Cancer Epidemiology 72 (2021) 101940

Contents lists available at ScienceDirect

Cancer Epidemiology

journal homepage: www.elsevier.com/locate/canep

Follow-up of women screened for cervical cancer in São Paulo, Brazil: An analysis of the times to diagnostic investigation and treatment

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ARTICLE INFO

Keywords:
Uterine cervical neoplasms
Mass screening
Cohort studies
Health planning

ABSTRACT

Background: Cervical cancer incidence and mortality rates are higher in Brazil than in western countries. Access to cytology-based screening has increased in the country in recent decades, but few studies have assessed the quality of the follow-up care of women with abnormal screening tests that require further investigation.
Methods: A record-linkage cohort study was conducted in São Paulo state. Women aged 25+ years, who were screened in 2010, and whose test revealed a high-grade, or more severe, lesion were eligible. Follow-up information on diagnostic investigations, treatments and mortality was obtained through record-linkage of health databases. The Kaplan-Meier method was used to estimate median times between screening and diagnostic investigation, and diagnosis and treatment initiation. Cox survival models were used to identify correlates of the length of these time intervals.
Results: 4300 women had a high-grade, or more severe, test result. Of these, 2788 (64.8 %) had a diagnostic investigation record, 1763 (41 %) a confirmed diagnosis of a precursor lesion or cancer, and 1247 (70.7 %) a treatment record. The median time to diagnosis was 190 days, with the probability of undergoing a diagnostic investigation within 30 days of the abnormal screening test being 7%. The median time to treatment was 81 days, with the probability of undergoing treatment within 60 days of a confirmed diagnosis being 44 %. Delays in diagnosis and treatment were associated with area-based healthcare indicators.
Conclusion: Times to diagnosis and treatment were long, well above recommendations. Strategies to improve follow-up care must be prioritized to ensure screening reduces cervical cancer incidence and mortality.

1. Introduction

Cervical cancer – a preventable and potentially curable disease – affected over 500 thousand women, and killed over 300 thousand, worldwide in 2018. Therefore, a strategy for eliminating cervical cancer as a public health problem has been adopted by the World Health Organization, which includes HPV vaccination, screening, and appropriate management of pre-neoplastic lesions and invasive cancer [1].

Mortality from cervical cancer is higher in Brazil than in high-income countries. Brazil has a population of about 210 million inhabitants, of which almost 60 million are women in the target age group for cervical cancer screening (25–64 years). The country has a universal health system – the Unified Health System (SUS) – used by about 80 % of its population [2]. HPV vaccination of adolescent girls was implemented nationally in 2014, with the first dose of the vaccine having achieved a coverage above 80 % [3].

Cervical cancer screening based on cytology was initiated in the 1980s, but it is still carried out in an opportunistic way, and early cancer detection strategies, while guided by national guidelines, are implemented differently by municipal and state managers [4,5]. Consequently, marked geographical differences have been observed in the uptake of screening, access to diagnosis and treatment of cervical cancer

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https://doi.org/10.1016/j.canep.2021.101940
Received 5 November 2020; Received in revised form 5 April 2021; Accepted 12 April 2021
Available online 24 April 2021

and its precursors, as well as in the incidence of, and mortality from, the disease [6,7].

For a screening program to be effective in reducing incidence of, and mortality from, cervical cancer it must have not only high coverage but also provide adequate mechanisms to ensure the appropriate follow-up of women with screen-detected cervical abnormalities requiring diagnostic investigation and, eventually, treatment [8]. Monitoring and evaluation of the quality of follow-up care in Brazil has been hampered by the fragmented nature of its national health information systems [9] coupled with the lack of a unique personal identifier to allow record linkage across multiple databases. A national health card, which assigns a unique identifier to each SUS user, is being gradually implemented in the country, but it is not yet universally used. Consequently, although several studies have evaluated cervical screening coverage in Brazil (e.g. 10–12), few have so far assessed the quality of follow-up care [13,14].

This study used routinely collected data from different national health information systems to assess the quality of the follow-up care given to women with screening abnormalities by examining the length of the time intervals between screening and diagnosis, and between diagnosis and treatment initiation, for high-grade or more severe cytological lesions in the state of São Paulo, the most populous state in Brazil with almost 46 million inhabitants, corresponding to 20 % of the country's total population.

2. Methods

2.1. Study population and follow up

We identified a cohort of women living in the state of São Paulo, aged 25 years or older, who were screened for cervical cancer in SUS in 2010, and whose screening test result was recorded in the cervical cancer information system (SISCOLO) as being a high-grade cervical lesion, squamous cell carcinoma, or adenocarcinoma.

According to the Brazilian national screening guidelines [5] women aged 25–64 years should have a Pap smear test every 3 years whilst older women who had never had a Pap smear should have two smear tests with an interval of one to three years. If these are normal, women are exempted from additional tests. Thus, all women screened in 2010 who had a high-grade, or a more severe, cytological lesion, and who were aged 25 years and over, were regarded as potentially eligible for this study.

