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Adherence to the Pre-Exposure Prophylaxis to the HIV: how are we doing it in Brazil?

Adesão à Profilaxia Pré-Exposição ao HIV: como estamos no Brasil?

Adherencia a la profilaxis previa a la exposición al VIH: ¿cómo estamos en Brasil?

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ABSTRACT

Introduction: The recent insertion of the Pre-Exposure Prophylaxis to the HIV as a strategy of controlling HIV infection in the Unified Health System, and the studies related to the thematic can enhance its effectiveness in the control of HIV infection. The study aims to analyze the current scenario of adherence to HIV Pre-Exposure Prophylaxis in Brazil and understand the barriers and facilitative aspects for effective adherence. **Outline:** This is an integrative literature review study, carried out in the main databases. The inclusion criteria applied were primary studies and published until September 2019. **Results:** It was observed high adherence to the Pre-Exposure Prophylaxis for the HIV. The barriers and facilitative aspects for adherence to HIV Pre-Exposure Prophylaxis are associated with social stigma, lack of knowledge about the efficacy and safety of prophylaxis and, especially, low awareness of sexual practices and high-risk behaviors for the HIV transmission. **Implications:** High adherence to HIV Pre-Exposure Prophylaxis was observed in the most vulnerable population segments. Barriers to adherence to HIV Pre-Exposure Prophylaxis can be overcome with greater investment in the dissemination of its benefits to the population.

DESCRIPTORS

Infection Control; HIV; Pre-Exposure Prophylaxis; Medication Adherence; Brazil.

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INTRODUCTION

By the year 2019, approximately 38 million people were diagnosed with the Human Immunodeficiency Virus (HIV) in the world, and 1.7 million people were infected in that same year.¹

In Brazil, there exist 830 thousand people living with HIV/Aids, with prevalence of 0.4% in the general population, 18.4% in the Men who have Sex with Men (MSM) population, 31.2% in the transgender women and transvestite population, and 5.3% among the professionals of sex. Moreover, according to ANTRA, National Association of Transvestites and Transsexuals, 90% of the transgender women survives through prostitution.²

This population with higher prevalence for contaminating with the virus is called either key-population or populational segment, which corresponds to MSM, professionals of sex and transgender people. It is added to that a bigger contamination risk of, respectively, 22, 21 and 12 times in relation to the remain of the population.³

Such risks can be associated with risk behaviors with unprotected sexual practices, with elevated number of partners, amount and diversity of sexual partnerships and the professionalization of sex.^{4,5}

Prejudice and social stigma about these populations are evident, with clear social exclusion, which make them more vulnerable to the growing HIV epidemic.⁵ Another factors that we can highlight are the discriminatory attitudes of health professionals, contributing for a limitation and a distancing of these populational segments from the health services.³

These factors can interfere in the adherence to the prevention methods and/or in the seek for health services, especially, specialized diagnosis services, preventive medical exams and orientations about the control of HIV infection.³

Those data from the epidemiological profile highlight the need of strategies and public health policies intended to the key-population in question

for the control of HIV infection. The Combined Prevention offered in federal scope refers to the adequate treatment of people living with HIV, to the immunizations, undetectable viral load due antiretroviral therapy, to the continuing education of the health professionals for the orientation of combined prevention, the importance of using preservatives, rapid HIV test, opportune and adequate diagnosis of other sexually transmitted infections (STI), to the post-exposure prophylaxis (PEP), to the HIV infection Pre-Exposure Prophylaxis (PrEP), and to the management of the aforementioned vulnerabilities.⁵

In front of the great challenges for the control of HIV infection, the PrEP is a breakthrough in collective health practices, because it promotes simplified action of the user for the prevention of virus transmission and consolidates the trends of worldwide strategies for reducing the number of infected ones. The PrEP consists in the administration of a single daily dose, orally, of the pill composed by tenofovir and emtricitabine (TDF/FTC 300/200mg), commercially known as Truvada. In Brazil, the PrEP was incorporated in an effective manner to the Brazilian National Health System (SUS) in December 2017 through, at that time, the Department of Vigilance, Prevention and Control of the Sexually Transmitted Infections, of the HIV/Aids and of the Viral Hepatitis from the Ministry of Health.⁶⁻⁷

Other countries such as the United States (Food and Drug Administration - FDA) had already approved PrEP in July 2012, Kenya and South Africa in December 2015 and Canada and Peru in 2016.⁸

