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Original Article

The Impact of Alcohol and Illicit Drug use on Adherence to HIV Pre-exposure Prophylaxis among Men who have Sex with Men

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ABSTRACT

Objectives: To investigate the degree of Men who have Sex with Men (MSM) adherence to antiretrovirals Tenofovir/Emtricitabine (TFC/FTC), drugs for the Pre-exposure Prophylaxis to the human immunodeficiency virus (PrEP). **Methods:** This is a cross-sectional and retrospective study carried out in a reference service in infectology in Ceará-Brazil. MSM with at least three recorded medical follow-ups were included in the study. We considered as ideal adherence those users who took at least 80% of the doses within 90 days. Bivariate analysis (X^2 or Fisher's exact) was carried out to investigate the association between ideal adherence to PrEP and the use of alcohol and illicit drugs. Results with a *p*-value <0.05 were taken into consideration. **Results:** A total of 167 individuals participated in the survey. MSM stopped taking 668 doses of PrEP in three months, of which 16.2% (*n*=27) had an adherence rate >80%. Nevertheless, alcohol and illicit drug use accounted for 41.4% (*n*=69). Among the most commonly used narcotics were marijuana and cocaine, 42.7% (*n*=35) and 18.3% (*n*=15), respectively. It was observed that optimal adherence (>80%) was better in individuals who did not use alcohol and illicit drugs compared to those who did (*p*=0.003). **Conclusion:** MSM adhered satisfactorily to PrEP; however, it was observed that individuals who used illicit drugs and alcohol when had their degree of adherence to TDF/FTC weakened when compared to those who did not use them. Thus, it becomes necessary to pay attention to such aspects to provide alternatives for increasing adherence in high-priority populations.

Key words: Alcohol, HIV, Illicit Drugs, Men who have Sex with Men, Risk Groups, Sexuality.

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INTRODUCTION

There is a downward trend in the incidence of Human Immunodeficiency Virus (HIV) infection in many countries; however, among men who have sex with men (MSM), the epidemic has grown disproportionately.[1,2] In low- and middle-income countries, MSM are estimated to be almost 24 times more likely to become infected with HIV compared to the general population.[3,4] Even in high-income countries, the HIV epidemic reemerges among MSM as a severe public health problem.[2]

In Brazil, the epidemic of Acquired Immunodeficiency Syndrome (AIDS) associated with HIV infection is concentrated in some population segments, which account for most new cases of infection, such as gay and other MSM, transgender people, and sex workers. In addition, the growth of HIV infection in young people is noteworthy.[5] It is estimated that since the emergence of AIDS in Brazil in 1980, by June 2020, about 1,011,617 people were living with the syndrome.[6]

In Ceará, specifically, a total of 14,647 AIDS cases were notified between the years 1981 to December 2020, with an average of 930 new cases in the last five years. Also, it is possible to highlight the growth of HIV cases in males, where it is historically observed that from 2009 to November 2019, most infected men reported having sex only with men, thus identifying the primary mode of transmission.[7]

Considering this scenario, in 2015, the World Health Organization (WHO) and the United Nations Program on HIV/AIDS (UNAIDS) prepared a document called *Oral Pre-Exposure Prophylaxis: Putting a new choice in context*. This document proposes combined prevention actions against HIV infection to control the epidemic in the member countries of the United Nations (UN), one of the measures being the Pre-Exposure Prophylaxis to HIV (PrEP).[8]

In this context, PrEP consists of the use of antiretroviral drugs (ARV), such as Tenofovir (TDF) associated with Emtricitabine (FTC), attending sexual practices, with a protection level of 96% (90 to >99%) in anal intercourse, when used daily.[9] This strategy has proven effective and safe in people at increased risk of acquiring the infection.[10]

In 2010, the *Pre-Exposure Prophylaxis Initiative* (iPrEx) became the first randomized controlled trial to demonstrate the efficacy of PrEP in MSM, finding a 44% risk reduction in the experimental group receiving co-formulated TDF/FTC tablets compared to placebo.[11] This success has since been replicated in several other studies.[12-15]