Women who had a record, in 2009, of an abnormal test (atypical cells, low- or high-grade lesions, and carcinomas) or a record of a treatment for precursor lesions or cervical cancer, were regarded as prevalent cases and excluded to ensure that only those with a newly screen-detected abnormality in 2010 were included in the study. Women residing in the Campinas health administration were also excluded from the study because their main referral health facility, i.e. the local University, operates outside SUS and, hence, does not use its health information systems.

The eligible cohort was followed up to the end of 2013 through probabilistic linkage of several health information systems. The follow-up period reflected data availability and completeness as, from 2013 onwards, SISCOLO began to be gradually replaced with a new online system (SISCAN), with many health facilities experiencing temporary problems with the computerization of their records.

SISCOLO provided data on screening tests and biopsy results. Results of all Pap Smear tests and histological exams performed in SUS must be registered in this health information system, which also collects data on the woman (name, date of birth, address, mother's name) and the health services (e.g. type of healthcare unit, location). Data on biopsies not registered in SISCOLO as well as on large-loop excision of the transformation zone, chemotherapy and radiotherapy were obtained through linkage to the SUS Outpatient Information System (SIA/SUS) Data on conization and surgical procedures (i.e. hysterectomy, trachelectomy) were obtained from the SUS Hospital Information System (SIH/SUS), and data on deaths from the Mortality Information System (SIM).

Probabilistic record linkages were performed using the Reclink software, which generates a summary score of the degree of agreement between pairs of records on *a priori* defined fields [15]. The software is widely used in research conducted in Brazil, with sensitivity values ranging from 86 % to 91 %, and specificity from 99 % to 100 % [16–18]. In a record-linkage study based on databases similar to those used in the present study, sensitivity for cervical cancer data was 97.5 % and specificity 99.3 % [19]. In the present study, the probabilistic record linkage was based on all the available personal identification fields (i.e. woman's name, date of birth and address, and mother's name). The pairs of records that did not obtain the maximum Reclink agreement score were visually inspected and classified as being concordant or discordant.

2.2. Data analysis

The primary outcomes of the study were the length of the time interval between a screen-detected high-grade, or more severe, lesion and the final diagnosis (time to diagnosis) and the length of the time interval between a confirmed diagnosis and initiation of treatment (time to treatment). Time to diagnosis was calculated by the difference (in days) between the date of the release of the screening test report and the date of the first of the following events: (i) release of the biopsy's result; (ii) registration of an excisional treatment; (iii) registration of a repeat screening test with a normal result or minor lesions within six months of the original test; (iv) date of death; or (v) the last day of the follow-up period (31st December 2013). Women in (iv) and (v) were assumed to have remained undiagnosed until the date of their death or the end of follow-up, respectively.

Women with a high-grade lesion for whom no biopsy record was found, but who had a record of excisional treatment, were assumed to have undergone the 'see-and-treat' method, whereby they were submitted to excisional treatment of the lesion without undergoing a biopsy. In these circumstances, the treatment procedure was also the diagnostic investigation [20,21], and, hence, the date of treatment was considered to be also the date of the diagnosis.

According to the clinical guidelines of the Ministry of Health [5], women whose cytological test was classified as a high-grade lesion, but whose colposcopy was normal, should repeat the cytology test within six months, or had their original cytology slides reviewed, with their clinical management being reassessed according to the new result. As data on colposcopy results is not captured by the existing health information systems, a repeat cytological test was considered a diagnostic investigation procedure if: (i) it was conducted within 6 months of the original cytology; (ii) it was normal or revealed only minor abnormalities; and (iii) no biopsy or treatment records for the women were found.

Analysis of time to treatment was restricted to women with a confirmed diagnosis, that is, those with a record of a biopsy result of a CIN2, CIN3, squamous cell carcinoma or adenocarcinoma or, in the absence of a biopsy record, those with a record of an excisional procedure (as discussed above). Time between confirmed diagnosis and treatment was calculated by the difference (in days) between the date of the biopsy result and the date of the first of the following events: (i) first treatment received; (ii) registration of an excisional treatment (for women who were subjected to the see-and-treat method, the diagnosis and treatment dates were the same); (iii) death; or (v) last day of the follow-up period (31st December 2013). Hence, women with a confirmed diagnosis but for whom no treatment or death record was found in the health information systems were assumed to have remained untreated during the follow-up period.

Women who had no diagnosis nor treatment records in the health information systems, but for whom a death record was found in SIM, were assumed to have remained undiagnosed and untreated until their death and, hence, their follow-up was censored on that date. Women with no diagnostic, treatment nor death records were assumed to have

remained undiagnosed and untreated until the end of the follow-up period. Women with a treatment record (i.e. of surgery, chemotherapy, or radiotherapy) but no record of a diagnostic investigation (n = 428) were excluded as it was not possible to calculate the length of the time intervals between screening and diagnosis, and between diagnosis and treatment.

