J Ambulatory Care Manage
Vol. 40, No. 2 Supp, pp. S24–S34

OPEN

Primary Health Care and Cervical Cancer Mortality Rates in Brazil

A Longitudinal Ecological Study

Thiago Augusto Hernandes Rocha, MSc; Núbia Cristina da Silva, PhD; Erika Bárbara Abreu Fonseca Thomaz, PhD; Rejane Christine de Sousa Queiroz, PhD; Marta Rovery de Souza, PhD; Adriana Lein, MSc; João Victor Muniz Rocha, MSc; Viviane Alvares, MSc; Dante Grapiuna de Almeida, BCompSc; Allan Claudius Queiroz Barbosa, PhD; Elaine Thumé, PhD; Catherine Staton, PhD; João Ricardo Nickenig Vissoci, PhD; Luiz Augusto Facchini, PhD

Abstract: Cervical cancer is a common neoplasm that is responsible for nearly 230 000 deaths annually in Brazil. Despite this burden, cervical cancer is considered preventable with appropriate care. We conducted a longitudinal ecological study from 2002 to 2012 to examine the relationship between the delivery of preventive primary care and cervical cancer mortality rates in Brazil. Brazilian states and the federal district were the unit of analysis (N = 27). Results suggest that primary health care has contributed to reducing cervical cancer mortality rates in Brazil; however, the full potential of preventive care has yet to be realized. **Key words:** *health care quality assessment, longitudinal studies, mortality, primary health care, uterine cervical neoplasms*

Author Affiliations: *School of Economics, Center of Post-graduate and Research in Administration (Mr Rocha), Observatory of Human Resources in Health, Faculty of Economics (Dr da Silva and Messrs Rocha and de Almeida, and Ms Alvares), and Department of Administrative Sciences, Faculty of Economics (Dr Barbosa), Federal University of Minas Gerais, Belo Horizonte, Minas Gerais, Brazil; Department of Public Health, Federal University of Maranhão, São Luís, Maranhão, Brazil (Drs Thomaz and de Sousa Queiroz); Department of Public Health, Federal University of Goiás, Goiânia, Goiás, Brazil (Dr de Souza); Duke Global Health Institute, Duke University, Durham, North Carolina (Ms Lein and Drs Staton and Vissoci); and Department of Social Medicine, Faculty of Medicine, Federal University of Pelotas, Pelotas, Rio Grande do Sul, Brazil (Drs Thumé and Facchini).*

This research was funded by the Foundation for Research and Scientific and Technological Development of Maranhão (FAPEMA), Brazil. The authors thank the Brazilian government for the provision of the various open access databases and the participants of the 3 surveys whose data were used in this research.

The authors declare there is no conflict of interests considering the present article.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.ambulatorycaremanagement.com).

Correspondence: *Thiago Augusto Hernandes Rocha, MSc, School of Economics, Center of Post-graduate and Research in Administration, Federal University of Minas Gerais, Belo Horizonte 30270901, Minas Gerais, Brazil (rochahernandes3@gmail.com).*

DOI: 10.1097/JAC.0000000000000185

CERVICAL CANCER is the third most frequent neoplasm among women worldwide (Hernandez-Hernandez et al., 2015). Moreover, the incidence of cervical cancer is 2-fold in low- and middle-income countries when compared with high-income countries (Benjamin et al., 2014). Cervical cancer incidence in Brazil reflects this disparity and contributes to 230 000 deaths annually (Benjamin et al., 2014; de Oliveira et al., 2015; Ministério da Saúde, 2014). Cervical cancer is preventable, and survival is related to timeliness of care and could be increased by expanding access to health services. A projected 150 000 lives could be saved by 2030 through the application of appropriate detection and prevention (Hernandez-Hernandez et al., 2015).

Several factors have been discussed as barriers to accessing preventable health services (Bang et al., 2012; Oscarsson et al., 2008), namely, low socioeconomic status and inadequate coverage of cervical cancer screening (Bigby & Holmes, 2005). The Papanicolaou test has been the primary instrument to detect the disease in its early stages (Roland et al., 2013), contributing to the reduction of mortality in women (Habbema et al., 2012). Besides vaccination against human papillomavirus (HPV), the development of health prevention and promotion measures, in the context of primary care (PC), serves as an example of actions to avoid this neoplasm (Weinstein et al., 2009).

