Socio-demographic and clinical determinants of late presentation among patients newly diagnosed with HIV in the Eastern Cape, South Africa

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Abstract

South Africa recently implemented the 'test and treat' strategy for all HIV-infected individuals receiving diagnosis at the health facility level. However, the impact of this programme in terms of the prevention of HIV transmission, morbidity and mortality associated with HIV can only be maximized if patients are diagnosed early. This study determines the prevalence of late presentation among newly diagnosed HIV-infected individuals and also examines the socio-demographic and clinical determinants for late presentation in health facilities in the Eastern Cape Province, South Africa.

In this cross-sectional study, a total of 335 newly diagnosed patients were recruited consecutively between August 2016 and July 2017. Late presenter for HIV care was defined in accordance with the European Late Presenter Consensus working group as a patient who reports for care when the CD4 count is below 350 cells/μL and/or when there is an established AIDS-defining clinical condition, irrespective of CD4 count. Adjusted and unadjusted logistic regression analysis was used to examine the determinants of late HIV diagnosis.

Participants' mean age was 33.6 (SD: 10.6). Almost 96% of the participants believed their route of HIV infection was heterosexual sex. Most newly diagnosed HIV-infected patients (60%) were late presenters (CD4+ count ≤350 cells/μL and/or having an AIDS-defining illness in World Health Organisation (WHO)-defined stage III/IV), with 35% presenting with Acquired Immune Deficiency Syndrome (AIDS)-related complications. In the adjusted model, only male sex (AOR: 2.81; CI: 1.51–5.23), no formal education (AOR: 5.63; CI: 1.68–18.85), and overweight body mass category (AOR: 2.45; CI: 1.04–5.75) were independently associated with late HIV diagnosis.

The majority of newly diagnosed HIV-infected individuals were late presenters. To maximize the impact of the 'test and treat' policy aimed at reducing new HIV transmissions and preventing the morbidity and mortality associated with HIV, there is a need for programmes to improve early detection of HIV in the study settings. This programme should target males and individuals with no formal education for maximum impact.

Abbreviations: AIDS = acquired immune deficiency syndrome, ART = antiretroviral therapy, ARV = anti-retroviral, HCT = HIV counselling and testing, HIV = human immunodeficiency-virus, HIVAN = HIV-associated nephropathy, PLHIV = national department of health, people living with HIV, PMTCT = prevention of mother to child transmission of HIV, VCT = voluntary counselling and testing center, WHO = World Health Organisation.

Keywords: AIDS, HIV-infected patient, late presentation for care

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1. Introduction

Late presentation or detection of HIV-infected individuals remains a source of impediment to the eradication of infections and HIV-related mortality.[1] Accessing HIV care at a late stage of the disease has been shown to be detrimental to the health of infected persons and society at large.[2–4] Also, presenting late for HIV care does not only further HIV transmission,[5–8] but also drives AIDS-related deaths.[9,10] Several studies have documented the benefit of early and timely initiation of anti-retroviral therapy (ART) in HIV-infected individuals.[11–14] Recently, Cohen et al[12] have greatly influenced policies across the world by advocating for earlier initiation of ART to HIV-infected individuals, irrespective of their CD4 count.[15,16] Notably, the early use of ART depletes the size of the HIV reservoir[17,18] and ensures that patients who start ART do so with preserved immune function. The patient who presents late for HIV care is at risk of clinical complications. It is still debatable if the immune function ever returns to the pre-infective state of normal function, with studies of long-term cohorts indicating that patients who adhere to ART treatment have a normal life expectancy, similar to that of non-HIV infected persons.[19]

The late presentation of HIV infection was defined by the European Late Presenter Consensus working group as a patient who reports for care when the CD4 count is below 350 cells/μL or who has an established AIDS-defining clinical condition, irrespective of the CD4 count.[20] This definition is aimed at allowing for coordinated care and a uniform approach to the management of HIV disease to improve the standard of care of late HIV presenters. Another study proposed a definition of late presenters as patients who present with a CD4 count <200 cells/μL and/or have an AIDS-defining illness within a month after HIV diagnosis, or patients with a first-reported CD4 count <350 cells/μL or an AIDS-defining illness within a month after HIV diagnosis.[21] A common definition of late presentation of HIV infection was advocated to ensure uniformity of care.[22] However, no such standard definition exists in the South African context to describe the cohort of HIV-infected individuals who present late with HIV infection.

