

Original Article

The effect of attention deficit and hyperactivity disorder on ART and appointment adherence among adults living with HIV

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Abstract

Introduction: The most prominent characteristic of adult attention deficit hyperactivity disorder (ADHD) is impulsive behavior and deficits in executive functions, which require long-term organization and discipline. This may have serious implications in terms of adherence to treatment among adults living with HIV (PLWH). This study aimed to determine the prevalence of ADHD among non-perinatally infected PLWH and its effect on adherence to antiretroviral treatment (ART) and scheduled appointments.

Methodology: The PLWH admitted to our centers between January 2012 and February 2016 were invited to the study. ADHD diagnosis was made according to the novel criteria guided interviews. The first ART interruption for ≥ 6 days per month ($\leq 80\%$) was defined as ‘‘ART-event’’ and the first non-attendance of any scheduled appointment was defined as ‘‘appointment-event’’. Kaplan-Meier plot with a Log-rank test was used for event-free adherence (EFA).

Results: Twenty-five patients out of 85 were diagnosed with ADHD (29.4 %) which was significantly higher than the highest percentage reported (7.3 %) for the general population ($p < 0.0001$). Both ART-event ($p = 0.0002$) and appointment-event ($p = 0.02$) were significantly higher among ADHD participants compared to those without. Additionally, both ART-EFA ($p = 0.00014$) and appointment-EFA ($p = 0.023$) were significantly shorter among ADHD participants compared to those without.

Conclusion: ADHD is significantly higher in adult PLWH and people with ADHD had a significant tendency for non-adherence to ART and follow-up. Screening for ADHD as well as providing treatment when required would be beneficial to achieve and maintain virologic success.

Key words: adherence; antiretroviral therapy; appointment adherence; human immunodeficiency; virus; attention deficit hyperactivity disorder.

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Introduction

Human immunodeficiency virus (HIV) infection is a chronic condition, which requires regular follow-up and accurate treatment. People living with HIV (PLWH) can live a long and healthy life with early and appropriate antiretroviral treatment (ART) if they are highly adherent to their treatment regimens [1]. Although virologic success rates are high with novel antiretroviral drugs due to easier dosing regimens and fewer side effects compared to historical drugs, the level of adherence drops as the duration of treatment is prolonged for life long [2]. However, adherence to treatment has a pivotal role in achieving virologic suppression, which is associated with lower

transmission rates and a higher quality of life for PLWH [3]. Earlier studies showed that a high level of adherence ($> 95\%$) was required for virologic success and that virologic failure rates increased with lower levels of adherence [4]. However, the global rate of optimum adherence currently does not exceed 70% [5-7]. Many obstacles were identified for poor adherence such as interruption of drug access, adverse drug events, psychological problems, forgetfulness, and fear of stigma and discrimination [8-11]. On the other hand, various studies reported a higher prevalence of psychiatric disorders among PLWH compared to the general population [12,13]. A meta-analysis indicated that depression and anxiety disorders were two-fold

higher among PLWH compared to the general population [14]. Additionally, the psychiatric morbidity among PLWH showed that 24% of the cases had mood disorders, 19% had major depressive disorder, 1% had anxiety disorder, 7% had adjustment disorder, 1% had psychotic disorder and 17% had a history of substance abuse [15]. Depression, cognitive disorders, alcohol and substance abuse have been reported to be associated with poor prognosis in addition to ART non-adherence [16-20].

Attention deficit and hyperactivity disorder (ADHD) is a condition, which usually develops during childhood and may result in cognitive and social problems [21]. However, ADHD is a disorder that can also be seen in adulthood. Additionally, the most prominent characteristics of adult ADHD is impulsive behavior and deficits in executive functions, which require long-term organization and discipline, unless they have high motivation [22]. Adolescents with ADHD have an early sexual debut and similarly, ADHD in adulthood might have been a factor for vulnerability to HIV transmission due to ADHD-related impulsivity [23,24]. Although adults may also suffer from ADHD it is difficult to recognize during adulthood because it may have atypical manifestations ranging from socioeconomic problems to risky sexual behavior [25-28]. Therefore, adult-ADHD may be an important comorbidity resulted with a negative effect on prognosis in PLWH. On the other hand, awareness for ADHD in adulthood is very limited among HIV clinicians, which usually results with a misinterpretation of the concentration defect and carelessness, which usually results with non-adherence to treatment and to scheduled clinic appointments in PLWH with ADHD, as a natural personal trait and missing the opportunity for intervention [29]. Thus, adult-ADHD may be an important comorbidity to be screened for in PLWH with a higher prevalence of poor prognosis associated with ART non-adherence compared to ADHD negative participants.

A brief review of the literature for ADHD in PLWH showed that most of the studies were focused on children or adolescents with perinatally acquired HIV infection [24,30-36]. However, up to date only one cross-sectional study restricted to male participants, assessed adult-ADHD as an important psychiatric condition among PLWH in the literature [23]. Despite this study on restricted sub-population, there is no study investigating the effects of adult-ADHD over 18 years of age who have not been perinatally exposed to HIV [23,24,30-36]. Therefore, adult-ADHD may be a

hidden factor to be screened for in PLWH with a higher prevalence compared to HIV negative participants [23].

