

The effects of alcohol use on people living with HIV/Aids: an integrative review

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ABSTRACT

The aim of this study was to analyze the scientific production on the effects of alcohol use on people with HIV/Aids. This is an integrative review carried out in October 2017 using the following databases: LILACS, SciELO, MEDLINE, CINAHL, Scopus, Cochrane and Web of Science. The descriptors "Acquired Immunodeficiency Syndrome", "HIV" and "Alcohol" were used in Portuguese, English and Spanish, with the Boolean operator "AND". A total of 2,355 articles were found, and 46 were selected for the study. The data were organized into four thematic categories: the effects of alcohol on adherence to antiretroviral therapy; neurological and metabolic effects of alcohol; increased risk of HIV transmission and disease progression. It is concluded that HIV/Aids and alcohol consumption have a synergistic effect on the lives of people with HIV, causing them greater health harm (with emphasis on neurological and metabolic alterations), low adherence to treatment, increased virus transmission and disease progression.

Descriptors: HIV; Ethanol; Acquired Immunodeficiency Syndrome.

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INTRODUCTION

Despite advances in reducing the spread of the acquired immunodeficiency virus (HIV), the number of people affected by it continues to rise worldwide⁽¹⁾. Associated with this, alcohol abuse is observed in this population; which is a serious health problem with social, economic and psychological repercussions⁽²⁾.

With the use of antiretroviral therapy (ART), there has been a significant reduction in morbidity and mortality associated with HIV; which makes it a chronic disease. This fact led to an increase in life expectancy and the susceptibility to the acquisition of risk habits, such as alcohol consumption, which tends to be more prevalent in people living with HIV/Aids (PLHA) when compared to the general population⁽¹⁻²⁾. It is estimated that 44.0% of these individuals have problems with the use of alcohol and other drugs⁽³⁾.

Alcohol consumption negatively influences the health status of PLHA⁽⁴⁾ and is associated with unprotected sex (without the use of condoms)⁽¹⁾, which increases the likelihood of transmitting HIV and other sexually transmitted infections⁽²⁾. Moreover, it may compromise quality of life and adherence to treatment, accelerating the progression of the disease⁽³⁾.

In light of this, it is essential for health professionals (especially nurses) to know the effects of alcohol use in PLHA, in order to prevent or reduce harm associated with this substance, by stimulating the acquisition of healthy lifestyle habits and self-care.

Aiming to contribute to the health care of PLHA, the goal of this study is to analyze the scientific productions about the effects of alcohol use on people living with HIV/Aids.

METHOD

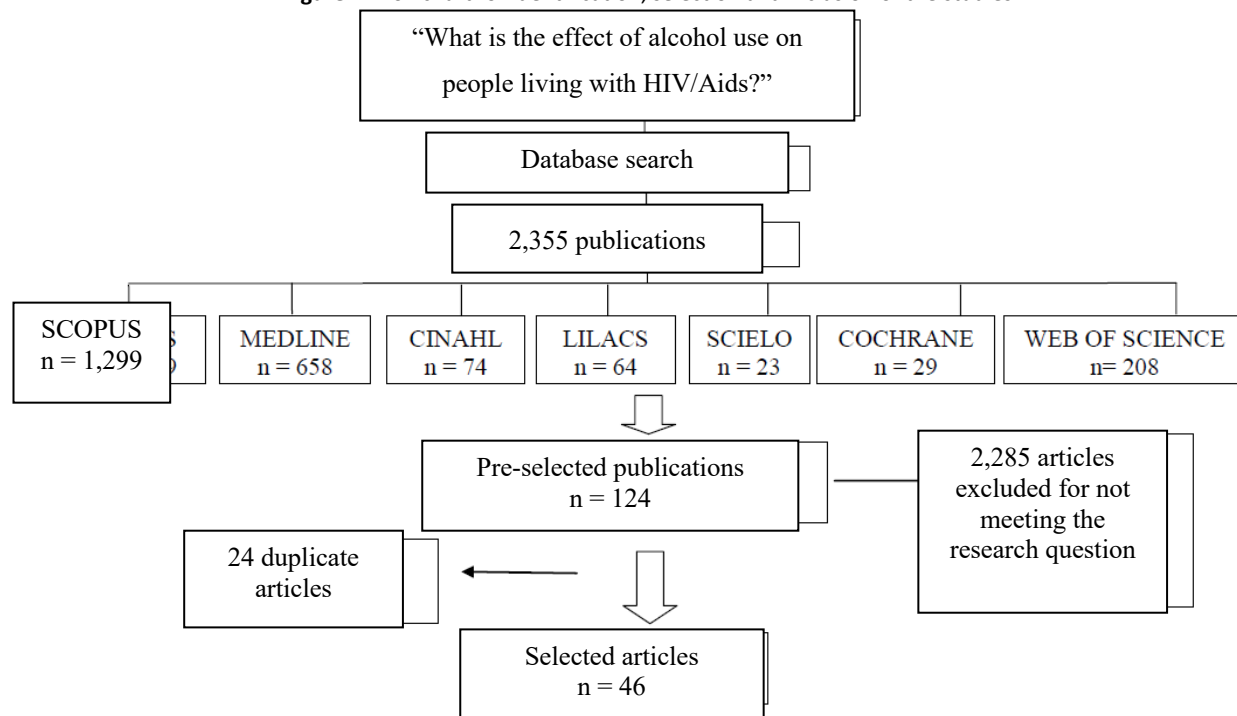
This is an integrative literature review developed through the following stages: elaboration of the guiding question, literature search, data collection, critical analysis of the results, and presentation of the integrative review⁽⁵⁾.

