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Association of sociodemographic and clinical variables with time to start prostate cancer treatment

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Abstract *Introduction: Disparities in prostate cancer care have been evidenced and associated with sociodemographic and clinical factors, which establish the time for diagnosis and initiation of treatment. Objective: To evaluate the association of sociodemographic and clinical variables with the onset of prostate cancer treatment. Methods: This is a prospective longitudinal cohort study with secondary data with a population of men with prostate cancer attended in the periods 2010-2011 and 2013-2014 at the Santa Rita de Cássia Hospital in Vitória, Espírito Santo, Brazil. Results: The study population consisted of 1,388 men. Of the total, those younger than 70 years (OR = 1.85; CI = 1.49-2.31), nonwhite (OR = 1.30; CI = 1.00-1.70), less than 8 years of schooling (OR = 1.52; CI = 1.06-2.17) and referred by the Unified Health System services (OR = 2.52; CI = 1.84-3.46) were more likely to have a delayed treatment. Similarly, the lower the Gleason score (OR = 1.78; CI = 1.37-2.32) and Prostate-Specific Antigens levels (OR = 2.71; CI = 2.07-3.54), the greater the likelihood of delay for the onset of treatment. Conclusion: Therefore, sociodemographic and clinical characteristics exerted a strong influence on the access to prostate cancer treatment.*

Keywords *Health services accessibility, Health equity, Time-to-treatment, Prostatic neoplasms*

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Introduction

Prostate cancer is the second most common form of cancer among men and the fifth leading cause of death for men around the world[1]. In Brazil, 61,200 new cases are estimated for the biennium 2016/2017, representing an estimated risk of 61.82 cases per 100,000 men[2]. It has a growing mortality and incidence rate, although its magnitude is lower[2].

Although survival rates after the diagnosis of prostate cancer have improved in the last two decades, survival analyses of socioeconomic status suggest inequalities, indicating a worse prognosis for lower income individuals[3]. Black men also have a higher risk of being affected and dying from this type of cancer, which may be related to the difficult access to health services and different therapeutic approach[4,5].

The study revealed that men diagnosed in health systems that serve mainly populations of low socioeconomic status tend to have a significantly higher risk and disease staging compared to those seen in other services (even at comparable ages), a phenomenon that cannot be explained only by racial distributions[6]. Thus, unequal access to health services clearly plays a crucial role in delayed diagnosis and treatment[7].

In 2012, the Brazilian government published Law 12.732, which establishes a 60-day deadline for the onset of treatment in the Unified Health System (SUS) after diagnosis for all types of neoplasms, with the objective of minimizing and eliminating gaps in the access to cancer treatment[8]. A universal and comprehensive approach, according to the doctrinal precepts of SUS is required to achieve this.

Thus, in order to verify whether access to prostate cancer treatment has been equitably promoted by the health care network, this study aims to evaluate the association of sociodemographic and clinical variables with the time to begin treatment of men attended at a an oncology hospital of reference in the State of Espírito Santo, Brazil.

Methods

This is a prospective longitudinal cohort study with secondary data. The study population consisted of men with prostate cancer treated in the period from 2010 to 2014, except for the year 2012, at the Hospital Santa Rita de Cássia Hospital – Women's Association of Education and Fight against Cancer (HSRC-AFECC), located in the municipality of Vitória, Espírito Santo, Brazil. The hospital is accredited by the SUS as a High Complexity Oncology Center (CACON) and is a reference in the State of Espírito Santo.

We excluded men who started treatment at another hospital, in active surveillance, with treatment paid by health plans or private outlay, as well as cases with incomplete records of time-related variables. The exclusion of these individuals is justified because the study was carried out in a reference hospital and it was interested in evaluating the population at all stages of the treatment funded by SUS. Cases diagnosed in 2012 were not included in the survey in order to avoid the possible effect of adapting the service to comply with Law 12.732. Thus, since 2012 was the year of implementation, it was decided not to include it.

Data were extracted from the Tumor Registry Data Sheets that provide data for the Hospital Cancer Records Information System (SISRHC) and medical records. For the collection of data that were not included in the Tumor Registry Data Sheets, a specific tool developed by the researcher was used to analyze medical records and contained the following variables: clinical staging, Gleason score, prostate-specific antigen (PSA) levels, outcome, date of last consultation and of referral to HSRC-AFECC.