However, previous literature has noted that adherence is a critical link in the continued use of PrEP by MSM. The success of the PrEP intervention is closely related to the ability to maintain good adherence to the method.[16] In 2013, a substudy correlated to the *Partners PrEP Study* (PARCEIROS) found that high adherence to PrEP (>80%) was associated with its effectiveness in 100% of individuals (95% CI, 83.7 to 100%).[17] On the other hand, in 2015, the *Vaginal and Oral Interventions to Control the Epidemic* (VOICE) study, which aimed to demonstrate the clinical effectiveness of PrEP in young African women, revealed that only 30% of plasma samples analyzed contained detectable level of TDF.[18]

Thus, one of the factors that may be determinant for PrEP adherence, according to Hojilla *et al.* (2018),[19] is related to the routine use of alcohol, illicit drugs, and erection stimulants, since the authors identified in their

research the association between PrEP users' seroconversion, low adherence to the method and the consumption of alcohol and other drugs.

Although there are studies related to various aspects of PrEP, Brazil, and especially Ceará, lacks research involving this theme, considering that the method became part of the prevention strategies offered by the Ministry of Health (MH), through the Unified Health System (SUS), in December 2017. In this sense, the present study aimed to investigate the degree of adherence of MSM to antiretroviral TFC/FTC, PrEP drugs, given the self-reported adherence during monitoring consultations, as well as assess the existence of an association between the consumption of alcohol and illicit drugs in adherence to the method.

MATERIALS AND METHODS

This is an analytical, retrospective, cross-sectional study with a quantitative approach. The secondary data collection occurred during January and May 2020, through the System of Logistic Control of Medications (SICLOM), accessed in the Coordinators of Pharmaceutical Assistance (COASF), an agency linked to the Health Secretariat of the State of Ceará (SES-CE).

MSM in PrEP follow-up in a reference center in Ceará, duly registered in SICLOM in the period from January 2018 to December 2019, and who had at least three consultations registered in the system, participated in the study. Subjects with suspected immunological window, with inconclusive or confirmatory rapid or laboratory tests for HIV and users on antiretroviral therapy, considered exclusion criteria for indication, initiation, and continuity of PrEP were excluded.

The variables addressed refer to socio-demographic characteristics, sexual habits, degree of adherence, and history of alcohol and other drug use, classified as licit and illicit, of PrEP users (Table 1).

Table 1: Characterization of the variables selected for the study. Ceará, 2020.

Aspects: Socio-demographic	
Variable	**Metrics**
Age	Variable calculated in years based on the date of birth reported by the surveyed individual taking PrEP.
City of residence	Variable representing the city in which the surveyed individual currently taking PrEP resides.
Sexual orientation	Variable representing the sexual orientation of the individual using PrEP among the following: Heterosexual Homosexual, Gay, and Lesbian Bisexual.
Gender identity	Variable representing the gender identity of the individual using PrEP among the following: Male, Female, Transsexual Woman, Transvestite/Transvestite Woman, and Transsexual Man.
Race/color	Variable representing the race/color declared by the PrEP user among the following: White, Black, Race/Color, Yellow, Brown, and Indigenous.
Education	Variable representing the level of education (in years of study) declared by the PrEP user among the following: None/No Formal Education, 1 to 3 years, 4 to 7 years, 8 to 11 years, and 12 and more years.
Medical follow-up	Variable representing the type of medical follow-up of the PrEP user, among the following: Public and Private
Sexual behavior and use of alcohol and other drugs by PrEP users	
Reason for choosing PrEP	Variable representing why the individual sought PrEP, among the following: Referral by a health care provider, made aware by print/internet communication/peer/friend campaign/educator, or guidance from Non-Governmental Organizations (NGOs)
Frequency of PEP use	Variable representing the number of times the individual had used PEP in the past 12 months before choosing to use PrEP.
Frequency of sexual intercourse	Variable representing the number of times the individual used condoms during sexual intercourse in the last 3 months, before choosing PrEP and 180 days after using it.
Frequency of condom use in sexual intercourse	Variable representing the number of times the individual used condoms during sexual intercourse in the last 3 months, before using PrEP and 180 days after using it.
Type of sexual intercourse without condoms	Variable representing the type of sexual relation that the individual had, in the last 6 months, before the use of PrEP and 180 days after its use, among the following: Anal Insertive (penetrating the anus), Anal Receptive (being penetrated in the anus), Vaginal Insertive (penetrating the vagina), Vaginal Receptive (being penetrated in the vagina) and Not applicable.
Sexual intercourse with PLHIV	Dummy variable (yes/no/don't know) for unprotected sex by PrEP user with HIV+ partner in the past 6 months.
Receiving some sort of remuneration in exchange for sex.	Dummy variable (yes/no) reflecting the receipt of remuneration in exchange for sex in the past 6 months by individuals who opted for PrEP.
Alcohol Use	Dummy variable (yes/no) shows whether the individual using PrEP had 5 or more alcoholic drinks during approximately two hours in the last 3 months.
Use of other substances	Variable reflecting the individual PrEP user's use of the following substances: Poppers, Cocaine/Coca paste, Crack, Marijuana, Club drugs (ketamine, ecstasy, LSD, GHB, bath salts, etc.), Erection stimulants (Sildenafil, Viagra®, Cialis®, Levitra®, Helleva®), Solvent and I have not used any of the above.
Injecting drug use	Variable detailing the use by PrEP-using individuals of injectable drugs without a prescription, categorized into: No, Never, Yes in the past 3 months, and Yes but not in the past 3 months.
History of adherence and adverse reactions to PrEP drug	
Frequency of missed doses of TDF/FTC	Variable that reflects the number of times the individual has stopped taking one of the doses of the drug over 30 days.
Reason for not using the doses of TDF/FTC	Variable that reflects why the individual stopped taking one of the doses of the medication, among the following: forgot, travel/away from home, ran out of medication, adverse effects, didn't stop taking, other reasons.
Adverse drug reactions	Variable that reflects possible adverse reaction to the medication since the last medical appointment, among the following: I had no adverse reaction, diarrhea, flatulence, nausea, vomiting, abdominal pain, other.
Persistence of the adverse reaction	Dummy variable (yes/no/not applicable) reflecting the persistence of the adverse reaction.