The following guiding question was formulated based on the PICO strategy⁽⁶⁾: "What is the effect of alcohol use on people living with HIV/Aids?". The inclusion criteria consisted of complete articles available electronically in Portuguese, English and Spanish, with no temporal cut. Duplicate publications were excluded and grouped in the database together with other articles that either did not respond to the research question or involved animals.

The electronic search was conducted simultaneously by two reviewers, in October 2017, in five databases: Cumulative Index to Nursing and Allied Health Literature (CINAHL), Latin American and Caribbean Health Sciences Literature (LILACS), Scientific Electronic Library Online (SciELO), Web of Science, and Scopus. The Medical Literature Analysis and Retrieval System Online portal (MEDLINE/PubMed) and the Cochrane Library were also searched. The descriptors used were "Acquired Immunodeficiency Syndrome", "HIV" and "Alcohol", available at the Medical Subject Headings (MeSH), produced by the National Library of Medicine, and at the Health Sciences Descriptors (DeCS); in Portuguese, English and Spanish, using the Boolean operator "AND".

From the crossings that arose, a total of 2,355 articles were found, of which 46 were selected. Twenty-four duplicate publications were excluded, together with 2,285 articles addressing the relationship between alcohol and other drugs in uninfected people, and risk behaviors for HIV acquisition. Figure 1 shows the identification, selection and inclusion of the scientific productions.

Figure 1: Flowchart for identification, selection and inclusion of the studies.



Data analysis was done by the translation and full reading of the articles, by two authors, independently. In case of doubts, there was a meeting between the reviewers for consensus. The information was transcribed and organized using a validated instrument⁽⁷⁾ that investigated: the methodological development, the effects of alcohol use on PLHA, the conclusion, and the levels of evidence.

The levels of evidence were determined as follows: Level I - Evidence from a systematic review or meta-analysis of multiple randomized controlled clinical studies or from clinical guidelines based on systematic reviews of randomized controlled trials; Level II - Evidence from individual randomized controlled studies; Level III - Evidence from experimental studies without randomization; Level IV - Evidence from cohort or case-control studies; Level V - Evidence from a systematic review of descriptive and qualitative studies; Level VI - Evidence from a descriptive or qualitative study; Level VII - Evidence obtained from opinions of authorities or expert committees report⁽⁸⁾.

After the analysis, the effects of alcohol use on PLHA were grouped into four categories: 1. Neurological and metabolic effects of alcohol; 2. Effects of alcohol on ART adherence; 3. Increased risk of HIV transmission, and 4. Increased disease progression. The findings were discussed based on the scientific literature on the subject, respecting copyright and the integrity of the articles, so that no modification of content was made for the benefit of this research.

RESULTS

Regarding the characterization of the articles selected, the year of publication ranged from 1993 to 2017. Eleven were published in European countries^(10,12,15-16,20,24,36-37,45,49,51), twenty-eight in the United States^(17-19,21-22,25-33,38-44,46-48,50,52-54), four in Brazil^(9,23,34-35), two in the Asian continent⁽¹³⁻¹⁴⁾ and one in the African continent⁽¹¹⁾ (Table

1). The analysis of the levels of evidence showed the following distribution: two level I⁽⁴⁰⁻⁴¹⁾, two level II^(17,26), fifteen level IV^(15-16,27,30,32-33,39,38,42-47,49,51-42), six level V^(18,29,35-38), and twenty-one level VI^(9-14,19-25,28,31,34,43,48,50,53-54).

Table 1: Characterization of the studies according to journal, year, country, type of study, and outcome in PLHA. Fortaleza, Ceará, Brazil, 2017.

Journal	Year	Country	Type of study	Outcome in PLHA
BMC Infect Dis. ⁽⁹⁾	2017	Brazil	Cross-sectional study	Low CD4+ T lymphocyte count
Addict Behav. ⁽¹⁰⁾	2016	England	Cross-sectional study	Increased anxiety sensitivity
PloS one. ⁽¹¹⁾	2015	South Africa	Cross-sectional study	Failure and interruption of treatment
AIDS Care. ⁽¹²⁾	2015	England	Cross-sectional study	CD4+ T lymphocyte count less than 200 cells / mm ³
AIDS Care. ⁽¹³⁾	2015	Russia	Cross-sectional study	Reduced adherence to ART
BMC Public Health ⁽¹⁴⁾	2014	Vietnam	Cross-sectional study	Reduced adherence to ART and reduced quality of life
Curr Res HIV. ⁽¹⁵⁾	2014	Holland	Cohort study	Neurocognitive disorders, such as reduction of brain-derived neurotrophic factor
Brain Pathol. ⁽¹⁶⁾	2014	Switzerland	Cohort study	Elevated levels of neuroinflammation markers
Subst Abus. ⁽¹⁷⁾	2014	United States	Clinical trial	Prevalence of depressive symptoms
Behav Med. ⁽¹⁸⁾	2014	United States	Literature review	Reduced adherence to ART and risky sexual behavior
AIDS Res Hum Retroviruses. ⁽¹⁹⁾	2014	United States	Cross-sectional study	Low virological suppression
Int J Behav Med. ⁽²⁰⁾	2014	Georgia	Cross-sectional study	Low viral suppression and lower adherence to treatment
Curr HIV Res. ⁽²¹⁾	2014	United States	Cross-sectional study	Progression to advanced stage / aids, low CD4 + T lymphocyte count, increased susceptibility to opportunistic infections and lower adherence to medications
Scientific World Journal. ⁽²²⁾	2013	United States	Cross-sectional study	Increased blood pressure
Brasília Med. ⁽²³⁾	2013	Brazil	Case report	Immune system dysfunction and thrombocytopenia, in addition to increased susceptibility to infectious and opportunistic diseases
HIV Med. ⁽²⁴⁾	2013	England	Cross-sectional study	Risky sexual behavior, such as intercourse without condoms and with serodiscordant partners
AIDS Res Hum Retroviruses. ⁽²⁵⁾	2013	United States	Cross-sectional study	Increased risk of non-adherence to pharmacological treatment
J Acquir Immune Defic Syndr. ⁽²⁶⁾	2012	United States	Clinical trial	Toxic effects on the body
Biol Psychiatry. ⁽²⁷⁾	2012	United States	Cohort study	Deeper and consistent cerebral volume loss
J Subst Use. ⁽²⁸⁾	2012	United States	Cross-sectional study	Multiple partners, unprotected sex
Expert Opin Drug Metab Toxicol. ⁽²⁹⁾	2012	United States	Systematic review	Increased neuronal toxicity; reduced adherence to ART and reduced quality of life; greater immune suppression and a faster progression to AIDS; exacerbation of neuroinflammation and neuropsychological impairment
AIDS Care. ⁽³⁰⁾	2011	United States	Cohort study	Reduced adherence to ART
Subst Abus. ⁽³¹⁾	2011	United States	Cross-sectional study	Non-adherence to ART
Drug Alcohol Depend. ⁽³²⁾	2011	United States	Cohort study	Depressive symptoms