The South African HIV guidelines have undergone numerous changes over the past few years, based on robust evidence supporting the treatment of all individuals diagnosed with HIV, irrespective of CD4 count[23] (the 'test and treat' strategy).[24] Preceding this change, immunological status (CD4 count) was crucial for ART initiation, which changed from 350 cells/uL to 500 cells/uL in 2015.[25] Of utmost importance is the adoption of a new HIV testing policy by both the World Health Organisation (WHO) and the South African Department of Health.[25]

In a study conducted in India, the percentage of patients who were detected with CD4 counts <200 and <350 cells/mm^3 ranged from 46% to 68.7% respectively.[26] In developed countries, the prevalence of late presenters varies between 5% and 30%, and can rise up to 50%, depending on access to care in certain areas.[27] In South Africa, the prevalence of patients who present for HIV care with a CD4 count of less than 200 cells/uL is about 33.6%.[28] However, this figure was cited in a study conducted in 2012, when the CD4 threshold for enrolling into the ART programme was 350 cells/uL or less.[29]

Late presentation of HIV infection might be indicative of lack of knowledge about HIV, cultural and social stigmas, and/or socioeconomic barriers which limit access to healthcare.[28,30] Distances of more than 5 km between patients' homes and health services was reported to have a substantial impact on timing of patients' presentation at health care facilities.[28] Patients in rural areas in the United States of America were reported to present late for HIV care.[27] In China, the province where a patient resides has been reported to have a bearing on the time of presentation for HIV care.[31] Socioeconomic circumstances have also been found to cause a delay in early presentation for treatment. Lack of housing or not having a permanent place of abode contributes to late presentation.[31] This was corroborated in a similar study conducted in India.[26] The role of being a migrant significantly impacted on how early such migrant HIV patients access care.[32] Other socioeconomic factors which contributed to late presentation included lower educational attainment and non-business occupation.[33] Demographic factors such as age, gender and occupational status of patients have an impact on the timing of presentation for HIV care. Male gender, non-pregnancy state and older age were associated with late presentation for HIV care.[28,31–33]

Local epidemiological data on late presentation among newly diagnosed HIV-infected individuals could be important for policy advocacy and health managers. This valuable data is currently lacking in the Eastern Cape, South Africa. Also, the 'test and treat' policy could be a game-changer, given that treatments are freely available for everyone diagnosed with HIV in South Africa. The policy could have an impact at the population level if individuals living with HIV receive early diagnosis. Given the individual and public health benefits of early diagnosis and timely ART initiation,[30] it is crucial to gain an understanding of the extent of late presentation of HIV infection in the Eastern Cape, South Africa. This study examined the socio-demographic and clinical factors for late presentation amongst newly diagnosed HIV-infected individuals within the context of the 'test and treat' strategy in some health facilities in Buffalo City Municipality in the Eastern Cape.

2. Methods

2.1. Study areas and study population

All newly HIV-diagnosed patients in the HIV testing sites of Cecilia Makiwane Hospital and four randomly selected HCT sites at Buffalo City Municipality community health centers who consented to participate in the study were recruited into the study between August 2016 and July 2017. Cecilia Makiwane Hospital (CMH) is a regional hospital situated in Mdantsane, the second largest township in South Africa. The hospital serves as a major referral center for the central region of Eastern Cape. Various patients, regardless of ethnicity, geographical residence and socioeconomic status visit and are referred to the hospital. The HCT sites at the Buffalo District Municipality community health centers also cater for a wider region than only Buffalo City Municipality, and frequently serve as the first point of call for patients at primary health care level. The hospital and the community health centers are situated in Buffalo City Local Municipality, in Amathole District Municipality, where the prevalence of HIV infection, as recorded by the antenatal clinic attendance (ANC) survey, is 12.7%.[34] The required sample size of 335 was based on the 12.7% HIV-prevalence rate in the study setting, a 95% confidence level and a ±3.57% confidence interval.

Participants were recruited over a period of 1 year. Participants were eligible if they were 15 years old or over, newly diagnosed with HIV and had no prior exposure to ART. The target population were all newly established HIV-positive patients in the Eastern Cape Province.