PrEP - HIV Pre-Exposure Prophylaxis; NGOs- Non-Governmental Organizations; PEP - HIV Postexposure Prophylaxis; PLHIV - People Living with HIV; HIV - Human Immunodeficiency Virus; LSD - lysergic acid diethylamide; GHB - gamma-hydroxybutyrate; TDF/FTC - Tenofovir/Emtricitabine. To measure the degree of adherence of individuals, we used part of the method described in the work of Montgomery *et al.* (2016),[15] which consisted of analyzing the self-report of the use of TDF/CTF by the user by filling out the PrEP monitoring form in SICLOM by the health professional, which allowed to evaluate the adherence behavior of users by the periodicity with which they stop taking the doses of the drug. Additionally, to measure level of adherence to PreP, the following scale was adopted: < 60% unsatisfactory, 60 and 79% as acceptable, and > 80% ideal adherence.[13]

The data collected were entered into Microsoft Excel software (version 2013) and subsequently exported to the Statistical Package for the Social Sciences (version 21), with the results expressed according to descriptive statistics. We performed bivariate analysis (X^2 or Fisher's exact) to investigate the existence of an association between the number of illicit drugs consumed and the number of doses of TDF/FTC not taken by MSM. Data were considered significant when $p<0.05$. Ethical aspects were respected, with approval from the Research Ethics Committee (CEP) of the Federal University of Ceará (UFC) and the Secretary of Health of the State of Ceará, process number 3.644.728/2019 and 3.765.612/2019, respectively. Moreover, the selected unit is linked to the SES-CE. It is considered a reference in the clinical management of infectious diseases, emphasizing the care of People Living with HIV (PLHIV), HIV Postexposure Prophylaxis (PEP), and PrEP, the latter having been incorporated in December 2017.

RESULTS

Of the 235 individuals using PrEP registered in the reference service, 167 subjects made up the study sample, considering that 66 individuals had no data on the return of thirty days of PrEP since they participated in the project COMBINA!- linked to the Faculty of Medicine, University of São Paulo; and 64 individuals, for not yet having registered in SICLOM, the third monitoring of PrEP. The subjects had a mean age of 32 years±8.6 (range 19 to 62 years), most were single (83.8%; *n*=140), living in Fortaleza (84.4%; *n*=141), with more than 12 years of schooling (*n*=133; 79.6%), and of mixed race/race (53.9%; *n*=90) (Table 2). The mean time of PrEP use was 17.9±5.6 months; range, 6 to 28 months.

