**Mental health and substance use in HIV-infected adolescents**

**Michael Evangeli1**

1 Department of Psychology, Royal Holloway University of London, Egham, Surrey, UK

Correspondence to Dr. Michael Evangeli, Department of Psychology, Royal Holloway University of London, Egham, Surrey, TW20 0EX, UK. Tel: 00441784443851. Fax: 01784472746. Email: michael.evangeli@rhul.ac.uk

**Abstract**

***Purpose of review***

Adolescents with HIV include both those infected perinatally and behaviourally. This population is confronted by normative challenges and HIV stressors as they move towards becoming increasingly independent adults. This review focuses on mental health and substance use in adolescents with HIV. These are important issues in their own right as well as having implications for antiretroviral (ART) adherence and HIV management.

***Recent findings***

Sixteen articles, published from 1st January 2016 to 1st September 2017, were included from 13 distinct studies, mostly from the US and Africa. Cross sectional designs predominated. There was only one intervention study. There was evidence of mental health and substance use difficulties, although not at a higher level than comparison groups. Consistent associations were found between (1) ART non-adherence and both mental health difficulties and substance use (2) environmental stressors and mental health difficulties.

***Summary***

Adolescents with HIV display considerable resilience. There is a need, however, for interventions for mental health difficulties and substance use, and for ART adherence interventions to consider these issues. Studies on mental health and substance use should cover a wider range of regions. Mitigating the impact and reducing exposure to environmental stressors is a priority.

**Key words: HIV; adolescents; mental health; substance use; young adults**

**Introduction**

There are large numbers of adolescents living with HIV globally, with nearly two million currently between 10 and 19 years. The majority have perinatally acquired HIV (PHIV) and live in sub-Saharan Africa, although there are also an estimated 250,000 new HIV infections among adolescents every year (young people with behaviourally acquired HIV: BHIV) ([1](#_ENREF_1)).

Adolescence commonly refers to the teenage years through to early adulthood. It is a time of exploration, where individuals establish their identity through making choices in areas such as relationships, work and ideology ([2](#_ENREF_2), [3](#_ENREF_3)). This period can be characterised by tension between autonomy and connectedness for the young person ([4](#_ENREF_4)) as they negotiate ‘progressive independence’ ([5](#_ENREF_5)) away from their family and towards their peers.

Adolescents with HIV face a number of sexual health, well-being and ART adherence challenges as well as negotiating normative adolescent tasks. Those with PHIV often have long histories of ART use with suboptimal regimens ([6](#_ENREF_6)), with variable rates of viral suppression, associated with poor ART adherence ([7](#_ENREF_7)). This population have frequently experienced multiple caretaking transitions and loss due to parental illness or death. Some young people with PHIV have subcortical white matter and fronto-striatal abnormalities that affect emotion and behaviour regulation and place them at risk for mental health difficulties ([8](#_ENREF_8)). They are more likely to have executive functioning problems (e.g., in working memory, processing speed and cognitive flexibility) and compromised verbal abilities ([9](#_ENREF_9), [10](#_ENREF_10)). Adjustment challenges for adolescents with either PHIV or BHIV include managing HIV stigma with anxiety about sharing one’s HIV status with others (onward disclosure) that may limit social support, concerns about onward HIV transmission, transitioning from paediatric to adult care, and other stressors associated with living with a chronic illness (e.g., hospitalisations, missed school, employment and social opportunities, and pain). These challenges often occur in the context of living in resource-limited environments.

There have been two comprehensive systematic reviews in recent years focussing on mental health and substance use in young people with HIV. Mellins and Malee ([8](#_ENREF_8)) focused specifically on mental health in young people with PHIV. They reported that many PHIV youth have adequate mental health, despite the fact that *risks* to poor mental health tended to be highlighted in research rather than *resilience*. They found higher rates of psychiatric disorders in young people with PHIV than the general population, but similar rates than in young people exposed to but not infected with PHIV. Mellins and Malee reported more depression and anxiety in females, and more behavioural problems in males. Parental mental health was associated with child mental health problems. Resilience factors included higher levels of caregiver support and more positive caregiver-child relationships. Finally they reported the paucity of interventions focused on mental health in this population, with the exception of one family intervention ([8](#_ENREF_8)).