Journal	Year	Country	Type of study	Outcome in PLHA
Alcohol Clin Exp Res. ⁽³³⁾	2011	United States	Cohort study	Increased mortality rate
J Bras Psiquiatr. ⁽³⁴⁾	2011	Brazil	Cross-sectional study	Increased risk of non-adherence to pharmacological treatment
J Bras Psiquiatr. ⁽³⁵⁾	2010	Brazil	Systematic review	Reduced adherence to ART
Drug Alcohol Depend. ⁽³⁶⁾	2010	Ireland	Systematic review	Reduced adherence to ART
Alcohol Alcohol. ⁽³⁷⁾	2010	England	Systematic review	Reduced adherence to ART
Curr HIV/AIDS Rep. ⁽³⁸⁾	2010	United States	Systematic review	Reduced adherence to ART
Alcohol Research and health. ⁽³⁹⁾	2010	United States	Systematic review	Ventricular hypertrophy, decrease in neuronal markers, significant harm to myelin sheath and degradation of bundles
AIDS Behav. ⁽⁴⁰⁾	2009	United States	Systematic review	Unprotected sex
J Acquir Immune Defic Syndr. ⁽⁴¹⁾	2009	United States	Systematic review	Low adherence to ART
AIDS Care. ⁽⁴²⁾	2009	United States	Cohort study	Depressive symptoms
AIDS Behav. ⁽⁴³⁾	2008	United States	Cross-sectional study	Unprotected sex and with multiple partners
Addiction (Abingdon, England). ⁽⁴⁴⁾	2008	United States	Cohort study	Depressive symptoms
Brain. ⁽⁴⁵⁾	2007	England	Cohort study	Decreased fractional anisotropy and increased mean diffusivity in the region of callus and fiber bundles of the brain
J Stud Alcohol Drugs. ⁽⁴⁶⁾	2007	United States	Cohort study	Decreased quality of life and increased psychiatric comorbidities
Neuroimage. ⁽⁴⁷⁾	2006	United States	Cohort study	Ventricular hypertrophy and enlargement of the frontal regions of the brain
Journal of clinical and experimental neuropsychology. ⁽⁴⁸⁾	2006	United States	Cross-sectional study	Decreases in neurocognitive performance
J Acquir Immune Defic Syndr. ⁽⁴⁹⁾	2003	England	Cohort study	Nutritional and metabolic deficiency and brain cell degradation
J R Soc Med. ⁽⁵⁰⁾	1996	United States	Cross-sectional study	Progression to advanced stage / Aids
Alcohol Clin Exp Res. ⁽⁵¹⁾	1995	England	Cohort study	Metabolic and cerebral alterations such as reduced white matter concentrations of phosphodiester and phosphocreatine
Biol Psychiatry. ⁽⁵²⁾	1995	United States	Case-control study	Damage to brain cells and central nervous system morbidity
Clin Infect Dis. ⁽⁵³⁾	1994	United States	Case study	Increased viral replication and progression to the more advanced stage of the disease
Neuropsychiatry Clin Neurosci. ⁽⁵⁴⁾	1993	United States	Cross-sectional study	Neuropsychological effects

Regarding the thematic categories, there was a predominance of articles that addressed the metabolic and neurological effects of alcohol (Category 1). Among these effects, brain cell degradation was highlighted, with the consequent elevation of neuroinflammation markers, besides neurocognitive disorders, such as dementia and memory loss. In relation to metabolic alterations, nutritional deficit stood out, with the reduction of micronutrients (such as vitamins A, B, C, D and E, in addition to the minerals zinc, iron and selenium), directly influencing the immune system dysfunction and susceptibility to infectious diseases. Alcohol also had a negative influence on the quality of life of these patients, reducing their perception of the domains of quality of life. Concerning the development of diseases, depressive disorders and systemic arterial hypertension were

highlighted, together with increased anxiety sensitivity. Furthermore, the risk of interactions between alcohol and other drugs was observed, which may lead to more toxicity to the organism (Tables 1 and 2).

