic after coming back from initiation. These findings suggest that boys attending traditional initiation in the Eastern Cape are struggling to take HIV medicines and to remain within the public health system.

Poly-victimisation predicts ART non-adherence among adolescents living with HIV: A recent paper explored which kinds of violence experiences were associated with reduced ART adherence among adolescents living with HIV. Analyses examined associations between non-adherence and nine violence types using sequential multivariate logistic regressions. Potential interactive and additive effects were tested with regression and marginal effects. Four violence types were independently associated with non-adherence: physical abuse by caregivers; witnessing domestic violence; teacher violence and verbal victimisation by healthcare staff.

Past-week non-adherence rose from 25% with no violence, to 74% with four types of violence exposure (Figure 14). Violence exposures at home, school and clinic are major and cumulating risks for adolescent ART non-adherence. Prevention, mitigation, and protection services may be essential.

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52 Cluver, Meinick, and others.
for the health and survival of adolescents living with HIV. Evidence-based programmes that address different types of programmes include: parenting programmes, school violence prevention, and healthcare provider training programmes.53

**Mental health & internalising and externalising symptoms**: Multiple linear regression analyses were conducted to determine whether hypothesised correlates accounted for unique variance in mental health scores. Better physical health was negatively associated with all measures of internalising symptoms such as perceived stigma and depression. Negative clinic interactions were associated with higher depression scores. Access to clinic support groups appeared to be protective against symptoms of both anxiety and depression. Emotional abuse and bullying victimisation were associated with worse outcomes on all mental health measures. Parenting-related factors, positive parenting was associated with better mental health across all measures and poor parental monitoring was associated with more anxiety and conduct problems.

**Suicidality and depression in adolescents living with HIV**: A moderated mediation model was employed to test for potential (a) effects of stigma on suicidal ideation and attempts, both direct and mediated through depression and (b) direct and stress-buffering effects of social support resources on depression and suicidal ideation and attempts. Almost half of the adolescents living with HIV in our study has experienced some level of HIV-related stigma. Higher perceived social support was directly associated with less depression, while being part of a clinic-based support group was not. However, the combination of having more available social support and participating in a clinic-based support group appeared to protect adolescents living with HIV who were experiencing HIV-related stigma from depression and suicidal thought and behaviours.

**Clinic-level factors and HIV outcomes**: The initial analyses on combinations of social protection interventions for reduced risky behaviours among adolescents living with HIV highlighted the importance of clinic-centred provisions to enhance the effect of ‘cash’ and ‘care’ interventions. Analyses of clinic-level factors focused on two key outcomes: retention in care and internalised stigma.
Retention in care: Associations between retention in care and health service factors were tested using sequential multivariate regression and marginal effects modelling. Full retention in care was defined as no past-year missed appointments and 85% past-week adherence. Analysis controlled for covariates of age, gender, urban/rural location, formal/informal housing, maternal and paternal orphanhood, vertical/horizontal HIV infection, overall health, length of time on ART and type of healthcare facility. Only 56% of adolescents living with HIV reported retention in care (full ART adherence and clinic attendance). Interestingly, retention in care was not significantly associated with the following clinic-related factors: healthcare staff were able to answer adolescent questions, adolescent received information, confidentiality of information, flexible hours, waiting time and travel time to clinic. On the other hand, a stocked clinic, staff with sufficient time to see adolescents, having someone to attend the clinic with, enough cash to get to the clinic, and kind staff were strongly associated with improved retention in care. Combinations of these five interventions helped STACK the odds for HIV+ adolescent retention in care. With access to none only 3% of adolescents were retained, with access to only one 5%–9% while those who accessed all five reported a 70% probability of being retained in care\(^\text{56}\).