Data were tabulated in the Microsoft Office Excel 2007 program and later analyzed through the Statistical Package for Social Sciences (SPSS), version 20.0. The statistical analysis used frequency calculations, measures of central tendency (mean and median) and variability (standard deviation). Chi-square tests of association between the times of diagnosis and the onset of treatment and between the first consultation and the onset of treatment with the sociodemographic and clinical variables of the study were applied. The level of significance was set at 0.05. Odds ratios were calculated and adjusted by the logistic regression model for all variables with a p-value < 0.10.

The project was submitted to the Research Ethics Committee of the Health Sciences Center of the Federal University of Espírito Santo and approved.

Results

In the study period, 1,940 men with a diagnosis of prostate cancer were attended at the HSRC-AFECC. Of this total, we excluded 304 (15.6%)

because they started treatment outside the HSRC-AFECC, 190 (9.8%) because they were on active surveillance and/or did not generate an income value, 34 (1.7 %) because their treatment was funded by a health plan or private outlay and 14 (0.7%) because they lacked information. The study population was arrived at 1,388 men.

Table 1 shows the results of the associations of sociodemographic variables and service times.

We found that the highest percentage of men who had started treatment within 60 days, counted from the first consultation at the HSRC-AFECC were those aged 71 years or older (p = 0.001). However, non-whites had a time interval greater than 60 days between the first consultation and treatment (p = 0.050). As for schooling, most of those enrolled started treatment within 60 days, both from the date of diagnosis (p = 0.027) and the date of the first consultation at the hospital (p = 0.022). Thus, being under 70 years of age, being non-white and having less than eight years of schooling were determinants of delayed treatment initiation.

In relation to the effects of Law 12.732, there was no difference in the time between diagnosis and the onset of treatment, however, there was a greater interval between the date of the first consultation and the onset of treatment (p = 0.020).

Subjects who were referred to the hospital without diagnostic confirmation had a shorter time to treatment, both from diagnosis (p = 0.001) and first consultation at the HSRC-AFECC (p = 0.001). This was the case with those whose referral origin was non-SUS services, most of which

Table 1. Sociodemographic characteristics of men with prostate cancer attended at the HSRC-AFECC, Vitória (ES), Brazil.

Variables	**Time between diagnosis and onset of treatment**					**Time between first consultation and onset of treatment**				
	Under 60 days		**60 days and over**			**Under 60 days**		**60 days and over**		
	N	**%**	**N**	**%**	**p-value**	**N**	**%**	**N**	**%**	**p-value**
Age										
Under 70 years	111	14%	661	86%	0.062	310	40%	462	60%	0.001
71 years and over	105	18%	474	82%		321	55%	258	45%	
Age group										
Under 54 years	13	15%	76	85%	0.088	32	36%	57	64%	0.001
55-59 years	14	12%	99	88%		50	44%	63	56%	
60-64 years	26	12%	188	88%		79	37%	135	63%	
65-69 years	49	16%	252	84%		135	45%	166	55%	
70-74 years	36	14%	223	86%		112	43%	147	57%	
75-79 years	46	20%	181	80%		136	60%	91	40%	
80 years and over	32	22%	116	78%		87	59%	61	41%	
Skin color / ethnicity										
White	46	16%	238	84%	0.865	146	51%	138	49%	0.050
Non white	157	16%	838	84%		446	45%	549	55%	
Years of schooling										
Under 8 years	158	16%	847	84%	0.027	464	46%	541	54%	0.022
9 years and over	32	23%	106	77%		78	57%	60	43%	
Law of 60 days										
Before the Law	109	16%	584	84%	0.789	345	50%	348	50%	0.020
After the Law	107	16%	551	84%		286	43%	372	57%	
Previous diagnosis										
No diagnosis and no treatment	58	32%	125	68%	0.001	18	10%	165	90%	0.001
With diagnosis and no treatment	158	14%	1010	86%		613	52%	555	48%	
Referral origin										
SUS	111	12%	787	88%	0.001	386	43%	512	57%	0.001
Non SUS	58	28%	148	72%		135	66%	71	34%	

showing a time interval of under 60 days to start treatment, counted from the first consultation to the institution (p = 0.001).

