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STUDENT NUMBER: DYSBRY001 **DATE:** 1 November 2018

The executive function outcomes associated with HIV-infected adolescents in South Africa

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Abstract

With 36.9 million individuals living with HIV globally, and South Africa contributing 7.1 million, it is no surprise that HIV-associated outcomes are being questioned. Given the frontal lobe damage associated with HIV, executive functions (EFs) are said to be particularly affected, potentially causing detrimental health-related behaviours (i.e., poor medication adherence). Adolescents are particularly vulnerable to contracting and spreading HIV given their risk-taking behaviour. Therefore, this study focusses on the EF outcomes associated with HIV-infected adolescents in South Africa. The EF outcomes of an HIV-infected sample (n = 12) were compared to a matched control sample (n = 12) and it was hypothesised that the HIV-infected sample would score significantly lower on the various measures administered. Anderson's (2002) model was used as a theoretical basis, giving rise to four EF domains (attentional control, cognitive flexibility, goal setting, information processing). A single measure was used to asses each domain, namely the NEPSY-II Inhibition condition of the *Inhibition* subtest for attentional control, the CMS *Numbers Backwards* subtest for cognitive flexibility, the DKEFS *Tower test* for goal setting and the WISC-IV *Coding* subtest for information processing. Numbers Forwards, PIQ and VIQ were also recorded as control variables. No significant differences were found between the clinical and control samples. However, between-group differences were apparent and in the expected direction. Given the lack of locally published research, this study contributes to the knowledge base on adolescent HIV-infected EF outcomes in low SES communities and highlights issues for future research.

Keywords: adolescents; executive function; human immunodeficiency virus (HIV); low SES

With 36.9 million individuals living with the Human Immunodeficiency Virus (HIV) globally (UNAIDS, 2017), it is no surprise that the associated outcomes are being questioned and investigated (Cross, Combrinck, & Joska, 2013). Recently, executive function (EF) outcomes have been explored given the frontal lobe damage associated with HIV (Duncan, Emslie, Williams, Johnson, & Freer, 1996; Puthanakit et al., 2013). A portion of this research has focused on South Africa – given its status of having the highest HIV epidemic in the world (UNAIDS, 2016) – but the absence of studies focusing specifically on adolescent EFs indicates locally published literature is limited (Cross et al., 2013; Hoare et al., 2013; Laughton, Cornell, Boivin, & Van Rie, 2013). Given the association between poor EF outcomes and HIV, and the large proportion of the HIV-infected population being adolescent, this paper compares the EF outcomes of HIV-infected to -uninfected individuals to assess whether there are significant differences that could potentially lead to detrimental health and behavioural outcomes (Cross et al., 2013; Laughton et al., 2013; Nichols et al., 2015).

HIV in Adolescence

Adolescence is a developmental stage that incorporates those aged 10 to 19 (World Health Organisation [WHO], 2018). Often associated with psychosocial unpredictability, they are a vulnerable proportion of the population, highly susceptible to risk-taking behaviour (Chan, Tsai, & Siedner, 2015; Pettifor, Stoner, Pike, & Bekker, 2018; Steinberg, 2007). Adolescents have become known as the most likely group of individuals to contract HIV globally (Shisana et al., 2014; Steinberg, 2005). Given their heightened susceptibility to the disease, and based on research performed on children (rather than adolescents specifically), it is inferred that HIV-infected adolescents will tend to have EF deficits beyond those of an HIV-uninfected adolescent (Phillips et al., 2016). However, limited research connects the developmental stage of adolescence to these HIV-infected EF outcomes, particularly in low- to middle-income countries, such as South Africa (Nichols et al., 2015; Phillips et al., 2016).

Executive Functioning

EFs are cognitive processes associated with the prefrontal cortex of the frontal lobes (Duncan et al., 1996; Puthanakit et al., 2013). However, with white matter tracts throughout the brain, they are said to operate globally, controlling functions such as working memory, planning, and attention (Anderson, 2002; Laughton et al., 2013; Puthanakit et al., 2013). With a broad base of research indicating that HIV leads to EF deficits, which may cause detrimental health-related behaviours (e.g., poor medication adherence) (Laughton et al., 2013; Nichols et al., 2015), it is vital that these deficits are understood amongst adolescents, given their risk-taking tendencies (Anand, Springer, Copenhaver, & Altice, 2010).

One such detrimental behaviour is non-adherence to antiretroviral (ARV) medication (Nichols et al., 2015). ARVs limit the effect of HIV on an individual, potentially reducing the effect of the disease on frontal lobes (Inzaule, Hamers, Kityo, Rinke de Wit, & Roura, 2016; Williams, 2014). Existing studies have looked more broadly at adolescent HIV neurocognitive impairment (e.g., Hoare et al., 2013; Phillips et al., 2016), whilst a limited number of studies look specifically at EFs but tend to include data on children too (i.e., Haase, Nicolau, Viana, de val Barreto, & Pinto, 2014).

Impacting the central nervous system (CNS) in the early stages of infection, HIV reduces connectivity in the frontostriatal pathway of the brain (Cross et al., 2013). This is deemed one of the most detrimental consequences as it leads to decreased information processing speed (Hoare et al., 2013). It is hypothesised by Steinberg (2005) that decreased processing speed is exacerbated in adolescents due to the neural and developmental changes they are already undergoing. This, in combination with a variety of other EF deficits, affects one's ability to perform certain activities of daily living, such as adhering to medication.

Executive Functioning in HIV-infected Adolescents. International research gives rise to mixed findings regarding the differences in EFs between HIV-infected and HIV-

uninfected adolescents. Most studies indicate some significant differences (i.e., Haase et al., 2014), whilst others show no difference at all (i.e., Nichols et al., 2015). An issue in identifying the EF outcomes in HIV-infected adolescents is that their brains are changing and descriptions of how they are changing differ. However, using a theoretical model created by Peter Anderson (2002), the neuropsychological changes in adolescent EFs can be conceptualised and applied to the case of HIV-affected outcomes.

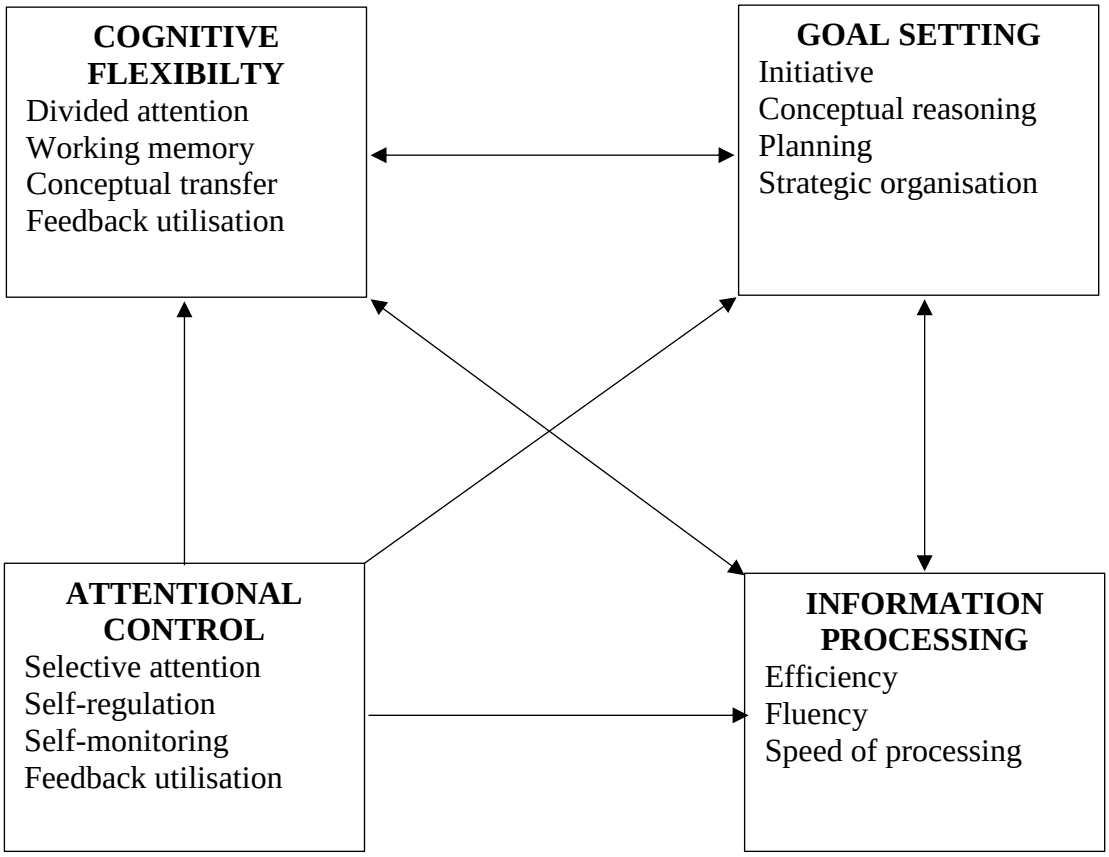

Figure 1. Peter Anderson's (2002) model of childhood

Anderson's Model of EF. Anderson (2002) describes EFs as being comprised of four discrete, but interconnected, domains operating together to allow executive control. These are outlined in Figure 1 above. Attentional control is said to be the most influential EF domain (Alexander & Stuss, 2000; Anderson, 2002). It is the domain that allows an individual to attend to specific stimuli for prolonged periods of focus, inhibit inappropriate

responses and regulate planned actions to execute them correctly. Cognitive flexibility is inclusive of working memory. It allows individuals to shift between different response sets given a variety of situations and learn from mistakes through the creation of new strategies (Anderson, 2002). Goal setting is also linked to cognitive flexibility (as well as the other two domains) as it focuses on strategy development, but incorporates pre-planning and problem-solving skills. Information processing, the fourth and final EF in Anderson's model, involves the fluency, efficiency and speed of output (2002). This is an indication that it is heavily reliant on the integrity of neural connections across the brain, which are affected when a person is living with HIV.