Adolescent transition out of paediatric care: Patient file data was extracted for all 10-19 year olds participants ever initiated on ART in 52 public healthcare facilities. Doctoral-candidate Roxanna Haghighat examined pathways in HIV care were identified by tracing movements across facility and care types. Associations between transition pathways and viral failure, mortality, loss to follow-up, and viral load change were tested in sequential multivariate regressions. Analyses controlled for sociodemographic and treatment-related variables. Thematic analyses of semi-structured healthcare provider interviews identified transition support available at included facilities. Only 20.4% of adolescents had transitioned out of paediatric HIV care. Two main pathways were identified: classical transition to adult HIV care (43.3%) and down-referral transition to primary healthcare clinics (56.7%). Across pathways, 27.3% experienced cyclical transition, or repeated movement between paediatric and non-paediatric care. Adolescents who experienced down-referral transition were less likely to demonstrate viral failure. Mortality and loss to follow-up were not associated with either pathway. Median post-transition viral load change was not clinically significant or associated with transition pathways. Interviews with healthcare providers found that informal “protocols” are implemented to mitigate risk of negative post-transition HIV outcomes.

\(^{56}\) Cluver, Pantelic, Toska, and others.
Internalised stigma: Similar factors were associated with internalised stigma: flexible hours, kind staff, and a well-stocked clinic. Adolescents who accessed neither of the three (flexible hours, kind staff and well-stocked clinics) were most likely to report internalised stigma (54%) compared to those who accessed all three (19%) (Figure 16).

Factors associated with HIV transmission risk: Longitudinal data analyses of adolescents living with HIV (n=983) explored which adolescents were most at risk of transmitting HIV to sexual partners, or children, and the potential risk factors for HIV transmission. 16% of adolescents reported both past-year sexual risk-taking and viral activity.

Factors associated with high HIV transmission risk were mode of infection, poverty, older age, and poor relationship dynamics. Mode of infection moderated the effect of poor relationship dynamics on HIV transmission risk: horizontally-infected adolescents reporting poor relationship dynamics were nearly 5 times more likely to report high HIV transmission risk than vertically infected adolescents in safe relationships (Figure 17).

Engagement with institutions among adolescents living with HIV: Additional findings57 explore how adolescents interact with institutions where they access care and HIV interventions. Using ethnographic data from a mixed rural-urban sample of adolescents living with HIV, Vale et al. explored how official documents (patient folders, patient cards, health notebook, birth certificates, etc.) bring adolescents living with HIV into state health services. These documents may enable access to essential medicines and other means of social support, including government social grants. But they may also be a source of fear and doubt among adolescents, particularly if their knowledge about the biomechanics of ART is limited, and if they rely on continued access to social grants as their primary or main means of material support.

Youth Engagement
Adolescents and young people need to be included in determining research agendas and outcomes to ensure their relevance to their lives and lived experiences. Though young people had long articulated the need for their meaningful involvement in scientific research, studies involving adolescents as their primary focus have rarely sought the input of young people. This is problematic given the centrality of adolescents in the AIDS epidemic in Southern and Eastern Africa.

Teen Advisory Group
Established in 2008, the aim of the study’s Teen Advisory Group (TAG) was to engage adolescents as advisors rather than only research participants. The research team engaged with the TAG through consultative activity-based weekend retreats throughout the course of the study. During Mzantsi Wakho, TAG weekends were hosted in Cape Town, South Africa in 2016, 2017 and 2018 with additional TAGs also hosted in Sierra Leone and Uganda in 2018.

TAG weekend retreats created a unique opportunity for adolescent and young people to have their voices heard. Research investigators encouraged TAG members to provide input on research methods to enhance acceptability of research methods and relevance of research objectives, discussed research findings to ensure appropriate interpretation, and brought together policymakers and adolescents to bridge the individual-structural decision-making divide. TAG workshops in 2015-2016 were critical to developing the content of the South African Adolescent and Youth Health Policy, lead-authored by Dr Rebecca Hodes and Prof Lucie Cluver.