Vreeman et al ([11](#_ENREF_11)) reviewed literature on mental health in adolescents with HIV. They reported that few studies included comparison groups and most of the studies took place in the US. Depression and anxiety were associated with lower antiretroviral adherence and unsuppressed viral loads. There were often no specialist adolescent services in lower and middle income countries, with a lack of screening of mental health problems and few interventions for these difficulties.

The aims of this review were to review the recent literature on both mental health difficulties and substance use in adolescents with HIV. As with Mellins and Malee ([8](#_ENREF_8)), mental health difficulties were defined broadly to include formal psychiatric diagnosis as well as clinically significant levels of psychological distress and emotional and behavioural problems.

**Methods**

# ***Study eligibility criteria***

Studies were included if they:

1. Presented data specifically relating to HIV-positive adolescents/young adults
2. Included assessments of mental health and/or substance use
3. Were published from 1st January 2016 to 1st September 2017
4. Reported primary empirical data
5. Were published in English
6. Were published in peer review journals

***Sources of information and search strategy***

Studies were retrieved from Pubmed/Medline, PsycINFO, and Web of Science databases. Searches were conducted using combinations of the following terms as keywords in titles and abstracts and using subject headings:

* ‘HIV’,
* ‘psych\*’, ‘depress\*’, ‘anx\*’, ‘affect’, ‘mental health’, ‘mood’, ‘wellbeing’, `well-being’, “quality of life”, ‘substance’,’drug’
* ‘child\*’, ‘adolescen\*’, ‘teen\*, ‘youth’

***Data collection***

# Following PRISMA guidelines ([12](#_ENREF_12)), data collection process had four stages (see Figure 1). Searches were carried out for the identification of studies, using pre-specified search criteria. All duplications were removed. Searches were completed on 3rd September 2017. The remaining titles and abstracts were then screened for eligibility. Articles considered relevant were retrieved in full text and eligibility of the retrieved articles was assessed.

**Figure 1 here**

**Results and Discussion**

Sixteen articles were included, relating to thirteen distinct studies (see Table I).

**Table I here**

***Study Characteristics and participants***

Five studies recruited solely from the US ([13-17](#_ENREF_13)) with two studies recruiting from both the US and Puerto Rico ([18](#_ENREF_18), [19](#_ENREF_19)). The remaining studies took place in Africa – Rwanda ([20](#_ENREF_20), [21](#_ENREF_21)), Uganda ([22](#_ENREF_22)), Tanzania ([23](#_ENREF_23)), Ghana ([24](#_ENREF_24)) and South Africa ([25](#_ENREF_25)). There were no studies from Asia, South America and Europe, however, despite significant numbers of adolescents with HIV in these regions ([26](#_ENREF_26)), and no studies on substance use outside of North America. There is clearly a need for studies across a wider range of contexts.

Most studies included between one hundred and five hundred young people with HIV, with sample sizes ranging from 40 ([24](#_ENREF_24)) to 2216 ([18](#_ENREF_18)). The studies covered a good range of ages, and samples represented both young people with BHIV and PHIV. A number of studies, however, did not report the mode of HIV infection. This is important to try to ascertain, given evidence of differences in mental health and substance use outcomes between the two populations from previous studies ([27](#_ENREF_27), [28](#_ENREF_28)). There is also evidence that youth with BHIV have more extensive experience of lifetime negative life events than youth with PHIV ([29](#_ENREF_29)) and different patterns of friendships, social support, onward HIV disclosure and sexual behaviour ([27](#_ENREF_27)) .