2.2. Study procedure

All newly diagnosed patients in the study period who gave written consent were asked to complete a questionnaire by trained research nurses at the clinics. A pre-validated questionnaire was used to obtain relevant demographic characteristics: age, sex, place of residence, employment status, and level of education. Additional information on the probable route of transmission was elicited from the participants. The data instrument was initially piloted with ten participants, and findings were used to improve the questionnaire for the study. Information on WHO clinical stage, CD4 count and other clinical conditions was obtained from patients' files and documented in the questionnaire. The research nurses measured the participants' weight and height in accordance with standard protocols.

The study protocol was approved by the University of Fort Hare Postgraduate Ethical Committee (REC 270710028RA level 01) and the Eastern Cape Health Department (approval number: EC_2016RP22_139). All respondents provided written consent. The respondents' rights to confidentiality and privacy were respected throughout the study.

2.3. Main outcome variable

Late presenter for HIV diagnoses and care was defined in accordance with the European Late Presenter Consensus working group as a patient who reports for care when the CD4 count is below 350 cells/ μL and/or when there is an established AIDS-defining clinical condition, irrespective of CD4 count. Patients were considered late presenters if their CD4 count was below 350 cells/μL or they had an established AIDS-defining clinical condition.

2.4. Data analysis

Data were coded and entered into the Statistical Package for Social Sciences (SPSS version 24, Chicago, IL). A simple frequency count was computed for all variables, and errors in data entries were corrected. Mean and standard deviations were estimated for age. Frequency counts and percentages were computed for categorical variables. Bivariate and multivariate analyses were used to examine the factors associated with late presentation. Adjusted and unadjusted logistic regression models were estimated at a 95% confidence interval. A *P* value of less than .05 was considered statistically significant.

3. Results

3.1. Sociodemographic

Of the 335 participants, 105 (31%) were men and 230 (69%) women. The mean age of the patients was 33.6 (SD: 10.6). The majority were single (81.4%), had a secondary education (54%) and were unemployed (60%). Concerning the pattern of infection, almost 96% of the participants believed they had acquired the HIV infection through heterosexual sex, while 3.6% of the participants had acquired the HIV infection through partners of the same sex. With regard to frequency of HIV testing, 90% of the study participants had undergone an HIV test within the last 5 years ().

3.2. Clinical parameters

3.2.1. Stages of presentation.
As shown in Figure 1, 60% of patients were late presenters, with 35% presenting with advanced disease. Over half the patients were asymptomatic. Most late presenters had developed an AIDS-defining condition such as tuberculosis (3%), oral candidiasis (1.5%), anemia (8.3%), meningitis (2%), and HIVAN (6%), with 21% presenting with oral candidiasis, anemia and tuberculosis (Table 2). In terms of WHO clinical staging, 51.4% were in clinical stage 1, 3% in stage 2, 36.6% in stage 3 and 9.1% in stage 4.

3.2.2. Determinants of late presentation among newly diagnosed patients.
The results of the bivariate analysis are presented in Table 3. The proportion of late presenters varies significantly by age, sex, educational level, and body mass index. Males (78.8%) were significantly more likely to be late presenters than females (50.9%). Similarly, individuals with no formal education were significantly more likely to be late presenters than those with higher education. Also, patients aged 36 years or over were significantly more likely to present late for treatment than those who were under 36 years old. Alcohol consumption, race, marital status and smoking did not significantly influence timing of presentation.

The results of adjusted and unadjusted logistic regression models are presented in Table 4. Male sex, age 36 or over, no formal education and underweight were independently associated with late presentation among newly diagnosed HIV-infected patients. In the adjusted model, only male sex, no formal education, and overweight body mass category were independently associated with late HIV diagnosis. Males were about three times more likely to present late than females. Patients who had no formal education were about 6 times more likely to be diagnosed late compared to those with tertiary levels of education. Compared to patients who were obese, overweight patients were more than twice as likely to present late for HIV diagnosis.