The probability of performing the diagnostic investigation procedure within 30 days after the altered screening test, and the probability of initiating treatment within 60 days after the confirmed diagnosis, as well as the corresponding median times, and their 95 % confidence intervals (95 % CI), were estimated using the Kaplan-Meier method.

Some of the women regarded as having remained undiagnosed and/or untreated during the follow-up period might have actually been diagnosed and/or treated in SUS, but due to administrative errors or record linkage problems, their diagnostic/treatment records were not traced in the health information systems. In addition, some women might have been diagnosed and treated outside SUS, i.e. in private healthcare facilities. Both circumstances would have led to an artificial increase in the length of the diagnostic and treatment intervals. To gauge this, times to diagnosis and treatment were also estimated among the subset of women for whom a diagnosis and/or treatment record was found.

Cox's proportional hazards model was used to identify factors associated with times to diagnosis and treatment. The quality of healthcare, and availability of diagnostic and treatment procedures for cervical cancer, varies across the various healthcare networks in the state of São Paulo. To account for this heterogeneity, due to unmeasured covariates, the regional health administration of residence of the women in the study was included in the Cox models as a frailty term [22]. The high percentages of missing data on socioeconomic variables (~75 % for ethnicity/skin color; ~65 % for schooling) precluded their use in the analysis. To overcome this limitation, two socio-economic measures of a woman's municipality of residence were taken as proxies for her individual-level socio-economic status. They were: (i) the municipality's primary healthcare (PHC) coverage, categorized as incipient (0 %–29 %), intermediate (30 %–70 %), and consolidated (>70 %) [23]; and (ii) the municipality's rate of gynecologists per 100,000 inhabitants, categorized as 0–5, 6–12, and >12. A linear trend analysis was performed for ordinal variables, categorized as having continuous scores.

The median times to diagnosis and treatment were estimated separately by place of residence according to mutually exclusive strata (capital, metropolitan, and inland). The capital was analysed separately