Sixteen studies addressed the effects of alcohol on ART adherence (Category 2), demonstrating that alcohol consumption reduces the ability to adhere to the therapeutic regimen in PLHA, which negatively influences health, due to the reduction of CD4 + T lymphocytes and increased viral load (Tables 1 and 2).

Category 3 demonstrates that alcohol use increases the chances of virus transmission and the possibility of reinfection, with a consequent increase in viral resistance. The lack of use of condoms draws attention and is linked to alcohol consumption during sex. These risky behaviors may be accompanied by the non-disclosure of the HIV-positive serological status to the partner, along with multiplicity of partners (Tables 1 and 2).

Regarding the increased disease progression (Category 4), viral load elevation and reduction in CD4 + T lymphocyte counts were identified, representing markers of disease progression. As a result, the patient's state of health is aggravated, leading to the final stage of the disease, which may cause death (Tables 1 and 2).

Table 2: Number of articles supporting each thematic category, according to the topics covered. Fortaleza, Ceará, Brazil 2017.

Category	Number of articles
Neurological and metabolic effects of alcohol	21
Effects of alcohol on ART adherence	16
Increased risk of HIV transmission	5
Increased disease progression	9
TOTAL	51*

* Note: Some articles were classified in more than one category.

DISCUSSION

This research helped describe the effects of alcohol on the metabolism, the central nervous system, adherence to ART and an increased risk of disease transmission and progression in PLHA. The analysis of the levels of evidence showed a predominance of level VI, that is, evidence from descriptive or qualitative studies⁽⁸⁾.

Regarding the neurological effects of alcohol consumption in PLHA, alcohol has been shown to produce morbidity in the central nervous system, especially in frontal regions of the brain, which control executive and motor functions⁽⁴⁷⁾. When a comorbidity exists, these effects tend to manifest earlier, leading to deleterious effects on the cerebral cortex⁽⁵²⁾, such as degradation of the cells, reduction of white⁽⁴⁵⁾ and gray brain matter⁽⁵¹⁾, reduction of the corpus callosum microstructure⁽⁴⁵⁾ and cerebral volume loss, especially in the lateral, frontal, temporal, parietal and occipital regions, besides the thalamus and corpus callosum⁽²⁷⁾. In addition, these were also identified: ventricular hypertrophy, significant harm to the myelin sheath, reduction in markers of living neurons^(39,47), and elevation of neuroinflammation markers⁽¹⁶⁾.

Evidence shows that neurological and cognitive disorders are accentuated over the years, as a result of the disease onset time; when there is a correlation with alcohol, these effects become even worse, causing considerable health harm to these patients^(15,36). The exaggerated use of alcohol in PLHA (an average of five to seven beverage doses per day, four days a week) was directly associated with a neurotrophic factor derived from the brain when compared to those who do not consume alcohol or those who use it sporadically; thus being a significant contributor to the development of neurocognitive disorders associated with HIV. Among these associated disorders dementia and memory loss stood out⁽¹⁵⁾.

Concerning the development of diseases, the risk of developing depressive symptoms was highlighted, which may be associated with the reduction of ART adherence and the progression of the disease^(38,44). Moreover, there is the additional risk of developing systemic hypertension⁽³³⁾ and anxiety sensitivity, which is considered a risk factor for the development of anxiety and depression disorders⁽¹⁰⁾.

Regarding the metabolic effects, it is worth noting that ethyl alcohol plays a significant adverse role on the thymus volume and on the reduction in platelet counts. Thrombocytopenia is directly related to the viral load and to the disease progression, being associated with increased morbidity and mortality due to the deterioration of CD4 + T lymphocytes⁽²³⁾, besides the higher risk of developing anemia⁽⁴⁹⁾.

Regarding the effect of alcohol on the adherence to ART, it was found that the higher the alcohol consumption, the higher the non-adherence rate to ART, which leads to the progression and multiplication of HIV^(34,36-37,41). Differences between genders were identified and it was observed that women who drink alcohol are more likely to not adhere to the treatment regimen when compared to men⁽³⁵⁾.

In addition, excessive alcohol consumption may cause interactions with medications and alter the drug binding protein, where ethanol competes with the drugs in the isozyme linkages of the metabolism process. Thus, these consumers may be at increased risk for adverse events, antiretroviral toxicity and ineffective therapy when compared to placebo groups⁽²⁶⁾, due to inadequate concentration of the drug in the plasma⁽³⁸⁾. These patients are more socially vulnerable and require harm reduction strategies to increase the chances of successful ART⁽²⁵⁾.

Considering the effects of alcohol and risk of HIV transmission, it has been shown that there is an increased risk of reinfection, dissemination and viral resistance, leading to negative health effects⁽³⁷⁾. Alcohol is considered an easily accessible drug and is present at occasions of socialization and celebrations where there are encounters between sexual partners, associated with the reduction of condom use in stable and casual relationships⁽⁵⁵⁾.

Alcohol consumption in PLHA can lead to the acquisition of risk behaviors, such as unprotected sexual practices and multiplicity of partners^(24,37,40). Evidence shows that each dose of alcohol consumed increases the chances of unprotected sexual intercourse by around 73%⁽⁵²⁾, however, it is not possible to take into account only alcohol as an influencing factor, since individual and situational circumstances are also involved⁽⁴³⁾.

Regarding the impact of the use of this substance on the progression of HIV/Aids, it has been observed that alcohol use has deleterious effects on the immune response, which may influence the increase of infections, disorders in B lymphocyte functions and chronic activation of T lymphocytes, accelerating the progression of the disease, leading to increased susceptibility to opportunistic infections such as tuberculosis, bacterial pneumonia and viral hepatitis⁽¹⁶⁾. It also produces effects on the transfer of intestinal bacteria that provoke immune activation against HIV, resulting in the progression of the disease⁽³⁸⁾.