Executive functioning developmental trajectory. With Anderson's (2002) model explained, one can discuss the developmental trajectory of EFs, which not only differ across, but within domains. When looking at attentional control, it is known that inhibited responses occur from as early as 12 months and continue to improve until age six (Diamond & Doar, 1989; Diamond & Goldman-Rakic, 1989). At age nine, just before adolescence, a child should be able to regulate actions well (Anderson, Anderson, & Lajoie, 1996). Information processing follows a slightly different trajectory, with the most significant advancements only evident after age nine (Kail, 1986). Efficiency and fluency continue to improve into adolescence but only minimally after 15 (Hale, 1990; Kail, 1986). This is similar to that of cognitive flexibility and goal setting as, in both cases, refinement is still taking place into adolescence (Anderson, Anderson, Northam, Jacobs, & Catroppa, 2001). The main difference between these two EF domains – that is, cognitive flexibility and goal setting – is that cognitive flexibility sees development of the switching of sets from as early as age three (Espy, 1997), whereas significant advancements are only seen at age seven for goal setting (Anderson et al., 1996; Krikorian & Bartok, 1998).

With the above information in mind, it is understandable that there may be issues in identifying exactly where the adolescent HIV-associated deficits in EFs lie given the wide range of executive developments already taking place. As outlined earlier, HIV is associated with decreased connectivity within the frontostriatal pathway (Cross et al., 2013). This neural network is primarily involved in speed of information processing; thus, HIV gives rise to abnormally slow output production. In adolescents, where information processing is still undergoing refinement, it is predicted that this outcome in particular will be exacerbated, as has been demonstrated in children (Murthy, Nayak, Joshi, & Ninawe, 2018; Puthanakit et al., 2013). However, this outcome has not been outlined in South African adolescent literature.

Executive functioning and low socioeconomic status (SES). An area of literature that has been explored extensively is the association between EFs and low SES backgrounds. Research indicates that low SES is negatively associated with executive functioning, particularly the domains of attentional control and cognitive flexibility (Hackman, Gallop, Evans, & Farah, 2015; Noble, Norman, & Farah, 2005; Sarsour et al., 2011). On top of this, with most longitudinal studies being performed from early childhood, low SES has also been found to be a predictor of poor EF development (Hook, Lawson, & Farah, 2013; Noble et al., 2005). This implies that adolescents living with HIV and living in low SES communities may experience exacerbated deficits. Again, issues may arise in locating the EF deficits directly associated with HIV. It is also noted that the link between low SES and poor EF development is based on international, rather than locally published literature.

Aims and Hypotheses

There is a significant gap in research pertaining to EF outcomes in HIV-infected adolescents in South Africa (Cross et al., 2013; Hoare et al., 2013; Nichols et al., 2015). This study aims to close this gap by identifying an EF outcomes profile (aligned with Anderson's (2002) model) for HIV-infected adolescents. Ultimately, it is hoped that this information

improves the HIV-infected EF outcomes knowledge base. Given the health and behavioural deficits associated with poor EF outcomes, such as defaulting on antiretroviral therapy, it is also hoped that the improved knowledge base will inform future interventions aimed at improving medication adherence within the adolescent age group (Nichols et al., 2015). There is a single, main hypothesis being tested:

1) The HIV-infected clinical sample will demonstrate significantly lower scores of executive functioning compared to a control group.

A further aim of the study is to create an EF neuropsychological profile for HIV-infected adolescents – specifically those living in South Africa – for future reference.

Methods

The current study forms part of a larger study: *Investigating the efficacy of a Goal Management Training (GMT) intervention in increasing adherence to antiretroviral therapy among adolescents living with HIV in South Africa*, run in association with the Desmond Tutu HIV Foundation. In terms of my role within the study, I assisted with the collection of data for some of the HIV-infected participants and all control participants. I was also responsible for the recruitment of all control participants. I cleaned, entered and analysed all data pertaining to the current study as well as assisted with the scoring of some of the HIV-infected and control participants.

Research Design and Setting

This study is quantitative, cross-sectional and exploratory in nature, following a between-subjects research design. Testing was performed on two groups: 1) an adolescent HIV-infected sample from the Hannan Crusaid Youth Development Programme (HCYDP), and 2) a matched community-recruited control group. Data collection took place in Gugulethu, at the Hannan Crusaid Treatment Centre, for the HIV-infected group and at the University of Cape Town (UCT) for controls.

The independent variable (IV) for the research study is the two groups, and the dependent variables (DV) are the various EF test scores. The HIV-infected sample's EF test scores were compared to those of the control group for the between-subjects component of this study and to create an HIV-infected adolescent EF outcomes profile.

Participants

Recruitment. The HIV-infected sample comprised of isiXhosa-speaking individuals from low socioeconomic status (SES) backgrounds, aged 14 to 16 years. The control group (i.e. non-HIV-infected individuals) was matched to the HIV-infected participants by age, sex and home-language, also residing in low SES areas. All HIV-infected participants were recruited from the HCYDP, whilst the matched controls were sampled from surrounding communities. This was achieved via word-of-mouth as staff members at UCT and personal contacts who reside in similar areas to the clinical population were asked if they have relatives or friends with HIV-uninfected children between the ages of 14 and 16 who would be willing to take part in our study. Once this was established, further questioning took place telephonically for matching purposes.

HIV-infected group exclusion criteria.

Secondary HIV co-morbid medication. Adolescents taking medication for secondary/co-morbid HIV-illnesses were not considered for the study. This included, but was not limited to, individuals on medication for comorbid HIV-related tuberculosis (TB). The premise upon which these individuals were excluded is that it has been found that administering co-morbid medication compromises adherence to ARV treatment which, in turn, affects executive functioning (e.g., Weiss et al., 2016). This is primarily because it is stated these medications should not be taken in conjunction with ARV treatment to begin with (Weiss et al., 2016).

Prenatal exposure to substance use. Prenatal exposure to substance use has been seen to confound a variety of HIV-related impairments, including EF outcomes (Mattson, Crocker, & Nguyen, 2011). A substance-related diagnosis or condition due to prenatal substance exposure, such as Foetal Alcohol Spectrum Disorder (FASD), may exacerbate the existing EF outcomes associated with HIV (Mattson et al., 2011). This was determined via self-report by the larger study where parents/caregivers were asked if their children may have been exposed to substances (i.e., alcohol or tobacco) *in utero* or had any past or existing diagnosed disorders.

Control group exclusion criteria. The primary exclusion criterion for the control group was whether they were HIV-infected or unsure of their HIV-status. This was determined via self-report when participants were asked whether they, or their mother, had being diagnosed with HIV. Given the potential consequences of prenatal HIV exposure, participants with an HIV-infected mother – regardless if the participant was HIV-uninfected – were excluded. Control participants also had to meet the matching criteria outlined above.

Power analysis. The study recruited 12 HIV-infected adolescents and 12 matched controls, with a total sample size of 24 ($N = 24$). Using an alpha level of .05 and a medium effect size of Cohen's $d = .50$, a statistical power of 0.22 was generated. This in an indication that the study is very underpowered. While data collection for the larger study is ongoing, scope and time constraints limited the number of participants I could include in my analyses.

Measures

Participants from both the HIV-infected and control group were isiXhosa-speaking, hence, interpreters were required for all testing sessions. The interpreters were provided with translated versions of all measures, which had also been back translated and approved. A single measure was used to asses each of Anderson's (2002) four EF domains (cognitive flexibility, goal setting, attentional control and information processing). SES, *Numbers*

Forwards, verbal, performance and full scale intelligence measures are also reported as these confound the EF scores if between-group differences are observed. Almost all measures have been successfully implemented in South Africa (see Hoare et al., 2013).

Socioeconomic status.

Sociodemographic Questionnaire. This is a questionnaire that incorporates questions on income, occupation and education to assess SES (see Appendix A). This was completed by parents/caregivers to determine that the inclusion criterion of low SES background was met. Given poor completion and return rates, school quintile was used to determine that the low SES criterion was met. School quintile is a univariate, contextual measure of SES, using the surrounding community as an indicator of poverty and how much families can afford for schooling (Department of Basic Education [DBE], 2006; Oakes & Rossi, 2003).

General intellectual functioning.

***Wechsler Abbreviated Scale of Intelligence* (WASI).** The WASI (Wechsler, 2011) is appropriate for individuals aged 6 to 90 years and reliability scores range from .81 to .93 across the four subtests. It is used to assess general intellectual functioning (full scale intelligence [IQ]), with the *Vocabulary* and *Similarities* subtests making up the Verbal IQ index whilst the *Block design* and *Matrix reasoning* subtests make up the Performance IQ index. Overall, the greater the score, the better your intelligence.

Vocabulary. This subtest is used to assess language development and vocabulary acquisition. There is a total of 42 items. The first four items are images that the participant is required to name. The remaining items are words read out by the investigator where the participant must provide a definition.

Similarities. This subtest assesses verbal concept formation and reasoning. It is a 26-item subtest that requires the participant to explain how two words are similar.

Block design. This subtest is used to assess perceptual organisation and visualization, visual-motor co-ordination and the ability to perceive abstract formations. The 13-item subtest requires that participants replicate patterns of cubes within a given amount of time.

Matrix reasoning. This subtest allows for the assessment of nonverbal reasoning. The 35-item subtest requires participants to select one of five possible missing pieces to complete a variety of matrices.

Executive function.

***Wechsler Intelligence Scale for Children* (WISC-IV).** This test has been normed for children aged six to 16 years, with internal reliability scores between .79 and .90 being reported across the 10 subtests (Kezer & Arik, 2012). The *Coding* subtest (a speed of processing measure) was used to assess the information processing EF domain. In this subtest, participants are required to copy a series of geometric shapes to corresponding boxes with numbers, to which they are paired, in a two-minute period of time.