Only one study specifically sampled young people with mental health or substance use problems, recruiting adolescents and young adults with depression ([13](#_ENREF_13)). It would be helpful for more studies to focus specifically on those with mental health and/or substances use difficulties to examine potential risk factors within these sub-populations. Most studies examined rates and relationships within a single group of young people with HIV, although five studies (four in the US) included comparison groups of young people not living with HIV ([14-16](#_ENREF_14), [19](#_ENREF_19), [20](#_ENREF_20)). There was one intervention study, in the US ([13](#_ENREF_13)). The remaining studies were observational, with the majority cross sectional in design. All of the cohort studies took place in the US or Puerto Rico.

The methods used to obtain data were generally self-report (questionnaires or interview), although caregiver and clinician-reported data were also used. Two US studies used gold standard mental health diagnostic interviews ([14](#_ENREF_14), [15](#_ENREF_15)). In general, causal models of mental health difficulties, adjustment or substance use did not appear to guide the selection of variables assessed in the studies. It may be useful to refer to these models in future studies, particularly as they frequently underlie associated interventions ([30](#_ENREF_30), [31](#_ENREF_31)).

***Mental Health***

Rates of mental health difficulties

A number of studies reported rates of mental health difficulties in young people with HIV, ([14](#_ENREF_14), [15](#_ENREF_15), [17](#_ENREF_17), [18](#_ENREF_18), [21](#_ENREF_21), [24](#_ENREF_24), [25](#_ENREF_25)) sometimes comparing these to other young people without HIV. Rates of clinically significant difficulties of internalising symptoms (e.g., depression and anxiety) ranged from 3% to 31%, with higher rates for anxiety than depression. Rates of self-harm/suicidality ranged from 12-24% with rates of externalising/behavioural disorders ranging from 6 to 15%. One US cohort study found no changes in rates of behavioural or mood disorders but a reduction in anxiety disorders over the teenage years ([14](#_ENREF_14)). A second US cohort study reported reductions in internalising symptoms but not externalising symptoms over time ([15](#_ENREF_15)).

There was no evidence of differences in rates of mental health difficulties between young people with PHIV and comparison groups, including those exposed to but uninfected with HIV, with BHIV or unaffected by HIV ([14](#_ENREF_14), [15](#_ENREF_15), [17](#_ENREF_17), [20](#_ENREF_20)) but one study found higher rates of suicidality in youth with BHIV compared to youth with PHIV ([17](#_ENREF_17)). The general lack of difference in mental health between young people perinatally infected with HIV and perinatally exposed but uninfected with HIV is consistent with the previous literature and suggests that risk factors for mental health difficulties in these populations are not specific to HIV ([8](#_ENREF_8)).

Associations between mental health and ART non-adherence

Three studies, all in Africa, reported on the relationship between mental health and ART non-adherence, with all showing a relationship between higher rates of mental health difficulties (psychological distress, depression, PTSD or conduct difficulties) and non-adherence ([21-23](#_ENREF_21)). These results are similar to previously reported findings ([32](#_ENREF_32)).

Other associations with mental health

A number of studies examined other correlates of mental health difficulties. There was consistent evidence that stressful life events (e.g., witnessing or being the victim of violence, daily hassles, experiencing hunger, being touched inappropriately) were associated with higher rates of mental health difficulties ([15](#_ENREF_15), [19](#_ENREF_19), [25](#_ENREF_25), [33](#_ENREF_33)). Similar associations have been reported in other reviews ([8](#_ENREF_8), [32](#_ENREF_32)). Reducing exposure to physical and sexual assault (as well as mitigating their impact), and ensuring that basic needs are met (e.g., having enough to eat) are priorities in improving the mental health of young people with HIV.

There was inconsistent evidence of relationships between mental health difficulties and both age ([15](#_ENREF_15), [17](#_ENREF_17)) and gender ([15](#_ENREF_15), [17](#_ENREF_17), [25](#_ENREF_25)). The lack of clear gender differences was not consistent with a previous review ([8](#_ENREF_8)). A range of *individual* psychological variables were related to mental health difficulties, for example, HIV concerns, HIV stigma, praying frequency, lower future orientation and future dreams, fatigue, not feeling safe, not belonging ([15](#_ENREF_15), [16](#_ENREF_16), [25](#_ENREF_25), [33](#_ENREF_33)). Finally, *relational* factors were examined in one study, which found that caregiver mental health problems and parent-child relationship problems were related to child behavioural functioning ([19](#_ENREF_19)).