The aim of this study was to determine the prevalence of adult ADHD among PLWH who were not perinatally infected and to assess the relationship between ADHD and long-term adherence to treatment and follow-up among PLWH.

Methodology

This study had two primary objectives: (a) to identify long-term adherence differences in non-perinatally infected PLWH with and without ADHD using the method of the event free survival analysis. (b) to compare the prevalence of ADHD among non-perinatally infected PLWH with the prevalence in the general population.

Ethical approval (code – date: 11-9/8 – November 22, 2011) was obtained from the Ege University Ethical Review Board. The study group included PLWH from Ege University and İzmir Atatürk Training and Research Hospital cohorts. All participants who presented to one of the centers mentioned above between January 2012 and February 2016 were invited to join the study without any selection process. All were informed about the purpose and design of the study. Participants who accepted to participate in the study were asked to sign the informed consent form before taking part and the informed consent was obtained from all individual participants included in the study. The Transparent Reporting of Evaluations with Nonrandomized Designs (TREND) guideline was followed for the design and reporting of this study [37].

Inclusion and exclusion criteria

Participants with confirmed HIV infection aged 18 years and older were included in the study if they had no confounding central nervous system disorder or active psychiatric disease. The exclusion criteria were withdrawal of consent, perinatal acquisition of infection, incomplete psychiatric evaluation, having symptomatic (active) psychiatric comorbidity, not completing the assessment process.

Diagnosis of Attention deficit and hyperactivity disorder

In order to assess the lifetime and current Axis I disorders, the Turkish version of the *Structured Clinical Interview for DSM-IV Axis I Disorders* (SCID-I) [38,39], and the Turkish version of the *17-item Hamilton Depression Rating Scale* [40,41], were completed for all participating PLWH by a psychiatrist. In addition, participants self-completed the Turkish

version of the *State-Trait Anxiety Inventory* (STAI) [42,43]. Turkish version of self-completed 25-item self-report *Wender Utah rating scale* (WURS-25), which was developed to diagnose adult-ADHD was used to screen for ADHD symptoms [44-46]. Besides, the Turkish version of WURS-25 which is a reliable and valid tool for assessing the childhood symptoms of ADHD in adults was used in addition to screening questions for possible ADHD in childhood [44,47]. The participants were evaluated for the presence of childhood ADHD symptoms according to DSM-IV diagnostic criteria [45]. In addition to WURS-25 a validated Turkish version of the *Adult ADHD Self-Report Scale* (ASRS) was used [38,48,49]. As detailed elsewhere it consists of 18 questions investigating adult ADHD symptoms as reported in the DSM-IV [38,39,48-51]. Six of these questions, have shown greater sensitivity and can be used as a separate screening tool, also known as Short Form-ASRS-Version 1.1 [51]. In the present study, short form ASRS was used initially; the complete form of the ASRS was used in addition to short form ASRS if the confirmation of the ADHD diagnosis was required [48,49,51]. Positive screening tests are not considered sufficient to diagnose adult ADHD, but they indicate that further investigation is required. Therefore, a blinded clinical reappraisal of the ASRS interviews should also be completed with additional data, such as the history of punishment or business problems [52].

All the ADHD-related data mentioned above was prospectively provided with assessment tools and interviews with an average of three stages: (a) descriptive data and HIV related conditions (~20 min). (b) self-reported surveys (~30 minutes). (c) clinical interviews by a psychiatrist (~40 minutes), respectively. Therefore, the evaluation period from invitation to the study until the diagnosis approximately lasted for at least 90 minutes per patient. In the case that an active (symptomatic) psychiatric comorbidity was detected or if the diagnosis was unclear, a clinical appointment was made for future psychiatric interview in order to confirm the diagnosis of adult ADHD. Therefore, the participants with additional psychiatric confounders were reevaluated for ADHD after they were treated and became asymptomatic.

Data definitions

Demographic details such as date of birth, gender, civil status and occupation were recorded. The total follow-up time since the HIV diagnosis, total duration of ART, adherence to ART and to scheduled clinic appointments, lost-to follow-up, diagnosis of ADHD

and the rates and duration of the appointment and ART adherence were recorded for each participant.

Participants who had an interruption in taking any of their antiretroviral drugs for at least 6 days per month ($\leq 80\%$ adherence) were defined as “ART event”. The time (year) from the first ART usage to the date of event was outcome variable of the event free adherence of the antiretroviral treatment (ART-EFA).

Participants who did not attend scheduled clinical appointments without an excuse were defined as “appointment event”. If the participants missed the scheduled clinical appointment, the first date of missing was recorded clearly [53]. The time (year) from the first admission to the first date of the event was outcome variable of the event free adherence the scheduled clinical appointment (Appointment-EFA). Those without an event were censored on the date of their last follow-up.

Table 1. Characteristics of the participants.