Children's Memory Scale (CMS). The CMS is normed for children aged five to 16 years (Cohen, 1997). The Numbers subtest was the only CMS subtest used in this study. Reliability coefficients range from .61 to .93 and content validity coefficients range from .06 to .96 (Cohen, 1997). *Numbers Backwards* (a measure of working memory) was used to assess the cognitive flexibility EF domain. The test involves repeating a series of digits backwards. The *Numbers Forwards* component assesses attention as a participant is simply required to repeat a set of digits.

Delis-Kaplan Executive Function System (DKEFS).

Tower test. This is a measure of planning and it was the only DKEFS subtest used in the study as it assesses the goal setting EF domain. The DKEFS battery has been normed for individuals aged eight to 89 years (Delis, Kaplan, & Kramer, 2001). The subtest measures both accuracy and efficiency when replicating a series of pegs in a tower formation. This

should be done in the fewest number of moves whilst only moving one peg at a time and without placing larger discs on top of smaller ones (Delis et al., 2001). A detailed DKEFS manual provides evidence of the validity and reliability of all subtests (Delis et al., 2001).

NEPSY-II. This neuropsychology battery has been normed and standardized for children aged five to 16 years with both strong content and construct validity (Korkman, Kirk, & Kemp, 2007). Only the Inhibition condition of the Inhibition subtest was used to assess the attentional control EF domain. The Inhibition condition is one of three conditions, namely Naming, Inhibition and Switching, in the subtest. The Inhibition condition requires participants to use alternative names for the same shapes. For example, on a sheet with circles and squares, one will have to name the circles "squares" and the squares "circles".

Procedure

Prior to the commencement of testing, parents/caregivers of both the HIV-infected and control group were offered a consent form to review and complete if they showed interest in participating in the study (see Appendix B and C). The adolescents from both groups were provided with an assent form to review and complete when interest in partaking in the study was shown (see Appendix D and E). Parents/caregivers and participants had the study explained to them in person or telephonically prior to the signing of consent/assent forms. These were collected prior to testing or brought to the testing site on the day of testing. All consent, assent and testing documents were translated into isiXhosa by the Stellenbosch University Language Centre. Testing was administered by myself, a neuropsychology Masters intern and two neuropsychology Masters students. Tests were administered to participants individually at the Hannan Crusaid Treatment Centre in Gugulethu and at UCT. Interpreters assisted with communication as participants were isiXhosa-speaking. Each testing session took between two to three hours to complete. Upon completion, participants were provided with R50 for transport and a R50 food voucher as compensation for their time.

Data Management and Statistical Analysis

Statistical procedure. All data was analysed using SPSS Version 25.

Scoring procedure. The scoring procedure outlined in each tests' administration manual was followed. All raw scores obtained were converted into age-adjusted scaled scores so that the appropriate comparisons between tests could be made.

Demographic information. Descriptive statistics are provided on the demographics of all participants. These include descriptors such as sex, age, school quintile and fee-paying status. Between-group differences for continuous variables were assessed using independent sample *t*-tests ($\alpha = .05$) to ensure the HIV-infected and control group were as closely matched as possible. Chi-square tests were used to assess categorical variables.

Executive function (EF).

Correlations. Pearson's *r* correlations were computed for the four EF measures to determine that they were assessing separate domains.

Analysis of variance. A one-way ANOVA was used to determine whether the HIV-infected group's mean test scores for each of the four EF domains differed significantly from the control group. Four analyses were run.

Multiple regression. A hierarchical regression was run for each of the four EF tests, controlling for the scores of *Numbers Forwards*, PIQ and VIQ. This determined whether other neuropsychological domains unduly influenced the outcome variables.

Ethical Considerations

Ethical clearance was granted by the University of Cape Town's Department of Psychology Research Ethics Committee (DPREC) and the Faculty of Health Sciences Human Research Ethics Committee (see Appendices F and G). An ethical amendment to include community controls was also approved by the DPREC (see Appendix H).

Informed Consent and Assent

Written consent from the parents/caregivers (see Appendices B and C) and assent from the participants (see Appendices D and E) was obtained prior to assessment and subsequent to being informed of the study.

Voluntary Participation

Participants and their parents/caregivers were notified that participation is voluntary and, if at any point, they wished to remove themselves from the study, or not start the study at all, they could and there were no consequences.

Confidentiality and Anonymity

Participants were assured of the confidentiality of the study. All information pertaining to the study was kept in a locked cabinet or within computer files that require passcodes to access. Participants were notified that only the researcher, her supervisors and co-investigators from the HCYDP were allowed access to confidential information. Anonymity was ensured as no identifiers (i.e. name and school) are reported in this study.

Risks and Benefits

Risks. Due to the long testing procedure, participant fatigue became apparent. However, participants were offered refreshments throughout the extended testing session and were allowed to take a break whenever they felt they needed to.

Benefits. To thank participants for their time, R50 food vouchers were offered as a token of appreciation. For those who travelled to the testing site, R50 was provided for transport. Accompanying parents/caregivers were also provided with transport reparation.

Debriefing. Participants will be provided with a summary of their performance upon completion of the larger study. This will also provide contact details should participants or their parents/caregivers have additional questions or concerns.

Results

Sample Characteristics

Table 1 indicates the sample characteristics of both the HIV-infected group and the control group. Independent sample *t*-tests established that the matching of the continuous variable (age) was appropriate, and no significant difference were detected. Chi-square tests of contingency determined that no significant differences existed between the clinical and control samples across all categorical variables (school quintile, fee-paying status and sex). Given that all participants were isiXhosa speaking, no statistics were computed. The above information indicates that the matching characteristics have not unduly influenced the EF outcome variables that will be elaborated on below.

Table 1

Sample Demographic Statistics (N = 24)

	Group				
	HIV-infected (*n* = 12)	Control (*n* = 12)			
Variable	*M (SD)*	*M (SD)*	*df*	*p*	ESE[a]
Age (years)	14.58 (0.79)	14.58 (0.67)	22	1.000	<.001
Sex (M:F)	3:9	3:9	1	1.000	<.001
Quintile[b] (1-5)	3.13[c, d] (0.35)	3.09 (0.70)	3	.416	.377
Fee-paying (Y:N)	1:7	1:11	1	.830	.047

Note. ESE = Estimate Size Estimate.

[a]*ESE*: Cohen's *d* for independent sample t-tests and ϕ for chi-square tests of contingency.

[b]*Quintile*: South African public school ranking system based on the wealth of the surrounding community (1 being the poorest and 5 being the wealthiest) to determine learner subsidisation. Data was retrieved from the Department of Basic Education [DBE] (2017).

[c]Three HIV-participants did not provide information on their school. [d]Quintile information was not provided for one school by the DBE (2017), thus, the group *n* was reduced to *n* = 8. This school is still classified as a no-fee school.

Control Variables

Descriptive statistics and between-group differences (calculated using one-way ANOVA and a significance level of $\alpha = .05$) were computed for the PIQ and VIQ scores, all WASI subtests and the *Numbers Forwards* subtest of the CMS. These are outlined in Table 2 below and no significant differences are observed. This indicates that, within this study, these domains of neuropsychological functioning are unlikely to significantly impact the EF outcomes being assessed. It was expected that the WASI subtest scores and the overall measures of IQ would be below international averages (Shuttleworth-Edwards et al., 2004). Some scores, specifically PIQ, are below the low SES South African average IQ score of approximately 80 (Shuttleworth-Edwards et al., 2004). However, previous South African IQ statistics, based on secondary school children, gave rise to similar, sometimes lower scores (see Lynn & Meisenberg, 2010; Skuy, Schutte, Fridjhon, & O'Carroll, 2001).

Table 2

Between-group Differences and Descriptive Statistics for Control Variables (N = 24)

	Group				
	HIV-infected (n = 12)	Control (n = 12)			
Variable	*M (SD)*	*M (SD)*	*F*	*p*	η^2
CMS					
Numbers Forwards[a]	5.42 (2.81)	5.58 (2.97)	0.02	.889	.001
WASI[a]					
Vocabulary	7.00 (3.10)	7.58 (3.65)	0.18	.678	.008
Similarities	4.17 (3.16)	6.33 (2.71)	3.26	.085	.129
Block Design	4.42 (2.43)	5.50 (3.00)	0.95	.342	.041
Matrix Reasoning	5.08 (2.91)	4.92 (2.78)	0.02	.887	.001
PIQ[b]	73.50 (11.02)	75.67 (11.69)	0.22	.645	.010
VIQ[b]	79.25 (13.18)	85.00 (13.17)	1.14	.297	.049

Note. WASI = Wechsler Abbreviated Scale of Intelligence; PIQ = Performance Intelligence Quotient; VIQ = Verbal Intelligence Quotient.

[a]*Numbers Forwards* and all subtests of the WASI are expressed as scaled-scores.

[b]PIQ and VIQ are expressed as scaled IQ scores.

Outcome Variables

Descriptive statistics. Table 3 outlines the descriptive statistics for the four measures of EF. It is noted that all standard deviations are within an acceptable range and, thus, are no cause for concern. The inter-correlations between the four EF domain measures were also assessed and found to be non-significant. Values ranged from r = -.10 to r = .37. This is an indication that the fours measures are likely assessing four discrete domains, as highlighted by Anderson (2002). Upon inspection of the means, it appears that only some differences in EF scores may exist – particularly processing speed, as demonstrated through the *Coding* subtest – but whether these differences are significant requires further analysis (as reported on below). The *Tower test* means are identical across the HIV-infected and control group.

ANOVA. A one-way ANOVA was performed for each of the four EF domains outlined in Anderson's (2002) model. All assumptions were met, but it is noted that certain variable distributions were slightly skewed. Given the robustness of the assumptions, I proceeded with the analyses, but caution should be exercised when generalising these findings to other populations (Field, 2009). All results are reported in Table 3 below.