Regarding the sexual habits of PrEP users, it was found that the average number of sexual partners was 11.5 ± 56.4 (range, 0 to 700) in the last three months before the indication of the method, in which the condom was only used every time in 26.3% (*n*=44) of sexual relations. Nevertheless, 41.9% (*n*=70) reported having sex without using a condom with PLHIV, and 92.2% (*n*=154) denied having sex in exchange for money, drugs, or housing. The most commonly practiced type of sex was insertive anal sex; 71.8 (*n*=135), followed by receptive anal; 28.2% (*n*=53). 12.6% (*n*=21) reported versatility in sexual intercourse.

The individuals studied stopped taking 668 doses of PrEP within 90 days, with 6.6% (*n*=11) taking between 53 and 14 doses (adherence grade <60%), 9.6% (*n*=16) between 55 and 69 doses (adherence grade between 60% and 79%), and 83.8% (*n*=140) between 72 and 90 doses (adherence grade > 80%). In addition, 52.7% (*n*=88) reported taking all doses of TDF/FTC. Forgetfulness (77.3%; *n*=51), travel (16.7%; *n*= 11), lack of the drug (4.5%; n=3), and adverse reactions (1.5%; *n*=1) were the causes for not taking the recommended doses.

Another characteristic investigated in the users was the consumption of alcohol and other drugs. The frequent use of licit and illicit drugs by the subjects was observed, especially for alcohol, which was reported frequent use by 66.5% (*n*=111) of individuals. Regarding illicit drugs, 38.9% (*n*=65) reported use, with marijuana being the most used narcotic; 42.7% (n=35), followed by cocaine; 18.3% (*n*=15), and poppers; 14.6% (*n*=12) (Table 3). The mean number of narcotic substances used by the individuals was 1.7±1.0.

Furthermore, we also investigated the existence of an association between the degree of adherence to the method and the consumption of alcohol and other drugs, where we saw that ideal adherence (>80%) was better in individuals who did not use alcohol and other drugs when compared to those who did (p=0.003). Furthermore, MSM who used three drugs or more had worse adherence when compared to those who used up to one drug (Table 4).

Table 2: Socio-demographic characteristics of the study participants. Ceará, 2020.

	n	%
City of residency		
Fortaleza	141	84.4
Caucaia	5	3.0
Maracanaú	4	2.4
Canindé	3	1.8
Other cities*	14	8.4
Race/color		
Brown	90	53.9
White	61	36.5
Black	15	9.0
Yellow	1	0.6
Education		
4-7 years	1	0.6
8-11 years	33	19.8
12 years or more	133	79.6
Marital status		
Single	140	83.8
Common-law marriage	19	11.4
Married	5	3.0
Divorced	3	1.8

*Atalaia (AL); Pacatuba; Itaitinga; Sobral; Iguatu; Morada Nova; Beberibe; Quixadá; Santo André (SP); Horizonte.Concerning the reason why individuals sought PrEP, 58.1% (*n*=97) reported being stimulated through communication, such as the internet/television, 38.3% (*n*=64) were referred by health professionals, and 3.6% (*n*=6) were referred by Non-Governmental Organizations (NGOs). In addition, we observed that 15.6% (*n*=26) used HIV Post-Exposure Prophylaxis (PEP) at least two times in the 12 months.

Table 3: Alcohol and illicit drug use reported by men who have sex with men at the initial PrEP consultation. Ceará, 2020.

	n	%
Regular alcohol consumption		
Yes	111	66.5
No	56	33.5
Consumption of illicit drugs		
Yes	65	38.9
No	102	61.1
Illicit substances used		
Marijuana	35	42.7
Cocaine	15	18.3
Poppers	12	14.6
Solvents	11	13.4
Club drugs*	8	9.8
Crack	1	1.2
Use of injectable drugs without a doctor's prescription		
No	145	86.8
Yes	22	13.2

* Group of recreational drugs, e.g., Ecstasy, amphetamines, methamphetamines, Lysergic Acid Diethylamide (LSD).