Participatory Research
Qualitative and quantitative components of Mzantsi Wakho were combined in order to explore the aspirations of adolescents living with HIV for health and development. This was investigated through two participatory exercises: “Dream Clinics” and “Yummy or crummy? You are the Master Chef”. These youth-friendly exercises captured the utility of participatory research with adolescents living with HIV, and revealed synergies between healthcare provision and access, infrastructure, water and
sanitation, and nutrition (Figure 18). Findings confirmed that food and water are critical to ART adherence among adolescents living with HIV, interlinking SDGs 2 (food security), 3 (health), and 6 (water and sanitation).

During another participatory exercise, adolescents learned about the different SDGs and were asked to choose eight goals they feel are most important to them. Across countries, six of the SDGs within the top eight were the same (in no particular order) – no poverty; good health and wellbeing; quality education; clean water and sanitation; peace, justice and strong institutions; and climate action. In each country, groups of teens shared their top SDG with their peers through acting, songs, and poetry.

The team also facilitated an “intervention combinations” activity which explored the teens’ ideas on the best combination of a maximum of three interventions. Although there was some variation in the combinations, certain interventions were selected in all of the countries for the subgroups (teen parents, teens without family, and teens who are not in education, employment or training). For teen parents, TAG participants indicated that they would include parent training for teen parents in the combination. For teens without families, providing grants was selected in all countries. For teens not in education, employment or training, providing career support was vital. In each country, groups of teens presented their combination of interventions to their President or Minister of Social Welfare (acted out by one of the facilitators).

TAGs in South Africa and beyond: In April 2018, we ran our 10th retreat in Cape Town, South Africa, and will be documenting our lessons learned in a forthcoming paper. The reach of the TAGs has also been expanded beyond South Africa to include the voices of young people from Kampala, Uganda, and Kenema, Sierra Leone. These additional TAGs were implemented to gain insights into the priorities and aspirations of adolescents from different regions of the African continent and to hear their views on how best to support the most vulnerable groups of teens.
Sustainable Development Goals & Adolescent Survival

The sustainable development goals (SDGs) present an ambitious agenda for 2030, and a unique opportunity to develop targeted interventions for adolescents living with HIV. Evidence to date suggests that certain interventions can contribute to meeting the SDGs for adolescents\(^\text{59}\). The UN Development Programme (UNDP) has proposed that key interventions or programmes targeted at specific populations can work as development accelerators, efficiently leading to progress across multiple SDG targets. Resources specifically allocated to such development accelerators for vulnerable populations may highly efficient for achieving SDG targets for adolescents living with HIV. However, little is known about which SDGs are most relevant to adolescents living with HIV, or what accelerators could be most efficient.

Quantitative and qualitative analyses of the Mzantsi Wakho data looked at which SDGs protect adolescents living with HIV against mortality risk\(^\text{60}\). Of eight SDGs tested, four were strongly associated with reduced mortality risk (defined as risk of viral failure or symptomatic untreated TB) among adolescents living with HIV. The four SDGs were poverty reduction related (SDG 1+2), having a healthy caregiver (SDG 3), household employment (SDG 8) and protection from child abuse (SDG 16). Each individual SDG contributed to reducing high mortality risk. Adolescents who met all the SDGs experienced the lowest mortality risk (14%) compared to those who accessed none (51%) (Figure 21). These findings shed light on which SDGs we should focus on to support adolescents living with HIV to survive and thrive. In the post-MDG policy era, in which no SDG focuses specifically on adolescents or on HIV, this analysis fills a critical gap in determining the health, education and social outcomes of adolescents living with HIV in relation to the SDG goals.

A recently published article evaluates the impact of social support provisions on outcomes across multiple SDGs spanning health (SDG 3) education (SDG 4), gender equality (SDG 5) and peace (SDG 16). High parenting support, government cash transfers and schools without bullying were all shown


\(^{60}\) Cluver, Pantelic, Orkin, and others.
to be development accelerators, each associated with positive outcomes across at least three SDGs. For five SDG-aligned outcomes, combinations of two or more accelerators showed cumulative positive associations, suggesting synergies of combining provisions\textsuperscript{61}. For example, with no safe schools, cash transfers, or parenting support, the probability of adolescents reporting no emotional or physical abuse (SDG 16.2) was 25%. With cash transfer alone it was 37%, with safe school alone 42% and with parenting support alone 44%. With all three development accelerators combined, 76% reported no emotional or physical abuse (Figure 22). These findings provided an early proof-of-concept for development accelerators, which could guide decisions on efficient interventions towards achieving the SDGs for adolescents living with HIV.