Attentional control. Table 3 indicates that no significant difference is observed when comparing the *Inhibition* error score means of the HIV-infected and control groups. The estimated marginal means in Figure 2 indicate that the predicted directionality may exist, but this difference is only slight and the small effect size, η^2 = .001, also indicates no significant difference exists.

Cognitive flexibility. Table 3 confirms no significant difference exists between the mean *Numbers Backwards* scores of the HIV-infected and control group. However, as is seen in Figure 2, and given the directionality of the means, it appears that a difference may exist, but the underpowered sample size may be contributing to the lack of significance. It is also noted that, when removing an outlier, the difference tends more towards significance,

$F(1) = 2.81$, $p = .109$, $\eta^2 = .118$. This is a medium to large effect size and an indication that the underpowered sample size may be giving rise to the lack of significance.

Goal setting. Table 3 demonstrates that, as expected based on the means, the *Tower test* move-accuracy score means across the HIV-infected and control group are also not significantly different and are actually the same.

Information processing. The *Coding* scores are also not significantly different (see Table 3). With $p = .152$, this is the lowest significance observed across the four EF measures, excluding analyses run without outliers. Figure 2, again, indicates that the predicted directionality of the mean EF scores may be observed. A medium effect size, $\eta^2 = .091$, is an indication that statistical significance may be lacking due to the underpowered sample size.

Overall, the above results do not confirm the hypothesis that the HIV-infected clinical sample will demonstrate significantly lower scores of executive functioning compared to a control group. The group means are, however, in the expected direction for cognitive flexibility and information processing, as seen in Figure 2.

Table 3

Between-group Differences and Descriptive Statistics for Outcome Variables (N = 24)

	Group				
	HIV-infected (n = 12)	Control (n = 12)			
Variable	*M (SD)*	*M (SD)*	*F*	*p*	η^2
WISC-IV					
Coding	4.67 (2.10)	6.00 (2.30)	2.20	.152	.091
CMS					
Numbers Backwards	5.92 (2.87)	7.00 (2.89)	0.85	.367	.037
DKEFS					
Tower Tests	7.25 (3.17)	7.25 (2.83)	<0.01	1.000	<.001
NEPSY-II					
Inhibition (Errors)	9.67 (3.45)	9.83 (4.06)	0.01	.915	.001

Note. WISC-IV = Wechsler Intelligence Scale for Children; CMS = Children's Memory Scale; DKEFS = Delis-Kaplan Executive Function System

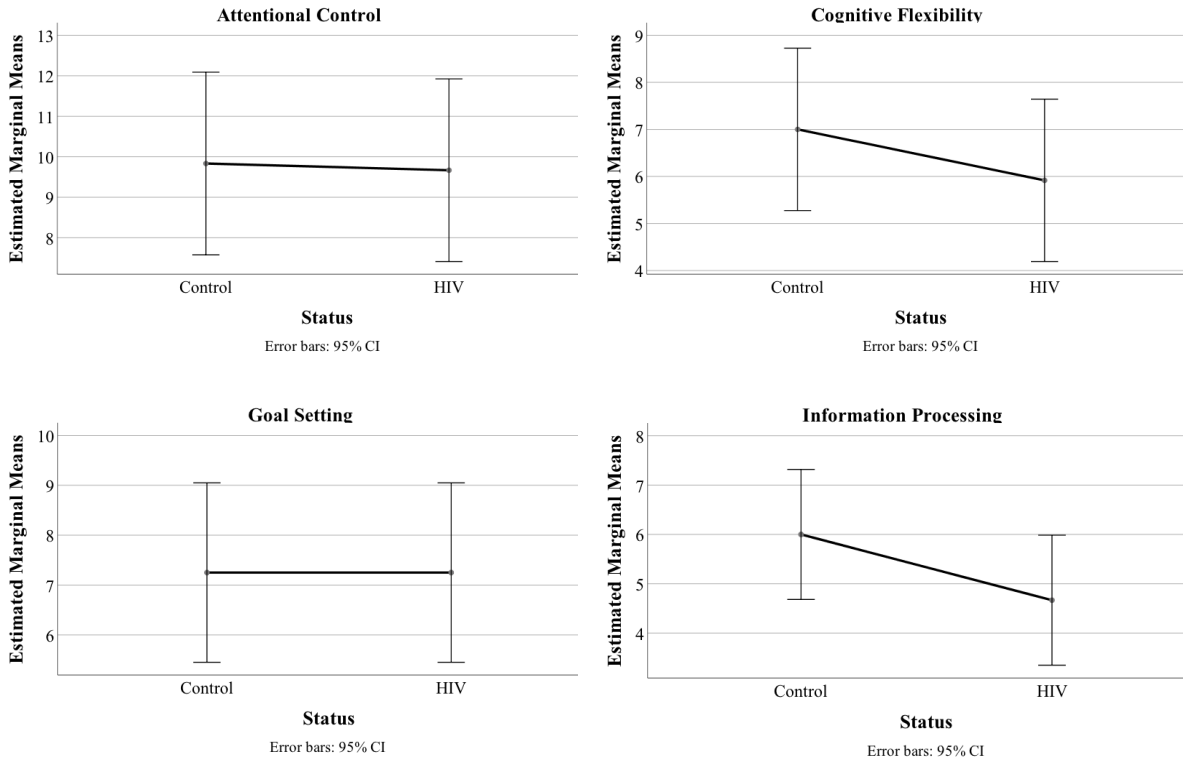

Figure 2. Estimated Marginal Mean Plots for the Four EF Domains.
Note. EF = Executive Function; CI = Confidence Interval.

Multiple regression. The scaled and standardised scores for *Numbers Forwards*, the WASI PIQ and VIQ indexes are used in the regression analyses below to see if they have confounding effects on the outcome variables. Basic attention (measured using *Numbers Forwards*) is a gateway function for other neuropsychological tasks, whilst poor intellectual functioning (measured by PIQ and VIQ) may undermine the neuropsychological testing of other domains (Mahone et al., 2002; Middlebrooks, Kerr, & Castel, 2017). HIV-status was inputted as the primary predictor of the various EF measures. The control variables outlined above were added as a block to each of the hierarchical regressions in step 1 to determine whether they had confounding effects on the outcome variables. Regarding the underlying regression assumptions, the residuals are mostly normally distributed and homoscedasticity is upheld. Linearity may be slightly problematic, thus, caution should be exercised when generalising the model (Field, 2009). The results are outlined in Table 4 below.

It is noted that the sample size (N = 24) is too small for regression analyses to measure the influence of age, sex and low SES (school quintile and fee-paying status act as proxies for this) on the outcome variables, thus, they were not entered.

Attentional control. As was observed in the lack of between-group differences above, HIV-status is not seen to be a significant predictor of attentional control. The change statistics indicate that the addition of HIV-status as a predictor made the regression less significant, $F(1, 19) = 0.07$, $p = .795$. The R^2 change value (< .01) also indicates that less of the variance in the *Inhibition* scores is explained by the presence of HIV than other variables. However, none of the potential confounding variables are returned as significant predictors.

Cognitive flexibility. The *Numbers Backwards* hierarchical regression indicates that none of the control variables are significant predictors of the working memory EF measure. However, *Numbers Forwards* tended most towards significance, potentially indicating the influence of basic attention on EF measures. The significance of the overall regression, prior to the inclusion of HIV, was close to the $p = .05$ threshold, $F(3, 20) = 2.59$, $p = .081$. The change statistics are, again, non-significant, $F(1, 19) = 0.68$, $p = .421$. This mirrors the between-group results obtained above: HIV is not a significant predictor of EF outcomes. However, as can be seen in Table 4 below, the negative directionality of the effect when HIV-status is added as a predictor is correct, $\beta = -.16$.

Goal setting. Given the ANOVA results for the *Tower test* move-accuracy mean scores, it was predicted and it is observed that HIV does not significantly predict the EF domain of planning. Prior to the inclusion of HIV-status, the regression with only the control variables as predictors was not significant, $F(3, 20) = 0.50$, $p = .684$. Change statistics, as observed above, indicate that the addition of HIV-status does not significantly influence the outcome variable, planning, $F(1, 19) < .01$, $p = .946$, but the directionality is correct, $\beta = -.02$.

Information processing. HIV does not significantly predict the *Coding* measure of processing speed. However, as was observed with cognitive flexibility, the directionality of the outcome variable change when HIV-status is added as a predictor is in the hypothesized, negative direction, β = -.23. It is also noted that none of the potentially confounding variables were significant. The overall regression was statistically significant at the .05 level both prior to – $F(3, 20) = 4.41$, $p = .015$ – and after the addition of HIV-status, $F(4, 20) = 3.85$, $p = .019$. This is appropriate for the main hypothesis, but concerning when considering the significance of the confounding effects observed. However, the change statistics indicate that the addition of HIV-status as a predictor does not significantly influence the outcome variable, $F(1, 19) = 1.69$, $p = .209$. R^2 change is .05, indicating that not much more of the variance in the outcome variable is explained by the addition of HIV-status.

The above results indicate that other neuropsychological domains, as those measured here, do not significantly impact the scores of executive functioning in the current study.