Thus, alcohol consumption in PLHA has a strong association with the increased morbidity and mortality of these individuals, since this comorbidity is directly related to markers of disease progression, factors that negatively influence the domains of quality of life⁽⁴⁶⁾. Evidence indicates that alcohol users were nine times more likely to have CD4 + T lymphocyte counts below 200 cells / mm³, and this association was independent of adherence to ART⁽¹²⁾. Besides the influence on the reduction of immune system cells, its relation to the increase

in viral load⁽³⁶⁻³⁷⁾ stands out, since alcohol consumption can suppress the immune system and stimulate virus replication^(32,52,56).

CONCLUSION

This review allowed the identification of several negative effects of alcohol consumption on PLHA, with an emphasis on neurological and metabolic changes, adherence to ART, increased HIV transmission and disease progression; indicating the need for educational strategies to prevent and reduce alcohol consumption, that seek to identify the main factors that lead to the consumption of this substance, in order to propose targeted measures and individualized care.

Studies with this approach may help nurses and other health professionals to recognize the impacts of alcohol use on this population, so as to instrumentalize them for the implementation of interventions according to the life context of each patient, and activate social support networks when necessary. It is recommended to carry out studies that evaluate the effectiveness of interventions with this purpose.

One limitation of this review was the lack of research on antiretrovirals that interact with alcohol, and studies that indicate the difference between the effects of alcohol on the female and male population.

REFERENCES

1. Luo X, Duan S, Duan Q, Pu Y, Yang Y, Ding Y, et al. Alcohol use and subsequent sex among HIV-infected patients in an ethnic minority area of Yunnan Province, China. *PLoS One*. [Internet]. 2013 [cited 08 set 2016];8(4):e61660. Available from: <http://dx.doi.org/10.1371/journal.pone.0061660>.
2. Molina PE, Bagby GJ, Nelson S. Biomedical consequences of alcohol use disorders in the HIV-infected host invited review. *Curr Res HIV*. [Internet]. 2014 [cited 08 set 2016];12(4):265-75. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4222574/>.
3. Orwat J, Saitz R, Tompkins CP, Cheng DM, Dentato MP, Samet JH. Substance abuse treatment utilization among adults living with HIV/AIDS and alcohol or drug problems. *J Subst Abuse Treat*. [Internet]. 2011 [cited 08 set 2016];41(3):233-42. Available from: <http://dx.doi.org/10.1016/j.jsat.2011.04.002>.
4. Wandera B, Tumwesigye NM, Nankabirwa JI, Kambugu AD, Parkes-Ratanshi R, Mafigiri DK, et al. Alcohol consumption among HIV-infected persons in a large urban HIV clinic in Kampala Uganda: a constellation of harmful behaviors. *PLoS One*. [Internet]. 2015 [cited 08 set 2016];10(5):e0126236. Available from: <http://dx.doi.org/10.1371/journal.pone.0126236>.
5. Cooper HM. *The integrative research review: a systematic approach*. Beverly Hills (CA): Sage Publications; 1984.
6. Souza MT, Silva MD, Carvalho R. Integrative review: what is it? How to do it? *Einstein*. [Internet]. 2010 [cited 08 set 2016];8(1):102-6. Available from: <http://dx.doi.org/10.1590/s1679-45082010rw1134>.
7. Ursi ES. *Prevenção de lesões de pele no perioperatório: revisão integrativa da literatura [dissertação]*. [Ribeirão Preto]: Escola de Enfermagem, Universidade Federal de São Paulo; 2005. Available from: <http://dx.doi.org/10.11606/D.22.2005.tde-18072005-095456>.
8. Melnyk BM, Fineout-Overholt E. Making the case for evidence-based practice. In: Melnyk BM, Fineout-Overholt E, editors. *Evidence-based practice in nursing & healthcare: a guide to best practice*. Philadelphia: Lippincott Williams & Wilkins; 2011.
9. Silva CM, Mendoza-Sassi RA, Mota LD, Nader MM, Martinez AMB. Alcohol use disorders among people living with HIV/AIDS in Southern Brazil: prevalence, risk factors and biological markers outcomes. *BMC infectious diseases*. [Internet]. 2017 [cited 04 nov 2017];17(1):263. Available from: <http://dx.doi.org/10.1186/s12879-017-2374-0>.
10. Paulus DJ, Jardin C, Bakhshaie J, Sharp C, Woods SP, Lemaire C, et al. Anxiety sensitivity and hazardous drinking among persons living with HIV/AIDS: An examination of the role of emotion dysregulation. *Addic Behav*. [Internet]. 2016 [cited 08 set 2016];63:141-8. Available from: <http://dx.doi.org/10.1016/j.addbeh.2016.07.013>.
11. Kader R, Govender R, Seedat S, Koch JR, Parry C. Understanding the impact of hazardous and harmful use of alcohol and/or other drugs on ARV adherence and disease progression. *PLoS One*. [Internet]. 2015 [cited 04 nov 2017];10(5):e0125088. Available from: <http://dx.doi.org/10.1371/journal.pone.0125088>.