Table 2 shows the clinical variables. We can observe that the greater the clinical staging, the Gleason score and PSA levels, the higher the probability of the treatment starting within 60 days, both when based on the date of diagnosis (p = 0.001) and the date of the first consultation at the HSRC-AFECC (p = 0.001). Men with more advanced disease have priority in establishing and initiating definitive treatment, whereas those with localized disease tend to wait longer to start treatment.

Table 3 shows crude and adjusted odds of the logistic regression model of the sociodemographic and clinical variables that showed p < 0.10, when associated to the time between diagnosis and first consultation at the specialized service. The adjusted OR showed a greater risk of delay in time between diagnosis and first consultation at the HSRC-AFECC of men who arrived at the institution with diagnosis (OR = 3.08; CI = 1.79-5.29), who were referred by SUS services (OR = 2.45, CI = 1.56-3.85), who had a Gleason score from 2 to 6 (OR = 2.59, CI = 1.55-4.32) and PSA levels below 10 ng/dL (OR = 4.42, CI = 2.59-7.54).

While Table 4 expresses crude and adjusted odds of sociodemographic and clinical variables associated with the time between the first consultation and onset of treatment at the HSRC-AFECC, we can identify that the adjusted OR poses a greater risk of delay for treatment in men with up to 54 years (OR = 2.59; CI = 1.13-5.96), non-white (OR = 1.45; CI = 1.01-2.11), with up to 8 years of study (OR = 2.04; CI = 1.20-3.48), originating from the SUS (OR = 2.26; CI = 1.49-3.44), with PSA below 10 ng/dL (OR = 2.38; CI = 1.60-3.54), and in those with PSA ranging from 10 to 19 ng/dL (OR = 2.18, CI = 1.43-3.33). However, reaching the hospital with diagnosis and no treatment was a protective factor (OR = 0.03; CI = 0.01-0.09).

Discussion

This study assumes the analysis of factors associated with delayed care, diagnosis and onset of treatment of men with prostate cancer attended at a state hospital of reference in oncology.

We observed that men older than 71 years mostly began treatment within 60 days of the first consultation at the institution, while those under 70 years of age exceeded this period. A study conducted in Canada[9] identified that individuals over 70 years of age had a longer delayed referral to the urologist. However, those under 70 took longer to receive the first fraction of ra-

Table 2. Clinical characteristics of men with prostate cancer attended at the HSRC-AFECC, Vitória (ES), Brazil.

Variables	Time between diagnosis and onset of treatment					Time between first consultation and onset of treatment				
	Under 60 days		60 days and over			Under 60 days		60 days and over		
	N	%	N	%	p-value	N	%	N	%	p-value
Staging										
1	7	9%	68	91%	0.001	29	39%	46	61%	0.001
2	28	10%	244	90%		118	43%	154	57%	
3	16	18%	71	82%		44	51%	43	49%	
4	57	40%	87	60%		92	64%	52	36%	
Gleason score										
2-6	58	9%	557	91%	0.001	246	40%	369	60%	0.001
7	54	15%	316	85%		180	49%	190	51%	
8-10	97	28%	253	72%		190	54%	160	46%	
PSA										
Less than 10	51	10%	478	90%	0.001	198	37%	331	63%	0.001
10-19	34	11%	265	89%		132	44%	167	56%	
20 and over	116	29%	282	71%		246	62%	152	38%	

Table 3. Absolute frequency and percentage of the total by time between diagnosis and first consultation and adjusted frequency of sociodemographic and clinical variables of men with prostate cancer attended at the HSRC-AFECC, Vitória (ES), Brazil.