Characteristic or finding	n (%) or median (min-max)
Age (years)	38 (23-65)
Gender (Male)	65 (76.5 %)
Marital status	
Married	38 (44.7 %)
Single	37 (43.5%)
Divorced	6 (7.1 %)
Widow	4 (4.7 %)
Education time (years)	8 (5-19)
Education level	
Elementary education	41 (48.2 %)
high school education	22 (25.9 %)
University	22 (25.9 %)
Employment rate	69 (81.2 %)
Self-reported income level	
Very - low	29 (34.1%)
Low	19 (22.4 %)
Moderate	13 (15.3 %)
Normal	5 (5.9 %)
Good	19 (22.4 %)
Legal punishment history	15 (17.6 %)
Hamilton depression score	8 (0-39)
STAI Tx-1	46 (20-76)
STAI Tx-2	50 (25-80)
WURS - 25	25 (0-80)
Positive ASRS interview	25 (29.4 %)
ART event	20 (23.5 %)
ART duration (years)	5 (1-17)
Appointment event	19 (22.4 %)
Follow-up duration (years)	6 (1-18)

ADHD; attention deficit hyperactivity disorder, ART; antiretroviral therapy, STAI-tx score; state-trait anxiety inventory text 1 and text 2 score, WURS-25; 25 item Wender Utah rating scale, ASRS; Adult ADHD Self-Report Scale, ART-event; an interruption in taking any of their antiretroviral drugs for at least 6 days per month, Appointment-event; an interruption in attending to the scheduled clinical appointments without an excuse.

Statistical analysis

Numbers and percentages were used for categorical data in descriptive analyses. The highest percentages for the normal population were compared with percentages in the study with the One Sample Chi-square Test. Continuous data were classified as parametric and non-parametric with skewness–kurtosis, Kolmogorov–Smirnov test, standard deviation/mean percentages and histogram graphics with normal distribution lines. For parametric and non-parametric data mean ± standard deviation with Student’s T Test and median (min–max) values with Mann-Whitney U Test were used respectively. Categorical data were compared with the chi-square or (if needed) the Fisher’s exact tests. The rates of the ART–event and Appointment–event in participants with and without ADHD were compared with the Chi-square test. The probabilities of EFA were analyzed using the plots and methods of Kaplan–Meier and were compared using the Log–rank test [54]. All p values were two-tailed. Statistically significant differences were assessed at an alpha level of < 0.05.

Results

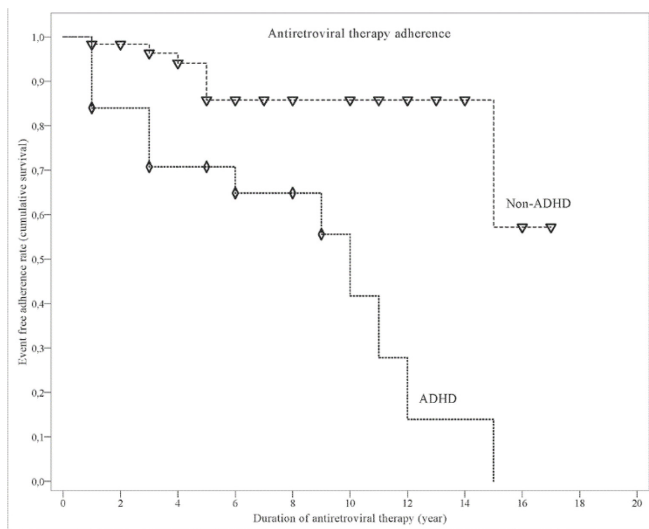
A total of 85 PLWH (20 females and 65 males) were included in the study and twenty-five participants (29.4 %) were diagnosed with ADHD. This rate (29.4 %) was significantly higher than the highest percentage reported for ADHD for the general population 7.3% ($\chi^2 = 61.413$ p < 0.0001) [52].

The characteristics and findings of the participants are shown in Table 1.

The state anxiety scores (STAI Text-1) for participants with and without ADHD were 47 ± 12 and 46.7 ± 13.7, respectively (p = 0.920). The trait anxiety scores (STAI Text-2) for participants with and without ADHD were 50.6 ± 11.7 and 49.2 ± 10.4, respectively (p = 0.586). The median Hamilton depression scores for participants with and without ADHD were 9 (min 0, max 9) and 7 (min 0, max 30), respectively (p = 0.136). The median WURS–25 for participants with and without ADHD were 39 (min 7, max 80) and 19 (min: 0, max 74), respectively (p = 0.00017). At the end of the assessment with ASRS and DSM interviews, twenty-five participants (29.4 %) were positive for ADHD.

During the follow-up period there were 20 (23.5 %) events of ART, with 13 events in ADHD participants and 7 events in non-ADHD participants (52 % vs. 11.7 %, Chi-Square, p = 0.0002). Kaplan–Meier plot with log-rank test demonstrated that the ART–EFA was significantly shorter among ADHD participants compared to those without (p = 0.00014) (Figure 1).

Figure 1. Event free antiretroviral treatment adherence among participants with and without attention deficit and hyperactivity disorder.



Participants who had used antiretroviral treatment (ART) for at least 15 days and had had an interruption in taking any of their antiretroviral drugs for at least 6 days in a month (≤ 80% adherence) were defined as event (ART non-adherence). Kaplan–Meier plots and log-rank tests demonstrated that event free antiretroviral treatment adherence (ART – EFA) was significantly shorter among ADHD participants compared to those without (Log-rank, $\chi^2 = 14.481$, p = 0.00014). ADHD; attention deficit and hyperactivity disorder, ◊ADHD, ▼Non-ADHD.