The criteria of indication for the PrEP are based on either receptive or inserted anal sexual intercourse, vaginal sexual intercourse without the use of condoms in the last six months, recurrent STI episodes, or the repeated use of PEP, without living or not with HIV.⁵ In the initial appointment are performed the respective screening exams: the HIV

rapid test, treponemal or non treponemal test for syphilis, tests for B and C hepatitis, investigation of other STI through urine and genital secretions exams, liver function and kidney function by the dosage serum creatinine and urea, creatinine clearance, evaluation of proteinuria, and the AST and ALT enzymes. If the test is negative for HIV, the results of the tests described must be awaited, with a return within 30 days to start the Pre-Exposure Prophylaxis.⁵

It is well elucidated in the literature the efficiency and the safety of the PrEP, being currently the most promising strategy in the control of HIV infection in the international scenario, with reductions of 44% in transmission and 95% in the incidence among MSM and transgender women.^{5,9} However, the effectiveness of PrEP is directly associated with medication adherence.

Considering the recent inclusion of PrEP in an effective way to the strategies of HIV infection control on the SUS, it is evident that, in the national scenario, the studies referring to the adherence to this prophylaxis are incipient in front of international scientific productions. In this sense, analyzing research investigating the adherence to PrEP in Brazil, as well as its barriers and its easier aspects, will contribute for the development of strategies which potentiates its effectiveness in the control of HIV infection. Starting from this problematic, the present study enquiries: “What is the scenario of adherence to the PrEP in Brazil?”

Thus, the study aimed to verify the scenario of the adherence to the PrEP in Brazil, its barriers and its facilitative aspects.

METHOD

It is an integrative review of literature,¹⁰ an evidence-based practice that summarizes the scientific literature and provides broad comprehension of particular phenomena. Its development included the following steps: establishment of the guide question, of the objective, of the descriptors for the searches in the data bases; definition of inclusion and exclusion criteria for sample selection; definition of the information to be extracted from the selected articles in the data bases; article analysis; and discussion of results.⁸ The strategy PICO was used for establishing the questions which guided this research, as follows: P: Brazil/Brazilians; I: PrEP; C: was not object of research; O: adherence to the PrEP. Therefore, the following questions was discriminated: What is the scenario of adherence to the PrEP in Brazil?

The following databases were prospected for the primary studies: PubMed, Web of Science, Scopus, Science Direct, CINAHL, Embase, and the Latin American and Caribbean Health Sciences Literature (LILACS). The controlled descriptors (terms MeSH, CINAHL headings and DeCS headings) and keywords used on each database were grouped in the following way:

*PubMed, Embase, Science Direct and Scopus	“Pre-Exposure Prophylaxis” and HIV and Brazil
*Web of Science	TS=Pre-Exposure Prophylaxis AND TS=hiv AND TS= Brazil
*CINAHL	“Pre-exposure prophylaxis” or prep or “preexposure prophylaxis” and HIV and Brazil
*LILACS	“profilaxia pré exposição” OR prep AND hiv AND Brasil

The inclusion criteria were: primary studies about the subject matter, published until September

2019, in Portuguese, English and Spanish languages. Review studies, opinions of experts, editorials, book

chapters, books, theses, dissertations, overviews and reviews were excluded. The study was carried out in October 2019 simultaneously by two independent