\textsuperscript{61} Cluver, Orkin, Campeau, and others.
EVIDENCE INTO ACTION

Purposeful and audience-specific dissemination of research progress and findings with stakeholders has been central to the work of Mzantsi Wakho. The team engaged with both academic and non-academic stakeholders involved in programme implementation and policy. Ongoing and iterative engagement with stakeholders has ensured that research questions and analyses directly responded to the needs of policy-makers and programme implementers. Once findings were rigorously tested, results and recommendations were shared with stakeholders without delay. Dissemination led to numerous opportunities to influence policies and guidelines as well as programme design catering to the needs of young people living with HIV. Evidence-based recommendations were shared with these stakeholders in the form of presentations, trainings, workshops, webinars, consultations as well as through general media to reach a wider public audience.

Dissemination activities were delivered by lead investigators and fieldwork team members, following extensive preparation and capacity building efforts. Feedback received during these events strengthened the team’s analyses and many presentations resulted in high-impact publications.

AIDS Impact ● International AIDS Society ● SA AIDS ● Association for the Social Sciences and Humanities in HIV (ASSHH) ● International Conference on AIDS and STIs in Africa (ICASA)

International AIDS Society (AIDS/IAS) ● The International Workshop on HIV and Hepatitis Observational Databases (IWHOD) ● Public Health Association of South Africa (PHASA) ● USAID Best Practices

1st Workshop HIV+ adolescents ● Men & Masculinities ● Public Health Association of South Africa (PHASA) ● South African Social Science and HIV Programme (SASH) Forum ● Young Families ● Med Humanities ● SAAIDS

Stakeholder Mapping

The team conducted a community audit and stakeholder mapping which resulted in expanding and strengthening the study’s dissemination networks. Throughout the initial study set-up and baseline data collection, the research team built a stakeholder matrix at the local (provincial), national, regional, and international level. Lead investigators (Cluver, Toska, Hodes, Orkin, Gardner, Boyes, Sherr) and fieldwork management held regular meetings with these stakeholders to present study findings, and to identify implications of research for programming and additional research gaps. The table of key actors listed below are those that were directly engaged as part of the team’s strategy.

| Summary of the key actors the research team has interacted with throughout the study |
|-----------------------------------------------|-----------------------------------------------|
| **International**                             | The Nuffield Foundation (UK), UNAIDS (Geneva), UNDP (HQ-USA), UNICEF Innocenti Office of Research (Italy), USAID/PEPFAR (Washington DC), World Bank (Washington DC), Children’s HIV Association (UK), Adolescent Treatment Coalition (IAS/ CIPHER), DFID (UK), UN Women (Washington DC), Houses of Parliament UK, UN Inter-Agency Task Team for Social Protection, UNAIDS, UN Development Programme, UNFPA, World Health Organisation, Global Fund |
| **National**                                  | National Departments of Health, National Department of Social Development, National Department of Basic Education, South African National AIDS Council, Medical Research Council, Beyond Zero, Kheth’impilo, National AIDS Councils and Ministries of Health across Africa, including Liberia, Sierra Leone, Tanzania, Zambia, Lesotho, Swaziland, Malawi and others. |
| **Local / Provincial**                        | Eastern Cape Departments of Health, of Social Development, and of Basic Education, Buffalo City Municipality, Frere Hospital, Lifeline/ Masithethe, Dimbaza Community Health Centre, SAPS, BCM Circumcision Programme, University of Fort Hare, Cecilia Makiwane Hospital, Bhisho Hospital, Duncan Village Day Hospital, Small Projects Foundation, Grey Hospital, All study health facilities (n=79), Schools in the catchment area |