Table 4: Bivariate analysis about the association between alcohol consumption and illicit drugs under the degree of adherence to PrEP by MSM. Ceará, 2020.

		Degree of adhesion > 80%		
	Total	No	Yes	*p*-Value
Drugs				
No	99 (59.3%)	9 (33.3%)	90 (64.3%)*	0.003
Yes	68 (40.7%)	18 (66.7%)*	50 (35.7%)	
Number of drugs (alcohol and illicit drugs)				
None	98 (58.7%)	8 (29.6%)	90 (64.3%)*	<0.001
1	36 (21.6%)	3 (11.1%)	33 (23.6%)*	
2	18 (10.8%)	3 (11.1%)	15 (10.7%)	
3	8 (4.8%)	6 (22.2%)*	2 (1.4%)	
4	7 (4.2%)	7 (25.9%)*	0 (0.0%)	

*$p<0.05$, Pearson's chi-square test (*n*, %).

Additionally, in the third clinical monitoring of PrEP, 3.6% (n=6) stopped using the method since there were changes in laboratory tests in two individuals, and four subjects decided not to continue. No intercurrence related to PrEP use by MSM was recorded during the analyzed period. There was no seroconversion to HIV in the individuals studied.

DISCUSSION

In Brazil, the HIV/AIDS epidemic is concentrated in some population segments that account for most new cases of infection, such as gay men and other men who have sex with men, transgender people, and sex workers. However, besides being at a higher risk of acquiring HIV, these people are often subject to discrimination, being targets of stigma and prejudice, thus increasing their vulnerability to HIV/AIDS.[5]

For these cases, PrEP is inserted as an additional prevention strategy available at SUS, aiming to reduce HIV transmission and contribute to achieving goals related to the end of the epidemic.[20] Under these aspects, it was observed that the users studied were mostly young adults, brown and white, residents of the capital (Fortaleza), and metropolitan region, with education of 12 years or more. These results contrast with the findings of Huang *et al.*,[13] who studied adherence to PrEP in an HIV care provider in the United States. However, we should draw attention to a part of the MSM population that could also possibly benefit from the use of PrEP; still, they apparently do not have the same access as the others, such as the black population and those with low education, either because of misinformation about the provision of the method or because of difficulty in accessing health services.[21] Above all, socioeconomic and cultural factors, stigmas related to sexuality, no concept of preventive care, and lack of risk perception are conditions that can distance people from other methods of protection against HIV.[22]

Considering this context, the media, such as the internet, was the main vehicle that led individuals to seek PrEP. This occurs due to the access to endless sources of information available on the internet, which plays a key role in shaping this active posture of the individual, who decides to expand his prevention strategies for HIV. The new virtual spaces for sharing information change or interfere with the relationship with doctors, who are no longer the supreme holders of knowledge and are now questioned by increasingly informed patients.[23]

Health professionals also have an essential role in identifying, guiding, and referring MSM at high risk of HIV infection to specialized services, especially those who constantly seek PEP in health facilities or with recurrent STI diagnosis. In this sense, a study conducted with Latin American MSM living in Texas, United States, reported that the primary source of information about PrEP was the internet (39%; *n*=62) followed by a sexual partner (37.1%; *n*=59), friend (29.6%; *n*=47) and/or health care professional (25.8%; *n*=41).[24]

Thus, one of the prerogatives for PrEP indication in Brazil is related to the risk behavior of individuals, as may be the case of gay men and other MSM, transgender people, sex workers, and serodiscordant couples, and these populations must fit at least one of the following criteria: a) frequent search for PEP, b) recurrent STI episodes; c) sexual intercourse with PLHIV without the use of condoms.[20] Moreover, it is worth drawing attention to the receptive anal intercourse practiced by the subjects since the chance of HIV infection may be up to 18 times higher than other types of intercourse, and PrEP is a crucial strategy for those not adept at using condoms.[25]

The effectiveness of PrEP depends on its adherence, as pointed out by several studies.[11,14,26,27] Thus, it was found that most MSM adhered to it, considering the self-report of adherence, in the 30-day recall period, through the survey conducted in the first three clinical monitoring of the method.