The mean duration of event free adherence in participants with and without ADHD was 8.4 (95% CI: 6.2 – 10.6) and 14.6 (95% CI: 13 – 16.2) years, respectively (Figure 1).

During the follow-up period there were 19 (22.4 %) events of appointment, with 10 events in ADHD participants and 9 events in non-ADHD participants (40% vs. 15 %, Chi-Square, p = 0.02). The appointment–EFA was significantly shorter among ADHD participants compared to those without (p = 0.023) (Figure 2). The mean duration of event free adherence in participants with and without ADHD was 10.8 (95% CI: 8.4–13.2) and 15.1 (95% CI: 13.4–16.8) years, respectively (Figure 2).

Discussion

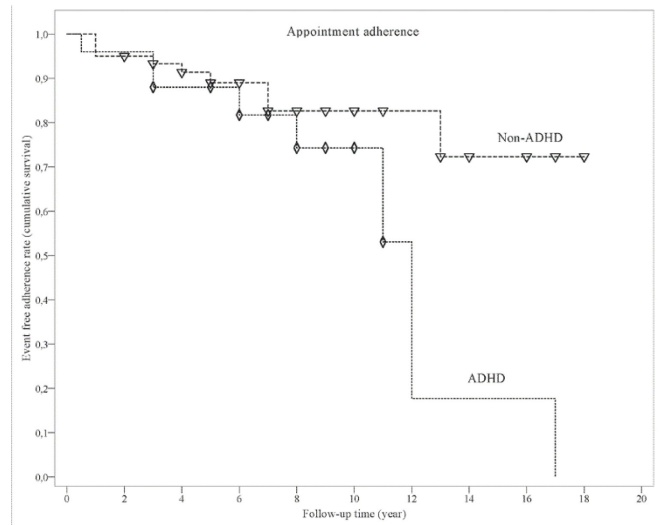
HIV infection has become a manageable chronic condition with the recent achievements in antiretroviral treatment. The duration and quality of life of the PLWH who initiate early antiretroviral treatment, attend scheduled appointments regularly and have long-term adherence to treatment is almost equivalent to those who are HIV negative [55]. Although full adherence to ART was defined as ≥ 95% a recent analysis reported that virologic success with novel drugs could be

achieved with adherence rates as low as to 80% [4,5,23]. However, adherence rates lower than 80% may result in virologic failure and resistance to antiretroviral drugs leading to the development of opportunistic diseases and restricting future treatment options [56-58]. Non-adherence to antiretroviral treatment also has social consequences, such as ongoing transmission of HIV and increased medical costs due to a high level of morbidity and mortality [59,60]. Failure to attend clinical appointments also may have negative outcomes such as delays in detecting and addressing laboratory abnormalities, especially virologic failure. Besides, non-attendance to clinical visits may cause delays in getting ART prescriptions on time [61].

Many obstacles were defined that prevented access to ART such as depression, cognitive disorders, alcohol abuse, substance abuse, lack of social support, lack of uninterrupted social security, interruptions in the drug supply, treatment fatigue, number of pills and drug side effects [10,17-19]. Although novel antiretroviral drugs are easier to use and have fewer side effects compared to historical drugs, full adherence rates globally are still lower than 70 % [5-7]. This study showed that ADHD might be a major factor to have a negative influence on adherence to treatment and attendance to the scheduled follow-up procedures in PLWH.

Attention deficit and hyperactivity disorder among adults has a range of manifestations from socioeconomic problems to risky sexual behavior [25]. Hyperactivity of younger ages usually diminishes in time being replaced with different manifestations that may be confused with other mental conditions [62,63]. Attention deficit becomes the major manifestation compared to hyperactivity in nine out of ten adult participants with ADHD and it usually manifests as disorganization, forgetfulness, distractibility, and poor school and work performance [62-65]. ADHD among PLWH was studied mostly in children and adolescents with perinatal exposure to HIV and up to date, ADHD was not listed as a psychiatric condition to create a barrier to adherence among patients with no perinatal HIV exposure [24,30-36]. Only one cross-sectional study that studied adult-ADHD among PLWH reported that participants with ADHD were less likely to be adherent to ART than those without; however, the study had a major limitation to include only male PLWH [23]. Our study clearly showed that ADHD was significantly more prevalent among PLWH than in the general population and that there was no gender-related difference [23,66,67]. In addition, we showed that not only there was non-adherence more common among participants with ADHD, but it also developed earlier

Figure 2. Event free appointment adherence among participants with and without attention deficit and hyperactivity disorder.



Participants who did not attend scheduled clinical appointments without an excuse were defined as an event (appointment non-adherence). Kaplan–Meier plots and log-rank tests demonstrated that event free appointment adherence (Appointment–EFA) was significantly shorter among ADHD participants compared to those without. (Log-rank, $\chi^2 = 5.158$, $p = 0.0231$). ADHD; attention deficit and hyperactivity disorder, \diamond ADHD, ∇ Non-ADHD.

compared to those without. Since the management of HIV infection requires strict discipline, an early diagnosis of ADHD that manifests with disorganization and forgetfulness, is crucial for the proper management of the HIV-infected patient.