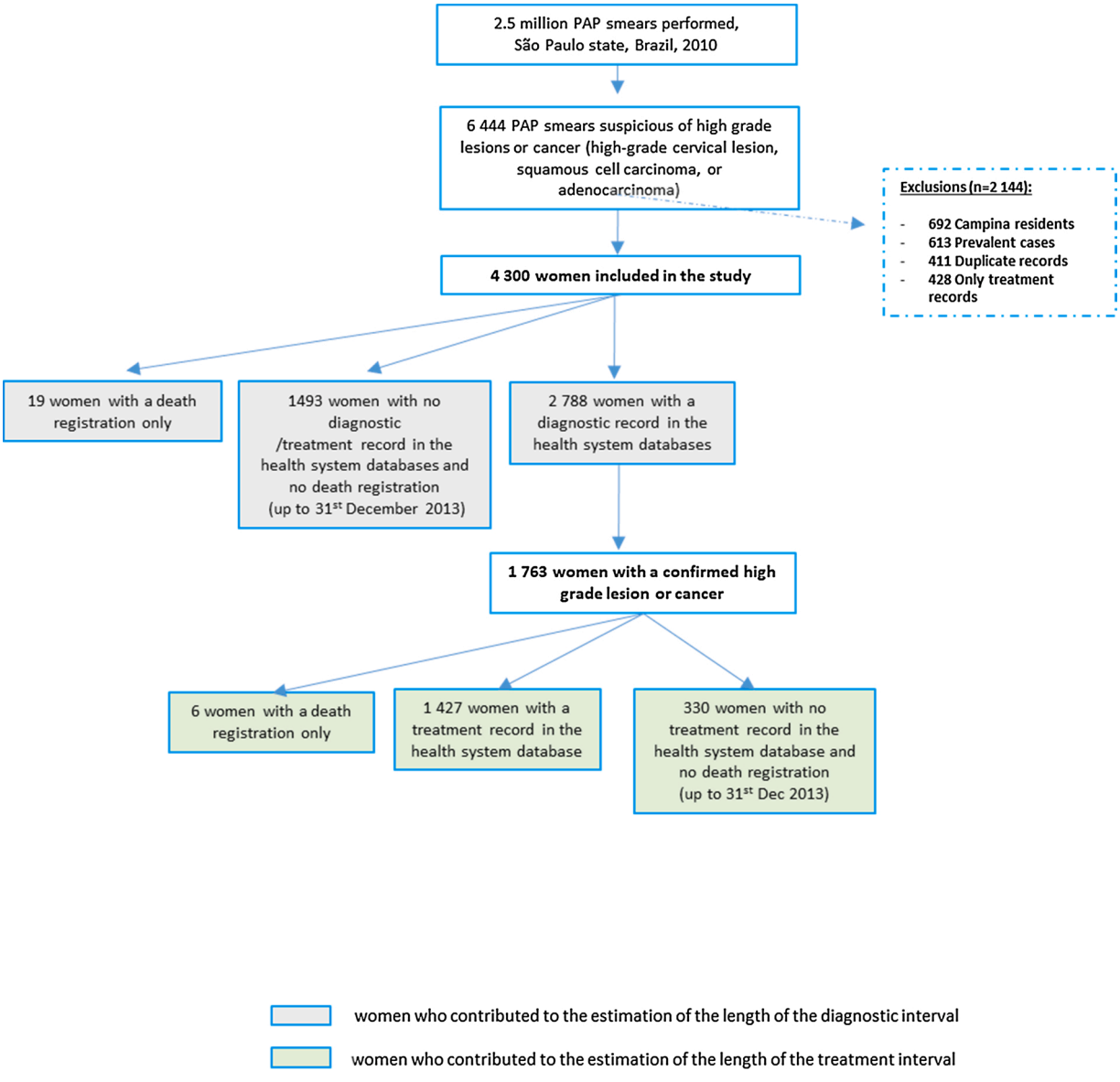

Fig. 1. Flowchart showing the selection of the study participants.

from the rest of the metropolitan region due to its greater concentration of diagnostic and treatment services, providing a different profile of access to healthcare services. Place of residence was not included in the Cox's proportional hazards model because the variable regional health administration, which reflects more closely the level of access to healthcare services, was already included in the model as a frailty term.

The proportional hazard assumption of each variable over time was assessed through graphical and statistical analyses of Schoenfeld's residuals [22]. This assumption was violated by one of the variables examined, i.e. type of healthcare unit where the diagnostic investigation was performed. Hence, type of healthcare unit was included in the adjusted Cox model only to allow estimation of hazard ratios adjusted for this variable, but without estimation of its coefficients. Statistical analyses were performed using the R program [24].

The Research Ethics Committee of the University of São Paulo approved the study.

3. Results

In all, 2.5 million cytopathological tests were recorded, in 2010, in the state of São Paulo, of which 6444 corresponded to a high-grade or more severe lesion. A total of 4300 women were included in the study cohort after removal of duplicate records and ineligible women (Fig. 1).

In all, 55.4 % of the 4300 eligible women were aged 25−40 years, 39.2 % resided in the capital, and 93.3 % had a high-grade lesion in the cytopathological test. Record linkage between the various health information systems retrieved diagnostic investigation records for 2788 (64.8 %) women, but only a death record for 19 women (0.4 %). For 1493 women (34.7 %) no diagnostic, treatment or death records were found (Fig. 1). (Table 1)

Among the 2788 women with a diagnostic investigation record, 68.7 % underwent biopsy, and 1763 (63.2 %) had diagnostic confirmation of a high-grade lesion or cancer.

The probability of undergoing a diagnostic investigation within 30 days of an abnormal screening test was 6.8 % (95 % CI = 6.0 %–7.5 %). The median time between the screening result and the diagnostic investigation was 190 days (95 % CI = 173–214) in São Paulo State overall, 198 days (95 % CI = 166–239) in the capital, 274 days (95 % CI = 212–351) in the metropolitan region (excluding the capital), and 149 days (95 % CI = 135–166) in the inland region (Fig. 2).

Median times ranged from 75 (95 % CI = 62–95) to 277 (95 % CI = 226–357) days across the 17 regional health administrations examined. The median times were shorter among residents of municipalities with consolidated PHC (144 days) and with the highest rates of gynecologists, i.e. ≥ 12 per 100,000 (99 days) (Table 2).

The univariate and multivariate analysis showed no association of age, primary health care coverage and rate of gynaecologists with time to diagnosis (Table 2).

A treatment record was found for 1427 (80.9 %) out of the 1763 women with a confirmed diagnosis of a high-grade lesion or cancer (Fig. 1), with conization being the most frequent treatment procedure (58 %). Of these, 962 (674%) underwent diagnostic investigation and treatment at the same health facility. Diagnosis and treatment were performed on the same day in 33 % (= 471/1427) of women (data not shown).

The median time to treatment varied across the 17 health administrations examined ranging from 0 to 142 days (data not shown). The probability of initiating treatment within 60 days after the confirmed diagnosis was 44 % (95 % CI 41.5 %–46.2 %). The median time between diagnosis and treatment initiation was 81 days (95 % CI = 74–89) in the state of São Paulo overall, 98 days (95 % CI = 83–116) in the capital, 57 days (95 % CI = 44–68) in the inland region, and 103 days (95 % CI = 86–124) in the metropolitan region, excluding the capital (Fig. 3).

The median times between diagnosis and treatment initiation were shorter among women aged over 40 years (72 days), residents in municipalities with consolidated PHC coverage (71 days), and residents of municipalities with a rate of gynecologists below 5/100,000 (70 days) (Table 3).

In the univariate Cox analysis, being over 40 years of age and having had the diagnostic investigation in hospital were significantly associated with shorter times between diagnosis and treatment initiation whilst residing in a municipality with a rate of gynecologists ≤ 5 per 100,000 was associated with a longer time. In the multivariate model being aged >40 years and residing in a municipality with incipient and intermediate PHC were associated with shorter times to treatment initiation, while residing in a municipality with a gynecologist rate <5 per 100,000 was associated with a longer time (Table 3).