Local Impact

A series of dissemination sessions were held with local stakeholders, NGOs and with the Eastern Cape Departments of Health, Basic Education and Social Development. The interactions described below express the two-way dialogue established between the team and local professionals. These resulted in reflections by district staff on how they support adolescents living with HIV and served as valuable opportunities for stakeholders to provide input into the study’s implementation and research aims.
The team delivered a more than 20 presentations to key local stakeholder groups including Learner Support Agents, programme officers and directors from the Department of Basic Education as well as healthcare providers working with the Department of Health. For example, the team presented to a 100-strong group of Learner Support Agents – a group of student support workers managed by the Department of Basic Education. This was key to sensitising Learner Support Agents to the special needs of adolescents affected by HIV. The feedback from the workshop participants was extremely positive. Research findings relating to schools were also presented to programmes officers and directors from the Department of Basic Education’s Research, Strategy, Curriculum and HIV directorates.

Mzantsi Wakho’s Senior Clinic Researcher, Senior Nurse Nontuthuzelo Bungane, joined the Faculty of Nursing at the University of Fort Hare (Alice and East London, South Africa) in mid-2017. During her tenure, she has been involved in training nursing students on HIV and paediatric practices, incorporating study findings where relevant. Senior Nurse Bungane continues to act as an essential point person in disseminating to large groups of health facility staff in upwards of 10 hospitals and health facilities in the district.

Lasting relationships and partnerships were established with district offices of local NGOs such as Beyond Zero and Kheth’impilo. These organisations provide training support for healthcare workers providing ART initiation services and patient advocates in the Eastern Cape. Throughout the project, the team also engaged with these organisations to provide extra support for programmes. Using the study’s research findings, the team informed programme development and implementation for Keth’impilo and Beyond Zero.

**National-level Impact**

National-level impact was broad and multi-faceted. Mzantsi Wakho findings and policy recommendations were communicated to stakeholders including: universities, NGOs, the South African National Departments of Health, Social development and Basic Education and other national authorities. Research findings were disseminated in conferences attended by policy-makers and implementers as well as at
academic conferences. Results also informed wide-reaching policy documents.

The most significant reach of the Mzantsi Wakho team to date has been the drafting of the 2017 South African National Adolescent & Youth Health Policy. As the writers of the policy, team members and colleagues conducted 7 Youth Health Policy Rapid Evidence Research Reviews in 2015, establishing the keys areas for inclusion in the policy. The majority of these highlighted the evidence supporting combination interventions for the improvement of health outcomes, including HIV prevention. The Rapid Evidence Research Reviews also emphasised the potential of social protection to effectively improve the sexual health of adolescents. The final policy document championed meaningful adolescent and youth engagement in its drafting and implementation.

As a result of this approach, and the study’s Teen Advisory Group (TAG), the national Department of Health established an Adolescent and Youth Advisory Panel which met for the first time in Cape Town in March 2018 (Figure 27). This panel comprises of nine youth representatives from each South African province. The panel advises the department in its implementation of the policy. In partnership with the Department of Health, the Desmond Tutu Foundation, and London School of Hygiene and Tropical Medicine, a training programme was convened to further support the implementation of the National Adolescent and Youth Health Policy. The Mzantsi Wakho team were invited to design and convene components of the training course for 36 governmental, NGO and civil society representatives in 2017 and 2018. Following the course, the team mentored multiple participants with their course follow up and assignments which involved disseminating and applying the principles of the policy in their workplaces.

Mzantsi Wakho team members have presented at several Pediatric Adolescent Treatment for Africa (PATA) training meetings for healthcare providers across the region, and the PATA Youth Summit in Johannesburg, with the theme: ‘Delivering on the frontline’. Dr Hodes presented a plenary on ‘A meal of medicines: why taking pills is different to eating sweets’.