Adults with ADHD that present to psychiatry clinics are usually diagnosed with major depression, generalized anxiety disorder, obsessive compulsive disorder in addition to their major diagnosis and they usually present to the clinic with symptoms related to those co-morbidities [62]. Moreover, conditions such as alcohol abuse (58.9 %), and suicide attempts (38.5%) are common among people with ADHD, which also contribute to the tendency of non-adherence [62]. This study pointed out that ADHD might create a serious risk for non-adherence to long-term ART usage, and to non-attendance to regular follow-up.

A high rate of adherence to antiretroviral treatment, which eventually results in a high treatment success rate, requires close contact between the HIV clinician and the psychiatrist. Considering that ADHD in adults may have different manifestations and atypical symptoms compared to children and adolescents, and that it may be obscured by the manifestations of co-morbid mental conditions, the diagnosis is likely to be missed in PLWH.

This study has several limitations that we considered when reviewing the results. First, this study did not show a correlation between other psychiatric comorbidities and non-adherence. This may be attributed to the fact that we did not include patients with active psychiatric conditions until they underwent remission. According to the planned methodology it was possible to control the confounding effects of psychiatric comorbidities and CNS related pathologies. However, other cases with factors that could negatively influence adherence were not taken into account and not included in the study. A second limitation is that, the dose-taking adherence was assessed by medical records of the clinician based on self-reporting by the patient. However, the technic of the “medical record of self-reporting” cannot be similar as the technic of the “measurement with the electronic monitoring cap attached to one of the pill bottles” [68].

Conclusion

The early initiation and the long-term maintenance of antiretroviral treatment requires full dedication and strict adherence in order to achieve long-term suppression. However, non-adherence to treatment and non-attendance to scheduled clinical visits are significantly more common and developed earlier among PLWH diagnosed with adult-ADHD compared to those without. Therefore, adult-ADHD may be considered a serious and hidden obstacle to the success of treatment among adults living with HIV. Early screening of PLWH for adult-ADHD as well as providing adequate support and treatment when required would be beneficial to ensure full adherence to ART and to achieve and maintain virologic suppression.

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References

1. Iacob SA, Iacob DG, Jugulete G (2017) Improving the adherence to antiretroviral therapy, a difficult but essential task for a successful HIV treatment-clinical points of view and practical considerations. *Front Pharmacol* 8: 831.
2. Belayihun B, Negus R (2015) Antiretroviral treatment adherence rate and associated factors among people living with HIV in Dubti Hospital, Afar Regional State, East Ethiopia. *Int Sch Res Notices*. Available: <http://downloads.hindawi.com/archive/2015/187360.pdf>. Accessed 11 September 2019.
3. Nelson M, Girard PM, Demasi R, Chen L, Smets E, Sekar V, Lavreys L (2010) Suboptimal adherence to darunavir/ritonavir has minimal effect on efficacy compared with lopinavir/ritonavir in treatment-naive, HIV-infected patients: 96 week ARTEMIS data. *J Antimicrob Chemother* 65: 1505-1509.
4. Paterson DL, Swindells S, Mohr J, Brester M, Vergis EN, Squier C, Wagener MM, Singh N (2000) Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Ann Intern Med* 133: 21-30.
5. Bezabhe WM, Chalmers L, Bereznicki LR, Peterson GM (2016) Adherence to antiretroviral therapy and virologic failure: a meta-analysis. *Med Baltim*. Available: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4839839/pdf/medi-95-e3361.pdf>. Accessed 10 September 2019.
6. Gardner EM, McLees MP, Steiner JF, Del Rio C, Burman WJ (2011) The spectrum of engagement in HIV care and its relevance to test-and-treat strategies for prevention of HIV infection. *Clin Infect Dis* 52: 793-800.
7. Ortego C, Huedo-Medina TB, Llorca J, Sevilla L, Santos P, Rodriguez E, Warren MR, Vejo J (2011) Adherence to highly active antiretroviral therapy (HAART): a meta-analysis. *AIDS Behav* 15: 1381-1396.
8. Adejumo O, Oladeji B, Akpa O, Malee K, Baiyewu O, Ogunniyi A, Evans S, Berzins B, Taiwo B (2016) Psychiatric disorders and adherence to antiretroviral therapy among a population of HIV-infected adults in Nigeria. *Int J STD AIDS* 27: 938-949.
9. Arreola S, Santos GM, Beck J, Sundararaj M, Wilson PA, Hebert P, Makofane K, Do TD, Ayala G (2015) Sexual stigma, criminalization, investment, and access to HIV services among men who have sex with men worldwide. *AIDS Behav* 19: 227-234.
10. Locher C, Messerli M, Gaab J, Gerger H (2019) Long-term effects of psychological interventions to improve adherence to antiretroviral treatment in HIV-infected persons: a systematic review and meta-analysis. *AIDS Patient Care STDS* 33: 131-144.
11. Mahajan AP, Sayles JN, Patel VA, Remien RH, Sawires SR, Ortiz DJ, Szekeres G, Coates TJ (2008) Stigma in the HIV/AIDS epidemic: a review of the literature and recommendations for the way forward. *Aids* 22 Suppl 2: S67-S79.
12. Morrison MF, Petitto JM, Ten Have T, Gettes DR, Chiappini MS, Weber AL, Brinker-Spence P, Bauer RM, Douglas SD, Evans DL (2002) Depressive and anxiety disorders in women with HIV infection. *Am J Psychiatry* 159: 789-796.
13. Peterson K, Togun T, Klis S, Menten J, Colebunders R (2012) Depression and posttraumatic stress disorder among HIV-infected Gambians on antiretroviral therapy. *AIDS Patient Care STDS* 26: 589-596.