According to a cohort study by Velloza *et al.* (2018),[28] users are required to take at least 80% of the recommended doses of PrEP, which would be somewhere around 5-6 pills per week, which the authors attested is enough to protect MSM against HIV. However, minimum pharmacokinetics have not yet been established for heterosexual women or men, and although previous studies have found an association between high levels of adherence and low HIV incidence. Research suggests that PrEP may be less tolerant of missed doses in vaginal exposure than in rectal exposure.[29,30] Increased adherence to PrEP among young MSM was also found in research by Myers and colleagues.[27]

Besides, the high tolerability of the use of TDF/FTC by MSM should be noted. Adverse reactions are primarily of gastrointestinal tract origin and more prevalent at the beginning of use but usually decrease within one month of use. Risk factors in long-term PrEP use include age, duration of TDF treatment, elevated baseline creatinine levels, and among people with African ancestry relative to Caucasians.[31]

Because of the significant behavioral requirements to maintain consistent daily pill intake, additional options as an alternative to TDF/FTC, including long-acting injectables, vaginal rings, and films, are being developed to increase the selection of PrEP products and allow people to make choices about which technology best fits their lifestyle.[32,33] This development scope is comparable to contraception, where increasing the number of contraceptive options has been shown to increase the overall acceptance of contraception significantly.[34]

One of the factors that increase the risk of HIV infection is related to the consumption of alcohol and licit and illicit drugs, either by sharing needles and uninhibited sexual risk behaviors influenced by drugs, as well as by the high prevalence of transactional sex and syndemic risk factors observed in this population (violence, poverty, impotence, and lack of access to care), and regarding PrEP, this habit can be a hindrance to its adherence.[35,36]

Hence, it was possible to observe that alcohol and illicit drugs directly influenced the ideal adherence to PrEP by MSM. The number of narcotics used is inversely proportional to good adherence to TDF/FTC. According to Lacob *et al.* (2017), due to drug dependence problems and the great diversity of illicit drugs available, the management of this population is particularly challenging, and this group is responsible for the growing number of new cases of HIV infection, besides the antiretroviral adherence being relatively low, around 63%.[37] However, the use of PrEP by drug users is advocated by Shrestha *et al.*(2017)[38]

One of the limitations of the study is related to data collection, which investigated the degree of adherence of MSM using TDF/FTC considering only their self-report. However, this technique alone does not make the study unfeasible since other studies have used this methodology alone or in combination.[13,15,39]

We expect that the results achieved in this research will serve to guide health professionals who work directly and indirectly with the MSM population and, in particular, PrEP users, to raise their interest in the factors that may compromise full adherence to the method, such as the consumption of licit and illicit drugs, to encourage the combined use of other methods for the prevention of HIV infection, as well as encourage the creation of public policies aimed at the population of MSM who use illicit drugs.

CONCLUSION

The results showed a satisfactory degree of adherence to PrEP by MSM. However, they also showed that illicit drugs are a risk factor for optimal adherence to the method. Thus, identifying the use of illicit drugs by MSM using PrEP is crucial in developing strategies to optimize its clinical and public health benefits in high-priority populations.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

MSM: Men who have Sex with Men; **TFC/FTC:** Tenofovir/Emtricitabine; **PrEP:** Pre-exposure Prophylaxis; **HIV:** Human Immunodeficiency Virus; **AIDS:** Acquired Immunodeficiency Syndrome; **WHO:** World Health Organization; **UNAIDS:** United Nations Program on HIV/AIDS; **UN:** United Nations; **ARV:** antiretroviral drugs; **iPrEx:** Pre-Exposure Prophylaxis Initiative; **PARCEIROS:** Partners PrEP Study; **VOICE:** Vaginal and Oral Interventions to Control the Epidemic; **MH:** Ministry of Health; **SUS:** Unified Health System; **SICLOM:** System of Logistic Control of Medications; **COASF:** Coordinators of Pharmaceutical Assistance; **SES-CE:** Secretariat of the State of Ceará; **NGO:** Non-Governmental Organizations; **PEP:** HIV Postexposure Prophylaxis; **PL-HIV:** People Living with HIV; **LSD:** lysergic acid diethylamide; **GHB:** Ggamma-hydroxybutyrate; **CEP:** Research Ethics Committee; **UFC:** of the Federal University of Ceará.

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