Table 4
Hierarchical Regression Analyses Controlling for Potential Confounding Variables (N = 24)

Variables Entered	*B*	*SE B*	*β*	*t*	*p*
HIV and Attentional Control, Controlling for Numbers Forwards, PIQ and VIQ.					
Step 2					
Constant	2.81	6.67		0.42	.679
Numbers Forwards	0.08	0.33	.06	0.23	.821
PIQ	-0.04	0.08	-.12	-0.51	.613
VIQ	0.11	0.07	.41	1.57	.133
HIV-status	0.41	1.57	.06	0.26	.795
HIV and Cognitive Flexibility, Controlling for Numbers Forwards, PIQ and VIQ.					
Step 2					
Constant	6.58	4.72		1.39	.179
Numbers Forwards	0.45	0.23	.44	1.93	.069
PIQ	-0.08	0.06	-.31	-1.44	.167
VIQ	0.05	0.05	.22	0.91	.373
HIV-status	-0.91	1.11	-.16	-0.82	.421
HIV and Goal Setting, Controlling for Numbers Forwards, PIQ and VIQ.					
Step 2					
Constant	11.35	5.58		2.03	.056
Numbers Forwards	0.17	0.28	.16	0.62	.544
PIQ	-0.08	0.07	-.29	-1.15	.265
VIQ	0.01	0.06	.04	0.13	.896
HIV-status	-0.09	1.31	-.02	-0.07	.946
HIV and Information Processing, Controlling for Numbers Forwards, PIQ and VIQ.					
Step 2					
Constant	-1.97	3.31		-0.59	.559
Numbers Forwards	0.26	0.16	.32	1.57	.134
PIQ	0.06	0.04	.27	1.41	.174
VIQ	0.03	0.04	.16	0.78	.448
HIV-status	-1.01	0.78	-0.23	-1.30	.209

Note. Each row summarises the results of a multiple regression analysis examining the effect of potential confounding variables on the relationship between HIV and executive functioning. Only Step 2 of the two-step hierarchical regression is shown as no significant changes were observed with the addition of HIV-status as a predictor. HIV = Human Immunodeficiency Virus; PIQ = Performance Intelligence Quotient; VIQ = Verbal Intelligence Quotient; *B* = unstandardised beta value; *SE B* = standard error of *B*; *β* = standardised beta value.

Discussion

The main aim of this study was to investigate whether the presence of HIV negatively influences scores of the four domains of executive functioning (attentional control, cognitive flexibility, goal setting and information processing) within an HIV-infected adolescent sample in South Africa. A single hypothesis was tested to assess this. The findings related to this hypothesis will be discussed in relation to recent and relevant literature below, before limitations and recommendations for future research are explored.

Control Variables

The control variables gave rise to unanticipated, but interesting findings regarding domains of neuropsychological functioning, excluding EFs. The scaled scores for all subtests of the WASI and the overall scores for PIQ and VIQ are slightly below, but mostly consistent with previously reported South African statistics for all participants within the study (Lynn & Meisenberg, 2010; Skuy et al., 2001). In Lynn and Meisenberg's (2010) systematic review, Full-scale Intelligence Quotient (FIQ) scores ranged from $M = 65$ to $M = 79$ in South Africa. Shuttleworth-Edwards et al. (2004) also highlight that South African IQ scores tend to be 20 IQ points lower than international averages. It is hypothesised, and has been observed in previous literature (i.e., Hook et al., 2013; Noble et al., 2005), that the below-average scores in this study are not only due to the presence of HIV, but also low SES.

The importance of this in relation to the control variables is that, when looking at potential confounding effects, it may be the effect of low SES rather than the other domains of neuropsychological functioning that are causing differences to be observed. This has been seen in previous South African and international literature (Hackman et al., 2015; Noble et al., 2005; Sarsour et al., 2011). Given the small sample size, and the poor completion and return rates of SES questionnaires, it was not appropriate to add school quintile (an SES proxy) to the regression analyses outlined in Table 4. However, the below-average PIQ and

VIQ scores across both the HIV-infected group and the control group indicate that the effect of low SES may be prevalent across the entire sample (N = 24).

Executive Functioning

The univariate analyses address the main hypothesis: the HIV-infected clinical sample will demonstrate significantly lower scores of executive functioning compared to a control group.

Contrary to *a priori* predictions, no significant between-group differences were observed across the HIV-infected and control groups for *attentional control*. The *Inhibition* subtest of the NEPSY-II Inhibition test was used to assess attentional control and, even though slight differences are observed when looking at the means, this difference was not large enough to warrant a statistically significant result. The same can be said for the measures of *cognitive flexibility* and *information processing*. *Cognitive flexibility* was assessed using the *Numbers Backwards* subtest of CMS. Although not statistically significant, mean differences are seen between the HIV-infected and control groups in the expected direction (i.e., the HIV-infected group scoring more poorly than the control group). *Information processing* was assessed using the *Coding* subtest of the WISC-IV. Once again, a significant difference was not observed, but a mean difference in the correct direction appears to exist. The measure of *goal setting*, the *Tower test* of DKEFS, shows no significant, or observed, between-group difference at all. Overall, one cannot confirm the hypothesis as the HIV-infected adolescent group did not score significantly lower than the control group across the four EF domains

With this in mind, it can be said that the results are inconsistent with locally and internationally published literature pertaining to EF outcomes HIV-infected individuals (Hoare et al., 2013; Cross et al., 2013). It is noted that this existing literature mostly pertains to younger children or adults – not specifically the adolescent age group – and this study

aimed to fill this gap in the literature. This will be touched on further, but the inconsistencies of this study need to be explored in relation to relevant literature.

The work of Cross et al. (2013), Phillips et al. (2016) and Hoare et al. (2013) highlights the importance of processing speed, specifically during the developmental phase of adolescence. It is proposed that processing speed is impaired in adolescents (HIV-infected or not) due to the changes these individuals are undergoing within the frontostriatal pathway of the frontal lobes (Steinberg, 2005). Given the HIV-associated neurological damage to this part of the brain, HIV is said to exacerbate these deficits further, giving rise to slow output production and information processing (Hoare et al., 2013). These findings have been observed in studies performed on children, but it is noted that little research exists within South Africa, specifically on adolescents (i.e., Murthy et al., 2018; Puthanakit et al., 2013). Regardless, the proposed directionality of HIV negatively impacting the EF domain of information processing is seen within this study (see Figure 2), but the lack of significance means the hypothesis cannot be confirmed. This could be due to a number of methodological limitations, the underpowered sample size being just one.

The use of a specific model of EF could be another reason discrepancies are seen between the findings of this study and previous literature. Anderson's (2002) model classifies all aspects of executive functioning into four discrete domains. In some ways, this is a strength of the study as few studies have utilised a theoretical model to conceptualise EFs in HIV-infected individuals. Previous research has tended to explore the topic more broadly through the utilization of substantially more measures than this study (Laughton et al., 2013). Previous literature has also tended to look more generally at the neurocognitive impairment associated with HIV, rather than focusing specifically on EF outcomes (Anand et al., 2010; Laughton et al., 2013). The use of more measures (i.e., for each of the EF domains outlined in Anderson's (2002) model) and a broader definition of EF may have made the findings more

consistent with previous work (i.e., Krikorian & Bartok, 1998; Phillips et al., 2016; Willen, Cuadra, Arheart, Post, & Govind, 2017). Given the lack of South African literature pertaining to HIV-infected EF outcomes in general, regardless of the research relating to adolescents, it may have been more appropriate for this study to be less specific.

The lack of locally published literature in the field of HIV-associated EF outcomes makes it difficult for this study to be compared in its entirety to another study and highlights the importance of future local research in the area. Findings from various studies were assessed when generating the *a priori* prediction that HIV-infected adolescents would score significantly lower on measures of EF outcomes compared to a control group (i.e., Cross et al., 2013; Phillips et al., 2016), but it is also noted that, in some instances, no significant differences were observed (Hoare et al., 2013; Nichols et al., 2015). In this study, ARV medication adherence could be contributing to non-significant results as research suggests that ARVs can limit HIV-related neuropsychological effects by potentially reducing the effect of the disease on frontal lobes (Inzaule et al., 2016; Williams, 2014). However, I did not obtain such data and, thus, it is not within this study's scope.

Small sample size is believed to be one of the biggest contributors to the lack of significant differences in this study. It is also hypothesised that low SES has a substantial effect on EF outcomes (Hook et al., 2013; Noble et al., 2005). In South Africa, the highest prevalence rates of HIV are found within the poorest communities (Laughton et al., 2013). This study recruited participants – both HIV-infected adolescents and controls – from such locations and, thus, the effect of low SES is likely to have been influential. Combined with this study's small sample size, the effects may have been exacerbated across the four EF domains, particularly attentional control and goal setting, which have been highlighted as being the most affected EFs in existing literature (Hackman et al., 2015; Noble et al., 2005; Sarsour et al., 2011).

Potential Confounds

The hierarchical regression analyses address the potential confounds of this study. The findings indicate that none of the control variables were statistically significant predictors of the four EF domains outlined in Anderson's (2002) model. It is noted that the regression run to predict information processing was significant overall, both before and after the inclusion of HIV-status as a predictor. Given the adolescent-associated deficits in processing speed (regardless of the presence of HIV), the significant outcome may be due such an effect (Steinberg, 2005).

Limitations and Recommendations for Future Research

A number of limitations within this study have already been highlighted above. Given the lack of significant results, but the correct directionality for certain measures, the small sample size appears to be one of the fundamental limitations of this study. This emerges as a trend observed in studies performing research in similar fields and it seems difficult to control for (Laughton et al., 2013; Phillips et al., 2016). The control recruitment process is where we particularly struggled with this study. With the HIV-infected sample being recruited through the HCYDP in Gugulethu, an application was submitted to, and approved by, the Department of Education (Appendix I) for the recruitment of controls through schools within similar geographic areas to the clinical sample. Schools were approached, but it became apparent that participants from the clinical sample and the control group may be coming from the same schools; meaning the status of the HIV-infected adolescents may have been exposed unwillingly. This could have detrimental consequences on the well-being of the participants, thus, the alternative recruitment process was followed.