4. Discussion

To our knowledge, this is the first study to examine the prevalence of late presentation and explore the determinants of late presentation among newly diagnosed HIV-infected individuals in the Eastern Cape Province, South Africa. Our study shows that most of the newly diagnosed patients presented late, with CD4 counts below 350 cells/ μL and advanced stages of disease. A retrospective study of 8138 newly diagnosed HIV-positive individuals in 35 clinics in South Africa reported a higher rate of late diagnosis, however, their definition of late presentation (CD4 count below 500 cells/ μL) differed from the definition used in this study.[35] Another South African study reported a lower prevalence of late HIV diagnosis; however, they included only patients with CD4 counts below 100 cells/ μL.[28]

The current study adds to the existing body of knowledge on the proportion of patients with delayed presentation for HIV care. Our finding provides recent data on late presentation and shows that late presentation is still a major challenge in the study setting. Late presentation for HIV diagnosis and care remains common practice, despite efforts to get patients to present early and access care. The goal of such efforts is obviously to prevent the morbidity and mortality associated with the late initiation of ART, and to ensure continuity of HIV care. The current study did not examine the trends in late presentation for HIV diagnosis over a period of time. As such, we are unable to determine whether there has been an improvement or a decline in the area of late presentation for HIV diagnosis in the study setting. A Spanish study shows that late presentation for HIV diagnosis and care have decreased substantially since 2001.[36] There is, therefore, a

Table 1

Characteristics and proportion of late presentation of HIV infection among newly diagnosed patients.

Variables	All participant	Male	Female	*P value*
Age**				
15–20	20 (6.0)	5 (4.8)	15 (6.6)	.004
21–30	126 (37.7)	25 (23.8)	101 (44.1)	
31–40	113 (33.8)	43 (41.0)	70 (30.6)	
41–50	48 (14.4)	19 (18.1)	29 (30.6)	
Above 50	27 (8.1)	13 (12.4)	14 (6.1)	
Marital Status*				
Single	271 (81.4)	78 (74.3)	193 (84.6)	.082
Married	53 (15.9)	23 (21.9)	30 (13.2)	
Formerly married	9 (2.7)	3 (2.9)	5 (2.2)	
Education level**				
None	42 (12.6)	20 (19.0)	22 (9.6)	.006
Primary	53 (15.9)	22 (21.0)	31 (13.6)	
Secondary	180 (54.1)	52 (49.5)	128 (56.1)	
Tertiary	58 (17.4)	11 (10.5)	47 (20.6)	
Religion**				
Christian	269 (80.8)	78 (74.3)	191 (83.8)	.087
Non-Christian	18 (5.4)	9 (8.6)	9 (3.9)	
No religion	46 (13.8)	18 (17.1)	28 (12.3)	
Employment Status*				
Unemployed	199 (59.6)	54 (51.4)	145 (63.3)	.004
Employed	135 (40.4)	51 (48.6)	84 (36.7)	
Race*				
Black	321 (96.1)	97 (92.4)	224 (97.8)	.054
White	6 (1.8)	4 (3.8)	2 (0.9)	
Coloured	7 (2.1)	4 (3.8)	3 (1.3)	
Alcohol use***				
Yes	90 (27.1)	44 (41.9)	46 (20.3)	.000
No	242 (72.9)	61 (58.1)	181 (79.7)	
Smoking status***				
Yes	57 (17.2)	44 (41.9)	13 (5.7)	.000
No	275 (82.8)	61 (58.1)	214 (94.3)	
Route of infection*				
Heterosexual	319 (95.5)	98 (93)	221 (96.5)	.303
MSM	12 (3.6)	5 (4.8)	7 (3.1)	
Maternal-fetal	3 (0.9)	2 (1.9)	1 (0.4)	
Last negative test**				
0–5	301 (90.4)	90 (85.7)	211 (92.5)	.107
6–10	29 (8.7)	13 (12.4)	16 (7.0)	
Above 10 years	3 (0.9)	2 (1.9)	1 (0.4)	

* One observation missing.
** Two observations missing.
*** Three observations missing.

need for trend analysis studies on late presentation among newly diagnosed HIV patients in South Africa.