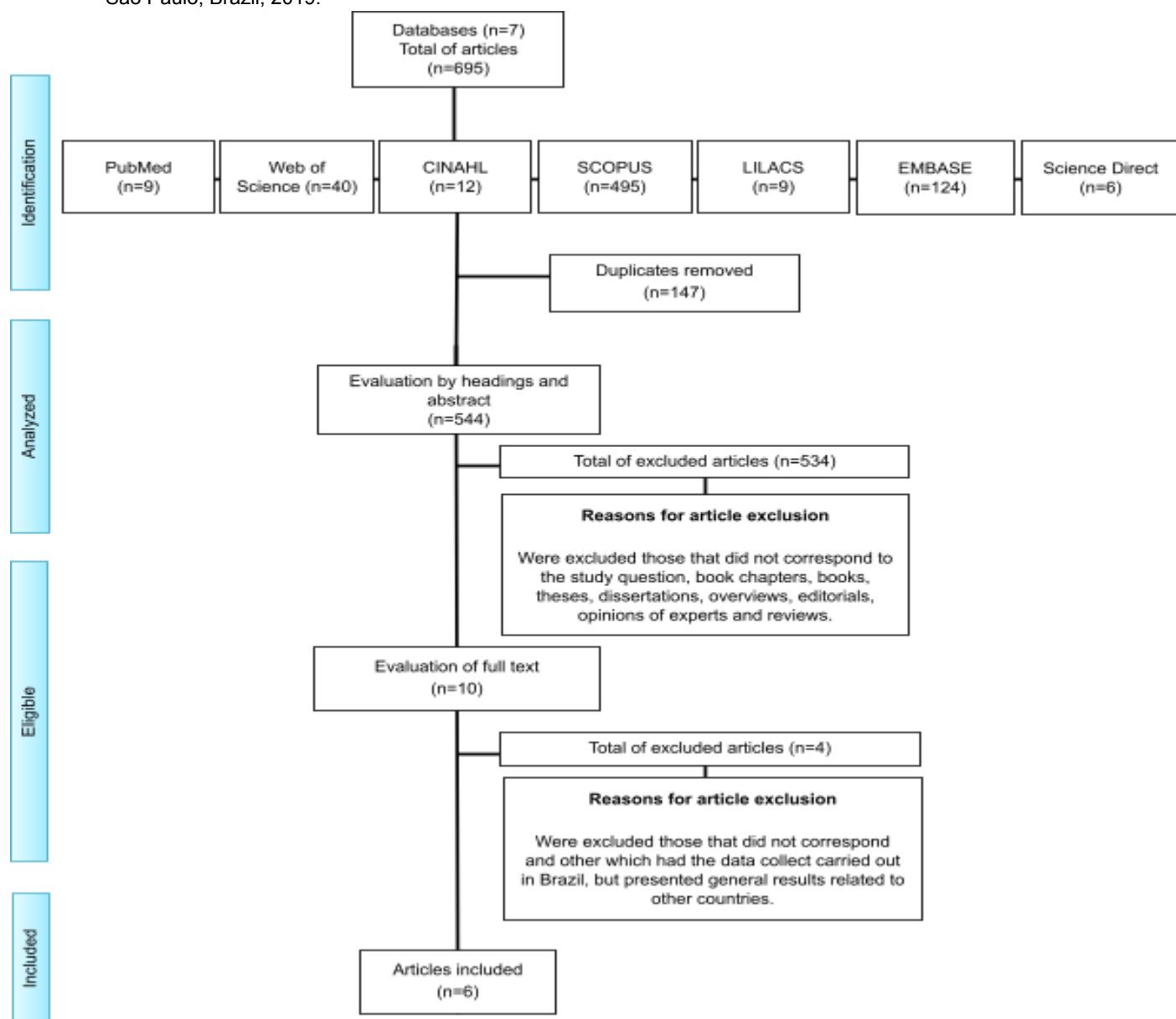
researchers and, at the end, reevaluated by a third researcher to verify the discordances. The study was conducted in six phases:

1. Search for studies in databases adopting pre-established descriptors;
2. Import of studies into EndNote Online software (Clarivate Analytics);
3. Exclusion of duplicate studies;
4. Peer evaluation of the headings and abstracts of the identified studies;
5. Peer review of the full texts of the studies identified in step 4;
6. Data extraction from the studies included in the review in accordance with URSI 2005.¹¹

The flowchart was guided by the Reporting Items for Systematic Reviews and Meta-Analyses, is

presented in Figure 1 and details the analysis process of the studies found.

Figure 1 – Selection process of the studies in the seven databases on the scenario of PrEP adherence in Brazil. Ribeirão Preto, São Paulo, Brazil, 2019.



RESULTS

The six articles included on this review are presented in the Chart 1.

Chart 1 – Articles included in the integrative review aiming to answer the guiding questions “What is the scenario of adherence to the PrEP in Brazil? Which are the barriers and facilitators for the adherence to the PrEP in Brazil?” Ribeirão Preto, São Paulo, Brazil, 2019.