Additional analyses of time to diagnosis restricted to women for whom a record of a diagnostic investigation procedure (n = 2788) or a death record (n = 19) was found in the health information systems, showed that the median time between an abnormal screening test result and the diagnostic investigation was, as expected, lower than among the whole study population (95 (95 % CI = 93–95) days versus 198 (95 % CI = 166–239) days, respectively), ranging from 83 (95 % CI = 90–95) days in the inland region to 97 (95 % CI 95-106) days in the capital (data not shown). The probability of undergoing the diagnostic investigation within 30 days of the abnormal screen test was 10.3 % (versus 6.8 % for the whole study population).

Similarly, analysis of time to treatment initiation restricted to

Table 1
Characteristics of the women participating in the study. São Paulo, 2010.

Characteristics	N	%
Age group (years)		
25−40	2383	55.4
>40	1917	44.6
Residence		
Capital	1688	39.3
Inland region	1244	28.9
Metropolitan area, excluding capital	1368	31.8
Screening test result:		
In situ adenocarcinoma	46	1.1
Invasive adenocarcinoma	52	1.2
Squamous cell carcinoma	188	4.4
High grade squamous intraepithelial lesion	4014	93.3
Previous Screening test		
Yes	3205	74.5
No	267	6.2
Don't know	385	9.0
No information	443	10.3
Follow up register		
Diagnosis investigation and treatment	1614	37.5
Only diagnosis investigation	1174	27.3
Only death	19	0.4
No information	1493	34.7
Diagnosis investigation procedure		
Biopsy	1914	44.5
Large-loop excision of the transformation zone (LLETZ)	207	4.8
Cytology	209	4.9
Conization	458	10.7
No diagnosis procedure register	1512	35.2
Diagnosis confirmation		
CIN * II+	1763	41.0%
CIN I/Benign	1025	23.8%
No diagnosis procedure register	1512	35.2 %
First treatment procedure		
Large-loop excision of the transformation zone (LLETZ)	420	9.8
Surgery (hysterectomy or trachelectomy)	148	3.4
Conization	936	21.8
Chemotherapy	42	1.0
Radiotherapy	68	1.6
Not recommended (Benign/CIN I)	1025	23.8
No treatment register	1661	38.6
Cytology repetition before diagnosis		
Yes	662	15.4
No	3638	84.6
Total	4300	**100.0**

* CIN: cervical intra-epithelial neoplasia (CIN).

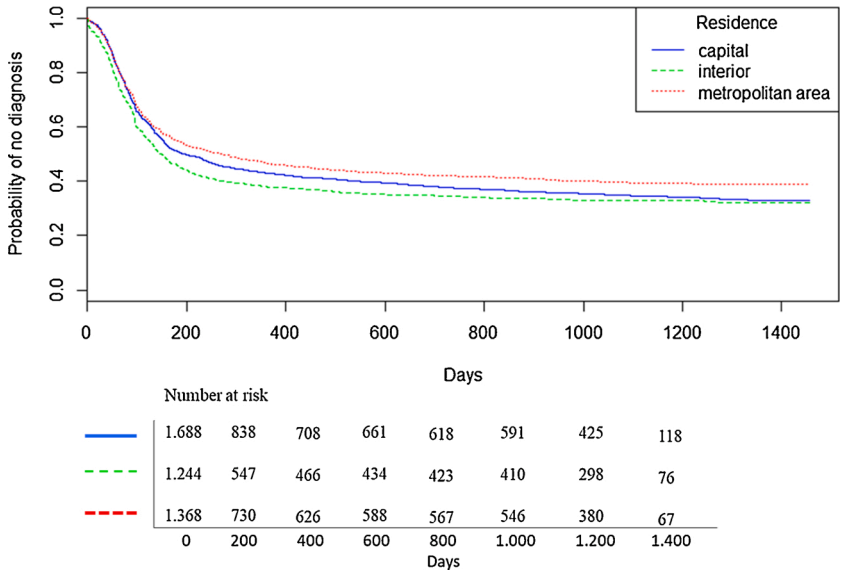

Fig. 2. Time to diagnostic investigation after a high-grade, or more severe, cytology test result, by place of residence. São Paulo, 2010–2013.

Table 2
Time between an abnormal screening test result and the diagnostic investigation, stratified by age and area-based socio-economic measures. São Paulo, 2010-2013 (N = 4300).