14. Ciesla JA, Roberts JE (2001) Meta-analysis of the relationship between HIV infection and risk for depressive disorders. *Am J Psychiatry* 158: 725-730.
15. Nebhinani N, Mattoo SK, Wanchu A (2011) Psychiatric morbidity in HIV-positive subjects: a study from India. *J Psychosom Res* 70: 449-454.
16. Collins PY, Holman AR, Freeman MC, Patel V (2006) What is the relevance of mental health to HIV/AIDS care and treatment programs in developing countries? A systematic review. *Aids* 20: 1571-1582.
17. Fernandez D, Salami I, Davis J, Mbah F, Kazeem A, Ash A, Babino J, Carter L, Salemi JL, Spooner KK, Olaleye OA, Salihu HM (2018) HIV-TB coinfection among 57 million pregnant women, obstetric complications, alcohol use, drug abuse, and depression. *J Pregnancy*. Available: <http://downloads.hindawi.com/journals/jp/2018/5896901.pdf>. Accessed 10 September 2019.
18. Gonzalez JS, Batchelder AW, Psaros C, Safren SA (2011) Depression and HIV/AIDS treatment nonadherence: a review and meta-analysis. *J Acquir Immune Defic Syndr* 58: 181-187.
19. Hendershot CS, Stoner SA, Pantalone DW, Simoni JM (2009) Alcohol use and antiretroviral adherence: review and meta-analysis. *J Acquir Immune Defic Syndr* 52: 180-202.
20. Mayston R, Kinyanda E, Chishinga N, Prince M, Patel V (2012) Mental disorder and the outcome of HIV/AIDS in low-income and middle-income countries: a systematic review. *Aids* 26 Suppl 2: S117-S135.
21. Matthews M, Nigg JT, Fair DA (2014) Attention deficit hyperactivity disorder. *Curr Top Behav Neurosci* 16: 235-266.
22. Barkley RA (1997) Behavioral inhibition, sustained attention, and executive functions: constructing a unifying theory of ADHD. *Psychol Bull* 121: 65-94.
23. Kumar S, Shekar A, Pandiyan K, Das G, Nahar A, Raveendra K, Hongally C (2014) Prevalence of adult attention deficit hyperactivity disorder and its correlates among recently diagnosed young adult males with HIV. *J AIDS Clin Res*. Available: <https://www.hilarispublisher.com/open-access/prevalence-of-adult-attention-deficit-hyperactivity-disorder-and-its-correlates-among-recently-diagnosed-young-adult-males-with-hiv-2155-6113.1000314.pdf>. Accessed 06 September 2019.
24. Mpango RS, Kinyanda E, Rukundo GZ, Levin J, Gadow KD, Patel V (2017) Prevalence and correlates for ADHD and relation with social and academic functioning among children and adolescents with HIV/AIDS in Uganda. *BMC Psychiatry* 17: 336.
25. Faraone SV, Biederman J, Mick E (2006) The age-dependent decline of attention deficit hyperactivity disorder: a meta-analysis of follow-up studies. *Psychol Med* 36: 159-165.
26. Hosain GM, Berenson AB, Tennen H, Bauer LO, Wu ZH (2012) Attention deficit hyperactivity symptoms and risky sexual behavior in young adult women. *J Womens Health (Larchmt)* 21: 463-468.
27. Volkow ND, Swanson JM (2013) Clinical practice: Adult attention deficit-hyperactivity disorder. *N Engl J Med* 369: 1935-1944.
28. Wender PH (1998) Attention-deficit hyperactivity disorder in adults. *Psychiatr Clin North Am* 21: 761-774.
29. Zalsman G, Shilton T (2016) Adult ADHD: A new disease? *Int J Psychiatry Clin Pract* 20: 70-76.
30. Adefalu MO, Tunde-Ayinmode MF, Issa BA, Adefalu AA, Adepoju SA (2018) Psychiatric morbidity in children with HIV/AIDS at a tertiary health institution in north-central Nigeria. *J Trop Pediatr* 64: 38-44.