Consistent with previous studies, most newly diagnosed patients are female.[28,31–33] This is in contrast to studies in Spain and Italy which reported a higher male preponderance of HIV infection.[36,37] The higher proportion of females in our study could be attributable to the health-seeking behavior disparity between the 2 genders. Also, gender differences in HIV prevalence rate have been reported, with females having a disproportionately higher HIV-prevalence rate than males.[34] The inference from our study is that the majority of patients who were newly diagnosed as HIV positive were women. This pattern was also found in three high-burden districts in South Africa between 2014 and 2015, where 69% of the study population were women. Another study showed an eight-fold higher rate of HIV infection amongst adolescent girls and young women aged 15 to 24 years when compared to their male peers in Sub-Saharan Africa.[38]

In this study, male gender was found to be an independent predictor of late presentation for HIV diagnosis. This finding is consistent with previous studies,[26,39] although an Ethiopian study reported a contrasting result, with females significantly more likely to be late presenters.[40] A study in China found no sex differences in the CD4 counts of newly diagnosed HIV-infected patients.[31] Females have far more opportunities to test for HIV than males do because of pregnancy and childbearing. The prevention of mother-to-child transmission of HIV programme (PMTCT) in South Africa, which made it mandatory for testing of all pregnant women for HIV during antenatal visits, provides opportunities for HIV diagnosis in women. Perhaps couples testing, especially during antenatal care, could be implemented in the study setting. This might not only strengthen the PMTCT programme in South Africa, but also increase the opportunities for men to get tested for HIV.

Our study shows that lack of formal education is significantly associated with late HIV diagnosis. This finding is in contrast to a
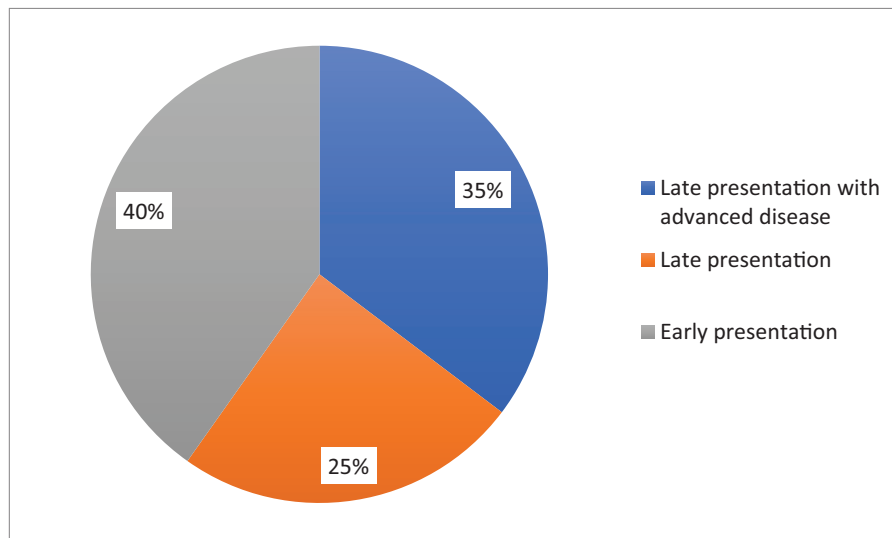
Figure 1. Stages of presentation for care.

study conducted in Denmark, which reported that no association existed between level of education and late presentation for HIV care.[39] Considering that Denmark is among countries with the highest levels of literacy, that finding is not comparable with the finding in this study. In addition, lower level of education was found to be associated with late presentation among newly diagnosed patients in other studies.[41,42] It is plausible that individuals with no formal education are less knowledgeable about HIV. Since this is the case, an intervention targeting these individuals is imperative.

Our study also shows that older age is associated with late diagnosis of HIV, which is consistent with findings in previous studies,[36,39,40] although it contrasts with findings in a study conducted in China.[31] Even though the effect of age on late presentation disappeared after controlling for other covariates, the consistency in the direction of the effect, as shown in the literature, suggests older age is a risk factor for late presentation for HIV diagnosis and care. Intervention that targets older people may have clinical benefits.

Our study shows that body mass index is associated with late diagnosis of HIV. It is plausible that patients seek care for rapid

Table 2

Clinical parameters at presentation.

Clinical parameter	Frequency (n = 335)	Percentage
Asymptomatic	175	52.0
pgl	1	0.63
Urti	2	1.25
Popular pruritic rash	5	3.13
Herpes zoster	3	1.88
Oral thrush	12	3.5
Anemia	28	8.3
Pulmonary tuberculosis	5	1.5
Anemia, ptb, oral thrush	70	21
Extra pulmonary tuberculosis	5	1.5
Meningitis	7	2.0
HIVAN	20	6.0
Meningitis, HIVAN	2	0.6

Table 3

Relationship between demographic variables and late presentation.