The team provided input into South Africa’s new National Strategic Plan on HIV, STIs and TB 2017-2022 which included:

- Prof Cluver provided input through a presentation to the South African National AIDS Council (SANAC) on 28 September 2016.
- Dr. Hodes gave inputs into SANAC’s report on socio-structural drivers of HIV, for inclusion in South Africa’s National Strategic Plan 2017-2022.
• L. Gittings attended and provided input into a consultation session on 20 September 2016.

In June 2018, Prof Cluver and Dr Toska held dissemination and research prioritization with Deputy Director General of Health, Dr Yogan Pillay, Deputy Direction General of Welfare Services, Mrs. Connie Nxumalo, and Deputy Director General of Education, Dr Granville Whittle in Pretoria, South Africa. These meetings highlighted future research gaps and how current Mzantsi Wakho findings can inform policy and programming.

Regional & International Impact

Lead study investigators have presented at multiple high-level meetings and contributed to key documents such as the UNAIDS Social Protection guidelines. In May 2016, dissemination of preliminary findings to high-level meetings and international stakeholders included consultations on the content of the UNAIDS Chapter on social protection. This was launched at AIDS2016. In April 2017, Prof Cluver presented at the UNAIDS/ World Bank/ UNICEF Social Protection Conference in Geneva. Throughout 2017 and 2018, Prof Cluver presented findings and priorities for adolescents living with HIV to National AIDS Councils across Africa as part of a series of UNAIDS Social Protection assessment meetings. While research settings differ between South Africa and countries in East, West, and Central Africa, the National AIDS Councils noted the transferability of the concepts and findings. This supported National AIDS Councils to inform programming for children and adolescents affected by HIV without having to run similar resource-intensive research studies.

Global Documents citing Mzantsi Wakho findings (examples)

1. UNAIDS 2016 World AIDS Day report
2. UNAIDS HIV care and support Reference document
3. UNAIDS Gap Analysis on Paediatric HIV Treatment and Support
5. UNICEF 2017 World AIDS Day report

In 2017, Dr. Toska presented Mzantsi Wakho findings and held a training for young activists living with HIV at the Intergenerational Summit organized by the International AIDS Society, the Adolescent Treatment Coalition, and PATA in Cape Town. Policy briefs of Mzantsi Wakho findings were distributed as potential tools for advocacy. Activists from 23 national, regional, and international networks of young people living with HIV were present.

Dr Toska and the Mzantsi Wakho team provided input into the development of guidelines that will inform the institutionalization of Adolescent and Youth Friendly Services, overseen by Craig Carty and UNFPA ESARO. Prof Cluver and Dr Toska were invited by UNFPA ESARO to be in the advisory panel for the rollout of these guidelines by UNFPA ESARO and WHO AFRO.

All lead investigators contributed to the WHO/ CIPHER adolescent and paediatric HIV research agenda, which has shaped current and future research and programmatic priorities. Hodes, Cluver and Toska continue to engage with the CIPHER research programme. Dr Toska received a CIPHER award for 2018-2020 to focus on additional analyses of the Mzantsi Wakho data centred on adolescent mothers living with HIV and their children. In March 2017, Toska and Cluver were technical experts for WHO’s scoping meeting on developing guidelines for user-initiated interventions for sexual and reproductive health.
Policy briefs were finalized based on Mzantsi Wakho research in collaboration with UNICEF-ESARO and Regional Inter-Agency Task Team on Children Affected by AIDS Eastern and Southern Africa (RIATT-ESA). All of the briefs can be found here: [https://www.unicef.org/esaro/5482_briefs.html](https://www.unicef.org/esaro/5482_briefs.html). The team is in the process of planning a second policy brief series with UNICEF ESARO, UNFPA ESARO, and UNAIDS.

**Evolution of HIV research:** With a broader focus on developments in HIV clinical, health and social sciences, we conducted a study on the evolution of HIV research as a domain of global knowledge. The study explored two key themes: (1) The significance of context - the ‘setting’ of HIV research; and (2) sex, race and risk – changing ideas about the social determinants of HIV transmission, including among adolescents. Based on familiarity with the research field, we were invited to author the Oxford Research Encyclopaedia’s entry on the ‘HIV/AIDS in South Africa’, which focuses on key research developments across the health and social sciences over the history of the epidemic.