The lack of significance, and the poor performance of all participants across both the control and outcome variables, led to consideration being given to the translated versions of the tests that were being administered. It became apparent during testing – based on the

knowledge of the translators assisting with test administration – that some of the translations could have been interpreted in several ways by the participants, or failed to be interpreted at all. The translated versions of all measures administered were translated, back translated and reviewed, but issues of equivalence still arose; an issue that is readily acknowledge in South African literature (Foxcroft & Aston, 2006). It is proposed, and has been previously, that future research performed within this area accounts for such issues. Local literature exists regarding the English versions of South African adapted measures (i.e., Cawthra, 2016), but the same needs to be done for other South African languages.

A final limitation that needs to be addressed, and one that could also be contributing to the low and non-significant scores reported above, is the use of a self-report measure of HIV-status. The HIV-infected group were recruited through the HCYDP and, thus, their status was known. However, the control group were asked whether or not they were HIV-infected whilst being informed of the study and, again, upon arrival at testing before giving assent. The scope of this study meant that resources were not available to test participants for HIV, as has been observed in other studies (e.g., Ezeamama et al., 2016). Self-reported status is not uncommon (i.e., Bell et al., 2008; Haase et al., 2014), but it does allow for participant dishonesty. Future research should consider this, although a larger sample size may account for individuals falsely confirming they are HIV-uninfected.

A further recommendation for future research is the inclusion of more measures to assess EF outcomes (Laughton et al., 2013; Phillips et al., 2016). With a greater pool of measures, as well as a larger sample size, it is proposed that statistically significant differences between the HIV-infected and control group may be achieved. If resources allow, the testing of all participants for HIV is also recommended as it removes any doubt that the participants belong in their assigned groups.

Conclusion

In a country where the risk of HIV is threatening to the entire population, but adolescents in particular, it is of the utmost importance that the outcomes associated with the disease are understood so that early detection, successful maintenance and future prevention are achieved. Investigations into these outcomes are crucial, but the area appears to be under-researched, with locally published research regarding the EF outcomes associated with HIV-infected adolescents lacking. This study makes a valuable contribution to existing research.

To my knowledge, this is the first study to explore the executive function outcomes associated with HIV-infected adolescents in South Africa. The non-significant differences obtained serve to inform future research investigating similar associations within a similarly matched sample. More specifically, it is proposed that future research adopts a larger battery of measures to assess EF outcomes. This, along with a substantially larger sample size, is likely to improve statistical significance, which will give rise to results that can be utilized to inform future interventions.

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Appendix A

SES Demographic Questionnaire

DEMOGRAPHIC QUESTIONNAIRE AND ASSET INDEX

GENERAL INFORMATION

Full name (Parent):	
Telephone:	Work: ( ) Home: ( ) Cell:
How would you describe your ethnicity / race?	1. Black 2. Coloured 3. White 4. Asian 5. Other(specify):
Home Language:	
Full name (Child):	
Gender:	M F
Date of Birth:	
Grade:	

HOUSEHOLD INCOME: (Please circle appropriate number)

Household income per year:	1. R0 2. R1 – R5 000 3. R5001 – R25 000 4. R25 000 – R100 000 5. R100 001+

PARENTAL EDUCATION: (Please circle appropriate number)

	Biological mother	Biological father	Guardian
Highest level of education reached? Mark one response for each person as follows:			
1. 0 years (No Grades / Standards) = No formal education (never went to school)	1.	1.	1.
2. 1-6 years (Grades 1-6 / Sub A-Std 4) = Less than primary education (didn't complete primary school)	2.	2.	2.
3. 7 years (Grade 7 / Std 5) = Primary education (completed primary school)	3.	3.	3.
4. 8-11 years (Grades 8-11 / Stds 6-9) = Some secondary education (didn't complete high school)	4.	4.	4.
5. 12 years (Grade 12 / Std 10) = Secondary education (completed senior school)	5.	5.	5.
6. 13+ years = Tertiary education (completed university / technikon / college)	6.	6.	6.
7. Don't know	7.	7.	7.

PARENTAL EMPLOYMENT: (Please circle appropriate number)

Hollingstead categories:	Biological mother	Biological father	Guardian
1. Higher executives, major professionals, owners of large businesses)	1.	1.	1.
2. Business managers of medium sized businesses, lesser professions (e.g. nurses, opticians, pharmacists, social workers, teachers)	2.	2.	2.
3. Administrative personnel, managers, minor professionals, owners / proprietors of small businesses (e.g. bakery, car dealership, engraving business, plumbing business, florist, decorator, actor, reporter, travel agent)	3.	3.	3.
4. Clerical and sales, technicians, small businesses (e.g. bank teller, bookkeeper, clerk, draftsperson, timekeeper, secretary)	4.	4.	4.
5. Skilled manual – usually having had training (e.g. baker, barber, chef, electrician, fireman, machinist, mechanic, painter, welder, police, plumber, electrician)	5.	5.	5.
6. Semi-skilled (e.g. hospital aide, painter, bartender, bus driver, cook, garage guard, checker, waiter, machine operator)	6.	6.	6.
7. Unskilled (e.g. attendant, janitor, construction helper, unspecified labour, porter, unemployed)	7.	7.	7.
8. Homemaker	8.	8.	8.
9. Student, disabled, no occupation	9.	9.	9.

MATERIAL AND FINANCIAL RESOURCES (ASSET INDEX): (Please circle appropriate number)

Which of the following items, in working order, does your household have?

Items	Yes	No
1. A refrigerator or freezer	1.	1.
2. A vacuum cleaner or polisher	2.	2.
3. A television	3.	3.
4. A hi-fi or music center (radio excluded)	4.	4.
5. A microwave oven	5.	5.
6. A washing machine	6.	6.
7. A video cassette recorder or dvd player	7.	7.

Which of the following do you have in your home?

Items	Yes	No
1. Running water	1.	1.
2. A domestic servant	2.	2.
3. At least one car	3.	3.
4. A flush toilet	4.	4.
5. A built-in kitchen sink	5.	5.
6. An electric stove or hotplate	6.	6.
7. A working telephone	7.	7.

Do you personally do any of the following?

Items	Yes	No
1. Shop at supermarkets	1.	1.
2. Use any financial services such as a bank account, ATM card or credit card	2.	2.
3. Have an account or credit card at a retail store	3.	3.

Appendix B

Parent/caregiver Consent Form

"Retaining HIV-infected youth in care: A model for transitioning adolescents receiving ART from paediatric to adult care" - Aim 1 Adolescent Parent/Caregiver Consent Form

Short title: HlangananiPlus HCT

Introduction
We are doing research in order to understand whether a youth programme that prepares youth to move from adolescent care to adult care including information around health education, communication and life skills, goal management, information about treatment and treatment adherence (commitment to taking treatment regularly) will help prepare the youth better when they are moved to the adult clinic. As you know, as youth get older, they will need to be moved to the adult clinic and will begin to receive their treatment and other health services thereon. We want to see if having a programme like this will help ease this process for your child as compared to the usual standard of care.

What is my child being asked to do? We are asking your child to be in a research study that will help us find out more about whether people his/her age will benefit from such a program, so that when they move, they are able to come to their regular appointments, continue coming to the clinic and take their treatment regularly and as discussed with their doctor. We ask you to fully read this form or have it read to you to decide if you want your child to join the study. Please ask if there is anything that is not clear or if you would like more information.

Why is my child being asked to help? We are asking you to help with this research because your child is between 14 and 24 years of age. One of the groups of people participating in the research is adolescents.

How many people are expected to participate in the research? 120 participants will be included this part of the study. They will be randomly put into two groups with 60 people in each group. One group will participate in the program and the other will receive the standard (usual) care at the Hannan Crusaid clinic in Gugulethu. Your child has been assigned to the group that will participate in the program.

Does my child have to take part? Not at all. You can decide that your child should not be included in the research. If you are unsure, you can make the decision about your child being in the research later by using the information included in this form and talking to our research staff. If you do decide that your child will take part in this research, we will ask you to sign this

form as a sign that you understand this information and that you agree for your child to be in the research. You will get a copy of the form to keep. Even if you agree for your child to be in the study now by signing this form, you can still change your mind at any time and withdraw your child from the study.

What will be done if my child takes part in this research study? If you agree for your child to participate in this study by signing this form, the interviewer will sit down with your child and ask him/her questions. The interviewer will begin by introducing and giving your child more details about the programme. Then they will ask your child questions about their background like school, age and gender. They will also ask your child about people he/she lives with at home, about his/her parents or care givers, whether they work or not. We will ask your child about knowledge of HIV and AIDS as well as their knowledge of treatment. This discussion will take roughly 30 minutes.

Second, your child will be asked to complete some games (e.g., problem solving and memory games) and puzzles tests to see whether he/she needs further help when it comes to treatment adherence. The whole process will take about 2 hours. You can stop if you are feeling tired and need to take a break, at any time.

Third, your child might be requested to take part in-depth interviews where the researcher will ask him/her more questions about their life history, about their parents, about their disclosure process. They will also ask your child about community perceptions of HIV, history of ARV treatment and adherence, barriers to and facilitators of treatment adherence, feelings around living with HIV, and their future plans.

Fourth, your child will be asked to come for sessions every week for 17 weeks, which will be held every Saturday at the scout hall near the Hannan clinic. During these sessions, that is when our training and activities will take place.

What if the questions upset my child? If your child feels uncomfortable answering any of the questions on the survey, he/ she does not have to answer. He/she will be able to stop being in the study at any time. Also, we have a counselor who will be working with us and if you are upset and need more assistance, the counselor will be there to assist you.

Does your child get paid to be a part of this study? You will not be paid for being in the study but we will pay your child's transport of R30 every time we meet for our sessions. Your child will also receive a meal after the session for lunch.

Will what my child says be kept confidential? Yes. All the information that is given to us will be kept confidential (private). Anonymity (your name and other details being unknown) and confidentiality is a high priority and every effort will be made to protect it. The information collected will be secured, locked and/or password-protected within the DTHC offices. To safe guard against any loss, the recording of your interview will be stored on a safe and secure online facility called shared-point that allows access of your interview to only staff members working on this project. A backup will be stored on only one computer that is protected by a password at our head offices. We will not use actual names, but instead use a number identification system to distinguish between participants. If the results of this research are published or presented, your name will not be included in the study.