Variables	Late	Early	P value
All	198 (59.8)	133 (40.2)	
Gender			
Male	82 (78.8)	22 (21.2)	.000
Female	115 (50.9)	111 (49.1)	
Age			
15–35	121 (55.5)	97 (44.5)	.026
36 and above	77 (68.1)	36 (31.9)	
Education level			
No formal education	35 (83.3)	7 (16.7)	.002
Primary	35 (66.0)	18 (34.0)	
Secondary	100 (56.5)	77 (43.5)	
Higher Education	28 (48.3)	30 (51.7)	
Marital status			
Single	163 (60.8)	105 (39.2)	.604
Currently married	30 (56.6)	23 (43.4)	
Previously married	5 (55.6)	4 (44.4)	
Race			
Black	188 (59.1)	130 (40.9)	.082
White	3 (50.0)	3 (50.0)	
Coloured	7 (100.0)	0 (0.0)	
Smoking status			
Yes	34 (60.7)	22 (39.3)	.889
No	163 (59.7)	110 (40.3)	
Alcohol consumption			
Yes	54 (60.7)	35 (39.3)	.858
No	143 (59.6)	97 (40.4)	
BMI			
Underweight	25 (78.1)	7 (21.9)	.014
Normal weight	95 (61.7)	59 (38.3)	
Overweight	37 (62.7)	22 (37.3)	
Obesity	17 (41.5)	24 (58.5)	
Last negative test			
0–5	175 (58.7)	123 (41.3)	.411
6–10	20 (71.4)	8 (28.6)	
Above 10 years	2 (66.7)	1 (33.3)	

Late presentation defined as CD4 count <350 cell/ML or presenting with AIDS-defining event, regardless of the CD4 cell count.

Table 4

Adjusted and unadjusted logistic regression models showing determinants of late HIV diagnosis.

Variables	Unadjusted Odds Ratio (95% CI)	Adjusted Odds Ratio (95%CI)
Sex		
Male	3.60 (2.10–6.16)[***]	2.81 (1.51–5.23)[*]
Female (Reference)	1	1
Age		
36 and above	1.72 (1.06–2.76)[*]	1.42 (0.79–2.57)
15–35 (Reference)	1	1
Education		
No formal education	5.36 (2.05–14.01)[*]	5.63 (1.68–18.85)[*]
Primary	2.08 (0.97–4.49)	1.44 (0.59–3.50)
Secondary	1.39 (0.77–2.52)	1.35 (0.71–2.55)
Higher Education (Reference)	1	
BMI		
Underweight	5.24 (1.85–14.84)[*]	2.94 (0.97–8.93)
Normal weight	2.27 (1.13–4.58)[*]	1.84 (0.87–3.87)
Overweight	2.37 (1.05–5.37)[*]	2.45 (1.04–5.75)[*]
Obesity (Reference)	1	1

[*] $P < 0.05$.
[***] $P < 0.001$.

weight loss, which is considered a severe symptom and thus influences patients' choice of seeking care in health facilities. The health belief model asserts that illness perception influences health-seeking behavior. Individuals who consider their symptoms to be less severe may not seek care in clinics and may prefer self-medication. Further studies are needed to establish the link between body mass index and late presentation for HIV care.

Even though this study contributes to the literature on late presentation for HIV care, the findings should be interpreted within its limitations. In this cross-sectional survey, we were not able to ascertain causality of associations with delayed presentation. The study also did not entirely explore the role of distance to health care facilities, health system-related factors and impact of patient-related factors such as stigma on late presentation for HIV care. Future studies could examine trends in late presentation and the effect of distance to health care facilities, health-system factors and stigma perceptions on late presentation for HIV care.

5. Conclusion

Late presentation for HIV care remains a major challenge in the study setting. To maximize the impact of the 'test and treat' policy aimed at reducing morbidity and mortality associated with HIV, there is a need for programmes to improve early detection of HIV in the study settings. This programme should target males and individuals with no formal education for maximum impact. Also, efforts are needed to encourage men to access and utilize existing health care facilities as well as improve access to formal education.

Acknowledgments

Author contributions

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