Interventions for mental health difficulties

There was only one intervention study (for either mental health difficulties or substance misuse) during the review period. This preliminary RCT of a combination cognitive behavioural therapy and medication management intervention for youth with HIV and depression showed promising evidence of reductions in depression versus treatment as usual ([13](#_ENREF_13)).

***Substance use***

Rates of substance use

Rates of substance use were reported in three studies, all in the US. These ranged from 4% to 37% dependent on age and whether substances were considered individually or in combination ([14](#_ENREF_14), [18](#_ENREF_18), [34](#_ENREF_34)). One study reported that 57% of their sample scored in the ‘at risk’ range for substance use problems ([35](#_ENREF_35)), with higher rates of smoking, slightly higher alcohol and marijuana use and similar levels of other illicit drug use to population norms. Rates of marijuana use increased over the teenage years in two cohort studies ([14](#_ENREF_14), [34](#_ENREF_34)) and substance use symptoms also increased in one of these studies ([34](#_ENREF_34)). Two studies reported no differences in substance use between young people with PHIV and exposed to but uninfected with HIV ([14](#_ENREF_14), [34](#_ENREF_34)).

Associations with substance use

Gamarel and colleagues examined correlates of substance use in two articles relating to the same sample ([18](#_ENREF_18), [35](#_ENREF_35)). Weekly alcohol use, weekly marijuana use and any other illicit drug use were all associated with ART non-adherence. Regarding demographic variables, substance use/misuse was associated with increased age, white ethnicity, MSM, and males. Environmental risk factors for marijuana/other illicit drug use and problematic substance use included involvement in the criminal justice system and unstable housing. Alcohol use was associated with being employed, whereas other illicit drug use (not alcohol or marijuana) was associated with being unemployed. Problematic drug use was also associated with BHIV, with weekly alcohol use associated with unprotected sexual intercourse with an HIV negative partner.

***Associations between mental health and substance use***

One study did not find a relationship between substance use and clinically significant levels of psychological symptoms, but did find an association between suicidal ideation and both marijuana use and other illicit drug use ([18](#_ENREF_18)). A second study found no association between anxiety disorders and marijuana use. Future behavioural and mood disorders were, however, related to earlier marijuana use, and earlier behavioural disorders predicted later marijuana use ([14](#_ENREF_14)). Perhaps surprisingly, there was no general association between substance use and mental health difficulties. Associations between specific substances and aspects of mental health were, however, seen. For example suicidal ideation was linked with marijuana and other illicit drug use in one study ([18](#_ENREF_18)), and although all evidence was observational, a study examining temporal relationships suggested that early onset marijuana use is a risk factor for subsequent mental health difficulties. This finding is consistent with literature on early onset substance use in other populations ([36](#_ENREF_36)).

**Conclusions**

This review confirmed the conclusion of other authors that the majority of adolescents with HIV are resilient, with most not presenting with mental health difficulties ([8](#_ENREF_8)). There was consistent evidence, however, of relationships between (a) environmental stressors and mental health difficulties (b) poorer mental health and ART non-adherence, and (c) substance use and non-adherence. Environmental stressors, psychological health (e.g., depression) and substance use are included in an influential model of ART adherence ([37](#_ENREF_37)). Efforts to reduce rates of ART non-adherence and improve rates of viral suppression in this population should include a focus on psychological health and mood, as some interventions do ([38](#_ENREF_38)), and substance use. There is also a clear need for interventions for those young people with HIV with mental health and substance use difficulties, and their absence in the literature has also been reported by other authors ([32](#_ENREF_32)).

Conclusions from this review must be interpreted in the light of decisions made about study inclusion and exclusion. In particular, it may have been that the exclusion of some studies focused on quality of life, a construct that is conceptually related to mental health, may have affected findings. Similarly, there may have been relevant data from studies that sampled both adolescents and either older or younger individuals. Unless there was specific data on adolescents, these studies were excluded.