Who should I contact for further information? If you have questions about the study, you can call the principal investigator, Millicent Atujuna, at 021 406 6961.

Who can I call for information about my child's rights as someone who is helping with research?
There is a group of doctors and researchers whose job it is to help see that research is done carefully and that people in the research are treated fairly and it is made as safe as possible. If you have any questions about these things, or if you have a complaint or complaints about your rights and wellbeing as a participant, please contact the Human Research Ethics Committee: Tel: 021 406 6492
E-mail: sumaya.ariefdien@uct.ac.za

STATEMENT OF CONSENT:

I have read the information about this study and understand the explanations of it that were verbally given to me. I have had my questions concerning the study answered and understand what will be required of my child if he/she takes part in this study.

You voluntarily consent to allow your child to participate in this study. You hereby authorize the collection, use and sharing of your child's performance and other data. By signing this form, you are not waiving any of your legal rights.

SIGNATURES

_____ _____
Signature of Person Consenting and Authorizing Date

_____ _____
Name of Child Age

_____ _____ _____
Study Staff Member Conducting IC Discussion (print) Study Staff Member's Signature Date

_____ _____ _____
Witness' Name (print) Witness' Signature Date

NOTE: This form with the original signatures MUST be retained on file by the principal investigator. A copy must be given to the participant. A copy should be placed in the participant's medical record, if applicable.

Appendix C

Parent/caregiver Control Consent Form

"The executive function outcomes associated with HIV-infected adolescents in South Africa" - Adolescent Parent/Caregiver Control Consent Form

Introduction
We are doing research in order to determine whether there are significant executive function (e.g., thinking, planning and flexibility) differences between HIV-infected adolescents and HIV-negative adolescents.

What is my child being asked to do? We are asking your child to be in a research study that will help us find out more about whether people his/her age differ from those who are HIV-infected when performing a variety of cognitive tasks. We ask you to fully read this form or have it read to you to decide if you want your child to join the study. Please ask if there is anything that is not clear or if you would like more information.

Why is my child being asked to help? We are asking your child to help with this research because your child is HIV-negative and between 14 and 16 years of age.

How many people are expected to participate in the research? 60 participants will be included in this part of the study. One group of 30 will be HIV-infected, and the remaining 30 will be HIV negative. Your child has been asked to be a part of the HIV negative group.

Does my child have to take part? Not at all. You can decide that you child should not to be included in the research. If you are unsure, you can make the decision about your child being in the research by using the information included in this form and talking to our research staff. If you do decide that your child will take part in this research, we will ask you to sign this form as a sign that you understand this information and that you agree for your child to be in the research. You will get a copy of the form to keep. Even if you agree for your child to be in the study now by signing this form, you can still change your mind at any time and withdraw your child from the study.

What will be done if my child takes part in this research study? If you agree for your child to participate in this study by signing this form, the interviewer will sit down with your child and ask him/her questions. The interviewer will begin by introducing and giving your child more details about the study. Then they will ask your child questions about their background like school, age and gender. They will also ask your child about people he/she lives with at

home, about his/her parents or care givers, whether they work or not. This discussion will take roughly 30 minutes.

Second, your child will be asked to complete some games (e.g., problem solving and memory games) and puzzles tests. The whole process will take about 2 hours. Your child can stop if they are feeling tired and need to take a break, at any time.

What if the questions upset my child? If your child feels uncomfortable answering any of the questions on the survey, he/ she does not have to answer. He/she will be able to stop being in the study at any time. Also, we have a counselor who will be working with us and if your child or you are upset and need more assistance, the counselor will be there to assist them.

Does your child get paid to be a part of this study? Your child will be not be paid for being in the study but we will pay your child's transport of R30 on the day he/she comes in for testing if he/she has to travel to the testing venue. Your child will also receive a R50 meal voucher after testing for lunch.

Will what my child says be kept confidential? Yes. All the information that is given to us will be kept confidential (private). Anonymity (your child's name and other details being unknown) and confidentiality is a high priority and every effort will be made to protect it. The information collected will be secured, locked and/or password-protected within the Department of Psychology at the University of Cape Town. We will not use actual names, but instead use a number identification system to distinguish between participants. If the results of this research are published or presented, your child's name will not be included in the study.

Who should I contact for further information? If you have questions about the study, you can call the principal investigator, Bryony Dyssell, on 072 232 7862.

Who can I call for information about my child's rights as someone who is helping with research?
There is a group of researchers whose job it is to help see that research is done carefully and that people in the research are treated fairly and it is made as safe as possible. If you have any questions about these things, or if you have a complaint or complaints about your rights and well-being as a participant, please contact the Department of Psychology Research Ethics Committee: Tel: 021 650 4104
E-mail: rosalind.adams@uct.ac.za

STATEMENT OF CONSENT:

I have read the information about this study and understand the explanations of it that were verbally given to me. I have had my questions concerning the study answered and understand what will be required of my child if he/she takes part in this study.

You voluntarily consent to allow your child to participate in this study. You hereby authorize the collection, use and sharing of your child's performance and other data. By signing this form, you are not waiving any of your legal rights.

SIGNATURES

_____ _____
Signature of Person Consenting and Authorizing Date

_____ _____
Name of Child Age

_____ _____ _____
Study Staff Member Conducting IC Discussion (print) Study Staff Member's Signature Date

_____ _____ _____
Witness' Name (print) Witness' Signature Date

NOTE: This form with the original signatures MUST be retained on file by the principal investigator. A copy must be given to the participant. A copy should be placed in the participant's medical record, if applicable.

Appendix D

Adolescent Assent Form

"Retaining HIV-infected youth in care: A model for transitioning adolescents receiving ART from paediatric to adult care" - Aim 1 Adolescent Assent Form

Short title: HlangananiPlus HCT

Note to research staff: Only adolescents who have provided you with a written parent or caregiver consent form can participate in the assent process. Parent or caregiver signatures should appear on the parent consent form.

Introduction

We are doing research in order to understand whether a youth programme that prepares youth to move from adolescent care to adult care including information around health education, communication and life skills, goal management, information about treatment and treatment adherence (commitment to taking treatment regularly) will help prepare the youth better when they are moved to the adult clinic. As you know, as youth get older, they will need to be moved to the adult clinic and will begin to receive their treatment and other health services thereon. We want to see if having a programme like this will help ease this process.

What am I being asked to do? We are asking you to be in a research study that will help us find out more about whether people your age will benefit from such a program so that when they move, they are able to come to their regular appointments, continue coming to the clinic and take their treatment regularly and as discussed with their doctor. We ask you to fully read this form or have it read to you to decide if you want to join the study. Please ask if there is anything that is not clear or if you would like more information.

Why am I being asked to help? We are asking you to help with this research because you are between 14 and 24 years of age. One of the groups of people participating in the research is adolescents.

How many people are expected to participate in the research? 120 participants will be included this part of the study. They will be randomly put into two groups with 60 people in each group. One group will participate in the program, and the other will receive the standard (usual) care at the Hannan Crusaid clinic in Gugulethu. You have been assigned to the group that will participate in the program.

Do I have to take part? Not at all. You can decide to not to be included in the research. If you are unsure, you can make the decision about being in the research by using the information included in this form and talking to our research staff. If you do decide to be in the research, we will ask you to sign this form as a sign that you understand this information and that you agree to be in the research. You will get a copy of the form to keep. Even if you agree to be in the study now by signing this form, you can still change your mind at any time and withdraw from the study.

What will be done if you take part in this research study? If you agree to participate in this study by signing this form, the interviewer will sit down with you and ask you questions. The interviewer will begin by introducing and giving you more details about the programme. Then they will ask you questions about your background like school, age and gender. They will also ask you about people you live with at home, about your parents or your care givers, whether they work or not. We will ask you about knowledge of HIV and AIDS as well as your knowledge of treatment. This discussion will take roughly 30 minutes.

Second, you will be asked to complete some games (e.g., problem solving and memory games) and puzzles, tests to see whether you need further help when it comes to treatment adherence. The whole process will take about 2 hours. You can stop if you are feeling tired and need to take a break, at any time.

Third, you might be requested to take part in-depth interviews where the researcher will ask you more questions about your life history, about your parents, about your disclosure process. They will also ask you about community perceptions of HIV, history of ARV treatment and adherence, barriers to and facilitators of treatment adherence, feelings around living with HIV, and your future plans.

Fourth, you will be asked to come for sessions every week, for 17 weeks, which will be held every Saturday at the scout hall near the Hannan clinic. During these sessions, that is when our training and activities will take place.

What if the questions upset me? If you feel uncomfortable answering any of the questions on the survey, you will still be able to stop being in the study at any time. Also, we have a counselor who will be working with us and if you are upset and need more assistance, the counselor will be there to assist you.

Do I get paid to be a part of this study? You will not be paid for being in the study but we will pay your transport of R30 every time we meet for our sessions. You will also receive a meal after the session for lunch.

Will what I say be kept confidential? Yes. All the information that is given to us will be kept confidential (private). Anonymity (your name and other details being unknown) and confidentiality is a high priority and every effort will be made to protect it. The information collected will be secured, locked and/or password-protected within the DTHC offices. To safe guard against any loss, the recording of your interview will be stored on a safe and secure online facility called shared-point that allows access of your interview to only staff members working on this project. A backup will be stored on only one computer that is protected by a password at our head offices. We will not use actual names, but instead use a number identification system to distinguish between participants. If the results of this research are published or presented, your name will not be included in the study.