12. Malbergier A, Amaral RA, Cardoso LD. Alcohol dependence and CD4 cell count: Is there a relationship? *AIDS Care*. [Internet]. 2015 [cited 09 set 2016];27(1):54-8. Available from: <http://dx.doi.org/10.1080/09540121.2014.947235>.
13. Pecoraro A, Mimiaga M, O'Cleirigh C, Safren SA, Blokhina E, Verbitskaya E, Yaroslavlseva T, Ustinov A, Lioznov DA, Zvartau E, Krupitsky E, Woody GE. Depression, substance use, viral load, and CD4+ count among patients who continued or left antiretroviral therapy for HIV in St. Petersburg, Russian Federation. *AIDS Care* [Internet]. 2015 [cited 06 nov 2017];27(1):86-92. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4221462/>.
14. Tran BX, Nguyen LT, Do CD, Nguyen QL, Maher RM. Associations between alcohol use disorders and adherence to antiretroviral treatment and quality of life amongst people living with HIV/AIDS. *BMC Public Health*. [Internet]. 2014 [cited 06 nov 2017];14(27):2-7. Available from: <https://bmcpublihealth.biomedcentral.com/articles/10.1186/1471-2458-14-27>.
15. Míguez-Burbano MJ, Espinoza L, Whitehead NE, Bryant VE, Vargas M, Cook RL, et al. Brain derived neurotrophic factor and cognitive status: the delicate balance among people living with HIV, with and without alcohol abuse. *Curr Res HIV*. [Internet]. 2014 [cited 08 set 2016];12(4):254-64. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/25053366>.
16. Zarh NM, Mayer D, Rohlfing T, Sullivan E, Pfefferbaum A. Imaging Neuroinflammation? A perspective from MR Spectroscopy. *Brain Pathol*. [Internet]. 2014 [cited 09 set 2016];24(6):654-64. Available from: <http://dx.doi.org/10.1111/bpa.12197>.
17. Williams EC, Bradley KA, Balderson BH, McClure JB, Grothaus L, McCoy K, et al. Alcohol and associated characteristics among older persons living with human immunodeficiency virus on antiretroviral therapy. Substance abuse. [Internet]. 2014 [cited 04 nov 2017];35(3):245-253. Available from: <http://dx.doi.org/10.1080/08897077.2014.890997>.
18. Durvasula R, Miller TR. Substance abuse treatment in persons with HIV/AIDS: challenges in managing triple diagnosis. *Behavioral Medicine*. [Internet]. 2014 [cited 04 nov 2017];40(2):43-52. Available from: <http://dx.doi.org/10.1080/08964289.2013.866540>.
19. Howe CJ, Cole SR, Napravnik S, Kaufman JS, Adimora AA, Elston B, et al. The role of at-risk alcohol/drug use and treatment in appointment attendance and virologic suppression among HIV(+) African Americans. [Internet]. 2014 [cited 04 nov 2017];30(3):233-240. Available from: <http://dx.doi.org/10.1089/AID.2013.0163>.
20. Kalichman SC, Grebler T, Amaral CM, McNERney M, White D, Kalichman MO, et al. Viral suppression and antiretroviral medication adherence among alcohol using HIV-positive adults. [Internet]. 2014 [cited 04 nov 2017];21(5):811-820. Available from: <http://dx.doi.org/10.1007/s12529-013-9353-7>.
21. Agudelo M, Khatavkar P, Yndart A, Yoo C, Rosenberg R, G Devieux J, et al. Alcohol Abuse and HIV Infection: Role of DRD2. *Current HIV research*. [Internet]. 2014 [cited 04 nov 2017];12(4):234-242. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/25053368>.
22. Ikeda MLR, Barcellos NT, Alencastro PR, Wolff FH, Brandão ABM, Fuchs FD, et al. Association of blood pressure and hypertension with alcohol consumption in HIV-infected white and nonwhite patients. *Scientific World Journal*. [Internet]. 2013 [cited 09 set 2016];(169825). Available from: <http://dx.doi.org/10.1155/2013/169825>.
23. Santos VM, Cruz LR, Paixão GTG, Mizuno CA, Teza ITV, Souza DWS. Plaquetopenia grave em paciente etilista com infecção por vírus da imunodeficiência humana. *Brasília Med*. [Internet]. 2013 [cited 10 set 2016];49(3):id672195. Available from: <http://bases.bireme.br/cgi-bin/wxislind.exe/iah/online/?IscScript=iah/iah.xis&src=google&base=LILACS&lang=p&nextAction=lnk&exprSearch=672195&indexSearch=ID>.
24. Kalichman SC, Grebler T, Amaral C, Mckerey M, White D, Kalichman M, et al. Assumed infectiousness, treatment adherence and sexual behaviours: Applying the swiss statement on infectiousness to HIV-positive alcohol drinkers. *HIV Med*. [Internet]. 2013 [cited 08 set 2016];14(5):263-72. Available from: <http://dx.doi.org/10.1111/j.1468-1293.2012.01062.x>.
25. Teixeira C, Dourado MDL, Santos MP, Brites C. Impact of use of alcohol and illicit drugs by AIDS patients on adherence to antiretroviral therapy in Bahia, Brazil. *AIDS Res Hum Retroviruses*. [Internet]. 2013 [cited 10 set 2016];29(5):799-804. Available from: <http://dx.doi.org/10.1089/AID.2012.0296>.
26. Mccance-Katz EF, Lum PJ, Beatty G, Gruber VA, Peters M, Rainey PM. Untreated HIV infection is associated with higher blood alcohol levels. *J Acquir Immune Defic Syndr*. [Internet]. 2012 [cited 10 set 2016];60(3):282-288. Available from: <http://dx.doi.org/10.1097/QAI.0b013e318256625f>.
27. Pfefferbaum A, Rosenbloom, MJ, Sassoon SA, Kemper CA, Deresinski S, Rohlfing T, et al. Regional brain structural dysmorphology in human immunodeficiency virus infection: Effects of acquired immune deficiency syndrome, alcoholism, and age. *Biol Psychiatry*. [Internet]. 2012 [cited 08 set 2016]. 72(5):361-70. Available from: <http://dx.doi.org/10.1016/j.biopsych.2012.02.018>.
28. Gerbi GB, Habtemariam T, Tameru B, Nganwa D, Robnett V. A comparative study of substance use before and after establishing HIV infection status among people living with HIV/AIDS *Journal of substance use*. [Internet]. 2011 [cited 04 nov 2017];16(6):464-475. Available from: <http://dx.doi.org/10.3109/14659891.2010.495820>.
29. Kumar S, Jin M, Ande A, Sinha N, Silverstein PS, Kumar A. Alcohol consumption effect on antiretroviral therapy and HIV-1 pathogenesis: role of cytochrome P450 isozymes. *Expert Opin Drug Metab Toxicol*. [Internet]. 2012 [cited 06 nov 2017];8(11):1363-75. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4033313/>.