Categories	Time between diagnosis and first consultation > 60 days							
	Odds Crude				Odds Adjusted			
	p-value	OR	LL 95%	UL 95%	p-value	OR	LL 95%	UL 95%
Age								
Under 70 years	0.063	1.32	0.99	1.77				
71 years and over		1.00						
Age group								
Under 54 years	0.185	1.61	0.80	3.27	0.793	1.15	0.40	3.28
55-59 years	0.055	1.95	0.99	3.86	0.325	1.65	0.61	4.48
60-64 years	0.017	1.99	1.13	3.52	0.655	1.19	0.55	2.57
65-69 years	0.168	1.42	0.86	2.33	0.551	0.81	0.41	1.62
70-74 years	0.046	1.71	1.01	2.89	0.163	1.68	0.81	3.47
75-79 years	0.752	1.09	0.65	1.80	0.562	0.81	0.40	1.64
80 years and over		1.00				1.00		
Years of schooling								
Under 8 years	0.028	1.62	1.05	2.49	0.065	1.70	0.97	3.00
9 years and over		1.00				1.00		
Previous diagnosis								
No diagnosis and no treatment		1.00				1.00		
With diagnosis and no treatment	0.001	2.97	2.08	4.22	0.001	3.08	1.79	5.29
Referral origin								
SUS	0.001	2.78	1.93	3.99	0.001	2.45	1.56	3.85
Non SUS		1.00				1.00		
Gleason score								
2-6	0.001	3.68	2.57	5.27	0.001	2.59	1.55	4.32
7	0.001	2.24	1.55	3.25	0.098	1.51	0.93	2.47
8-10		1.00				1.00		
PSA								
Less than 10	0.001	3.86	2.69	5.53	0.001	4.42	2.59	7.54
10-19	0.001	3.21	2.11	4.87	0.007	2.02	1.22	3.37
20 and over		1.00				1.00		

LL = Lower Limit; UL = Upper Limit.

diotherapy. A research conducted in Baltimore, USA[10] found that the mean age of men who had a delay of less than six months for surgery was 59 years, while the mean age of those who delayed more than six months for surgery was 61 years. In the United Kingdom[11], long intervals between diagnosis and surgery were associated with increased age and individuals over 65 years had on average 97 days of waiting for surgery. The results found in this research seem to indicate that the health institution has reduced obstacles to access and use of health actions, giving priority to meeting the individual needs of the elderly.

Skin color/ethnicity has been treated as a variable that conditions access to health services. In this study, more than half (55%) of non-whites took more than 60 days to start treatment from the first consultation, pointing to the interrelationships between the socioeconomic and racial inequalities that generate these gaps in access to health. In the United States[12], research also identified that black men were more likely to delay initiating treatment when compared to white men. Another American study[13] found that African Americans had the longest intervals between diagnosis and treatment in all risk groups, and this difference is exacerbated in the high-risk group. In Brazil[14], a research indicated that skin color influenced the type of treatment, in which blacks were less prone to the surgical procedure.

Table 4. Absolute frequency and percentage of the total by time between the consultation and the onset of treatment and adjusted frequency of sociodemographic and clinical variables of men with prostate cancer attended at the HSRC-AFECC, Vitória (ES), Brazil.

Variables	Time between first consultation and onset of treatment > 60 days							
	Odds Crude				Odds Adjusted			
	p-value	OR	LL 95%	UL 95%	p-value	OR	LL 95%	UL 95%
Age								
Under 70 years	0.001	1.85	1.49	2.31				
71 years and over		1.00						
Age group								
Under 54 years	0.001	2.54	1.48	4.37	0.025	2.59	1.13	5.96
55-59 years	0.020	1.80	1.10	2.95	0.021	2.40	1.14	5.05
60-64 years	0.001	2.44	1.59	3.74	0.014	2.22	1.18	4.18
65-69 years	0.006	1.75	1.18	2.61	0.053	1.81	0.99	3.32
70-74 years	0.003	1.87	1.24	2.82	0.086	1.71	0.93	3.16
75-79 years	0.828	0.95	0.63	1.45	0.665	0.87	0.45	1.66
80 years and over		1.00				1.00		
Skin color / ethnicity								
White		1.00				1.00		
Non white	0.050	1.30	1.00	1.70	0.052	1.45	1.00	2.11
Years of schooling								
Under 8 years	0.023	1.52	1.06	2.17	0.008	2.04	1.20	3.48
9 years and over		1.00				1.00		
Law of 60 days								
Before the Law		1.00				1.00		
After the Law	0.020	1.29	1.04	1.60	0.199	1.23	0.90	1.68
Previous diagnosis								
No diagnosis and no treatment		1.00				1.00		
With diagnosis and no treatment	0.001	0.10	0.06	0.16	0.001	0.03	0.01	0.09
Referral origin								
SUS	0.001	2.52	1.84	3.46	0.001	2.26	1.49	3.44
Non SUS		1.00				1.00		
Gleason score								
2-6	0.000	1.78	1.37	2.32	0.032	1.58	1.04	2.40
7	0.131	1.25	0.94	1.68	0.074	1.49	0.96	2.31
8-10		1.00						
PSA								
Less than 10	0.001	2.71	2.07	3.54	0.001	2.38	1.60	3.54
10-19	0.001	2.05	1.51	2.78	0.001	2.18	1.43	3.33
20 and over		1.00						

LL = Lower Limit; UL = Upper Limit.