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Who can I call for information about my rights as someone who is helping with research? There is a group of doctors and researchers whose job it is to help see that research is done carefully and that people in the research are treated fairly and it is made as safe as possible. If you have any questions about these things, or if you have a complaint or complaints about your rights and wellbeing as a research participant, please contact the Human Research Ethics Committee: Tel: 021 406 6492 E-mail: sumaya.ariefdien@uct.ac.za

STATEMENT OF CONSENT:

I have read the information about this study and understand the explanations of it that were verbally given to me. I have had my questions concerning the study answered and understand what will be required of me if I take part in this study.

SIGNATURES

_____	_____	_____
Volunteer's Name (print)	Volunteer's Signature	Date
_____	_____	_____
Study Staff Member Conducting IC Discussion (print)	Study Staff Member's Signature	Date
_____	_____	_____
Witness' Name (print)	Witness' Signature	Date

NOTE: This form with the original signatures MUST be retained on file by the principal investigator. A copy must be given to the participant. A copy should be placed in the participant's medical record, if applicable.

Appendix E

Adolescent Control Assent Form

"The executive function outcomes associated with HIV-infected adolescents in South Africa" - Adolescent Control Assent Form

Note to research staff: Only adolescents who have provided you with a written parent or caregiver consent form can participate in the assent process. Parent or caregiver signatures should appear on the parent consent form.

Introduction
We are doing research in order to determine whether there are significant executive function (e.g., thinking, planning and flexibility) differences between HIV-infected adolescents and HIV-negative adolescents.

What am I being asked to do? We are asking you to be in a research study that will help us find out more about whether people your age differ from those who are HIV-infected when performing a variety of cognitive tasks. We ask you to fully read this form or have it read to you to decide if you want to join the study. Please ask if there is anything that is not clear or if you would like more information.

Why am I being asked to help? We are asking you to help with this research because you are HIV-negative and between 14 and 16 years of age.

How many people are expected to participate in the research? 60 participants will be included in this study. One group of 30 will be HIV-infected, and the remaining 30 will be HIV negative. You have been asked to be a part of the HIV negative group.

Do I have to take part? Not at all. You can decide not to be included in the research. If you are unsure, you can make the decision about being in the research by using the information included in this form and talking to our research staff. If you do decide to be in the research, we will ask you to sign this form as a sign that you understand this information and that you agree to be in the research. You will get a copy of the form to keep. Even if you agree to be in the study now by signing this form, you can still change your mind at any time and withdraw from the study.

What will be done if you take part in this research study? If you agree to participate in this study by signing this form, the interviewer will sit down with you and ask you questions. The interviewer will begin by introducing and giving you more details about the study. Then they

will ask you questions about your background like school, age and gender. They will also ask you about people you live with at home, about your parents or care givers, whether they work or not. This discussion will take roughly 30 minutes.

Second, you will be asked to complete some games (e.g., problem solving and memory games) and puzzle tests. The whole process will take about 2 hours. You can stop if you are feeling tired and need to take a break, at any time.

What if the questions upset me? If you feel uncomfortable answering any of the questions on the survey, you will still be able to stop being in the study at any time. Also, we have a counselor who will be working with us and if you are upset and need more assistance, the counselor will be there to assist you.

Do I get paid to be a part of this study? You will not be paid for being in the study but we will pay your transport of R30 on the day you come in for testing if you need to travel to the testing venue. You will also receive a R50 meal voucher after testing for lunch.

Will what I say be kept confidential? Yes. All the information that is given to us will be kept confidential (private). Anonymity (your name and other details being unknown) and confidentiality is a high priority and every effort will be made to protect it. The information collected will be secured, locked and/or password-protected within the Department of Psychology at the University of Cape Town. We will not use actual names, but instead use a number identification system to distinguish between participants. If the results of this research are published or presented, your name will not be included in the study.

Who should I contact for further information? If you have questions about the study, you can call the principal investigator, Bryony Dyssell, on 072 232 7862.

Who can I call for information about my rights as someone who is helping with research? There is a group of researchers whose job it is to help see that research is done carefully and that people in the research are treated fairly and it is made as safe as possible. If you have any questions about these things, or if you have a complaint or complaints about your rights and well-being as a research participant, please contact the Department of Psychology Research Ethics Committee: Tel: 021 650 4104, E-mail: rosalind.adams@uct.ac.za

STATEMENT OF CONSENT:

I have read the information about this study and understand the explanations of it that were verbally given to me. I have had my questions concerning the study answered and understand what will be required of me if I take part in this study.

SIGNATURES

_____	_____	_____
Volunteer's Name (print)	Volunteer's Signature	Date

_____	_____	_____
Study Staff Member Conducting IC Discussion (print)	Study Staff Member's Signature	Date

_____	_____	_____
Witness' Name (print)	Witness' Signature	Date

NOTE: This form with the original signatures MUST be retained on file by the principal investigator. A copy must be given to the participant. A copy should be placed in the participant's medical record, if applicable.

Appendix F

Department of Psychology Ethical Clearance

UNIVERSITY OF CAPE TOWN

Department of Psychology

University of Cape Town Rondebosch 7701 South Africa
Telephone (021) 650 3417
Fax No. (021) 650 4104

05 June 2018

Bryony Dyssell
Department of Psychology
University of Cape Town
Rondebosch 7701

Dear Bryony

I am pleased to inform you that ethical clearance has been given by an Ethics Review Committee of the Faculty of Humanities for your study, *The executive function outcomes associated with HIV-positive adolescents in South Africa*. The reference number is PSY2018-032.

I wish you all the best for your study.

Yours sincerely

University of Cape Town
ΨPSYCHOLOGY DEPARTMENT
Upper Campus
Rondebosch

Lauren Wild (PhD)
Associate Professor
Chair: Ethics Review Committee

Appendix G

Faculty of Health Sciences Ethical Clearance

HEALTH IMPACT ASSESSMENT
HEALTH RESEARCH SUB DIRECTORATE
Health.Research@westerncape.gov.za
tel: +27 21 483 0866: fax: +27 21 483 9895
5th Floor, Norton Rose House,, 8 Riebeek Street, Cape Town, 8001
www.capegateway.gov.za)

REFERENCE: WC_201711_003
ENQUIRIES: Dr Sabela Petros

University of Cape Town

Anzio Road

Observatory

Cape Town

7925

For attention: Dr Millicent Atujuna

Re: Retaining HIV-positive youth in care: A model for transitioning adolescents receiving ART from paediatric to adult care: HlangananiPlus.

Thank you for submitting your proposal to undertake the above-mentioned study. We are pleased to inform you that the department has granted you approval for your research. Please contact following people to assist you with any further enquiries in accessing the following sites:

Gugulethu CHC	**Mr Lunga Makamba**	**021 633 0020**

Kindly ensure that the following are adhered to:

1. Arrangements can be made with managers, providing that normal activities at requested facilities are not interrupted.
2. Researchers, in accessing provincial health facilities, are expressing consent to provide the department with an electronic copy of the final feedback (**annexure 9**) within six months of completion of research. This can be submitted to the provincial Research Co-ordinator (Health.Research@westerncape.gov.za).

3. In the event where the research project goes beyond the *estimated completion* date which was submitted, researchers are expected to complete and submit a progress report (**Annexure 8**) to the provincial Research Co-ordinator (Health.Research@westerncape.gov.za).

4. The reference number above should be quoted in all future correspondence.

Yours sincerely

AJ HAWKRIDGE.

DR A HAWKRIDGE

DIRECTOR: HEALTH IMPACT ASSESSMENT

DATE: 1/12/2017.

CC: **P OLCKERS** **DIRECTOR: KLIPFONTEIN/ MITCHELLS PLAIN**

Appendix H

Department of Psychology Ethics Amendment

UNIVERSITY OF CAPE TOWN

Department of Psychology

University of Cape Town Rondebosch 7701 South Africa
Telephone (021) 650 3417
Fax No. (021) 650 4104

15 August 2018

Ms Bryony Dyssell
Department of Psychology
University of Cape Town
Rondebosch 7701

Dear Ms Dyssell

I am pleased to inform you that ethical clearance has been given by an Ethics Review Committee of the Faculty of Humanities for the amended protocol, submitted 15 August 2018, to your study, *The executive function outcomes associated with HIV-positive adolescents in South Africa.* The reference number remains PSY2018-032.

I wish you all the best for your study.

Yours sincerely,

Lauren Wild (PhD)
Associate Professor
Chair: Ethics Review Committee

Appendix I

Department of Education Ethical Clearance

REFERENCE: 20180614–3311
ENQUIRIES: Dr A T Wyngaard

Ms Bryony Dyssell
PO Box 2188
Somerset West
7129

Dear Ms Bryony Dyssell

RESEARCH PROPOSAL: THE EXECUTIVE FUNCTION OUTCOMES ASSOCIATED WITH HIV-POSITIVE ADOLESCENTS IN SOUTH AFRICA

Your application to conduct the above-mentioned research in schools in the Western Cape has been approved subject to the following conditions:

1. Principals, educators and learners are under no obligation to assist you in your investigation.
2. Principals, educators, learners and schools should not be identifiable in any way from the results of the investigation.
3. You make all the arrangements concerning your investigation.
4. Educators' programmes are not to be interrupted.
5. The Study is to be conducted from **17 July 2018 till 28 September 2018**
6. No research can be conducted during the fourth term as schools are preparing and finalizing syllabi for examinations (October to December).
7. Should you wish to extend the period of your survey, please contact Dr A.T Wyngaard at the contact numbers above quoting the reference number?
8. A photocopy of this letter is submitted to the principal where the intended research is to be conducted.
9. Your research will be limited to the list of schools as forwarded to the Western Cape Education Department.
10. A brief summary of the content, findings and recommendations is provided to the Director: Research Services.
11. The Department receives a copy of the completed report/dissertation/thesis addressed to:

The Director: Research Services
Western Cape Education Department
Private Bag X9114
CAPE TOWN
8000

We wish you success in your research.

Kind regards.
Signed: Dr Audrey T Wyngaard
Directorate: Research
DATE: 14 June 2018