**UK Impact**

In addition to global, regional, national and local dissemination, the research team also disseminated findings to UK-based audiences throughout the study. A selection of these include:

- **Academic and conference presentations** at the London School of Hygiene and Tropical Medicine: Social Protection, TB and HIV (2017) and University of Cambridge Policy Engagement Forum, Cambridge (September, 2014). As well as, several PhD research presentations at the University of Oxford on adolescents and antiretroviral treatment (ART) adherence.
- **Public Engagement** through a workshop at the University of Oxford’s Ashmolean Museum ‘LiveFriday’ series (May 2015)
- **Press releases:** ESRC Blog, AVERT article, Oxford Research Impact series.

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63 Rebecca Hodes, *HIV/AIDS in South Africa* (Oxford University Press, 2018), i.
Media Impact
A series of podcasts showcasing different aspects of the Mzantsi Wakho research project has recently gone live, and can be accessed at http://www.mzantsiwakho.org.za/news/mzantsi-wakho-podcast-episode-01

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Further Research and Analysis

Funding awarded by the Nuffield Foundation has supported the team’s successful completion the world’s largest longitudinal cohort study of adolescents living with HIV. The significant academic and policy impact of this research has created meaningful opportunity for several sub-studies to be carried forward. Subsequent research projects will continue to deliver rigorous evidence-based findings that will support young people in South Africa and the region.

HEY BABY (Helping Empower Youth Brought up in Adversity with their Babies and Young children) – 2018-2021. In 2016-2017, it became clear that HIV-positive adolescent mothers were struggling to disclose their status to our research team, dropping out of HIV care, and more likely to be defaulting from ART. We have developed a sub-study including HIV-positive and HIV-uninfected adolescent mothers and their children. This includes a sub-group of adolescent mothers who participated in Mzantsi Wakho. HEY BABY study tools were piloted in 2017 and in 2018, funding applications were successful for two rounds of mother-child data collection (2018 and 2020). Ethical approval was given from the Universities of Oxford (IDERC Ref No: R48876/RE001) and Cape Town (HREC REF 226/2017), and the South African Department of Health. The study aims to understand resilience-promoting factors for adolescent parents who are HIV-infected and affected. It includes an adolescent parent questionnaire which investigates the experience of pregnancy and parenthood, as well as their infants’ health, nutrition and care, and uses the Mullen Scales of Early Learning which measures child cognitive ability and motor development. The study was officially launched in March 2018 and has successfully recruited 973 young mothers and 1,064 children to date. Follow-up data collection has been awarded funding by ERC, MRC and CIPHER for 2020-2021.

UPLIFT Adolescent and youth living with HIV 2018-2027: Understanding Predictors of Lifelong Initiation and Follow-up Treatment for adolescents and youth living with HIV (UPLIFT) aims to establish a lifelong social science cohort for adolescents and youth living with HIV. It will combine three rounds of self-reported data from the Mzantsi Wakho participants (2014-2018) with health outcomes (mortality, viral suppression, TB infection, STIs, and CD4 count) to identify what childhood and adolescent-experiences shape later health outcomes in adolescents and youth living with HIV. In 2015-2016, the clinic-based research team went to more than 50 health facilities to locate and extract data from patient files for the 1,050 HIV-positive adolescents recruited in the baseline Mzantsi Wakho cohort. It was clear from these efforts, that the majority (75%) of adolescent patient files did not include recent viral load/ CD4 measurements.

The most reliable and exhaustive source of such data for the adolescents in the Mzantsi Wakho participants is the National Health Laboratory Services of South Africa (NHLS). Consent was obtained
from all participants and their caregivers during the third wave of the study to access this data. A partnership with NHLS was established in 2018 with the purpose of developing an algorithm that will match socio-demographic details of Mzantsi Wakho participants with biomarkers records in the NHLS data warehouse. Data from NHLS data warehouse will be extracted and matched every 2 years and analyses will be conducted by Dr Toska, Prof Cluver and quantitative researchers in training.