**Key points**

* **The majority of adolescents with HIV did not have mental health or substance use difficulties.**
* **Consistent associations were found between antiretroviral non-adherence and both mental health difficulties and substance use.**
* **There are global gaps in evidence relating to substance use and mental health in adolescents with HIV.**
* **The consistent relationships between environmental stressors and mental health difficulties suggests that mitigating the impact and reducing the frequency of environmental stressors is a priority.**
* **There is a need for more studies evaluating interventions to reduce mental health difficulties or substance misuse, and for ART adherence interventions to cover these issues.**

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**Conflicts of interest**

The author declares no conflict of interest.

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**Figure 1: Study search process**

Full-text articles excluded
(n = 33):

Sample not living with HIV/unclear HIV status (n=10); focus not on mental health or substance use (n=9); results not disaggregated by age range or mental health status (n=9); sample noy within age range (n=3); secondary data (n=1); not published in peer review journal (n=1)

264 Records identified through PubMed (n=82); Psycinfo (n=62); Web of Science (n=120)

Records after duplicates removed (n = 141)

Records excluded
(n =92)

Studies included
(n = 16)

Full-text articles assessed for eligibility (n = 49)

Records screened
(n = 141)

## Identification

## Eligibility

## Included

## Screening

**Table I: Included studies**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Authors** | **Location** | **Sample**  | **Design/Methodology** | **Findings**  |
| **Brown et al (2016)** | US | 42 HIV+ (13 female (F); 4 with perinatally acquired HIV – PHIV+) with depression. Mean age 22 years (18-24).  | RCT. 24 week cognitive behavioural therapy/medication management (COMB) vs Treatment as usual (TAU). Clinician and self-report. | Greater reduction in depression symptoms and hopelessness, and higher rate of remission from depression in COMB versus TAU. |
| **Dow et al (2016)** | Tanzania | 182 HIV+ (99 F). Mode of infection not reported. Mean age 17 years (12-24). | Cross-sectional. Structured questionnaire.  | Higher HIV stigma and ART non-adherence associated with higher depression and PTSD scores. CD4 not associated with mental health.  |
| **Elkington et al (2016)** | US | 206 PHIV+ (105 F) and 134 perinatally exposed but uninfected with HIV (PHIV-). Mean age of PHIV+ group – 13 years at baseline (9-16) | Cohort study. Three diagnostic interviews over 5 years.  | PHIV+: Any marijuana use increased over time; no change over time in behavioural or mood disorders; reduction in anxiety disorders over time. No differences in disorders: PHIV+ and PHIV-. Marijuana predicted future behavioural and mood disorders in both groups. Behavioural disorders predicted marijuana. Anxiety not associated with marijuana. |
| **Enimil et al (2016)** | Ghana | 40 PHIV+ (20 F). Mean age 16 years (12-19) | Cross sectional. Self-report.  | 3% above depression cut-off. Lower QoL than norms in all domains and regional norms on physical and psychological health.  |
| **Gamarel et al (2016a)** | US and Puerto Rico | 2216 HIV+ (719 female, 84 transgender; 612 PHIV+). Mean age 22 years (12-26). | Cross-sectional. Self-report.  | 31 % psychological symptoms above clinical cut-off (not associated with substance use). 15% reported lifetime suicidal ideation. 28% marijuana use, 21% alcohol use – both weekly or more; 23% any other illicit drug use – last 3 months. Alcohol, marijuana, other drug use associations: increased age, white, MSM, ART non adherence. Alcohol, marijuana use association: males. Marijuana, other drug use associations: juvenile justice involvement, suicidal ideation. Other drug use associations: unstable housing, unemployment. Alcohol use associations: employment and UPSI with HIV- partner. |