Ethnical disparities in prostate cancer care have been documented in all neoplasm management stages, from introduction, diagnosis, treatment, survival to death, and black men had the highest burden in the whole care process[15]. Such disparities are complex and involve determinants of biological, socioeconomic and sociocultural nature[15-17]. Despite the recent debate on prejudice and discrimination, as in other societies marked by a history of colonization and slavery, ethnic and racial prejudice is still very much alive in Brazil, as are inequalities unfavorable to blacks, browns and indigenous people[18].

Regarding the constraints or inequalities in access to diagnostic procedures and treatment in Brazil, it is important to note that people who identify their ethnicity or skin color as brown or black tend to belong to lower income and schooling groups[19]. Schooling influenced both the time between diagnosis and treatment and between the first consultation at the HSRC-AFECC and the onset of treatment. In both cases, men under eight schooling years generally started treatment at a time interval greater than 60 days, while the ones with higher schooling years received the first treatment at a shorter interval. In the two US studies cited above[12,13], both found that black men were younger, had lower income and with a lower educational level when compared to whites. However, a Spanish study[20] did not find an association between the time elapsed from the diagnosis to the first treatment with the educational level. Although inequalities by schooling level in the use of health services are decreasing consistently in Brazil[19], it is still a huge challenge. However, these inequalities can also be attributed to different behaviors when seeking health care. People in the lower schooling groups may postpone the decision to seek health care due to negative experiences to obtain care in the basic network, or prejudices and fears related to the rectal touch problematized by hegemonic masculinity[21], or due to other factors such as the impossibility of missing work.

Regarding Law 12.732, it can be seen that it has not yet had any impact on the time between diagnosis and treatment in the hospital institution, only negatively affecting the interval between the first consultation and the treatment. In the years following the Law, approximately 60% of men with prostate cancer started receiving therapy after 60 days of the first hospital visit. Surveys regarding the waiting time for the treatment of men with prostate cancer in the country are incipient and did not exist in the period after the publication of the Law. In this context, an important aspect to be considered concerns recommendations for the prevention and treatment of prostate cancer, which are both diverse and somewhat controversial between different takes[21], including the indication of expectant behavior as a therapeutic approach, especially for older individuals or those with other important health problems.

It was observed that arriving at the hospital without diagnosis and without treatment presupposes a greater probability of starting the treatment within 60 days, counted both from the first consultation at the institution and from the date of diagnosis. This fact is also identified in a study that analyzed the time between diagnosis and treatment of elderly women with breast cancer, reporting that women who received the diagnosis and all the treatment in the service evaluated achieved better times[22]. However, previous research in the HSRC-AFECC[23] identified that men who arrived with diagnosis and without treatment were less likely to be in the late stage, whereas those who came without diagnosis and without treatment tended to have more advanced stages. In this case, it is necessary to consider, in particular, the poor organization of the regionalized service network, with mechanisms that are still ineffective in terms of regulation and referrals and counter-referrals due to structural, procedural and political obstacles, such as imbalance of power between among network members, the lack of accountability of stakeholders involved, administrative discontinuities and high turnover of managers.

Regarding the origin of referrals, men referred by establishments of the SUS had longer intervals between the diagnosis and the treatment and consultation and the treatment, in comparison with individuals referred by private health establishments. A North American study[15] highlighted that adequate coverage of health plans can be an important determinant in the detection of the tumor of prostate cancer in curable stage, enabling a timely treatment and reducing disparity. Another study developed in the United States[24] found an association between having a public health plan with conservative treatment, as well as advanced age, blacks, singles, PSA above 20 ng/dl, low Gleason score (2-4) and comorbidities. A study conducted in the State of São Paulo[14] described the profile of men with prostate cancer from the SUS as being black, elderly, with high PSA, greater probability of metastasis and less likely to receive definitive treatment, such as surgery. Findings of the Brazilian research show similarities with the aforementioned American research, although both were carried out in different health system contexts, one of which was universal, and the other not. While the use of services varies widely between those who have health plans and those who do not, we have found that the gap between these two groups is decreasing[19]. However, according to these authors, as the private sector market increases, interactions between public and private sectors create contradictions and unfair competition, generating negative results in equity, access to health services and health conditions[19,21]. The different care between SUS and Non-SUS remind us the double gateway issue, which refers to institutions that attend SUS patients and private patients, as is the case of the HSRC-AFECC, which is a philanthropic hospital. This highlights possible shortcuts that individuals with a health or private plan use to jump the waiting queue for care in the hospital paid by the SUS. In healthcare establishments with a double gateway, there is a clear tendency to prioritize private care over patients funded by the public system[25-27]. Criticisms point to the fact that the "double gateway" generates a double waiting queue and course within the institution, therefore segregating and/or excluding not only from the outside, but also within the hospital[26].