31. Chernoff M, Angelidou KN, Williams PL, Brouwers P, Warsaw M, Nachman S (2018) Assessing psychiatric symptoms in youth affected by hiv: comparing a brief self-administered rating scale with a structured diagnostic interview. *J Clin Psychol Med Settings* 25: 420-428.
32. Kacanek D, Angelidou K, Williams PL, Chernoff M, Gadow KD, Nachman S (2015) Psychiatric symptoms and antiretroviral nonadherence in US youth with perinatal HIV: a longitudinal study. *Aids* 29: 1227-1237.
33. Mellins CA, Smith R, O'Driscoll P, Magder LS, Brouwers P, Chase C, Blasini I, Hittleman J, Llorente A, Matzen E (2003) High rates of behavioral problems in perinatally HIV-infected children are not linked to HIV disease. *Pediatrics* 111: 384-393.
34. Mpango RS, Kinyanda E, Rukundo GZ, Osafo J, Gadow KD (2018) Exploration of the understanding and etiology of ADHD in HIV/AIDS as observed by adolescents with HIV/AIDS, caregivers and health workers- using case vignettes. *Afr Health Sci* 18: 488-495.
35. Scharko AM (2006) DSM psychiatric disorders in the context of pediatric HIV/AIDS. *AIDS Care* 18: 441-445.
36. Visser MJ, Hecker HE, Jordaen J (2018) A comparative study of the psychological problems of HIV-infected and HIV-uninfected children in a South African sample. *AIDS Care* 30: 596-603.
37. Des Jarlais DC, Lyles C, Crepaz N (2004) Improving the reporting quality of nonrandomized evaluations of behavioral and public health interventions: the TREND statement. *Am J Public Health* 94: 361-366.
38. First MB, Gibbon M, Spitzer RL, Benjamin LS and Williams JB (1997) Structured clinical interview for DSM-IV® axis II personality disorders SCID-II, 1th edition. New York: American Psychiatric Pub. 91 p.
39. Özkürkçügil A, Aydemir Ö, Yıldız M, Esen-Danaci A, Köroğlu E (1999) Adaptation into Turkish and reliability of structured clinical interview for DSM-IV (SCID). *İlaç ve Tedavi Dergisi* 12: 233-236.
40. Akdemir A, Turkcapar MH, Orsel SD, Demirergi N, Dag I, Ozbay MH (2001) Reliability and validity of the Turkish version of the Hamilton depression rating scale. *Compr Psychiatry* 42: 161-165.
41. Hamilton M (1960) A rating scale for depression. *J Neurol Neurosurg Psychiatry* 23: 56-62.
42. Öner N and Lecompte WA (1985) Durumluk-süreklilik kaygı envanteri el kitabı, 2th edition. İstanbul: Boğaziçi üniversitesi yayımları 26 p. [Book in Turkish].
43. Spielberger CD, Gorsuch RL, Lushene R, Vagg PR and Jacobs GA (1983) State-trait anxiety inventory for adults: Manual, instrument, and scoring guide, 1th edition. Palo Alto: Consulting Psychologists Press. 75 p.
44. Öncü B, Ölmez Ş, Şentürk V (2005) Validity and reliability of the Turkish version of the Wender Utah rating scale for attention-deficit / hyperactivity disorder in adults. *Turk J Psychiatry* 16: 252-259.
45. Turkyilmaz E, Yavuz BG, Karamustafalioglu O, Ozer OA, Bakim B (2012) Prevalence of adult attention deficit hyperactivity disorder in the relatives of patients with bipolar disorder. *Int J Psychiatry Clin Pract* 16: 223-228.
46. Ward MF, Wender PH, Reimherr FW (1993) The Wender Utah rating scale: an aid in the retrospective diagnosis of childhood attention deficit hyperactivity disorder. *Am J Psychiatry* 150: 885-890.