Title	Authors' names and publication year	Objective	Method	Main results
<i>Retention, engagement, and adherence to pre-exposure prophylaxis for men who have sex with men and transgender women in PrEP Brasil: 48 week results of a demonstration study.</i> ¹²	Grinsztejn, Beatriz Hoagland, Brenda Moreira, Ronaldo I Kallas, Esper G Madruga, Jose V Goulart, Silvia Leite, Iuri C. Year 2018	To evaluate, into a 48-week period, the retention, commitment, the adherence, the sexual behaviors and the incidence of sexually transmitted diseases.	Kind of study: open-label, demonstrative. Setting: Rio de Janeiro and São Paulo.	The PrEP displayed to be viable and effective and the fact of the medication being available at no charge made possible to reach high levels of adherence, without compensation of risks.
<i>High pre-exposure prophylaxis uptake and early adherence among men who have sex with men and transgender women at risk for HIV Infection: The PrEP Brasil demonstration project.</i> ¹³	Hoagland B, Moreira RI, De Boni RB, Kallas EG, Madruga JV, Vasconcelos R, Goulart S, Torres TS, Marins LMS, Anderson PL, Luz PM, Costa Leite ID, Liu AY, Veloso VG, Grinsztejn B. Year 2017	To evaluate the getting and the adherence to the PrEP and to describe the demographic characteristics and the risks of the population under study: Men who have sex with men and trans Women.	Kind of study: demonstration, multicenter, prospective, open label. Setting: Rio de Janeiro and São Paulo.	It was observed a high adherence to the medication. It was possible to identify a high protection in the individuals that made the correct use of the drug prophylaxis with 78.5% as protective range when taking four or more doses per week. The main barrier pointed out in this study was the fear of side effects.
<i>Performance of HIV pre-exposure prophylaxis indirect adherence measures among men who have sex with men and transgender women: Results from the PrEP Brasil Study.</i> ¹⁴	Marins LMS, Torres TS, Leite IDC, Moreira RI, Luz PM, Hoagland B, Kallas EG, Madruga JV, Liu AY, Anderson PL, Grinsztejn B, Veloso VG Year 2019	To examine the concordance among three indirect measuring methods of adherence with the blood levels of the medications inside the high protection range measured from the dried blood stain (DBS) among the retained partakers during 48 week in the Study PrEP Brasil.	Kind of study: demonstration, multicentre, open label. Setting: Rio de Janeiro and São Paulo.	There was a high adherence among the partakers in the 48-week period. There were no meaningful differences among the three indirect measures of adherence in the capability of discerning the partakers with and without levels of protection of the drugs ($p=0.44$). These measures can be useful in the monitoring of PrEP use among MSM and trans women retained in one PrEP program and in the orientation of the need for adherence interventions. In this study, barriers and facilitators of medication adherence to PrEP were not identified.
<i>Barriers and facilitators to PrEP for transwomen in Brazil.</i> ¹⁵	Wilson EC, Jalil EM, Castro C, Martinez Fernandez N, Kamel L, Grinsztejn B Year 2019	To determine the consciousness and the interest in PrEP and to identify the barriers and the facilitators for adoption and adherence to PrEP among trans women who access PrPE in Brazil through Unified Health System (SUS).	Kind of study: qualitative Setting: Rio de Janeiro.	It was evidenced a high adherence, but less than in the MSM population and, also, as potential barriers for the adherence to PrEP. Among them, we can highlight: the refusal for being underwent to HIV test, the fear of favoring a risk behavior after the start of the PrEP or the fact of it becoming a “obligation”. There were added up, to the discussion about the theme, the discrimination or the association of the drug with getting sick or the drug associated to the seropositivity. The study identified some facilitative aspects related to the technological tools like apps for smartphones and the social networks.
<i>Awareness, Willingness, and PrEP Eligibility</i>	Jalil EM, Grinsztejn B, Velasque L, Ramos Makkeda A,	To estimate the consciousness and the will of using the	Kind of study: sampling survey.	The data showed that 38% of the partakers had never heard about PrEP and 48.7% already have. Among the group of persons