30. Cohn SE, Jiang H, McCutchan JA, Koletar SL, Murphy RL, Robertson KR, de St Maurice AM, Currier JS, Williams PL. Association of ongoing drug and alcohol use with non-adherence to antiretroviral therapy and higher risk of AIDS and death: results from ACTG 362. *AIDS Care* [Internet]. 2011 [cited 06nov2017];23(6):775-85. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3095689/>.
31. Broyles LM, Gordon AJ, Sereika SM, Ryan CM, Erlen JA. Predictive Utility of Brief Alcohol Use Disorders Identification Test (AUDIT) for human immunodeficiency virus antiretroviral medication nonadherence. *Substance abuse*. [Internet]. 2011 [cited 04 nov 2017];32(4):252-261. Available from: <http://dx.doi.org/10.1080/08897077.2011.599255>.
32. Sullivan LE, Goulet JL, Justice AC, Fiellin DA. Alcohol consumption and depressive symptoms over time: a longitudinal study of patients with and without HIV infection. *Drug and alcohol dependence*. [Internet]. 2011 [cited 04 nov2017];117(2):158-163. Available from: <http://dx.doi.org/10.1016/j.drugalcdep.2011.01.014>.
33. DeLorenze GN, Weisner C, Tsai AL, Satre DD, Quesenberry Jr CP. Excess mortality among HIV-infected patients diagnosed with substance use dependence or abuse receiving care in a fully integrated medical care program. *Alcoholism: Clinical and Experimental Research*. [Internet]. 2011 [cited 04 nov 2017];35(2):203-210. Available from: <http://dx.doi.org/10.1111/j.1530-0277.2010.01335.x>.
34. Rego SRB, Oliveira CFA, Rego DMS, Júnior RFS, Silva VB. Estudo do autorrelato de adesão e uso problemático de álcool em uma população de indivíduos com aids em uso de HAART. *J Bras Psiquiatr*. [Internet]. 2011 [cited 10 set 2016];60(1):46-9. Available from: <http://dx.doi.org/10.1590/S0047-20852011000100009>.
35. Rego SEM, Rego DMS. Associação entre uso de álcool em indivíduos com aids e adesão ao tratamento antirretroviral: Uma revisão da literatura. *J Bras Psiquiatr*. [Internet]. 2010 [cited 08 set 2016];59(1):70-3. Available from: <http://dx.doi.org/10.1590/S0047-20852010000100011>.
36. Azar MM, Springer SA, Meyer JP, Altice FL. A systematic review of the impact of alcohol use disorders on HIV treatment outcomes, adherence to antiretroviral therapy and health care utilization. *Drug Alcohol Depend*. [Internet]. 2010 [cited 08 set 2016];112(3):178-93. Available from: <http://dx.doi.org/10.1016/j.drugalcdep.2010.06.014>.
37. Shuper PA, Neuman M, Kanteres F, Baliunas D, Joharchi N, Rehm J. Causal considerations on alcohol and HIV/AIDS - A systematic review. *Alcohol Alcohol*. [Internet]. 2010 [cited set 2016];45(2):159-166. Available from: <http://dx.doi.org/10.1093/alcalc/agg091>.
38. Hahn JA, Samet JH. Alcohol and HIV disease progression: weighing the evidence. *Curr HIV/AIDS Rep*. [Internet]. 2010 [cited 08 set 2016];7(4):226-33. Available from: <http://dx.doi.org/10.1007/s11904-010-0060-6>.
39. Rosenbloom MJ, Sullivan EV, Pfefferbaum A. Focus on the brain: HIV infection and alcoholism comorbidity effects on brain structure and function. *Alcohol Research e health*. [Internet]. 2010 [cited 08 set 2016];33(3):247-57. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3860510/>.
40. Shuper PA, Joharchi N, Irving H, Rehm J. Alcohol as a correlate of unprotected sexual behavior among people living with HIV/AIDS: Review and meta-analysis. *AIDS Behav*. [Internet]. 2009 [cited 09 set 2016];13(6):1021-36. Available from: <http://dx.doi.org/10.1007/s10461-009-9589-z>.
41. Hendershot CS, Stoner SA, Pantalone DW, Simoni JM. Alcohol use and antiretroviral adherence: Review and meta-analysis. *J Acquir Immune Defic Syndr*. [Internet]. 2009 [cited 10 set 2016];52(2):180-202. Available from: <http://dx.doi.org/10.1097/QAI.0b013e3181b18b6e>.
42. Ghebremichael M, Paintsil E, Ickovics JR, Vlahov D, Schuman P, Boland R, et al. Longitudinal association of alcohol use with HIV disease progression and psychological health of women with HIV. *AIDS care*. [Internet]. 2009 [cited 04 nov 2017];21(7):834-841. Available from: <http://dx.doi.org/10.1080/09540120802537864>.
43. Barta WD, Portnoy DB, Kiene SM, Tennen H, Abu-Hasaballah KS, Ferrer R. A daily process investigation of alcohol-involved sexual risk behavior among economically disadvantaged problem drinkers living with HIV/AIDS. *AIDS Behav*. [Internet]. 2008 [cited 09 set 2016];12(5):729-40. Available from: <http://dx.doi.org/10.1007/s10461-007-9342-4>.
44. Sullivan LE, Saitz R, Cheng DM, Libman H, Nunes D, Samet JH. The impact of alcohol use on depressive symptoms in HIV-infected patients. *Addiction (Abingdon, England)*. [Internet]. 2008 [cited em 10 set 2016];103(9):1461-1467. Available from: <http://dx.doi.org/10.1111/j.1360-0443.2008.02245.x>.
45. Pfefferbaum A, Rosenbloom MJ, Adalsteinsson E, Sullivan EV. Diffusion tensor imaging with quantitative fibre tracking in HIV infection and alcoholism comorbidity: synergistic white matter damage. *Brain*. [Internet]. 2007 [cited 09 set 2016];130(Pt 1):48-64. Available from: <http://dx.doi.org/10.1093/brain/awl242>.
46. Rosenbloom MJ, Sullivan EV, Sassoon SA, O'Reilly A, Fama R, Kemper CA, et al. Alcoholism, HIV infection, and their comorbidity: factors affecting self-rated health-related quality of life. *J Stud Alcohol Drugs*. [Internet]. 2007 [cited 10 set 2016];68(1):115-25. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/17149525>.
47. Pfefferbaum A, Rosenbloom MJ, Rohlfing T, Adalsteinsson E, Kemper CA, Deresinski S, et al. Contribution of alcoholism to brain dysmorphology in HIV infection: Effects on the ventricles and corpus callosum. *Neuroimage*. [Internet]. 2006 [cited 09 set 2016];33(1):239-51. Available from: <http://dx.doi.org/10.1016/j.neuroimage.2006.05.052>.
48. Durvasula RS, Myers HF, Mason K, Hinkin C. Relationship between alcohol use/abuse, HIV infection and neuropsychological performance in African American men. *Journal of clinical and experimental neuropsychology*. [Internet]. 2006 [cited 04 nov 2017];28(3):383-404. Available from: <http://dx.doi.org/10.1080/13803390590935408>.