Characteristics	N	Median time (days)	Crude HR[a]	95 % CI	Adjusted HR[b]	95 % CI
Age group (years)						
25–40	2383	204	1	–	1	–
>40	1917	179	1.06	0.99–1.15	1.04	0.96–1.12
Primary healthcare (PHC) coverage[c]						
Incipient (<30 %)	503	265	0.89	0.75–1.05	0.90	0.75–1.06
Intermediate (30 %–70 %)	3167	200	0.99	0.86–1.14	1.01	0.88–1.17
Consolidate (>70 %)	630	144	1	–	1	–
*p**			0.79		0.66	
Rate of gynaecologists (/100,000 inhabitants)[c]						
≤ 5	1305	181	0.98	0.85–1.12	0.98	0.85–1.13
6–12	2567	220	0.89	0.75–1.06	0.88	0.74–1.05
>12	428	147	1	1	1	–
*p**			0.17		0.15	

CI: confidence interval; HR: hazard ratio.
* χ^2 for linear trend.
[a] HR estimates from a Cox's proportional hazard model with regional health administration of residence as a frailty term (see Data Analysis section).
[b] HR estimates from a Cox's proportional hazard model which included all the variables in the table (i.e. age of the women, PHC coverage and rate of gynecologists) as well as regional health administration of residence as a frailty term (see Data Analysis section).
[c] PHC coverage and rate of gynecologists of the woman's municipality of residence.

women with a confirmed diagnosis of precursor lesion or cancer for whom a treatment record (n = 1427), or a death record (n = 6), was found in the health information systems showed that the median time was also shorter than among all women with a confirmed diagnosis (48 (95 % CI = 41–57) days versus 81 (95 % CI = 74–89) days), ranging from 33 (95 % CI = 17–48) days in the inland region to 61 (95 % CI = 45–78) days in the metropolitan region, excluding the capital (data not shown).

No diagnostic records were found in the health information systems for 35.2 % (= 1512/4300) of the participants (Fig. 1; Table 4). Relative to women with a diagnostic record, higher proportions of those without such records resided in municipalities with incipient PHC coverage or in those with <5 gynecologists per 100,000 inhabitants (Table 4). In all, no treatment records could be found in the health information systems for 18.9 % (336/1763) of the women with a confirmed high-grade lesion or cancer. Relative to women with a treatment record, high proportions of those without such records were younger, resided in municipalities with higher rates of gynecologists, and were diagnosed in primary and secondary care health services (Table 4).

4. Discussion

In the state of São Paulo, the time interval between an altered screening test and the diagnostic investigation was unacceptably long (median = 190 days), with only 6.8 % of women having undergone a diagnostic investigation within the 30-day interval recommended by organized screening programs. [25,26]

In the present study, 35 % of women, i.e. approximately one in every three, screened in 2010 and whose test result was consistent with the presence of a high-grade cervical lesion, squamous cell carcinoma or an adenocarcinoma, did not appear to have undergone any diagnostic investigation within the next 3 years.

The 2015–2016 biennial report of the National Health System (NHS) Cervical Screening Programme in England showed that 88 % of women referred for colposcopy with a high-grade lesion, or a more severe diagnosis, were treated (52 %), or had a biopsy (37 %), on the same day. This Programme aims to ensure that 90 % of women with a high-grade lesion are treated within four weeks after having the diagnosis confirmed by biopsy [27]. A U.S. study conducted in a screening

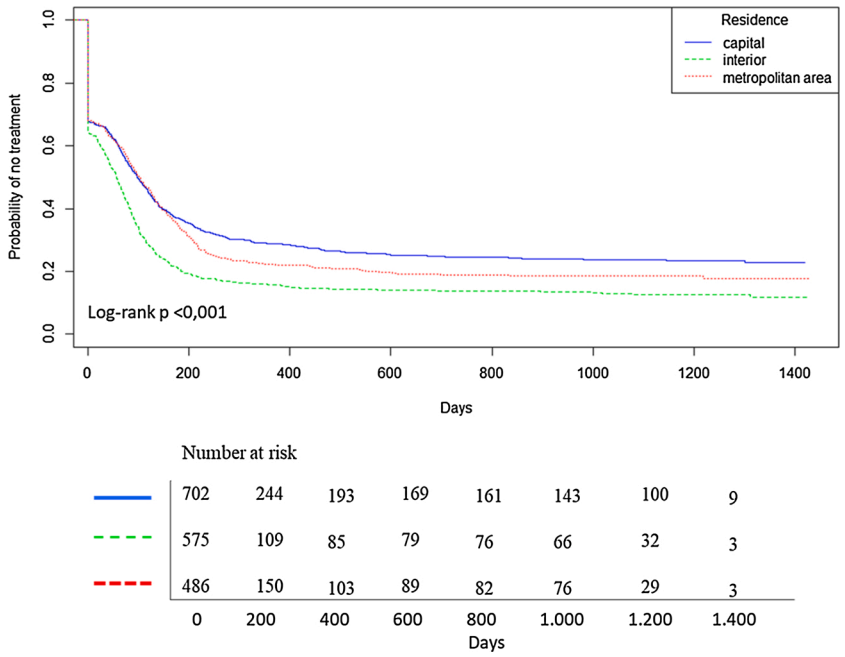

Fig. 3. Time to treatment initiation after a confirmed diagnosis (CIN2 +), by place of residence. São Paulo, 2010–2013.

Table 3
Time to treatment initiation for women with a confirmed diagnosis of a high-grade lesion or cancer, and its correlates. São Paulo, 2010–2013 (N = 1763).