<i>Among Transgender Women in Rio de Janeiro, Brazil.</i> ¹⁶	Luz PM, Moreira RI, Kamel L, Fernandes NM, Ferreira ACG, Hoagland B, Wagner S, Liu A, McFarland W, Buchbinder S, Veloso VG, Wilson E. Year 2018	PrEP and to examine the factors related to them.	Setting: Rio de Janeiro.	who did not have knowledge about the new strategy on health, 6.1% took PEP at least once. The study pointed out a high disposal for using PrEP among transwomen in Brazil. The PrEP was pointed out as promising strategy for preventing HIV with necessary disclosure about this prophylaxis for the highly vulnerable population.
<i>Knowledge and willingness to use pre-exposure prophylaxis among men who have sex with men in Northeastern Brazil.</i> ¹⁷	Magno L, Dourado I, Suttan Coats C, Wilhite D, da Silva LAV, Oni-Orisan O, Brown J, Soares F, Kerr L, Ransome Y, Chan PA, Nunn A. Year 2019	To explore the knowledge about the will of using PrEP among young MSM in Salvador, as well as, the other social factors, structural and behavioral that can affect the acceptability and adoption of PrEP in the public clinics in Brazil.	Kind of study: sampling survey. Setting: Rio de Janeiro.	The study pointed out that for raising awareness among young people it must be reinvigorated in the MSM activist community. The study consisted of evaluating the knowledge, the will and the barriers for the use of PrEP with a high degree of interest on its use. The knowledge about PrEP was related to the advanced age, school attainment and higher risk behavior related to greater risk perception. The study highlighted the importance of disseminating the new health strategy to less educated groups. The identified barriers were the lack of adequate knowledge about the real effectiveness, questions about the side effects of prophylaxis, the difficulties of access and the delay in care, as well as the lack of preparation of health professionals in the Unified Health System. The potential PrEP facilitators identified in the study are related to technology (radio, internet, cell phone and television, for example). Some reports cited the condom as a more culturally acceptable method, and other individuals that PrEP would allow the individual to be more "relaxed" if the partner were serodiscordant.

Adapted from URSI, 2005.⁹ Abbreviation: PrEP: Pre-Exposure Prophylaxis; HIV: Human Immunodeficiency Virus; MSM: Men who have Sex with Men; PEP: Post-Exposure Prophylaxis.

DISCUSSION

Brazil is the pioneer country of Latin America in the adoption of prophylactic measures for the control of HIV infection as Public Health Police and adopted in the public networks countrywide, being the PrEP offered with emphasis for the MSM, transgender people, professionals of sex and serodiscordant couples.⁵ Our study presented based on compiling the researches that investigated the barriers and the facilitative aspects for the adherence to the PrEP in Brazil. The founds of this review enabled an embracing view of the national scenario, as well as elucidate indicators for the development of strategies that enhance the access and use of this prophylaxis. In addition, the PrEP is an important and relevant theme, once it accompanies

the historical development of the public health of the Country.

The observation of the studies which compose this review indicates a high adherence to the PrEP by the MSM and a low adherence among the transgender women in the Southeast region of our country, related to the high social vulnerability, income and school attainment of those populations.¹⁴

The main identified barriers were: forgetting the doses, the changes in daily routine and the shortage of pills. The lack of knowledge about the prophylactic measure was considered a limiting factor. In addition, aspects such fear of drug effectiveness, non-functioning or malfunctioning of the drug therapy may leading to seroconversion were cited as potential barriers for the non-adherence to

the PrEP. Pharmaceutical side effects as abdominal pain, diarrhea, flatulence, nausea and vomit also were pointed out as potential barriers but were not cited among Brazilian researchers.¹⁴ The low awareness and the self-perception referring to the thought of “that’s never gonna happen to me” of people as to their sexual behaviors make them more vulnerable to the HIV infection.^{11,13} It can be said that despite of educational measures about the prevention, the general population is resistant to behavioral changes to mitigate the risk.¹⁵

Another data indicate that barriers related to the PrEP adherence are associated with the low school attainment and low incomes.^{12,15} Further, we can relate the unequal access to health care provided by SUS, solely because of the discrimination related to the gender identity.^{15,18} The reluctance on doing HIV test, the prejudice for the use of the PrEP, the fragility of the training of health professionals also are potential barriers for the prophylactic adherence.¹⁵ There are reports that health teams do not have the prepare e there are no specific trainings for taking care of transgender women.¹⁵

As to the facilitative aspects, keeping the drug in a visible place, for instance, in locals which daily activities are performed can facilitate the daily use of medications.^{14,16} In addition, the literature considers the SUS as the main facilitative agent, because it ensures the free access for the population.¹⁵

It is still possible to identify in the studies that the technology as smartphones and smartphone apps, WhatsApp and others are considered important tools in the access to the information and the spread of contents about the PrEP,¹⁵ although they are not accessible to everyone. Being this strategy contemporary and promising, may be explored by the public health agencies and scientific community, aiming to enhance the effectiveness of the PrEP,

regarding the aware and adherence, contributing for the control of HIV infection, the cost reduction and mortality associated with the infection.