Regarding the clinical variables, in both times, an association between advanced stage, high Gleason score and high PSA (above 20 ng/dL) was found, with shorter times to start treatment. In Canada[9], a research revealed that from the diagnosis to the start of radiotherapy, intermediate- and high-risk men had a shorter waiting time when compared to those at low risk. As in Spain[20], men with high PSA and high Gleason score obtained a lower interval between diagnosis and treatment.

Authors emphasize that for men of intermediate and high risk, the three-month period is acceptable for the choice of treatment, and the waiting lists of these patients should not exceed this period[27]. They further evidence that delayed treatment may favor the loss of the curability opportunity in men at high-risk, however, the delay may have no impact on the results among men with a lower risk tumor[27].

We found that determinants that condition the therapeutic approach of men with prostate cancer attended at the HSRC-AFECC, revealing inequitable access, since men of low socioeconomic level (non-white, less educated and SUS services users) are the ones with the greatest delays in the onset of treatment. Associations found between the times with the sociodemographic variables reveal differences that are unfair, as they harm the ones that need care the most, and there is no basis or recommendation for such an approach. This finding suppresses the principle of equity that should underlie the actions of health services, which seeks equal access of different population groups to SUS by reducing systematic differences that are unnecessary and avoidable[28].

However, regarding the findings of the research in relation to the clinical variables, it is in agreement with what is advocated in prostate cancer care. Individuals in more advanced stages take priority to start treatment, while those with earlier stages tend to wait longer for the definition of therapy, since prostate cancer is a slow-developing neoplasm in the vast majority of cases. However, Law 12.732 applies to all types of neoplasms, not going into detail about specificities of each cancer. Thus, the 60-day deadline to start treatment should be applied in all situations.

Disparate attendance in a service that is intended to be universal, comprehensive and equitable should never prevail; on the contrary, it is necessary to eliminate it from the work process. To this end, evaluating work and health service organization practice is a key tool for planning and promoting adaptations in the modalities of care. Thus, enabling minimum conditions of access to the population should be the basic premise of all services, since it is the gateway to interact with the health system. The growing population requires seeking formulas that meet quantitatively increasing needs and, at the same time, more equitably, efficiently and effectively[29].

Access does not only focus on characteristics related to geographical issues or the availability of a service at any given time and/or place[30,31], it is how people get in touch with the health system[32]. Ensuring this right to the population requires thinking of all the aspects that may affect the institutionalization of this analytical category, such as socioeconomic, cultural, demographic and relational factors[32-34]. Thus, having access as a tool for evaluating health actions presumes a greater vision of the processes operationalized by the SUS health care network, as well as the organization of work methods, within an ethical and right to citizenship[29] perspective.

The limitations of the study are related to possible information and selection bias, since a secondary data source was used and was subject to variations in records and incomplete information. Another limitation is the possible sampling bias, since a greater number of late-stage cases may have been referred to the HSRC-AFECC more frequently, since it is a reference institution in oncology[23].

Therefore, in order to overcome the challenges faced by the Brazilian health system, a deep review of public-private relationships and persistent inequalities will be necessary in order to ensure universal and equitable access at all levels of care. Managers and professionals must analyze the flows of care and attendance to promote adaptations in the organization and structure of the work process, in order to develop a humanized, welcoming and inequality-free practice.

Collaborations

RS Sacramento, LJ Simião, KCG Viana, MAC Andrade, MHC Amorim and E Zandonade participated in the different parts of the article.

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