Characteristics	N	Median time (days)	Crude HR[a]	95 % CI	Adjusted HR[b]	95 % CI
Age group (years)						
25–40	987	91	1	–	1	–
>40	776	72	**1.23**	1.10–1.36	1.13	1.02–1.26
Primary health care (PHC) coverage						
Incipient (<30 %)	208	78	1.14	0.92–1.41	1.44	1.16–1.80
Intermediate (30 %–70 %)	1.268	86	1.12	0.92–1.36	1.23	1.02–1.49
Consolidate (>70 %)	287	71	1	–	1	–
*p**			0.3		0.05	
Rate of gynecologists (/100,000 inhabitants)						
≤5	546	70	**0.80**	00.66–0.95	0.76	0.63–0.92
6–12	1.027	91	0.98	0.77–1.24	0.79	0.62–1.02
>12	190	75	1	–	1	–
*p**			<0.01		0.16	
Type of unit that performed the diagnosis[c]						
Primary health care	275	252	0.31	0.26–0.37		
Secondary health care	423	174	0.37	0.32–0.43		
Hospital	1061	0	1	–		

CI: confidence interval; HR: hazard ratio.
* χ^2 for linar trend.
[a] HR estimates from a Cox's proportional hazard model with regional health administration of residence as a frailty term (see Data Analysis section).
[b] HR estimates from a Cox's proportional hazard model which included all the variables in the table (i.e. age of the women, PHC coverage and rate of gynecologists) as well as regional health administration of residence as a frailty term (see Data Analysis section).
[c] Coefficients not calculated due to the loss of proportionality of the variable over time.

program directed at low-income women showed a median time of 48 days between suspicious cases and diagnoses in the years 2003–2009 [26].

In the present study, the median time between diagnosis and first treatment was 81 days (95 % CI = 74–89), well above the 60-day upper limit that the Brazilian law stipulates [28]. It should be noted, however, that this law refers to time to treatment of confirmed malignancy whilst the large majority of women in the present study had a confirmed diagnosis of a precursor lesion.

Women for whom no diagnostic, treatment or death records could be found in the SUS health information systems were considered in this study as having remained undiagnosed, or untreated, up to the end of the study period on the 31st December 2013. It is, however, possible that records could not be traced for some women due to administrative and linkage errors. Similarly, some women might have used private health services. Both these circumstances would have led to an overestimation of the lengths of the diagnostic and treatment intervals. But although the median time to diagnosis was shorter for the subset of women for whom a diagnostic record was found (95 days) than for the for the whole cohort (190 days), it was still well above the limit recommended by organized cervical screening programs. The median time to treatment was also shorter for the subset of women for whom a treatment record was found in the health information systems (48 days) than for all those with a confirmed diagnosis (81 days), and below the 60 days limit stipulated by the Brazilian law.

Accurate estimation of times to diagnosis and treatment would require active follow-up, as opposed to passive follow-up through record-linkage, of screen-detected women with abnormal test results to

Table 4
Characteristics of the study participants according to whether a diagnostic or treatment record was found in the health information systems. São Paulo, 2010-2013.

Characteristic	Diagnostic record		Treatment record[a]	
	Yes N (%)	No N (%)	Yes N (%)	No N (%)
Age group (years)				
25−40	1532 (54.9 %)	851 (56.3 %)	764 (53.5 %)	223(66.4 %)
>40	1256 (45.1 %)	661 (43.7 %)	663 (46.5 %)	113 (33.6 %)
p[*]	0.4		<0.001	
Primary healthcare (PHC) coverage				
Incipient (<30 %)	287(10.3 %)	216 (14.3 %)	168(11.8 %)	40 (11.9 %)
Intermediate (30 %–70 %)	2062 (74.0 %)	1105 (73.1 %)	1017 (71.3 %)	251 (74.7 %)
Consolidate (>70 %)	439 (15.7 %)	191 (12.6 %)	242(17.0 %)	45 (13.4 %)
p[*]		*<0.01*	*0.28*	
Rate of gynecologists (/100,000 inhabitants)				
≤5	828 (29.7 %)	477(31.5 %)	168(11.8 %)	22 (6.5 %)
6–12	1662 (59.6 %)	905 (59.9 %)	455(31.9 %)	91 (27.1 %)
>12	298 (10.7 %)	130 (8.6 %)	804 (56.3 %)	223 (66.4 %)
p[*]	0.07		0.01	
Type of unit where the diagnosis was performed[b]				
Primary health care	–	–	179 (12.5 %)	96 (28.8 %)
Secondary health care	–	–	290 (20.3 %)	133 (39.9 %)
Hospital	–	–	958 (67.1 %)	104 (31.2 %)
p[*]			<0.001	
Total	2788 (64.8 %)	1512 (35.2 %)	1427 (81.1 %)	336 (18.9 %)

[*] Chi-Square.
[a] Includes women with a death registration only (see Fig. 1).
[b] Information on this variable missing for three women.

ensure complete ascertainment of all diagnostic and treatment procedures regardless of whether they were performed in the public or private sector. Nevertheless, it is likely that the true median times to diagnosis and treatment lie somewhere between those estimated for the full cohort and those estimated for the subsets of women for whom diagnostic, or treatment, records were found in the SUS databases.