The main limitation of this study was the small number of articles included for results presentation. This limitation is due to, apart from the chosen including and excluding criteria, the recent insertion of the PrEP on the SUS. In addition, the studies included in this review were developed in privileged regions of our country, what can differ from the scenario of the others national contexts, being necessary caution when extrapolating our finds in territorial dimension.

It is emphasized that this integrative review contributes for disseminating the knowledge about PrEP for the society, for strengthening the continuous education of health professionals, for providing indexes for the development of strategies in order to improve the access and adherence to this prophylactic strategy, considering adherence scenario in Brazil, especially Southeast region, and to promote the discussion of the thematic in the literature.

CONCLUSION

In the key-populations it can be observed a high prophylactic strategy, mainly among MSM. However, the discussion of theme is incipient on the national scenario, but it is evident the advance, mainly, in respect to the Public Health Policies. Nevertheless, it is necessary to expand the studies about the PrEP, and to create strategies that reduces the barriers and strengthens the facilitative for its adherence. We stress that the extrapolation of the results of this study in territorial dimension must be performed carefully, once the available articles in the literature and included contemplate the Southeast region of the country.

RESUMO

Introdução: A inserção recente da Profilaxia Pré-Exposição ao HIV como uma estratégia de controle de infecção pelo HIV no Sistema Único de Saúde, bem como os estudos referentes à temática podem potencializar sua eficácia no controle da infecção pelo HIV. O estudo tem como objetivo analisar o cenário atual da adesão à Profilaxia Pré-Exposição ao HIV no Brasil e compreender as barreiras e os aspectos facilitadores para a efetiva adesão. **Delineamento:** Trata-se de um estudo de revisão integrativa da literatura, realizado nas principais bases de dados. Os critérios de inclusão aplicados foram estudos primários e publicados até setembro de 2019. **Resultados:** Observou-se alta adesão à Profilaxia Pré-Exposição ao HIV. As barreiras e os aspectos facilitadores para a adesão à Profilaxia Pré-Exposição ao HIV estão associados ao estigma social, déficit de conhecimento sobre a eficácia e a segurança da profilaxia e, principalmente, a baixa conscientização sobre as práticas sexuais e comportamentos de alto risco para a transmissão do HIV. **Implicações:** Observou-se alta adesão à Profilaxia Pré-Exposição ao HIV nos segmentos populacionais mais vulneráveis. As barreiras para a adesão à Profilaxia Pré-Exposição ao HIV podem ser superadas com maior investimento na divulgação dos seus benefícios para a população.

DESCRITORES

Controle de Infecções; HIV; Profilaxia Pré-Exposição; Adesão à Medicação; Brasil.

RESUMEN

Introducción: La reciente inserción de la Profilaxis Pre-Exposición al VIH como estrategia para el control de la infección por VIH en el Sistema Único de Salud, y los estudios relacionados con el tema pueden potenciar su efectividad en el control de la infección por VIH. El estudio tiene como objetivo analizar el escenario actual de adherencia a la profilaxis previa a la exposición al VIH en Brasil y comprender las barreras y aspectos facilitadores para una adherencia efectiva. **Delineación:** Se trata de un estudio de revisión integradora de la literatura, realizado en las principales bases de datos. Los criterios de inclusión aplicados fueron estudios primarios y publicados hasta septiembre de 2019. **Resultados:** Hubo una alta adherencia a la profilaxis previa a la exposición al VIH. Las barreras y aspectos facilitadores para la adherencia a la profilaxis previa a la exposición al VIH están asociados con el estigma social, el desconocimiento sobre la eficacia y seguridad de la profilaxis y, especialmente, la baja conciencia de las prácticas sexuales y las conductas de alto riesgo para la transmisión del VIH. **Implicaciones:** Se observó una alta adherencia a la profilaxis previa a la exposición al VIH en los segmentos de población más vulnerables. Las barreras para la adherencia a la profilaxis previa a la exposición al VIH pueden superarse con una mayor inversión en la difusión de sus beneficios a la población.

DESCRIPTORES

Control de Infecciones; VIH; Profilaxis Pre-Exposición; Cumplimiento de la Medicación; Brasil.

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COLLABORATIONS

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CONFLICTS OF INTEREST

There are no conflicts of interest to declare.