| **Gamarel et al (2016b)** | US and Puerto Rico | As above. | Cross-sectional. Self-report. | 57 % ‘at risk’ for substance use problems. Those at risk more likely to be older, white, behaviourally infected, identify as gay or lesbian, male or transgender female, have unstable housing, and report lifetime involvement in the criminal justice system  |
| **Hermetet-Lindsay et al (2017)** | US and Puerto Rico.  | 231 PHIV+ and 151 PHIV- (201 F). Mean age of PHIV+ at behavioural assessment - 15 years.  | Cohort study over 7 years. Self and caregiver report.  | Caregiver-child stress (caregiver mental health problems, life events, parent-child relationship problems) related to child and caregiver-reported behavioural functioning (BF). Cognitive functioning related to caregiver but not child-reported BF.  |
| **Mutumba et al (2016a)** | US | 166 PHIV+ and 114 PHIV- (129F). Mean age 12 years at BL (9-16).  | Cohort study. Interviews over 5 years.  | No difference between groups in mental health symptoms. Internalising symptoms decreased over time. Females increased more in internalising and externalising symptoms. Externalising symptoms and increases in internalising symptoms associated with life events, neighbourhood stressors. Older youths, males, those with lower future orientation scores reported greater externalising symptoms at BL.  |
| **Mutumba et al (2016b)** | Uganda | 464 HIV+ (249 F). Mode of infection not reported. Mean age 16 years (12-19). | Cross-sectional. Structured interview. | ART non-adherence associated with higher psychological distress  |
| **Mutumba et al (2016c)** | Uganda | As above | Cross sectional. Structured interview. | Daily hassles, negative life events, HIV concerns, HIV stigma, frequency of praying privately positively associated with psychological distress. Religious coping, satisfaction with social support, general coping style and behaviours negatively associated with distress.  |
| **Mutumba et al (2017)** | US | 196 PHIV+ and 129 PHIV- (162 F). Mean age 12 years at BL (9-16). | Cohort study. 3 time points over 5 years. Interviews.  | Substance use symptoms increased over time among PHIV+ but not PHIV-. Change in substance use symptoms was positively associated with an increasing number of negative life events. No difference between groups in substance use or substance use symptoms.  |
| **Nduwimana et al (2017)** | Rwanda | 218 HIV+ (infection mode not reported), 228 HIV-affected, 235 HIV unaffected (346 F). Mean age 14 years (10-17) | Cross-sectional. Interviews with child and caregiver. | Living with HIV not associated with depression, anxiety, conduct problems or irritability, after controlling for foster family status. |
| **Smith Fawsi et al (2016)** | Rwanda | 193 HIV+ (96 F). Mode of infection not reported. Aged 10-17 years. | Cross-sectional. Self and caregiver questionnaires.  | 26% depression symptoms, 12% self-harm. ART non-adherence significantly independently associated with caregiver-reported (but not self-reported) conduct problems and depression.  |
| **Tan et al (2017)** | US | 42 HIV+ (infection mode not reported), 42 community controls (55F overall; 13-18 years).  | Cross-sectional. Self-report measures. | In HIV+ group: Health related quality of life and subjective wellbeing negatively correlated, and fatigue positively correlated with psychopathology. Psychopathology negatively related to social-emotional strengths. |
| **Woollett et al (2017)** | South Africa | 343 HIV+ (181 F). Majority with PHIV+.Mean age 16 years (13-19).  | Cross-sectional. Self-report.  | 27% symptomatic for depression, anxiety, PTSD. 24% suicidality. Correlates of being symptomatic for depression, anxiety and PTSD: witnessing peer violence, hunger, experienced violence, not feeling safe, female, suicidality, not feeling belonging, being inappropriately touched, lack of perceived control over future, no dreams. |
| **Walsh et al (2017).** | US | 130 HIV+ (44% PHIV+; 58 F). Mean age 20 years (11-25) | Cross sectional. Self-report.  | 24% scored above depression cut-off. No relationship between depression and age, gender, race, ethnicity, mode of HIV infection or sexual orientation. Youth with behaviourally acquired HIV (BHIV+) more likely to report self-harm and/or suicidal ideation than PHIV+.  |