The proportion of women who resided in municipalities with incipient primary health care coverage was higher among those without a diagnostic record in the health information systems than among those with such records, reflecting perhaps the difficulties faced by those municipalities in referring women for further diagnostic evaluations. Similarly, the proportion of women who had their diagnosis confirmed in primary and secondary healthcare units was higher among those with no treatment records than among those with such records, pointing to barriers in the ability of these units to referring women to tertiary care.

This study shows that access to diagnostic investigation and treatment are obstacles to the follow-up of women with abnormal screen-detected cervical lesions in the Unified Health System (SUS) in the state of São Paulo, and that there are differences in follow-up within the state.

Increasing coverage of primary care programmes have been linked to improvements in several Brazilian health indicators [29,30]. In this study the time interval between screening and diagnosis was not associated with primary care coverage, possibly reflecting the limited capability of primary healthcare to deal with women who require more complex diagnostic investigations.

In contrast, time to treatment was shorter for women who reside in municipalities with incipient or intermediate primary healthcare coverage. This unexpected finding may indicate that small municipalities, without adequate diagnostic investigation services, may refer women who need to be further investigated directly to a referral treatment center. Direct referral to such treatment centers might prolong time to diagnosis as such centers have a limited capability; however, once women reach these centers the time from having a confirmed diagnosis to treatment initiation would be short.

In all, 33 % of women underwent the diagnostic investigation and treatment on the same day, which may be due to the greater dissemination and training of professionals to perform the see-and-treat method. This method is recommended by national guidelines to minimize follow-up losses and reduce costs associated with treatment.

The high proportion of women without a record of diagnostic investigation (35 %) and treatment (19 %) on SUS health information systems was the most important limitation of this study, as discussed above. The high proportion of missing data on the socioeconomic characteristics of the participants precluded the use of individual-level data on these variables in the analysis. Hence, area-based socio-economic indicators, based on a woman's municipality of residence, were used instead in attempt to overcome this limitation.

Most previous studies on factors associated with delays to diagnosis and treatment of cervical cancer focused on women's characteristics such as fear of diagnosis, lack of knowledge about the disease, schooling level, income, and ethnicity/skin color [31,32]. Some qualitative studies conducted in Brazil show that problems in the organization of health services also negatively affect time to treatment of the disease [33,34]. Our findings indicate that local healthcare networks, their resources and level of organization, influence time to diagnosis and time to treatment.

The low coverage of cervical screening in Brazil, which has been documented by previous studies [10,11], coupled with the poor follow-up of abnormalities highlighted in the present study, adversely affects the effectiveness of screening in curbing cervical cancer incidence and mortality in the country. Measures to expand and improve the quality of the follow-up care of women with screen-detected abnormalities should be put in place to ensure timely referral to appropriate diagnostic facilities and, if required, also to treatment in order to control the disease effectively. The SUS health information systems should also be improved to enable better, real-time, monitoring and evaluation of diagnostic and treatment procedures. Progress is already being made on this front. SISCAN, a national online information system, which is being gradually implemented to replace the health information systems used in this study, relies on the universal use of a unique identifier - the national health card number. This facilitates the follow-up of women as primary health care units, particularly those in populous areas, now have direct access to follow-up data, previously available only at the central level.

Authorship contribution

Ribeiro, CM: Substantial contributions to conception and design, acquisition of data, analysis and interpretation of data; drafting the article and final approval of the version to be published.

Silva, GA: Substantial contributions to conception and design, analysis and interpretation of data; revising the article critically for important intellectual content and final approval of the version to be published.

Silva, IS: Substantial contributions to conception and design, analysis and interpretation of data; revising the article critically for important intellectual content and final approval of the version to be published.

Neto, JE: Acquisition of data, revising the article critically for important intellectual content; and final approval of the version to be published.

Cury, LCPB: Acquisition of data, revising the article critically for important intellectual content; and final approval of the version to be published.

Funding

This work was funded by a joint UK-Brazil Newton Fund grant from Research Councils UK (http://www.newtonfund.ac.uk/) and Conselho Nacional das Fundacoes Estaduais de Amparo à Pesquisa (http://confap.org.br/).

CRediT authorship contribution statement

Caroline Madalena Ribeiro: Conceptualization, Methodology, Formal analysis, Investigation, Writing - original draft, Writing - review & editing. **Isabel dos Santos Silva:** Conceptualization, Methodology, Writing - review & editing, Resources. **José Eluf Neto:** Writing - review & editing. **Lise Cristina Pereira Baltar Cury:** Data curation. **Gulnar Azevedo e Silva:** Conceptualization, Methodology, Formal analysis, Resources, Writing - review & editing, Supervision.

Declaration of Competing Interest

None.

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