47. McIntosh D, Kutcher S, Binder C, Levitt A, Fallu A, Rosenbluth M (2009) Adult ADHD and comorbid depression: A consensus-derived diagnostic algorithm for ADHD. *Neuropsychiatr Dis Treat* 5: 137-150.
48. Dogan S, Öncü B, Varol-Saraçoğlu G, Küçükgöncü S (2009) Validity and reliability of the Turkish version of the Adult ADHD Self-Report Scale (ASRS-v1.1). *Anadolu Psikiyatri Derg* 10: 77-87.
49. Kessler RC, Adler LA, Gruber MJ, Sarawate CA, Spencer T, Van Brunt DL (2007) Validity of the World Health Organization adult ADHD self-report scale (ASRS) Screener in a representative sample of health plan members. *Int J Methods Psychiatr Res* 16: 52-65.
50. Barkley R, Murphy K and Fischer M (2008) *ADHD in adults: What the science says*, 1th edition. New York: The Guilford Press. 489 p.
51. Kessler RC, Adler L, Ames M, Demler O, Faraone S, Hiripi E, Howes MJ, Jin R, Secnik K, Spencer T, Ustun TB, Walters EE (2005) The World Health Organization Adult ADHD Self-Report Scale (ASRS): a short screening scale for use in the general population. *Psychol Med* 35: 245-256.
52. Valsecchi P, Nibbio G, Rosa J, Tamussi E, Turrina C, Sacchetti E, Vita A (2018) Adult ADHD: Prevalence and clinical correlates in a sample of Italian psychiatric outpatients. *J Atten Disord*. Available: <https://journals.sagepub.com/doi/pdf/10.1177/1087054718819824>. Accessed 07 September 2019.
53. Kahana SY, Jenkins RA, Bruce D, Fernandez MI, Hightow-Weidman LB, Bauermeister JA (2016) Structural determinants of antiretroviral therapy use, HIV care attendance, and viral suppression among adolescents and young adults living with HIV. *PLoS One* 11: e0151106.
54. Kaplan EL, Meier P (1958) Nonparametric estimation from incomplete observations. *J Am Stat Assoc* 53: 457-481.
55. May MT, Gompels M, Delpech V, Porter K, Orkin C, Kegg S, Hay P, Johnson M, Palfreeman A, Gilson R, Chadwick D, Martin F, Hill T, Walsh J, Post F, Fisher M, Ainsworth J, Jose S, Leen C, Nelson M, Anderson J, Sabin C (2014) Impact on life expectancy of HIV-1 positive individuals of CD4(+) cell count and viral load response to antiretroviral therapy. *Aids* 28: 1193-1202.
56. Bangsberg DR, Perry S, Charlebois ED, Clark RA, Roberston M, Zolopa AR, Moss A (2001) Non-adherence to highly active antiretroviral therapy predicts progression to AIDS. *Aids* 15: 1181-1183.
57. Clavel F, Hance AJ (2004) HIV drug resistance. *N Engl J Med* 350: 1023-1035.
58. Nachega JB, Hislop M, Dowdy DW, Lo M, Omer SB, Regensberg L, Chaisson RE, Maartens G (2006) Adherence to highly active antiretroviral therapy assessed by pharmacy claims predicts survival in HIV-infected South African adults. *J Acquir Immune Defic Syndr* 43: 78-84.
59. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, Hakim JG, Kumwenda J, Grinsztejn B, Pilotto JH, Godbole SV, Mehendale S, Chariyalertsak S, Santos BR, Mayer KH, Hoffman IF, Eshleman SH, Piwovar-Manning E, Wang L, Makhema J, Mills LA, de Bruyn G, Sanne I, Eron J, Gallant J, Havlir D, Swindells S, Ribaudo H, Elharrar V, Burns D, Taha TE, Nielsen-Saines K, Celentano D, Essex M, Fleming TR (2011) Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med* 365: 493-505.
60. Nachega JB, Leisegang R, Bishai D, Nguyen H, Hislop M, Cleary S, Regensberg L, Maartens G (2010) Association of antiretroviral therapy adherence and health care costs. *Ann Intern Med* 152: 18-25.
61. Gardner LI, Marks GB, O'Daniels CM, Wilson TE, Golin C, Wright J, Quinlivan EB, Bradley-Springer L, Thompson M, Raffanti S, Thrun M (2008) Implementation and evaluation of a clinic-based behavioral intervention: positive steps for patients with HIV. *AIDS Patient Care STDS* 22: 627-635.
62. Duran S, Fistikci N, Keyvan A, Bilici M, Caliskan M (2014) ADHD in adult psychiatric outpatients: prevalence and comorbidity. *Turk J Psychiatry* 25: 84-93.
63. Nierenberg AA, Miyahara S, Spencer T, Wisniewski SR, Otto MW, Simon N, Pollack MH, Ostacher MJ, Yan L, Siegel R, Sachs GS (2005) Clinical and diagnostic implications of lifetime attention-deficit/hyperactivity disorder comorbidity in adults with bipolar disorder: data from the first 1000 STEP-BD participants. *Biol Psychiatry* 57: 1467-1473.
64. Schmidt K, Froidson S (1990) Atypical outcome in attention deficit hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry* 29: 566-570.
65. Wilens TE, Biederman J, Wozniak J, Gunawardene S, Wong J, Monuteaux M (2003) Can adults with attention-deficit/hyperactivity disorder be distinguished from those with comorbid bipolar disorder? Findings from a sample of clinically referred adults. *Biol Psychiatry* 54: 1-8.
66. Fayyad J, De Graaf R, Kessler R, Alonso J, Angermeyer M, Demyttenaere K, De Girolamo G, Haro JM, Karam EG, Lara C, Lepine JP, Ormel J, Posada-Villa J, Zaslavsky AM, Jin R (2007) Cross-national prevalence and correlates of adult attention-deficit hyperactivity disorder. *Br J Psychiatry* 190: 402-409.
67. Kessler RC, Adler L, Barkley R, Biederman J, Conners CK, Demler O, Faraone SV, Greenhill LL, Howes MJ, Secnik K, Spencer T, Ustun TB, Walters EE, Zaslavsky AM (2006) The prevalence and correlates of adult ADHD in the United States: results from the national comorbidity survey replication. *Am J Psychiatry* 163: 716-723.
68. Wagner GJ, Linnemayr S, Ghosh-Dastidar B, Currier JS, Hoffman R, Schneider S (2016) Supporting treatment adherence readiness through training (START) for patients with HIV on antiretroviral therapy: study protocol for a randomized controlled trial. *Trials*. Available: <https://trialsjournal.biomedcentral.com/track/pdf/10.1186/s13063-016-1287-3>. Accessed 06 September 2019.

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