49. Conigliaro J, Gordon AJ, McGinnis KA, Rabeneck L, Justice AC. How harmful is hazardous alcohol use and abuse in HIV infection: Do health care providers know who is at risk? *J Acquir Immune Defic Syndr*. [Internet]. 2003 [cited 08 set 2016];33(4):521-25. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/12869842>.
50. Lake-Bakaar G, Grimson R. Alcohol abuse and stage of HIV disease in intravenous drug abusers. *Journal of the Royal Society of Medicine*. [Internet]. 1996 [cited 04 nov 2017];89(7):389-392. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1295853/>.
51. Meyerhoff DJ, Mackay S, Sappey-Mariner D, Deicken R, Calabrese G, Dillon WP, et al. Effects of chronic alcohol abuse and HIV infection on brain phosphorus metabolites. *Alcohol Clin Exp Res*. [Internet]. 1995 [cited 09 set 2016];19(3):685-92. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/7573794>.
52. Fein G, Biggins CA, Mackay S. Alcohol abuse and HIV infection have additive effects on frontal cortex function as measured by auditory evoked potential P3A latency. *Biol Psychiatry*. [Internet]. 1995 [cited 10 set 2016];37(3):183-95. Available from: [http://dx.doi.org/10.1016/0006-3223\(94\)00119-N](http://dx.doi.org/10.1016/0006-3223(94)00119-N).
53. Fong IW, Read S, Wainberg MA, Chia WK, Major C. Alcoholism and rapid progression to AIDS after seroconversion. *Clin Infect Dis*. [Internet]. 1994 [cited 10 set 2016];19(2):337-8. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/7986912>.
54. Bornstein RA, Fama R, Rosenberger P, Whitacre CC, Para MF, Nasrallah HA, et al. Drug and alcohol use and neuropsychological performance in asymptomatic HIV infection. *Journal of Neuropsychiatry and Clinical Neurosciences*, [Internet]. 1993 [cited 04 nov 2017];5:254-254. Available from: <http://dx.doi.org/10.1176/jnp.5.3.254>.
55. Barta WD, Tennen H, Kiene SM. Alcohol-involved sexual risk behavior among heavy drinkers living with HIV/AIDS: negative affect, self-efficacy, and sexual craving. *Psychol Addict Behav*. [Internet]. 2010 [cited 08 set 2016];24(4):563-70. Available from: <http://dx.doi.org/10.1037/a0021414>.
56. Bagby GJ, Zhang P, Purcell JE, Didier PJ, Nelson S. Chronic binge ethanol consumption accelerates progression of simian immunodeficiency virus disease. *Alcohol Clin Exp Res*. [Internet]. 2006 [cited 09 set 2016];30(10):1781-90. Available from: <http://dx.doi.org/10.1111/j.1530-0277.2006.00211.x>.