**ABCD: ASK, BOOST, CONNECT, DISCUSS** for improved mental health of adolescent mothers living with HIV in sub-Saharan Africa, is an initiative funded by the Gates Foundation & Grand Challenges Canada under a call for improved adolescent maternal mental health for the period of April 2018 to October 2019. ABCD is an adolescent co-developed package of care provided by young peer supporters living with HIV to reduce adolescent maternal mental health issues, with a focus on depression and self-care. Peer supporters in 4 Sub-Saharan African countries will use this mTraining & mSupervision tool (ABCD) to help young mothers living with HIV to access maternal depression care through: screening (ASK), evidence-based CBT-informed mental health support (BOOST), help with accessing services (CONNECT), and ongoing supervision and self-care (DISCUSS). The tool development is led by the Paediatric Adolescent Treatment for Africa (PATA) in collaboration with a joint research team at the Universities of Oxford and Cape Town (Toska, Wittesaele and Cluver).

**UKRI GCRF Accelerating Achievement for Africa’s Adolescents**

In early 2019 the UK Research and Innovation Council (UKRI) announced a long-term initiative which could significantly improve the health and life prospects of a generation of Africa’s youth. The **UKRI GCRF Accelerating Achievement for Africa’s Adolescents Hub** is led by an interdisciplinary team at Oxford University and the University of Cape Town, with University partners across Africa from South Sudan and the Democratic Republic of Congo to Lesotho and Tanzania. The Hub will work alongside international partners, governments across Africa, donors and young people themselves, to identify and test a range of ‘accelerator synergy’ service combinations, from across health, education, social and economic sectors. In doing so, they will determine which combinations, such as malaria prevention, business skills and violence prevention, offer teenagers across Africa the best opportunities to lead better, safer lives.
The following is a full list of the publications lead-authored or co-authored by the Mzantsi Wakho investigators until January, 2019.


18. Gittings, L. (2017). “He Can’t Say a Man’s Stuff to a Woman…” Perspectives on the Preferences of Men Living with HIV for Gender-Concordant Care Workers in Cape Town, South Africa. Men and Masculinities, 1097184X17732607.


34. Gittings, L. (2016). ‘When you visit a man you should prepare yourself’: male community care worker approaches to working with men living with HIV in Cape Town, South Africa. Culture, health & sexuality, 18(8), 936–950.
Publications under review

1. Sherr, L. Cluver L, Toska, E. He, E. (Revise and resubmit at AIDS Care). Mode of infection needs to be considered when understanding HIV in adolescent populations.
THE TEAM 2013-2018*

**Analysis and writing:** Mark Boyes, Laurence Campeau, Craig Carty, Lucie Cluver, Clare Dyer, Eda He, Lesley Gittings, Roxanna Haghighat, Rebecca Hodes, Franziska Meinck, Mosa Moshabela, Helen Natukunda, Mark Orkin, Marija Pantelic, Lorraine Sherr, Elona Toska, and Siyanai Zhou.

**Oxford team:** Lizzy Button, Jenny Doubt, Sarah Hoeksm, Colleen Kelly, Sally Medley, Maria Michaloupoulou, Melissa Pancoast, Louis Pilard, Amogh Sharma, and Camille Witesaele


**UCT team:** Nozuko Boqwana, Marius Coqui, Nondumiso Hlwele, Jane Kelly, Fundiswa Menziwa, Noxolo Myeketsi, Thobani Ncapai, Beth Vale, Sarah Walters, and Siyanai Zhou

**Clinic team:** Pumza Bellem, Nontuthuzelo Bungane, Zoliswa Marikeni, and Amanda Mbiko.

**Research assistants:** McKenzie Berezin, Shaan Bhambra, Niklas Bobrowitz, Khameer Kidia, Samantha Malungu, Amol Naik, Alice Redfern, and Alexa Yakubovich.

*alphabetically listed*