Spadea et al. (2010) highlight that countries with health systems that organize population-focused screening programs are more effective in reducing socioeconomic disparities in the early detection of cervical cancer than countries that opt for spontaneous testing.

In Brazil, the national PC program, the Family Health Strategy (FHS), coordinates community-based screening programs, which have been found to be more effective in lessening socioeconomic disparities in early detection than spontaneous diagnostic testing (Spadea et al., 2010). As of 2016, FHS consists of 40 155 primary care teams (PCTs) and operates in 98% of municipalities, covering 63.83% of the population (Ministério da Saúde, 2016).

Investments directed to primary health care (PHC) are important to ensure the strengthening of actions dedicated to prevention of diseases and promotion of health. From this perspective, the Program to Improve Access and Quality of Primary Health Care (PMAQ) is the largest PC monitoring initiative, with objectives of incentivizing evaluation and adherence to standards through internal assessments, measures of epidemiological indicators, and external diagnostic surveys of adequacy of infrastructure, work processes, and user satisfaction. The structure of PMAQ incentivizes adherence to quality standards at the level of PC through value-based payment mechanisms.

PMAQ has preventive programming targeted directly to cervical cancer screening and care management, consistent with priorities established by the World Health Organization (WHO) in the Global Action Plan for the Prevention and Control of Noncommunicable Diseases (WHO, 2013a). International initiatives to increase the early screening for cervical cancer can be observed in several European countries (WHO, 2007) and are part of the WHO action plan to control noncommunicable diseases (WHO, 2013b). Taking this into consideration, the topics evaluated by PMAQ are an alignment effort to international recommendations to minimize cervical cancer complications.

The creation of PMAQ marked the institutionalization of Brazilian PHC monitoring. With evaluations occurring every 2 years and based on recontracting with quality improvement goals, the program seeks to strengthen professional training strategies and work processes performed by health teams through increased financial incentives for better performance. This cyclical characteristic has searched for improvements in the provision of services by mobilizing health teams to meet recommended quality standards.

Spadea et al. (2010) highlight that PC doctors could assume a key role in cervical cancer screening and that organization of work processes of primary health care team (PHCT) could impact screening services for cervical cancer, creating conditions for early interventions. Such screening programs in asymptomatic women are critical to the reduction of morbidity and mortality (Limmer et al., 2014; Peirson et al., 2013). Yet, few studies exist regarding the relationship between components of the structure and work processes that facilitate preventive screenings and care management of cervical cancer at the level of PC and cervical cancer mortality rates. To contribute to the needed knowledge in this area, we aimed to analyze the temporal evolution of PC in Brazil-focused structural characteristics and work processes and to examine whether these components are associated with lower cervical cancer mortality rates, adjusting for socioeconomic status and health services coverage, which have been found to relate to cervical cancer mortality rates (Bigby & Holmes, 2005).

METHODS

This is an ecological longitudinal study that utilizes secondary data from 2002 to 2014 at the level of Brazil's 26 states and federal districts.

Sources of data and population

Secondary data were extracted from 3 national surveys. The first survey (2001-2002) is a diagnostic census of 13 973 PCTs and 2841 oral health teams (OHTs) that encompasses physical infrastructure, equipment, facilities, supplies, and human resources, as well as aspects of work processes related to care delivery and access to services. The second survey (2008) is a probabilistic sample representative of all states comprising 2133 PCTs and 1858 OHTs that measured parameters consistent with the first survey. The third survey (2012) is a part of the first cycle of PMAQ, spanning 17 202 PCTs and 12 403 OHTs. Data from PMAQ were also comparable in parameters with those of the previous 2 surveys. Data from PMAQ also had similarities regarding the parameters of previous 2 monitoring initiatives of 2002 and 2008.

Data analysis

Data from all 3 surveys were aggregated by state, creating a data set that allowed for comparisons over the 10-year period, and variables related to the structure and work processes necessary for the delivery of women's health services were selected. Data on socioeconomic determinants were further collected to adjust for the influence of potential confounders. For the outcome, the number of deaths due to cervical cancer from 2002 to 2014 was extracted and age-standardized as a rate using the direct method. Variables corresponding to work processes (grouped by PCT) and structural characteristics (grouped by health facility) that were available in the aforementioned surveys were aggregated by state and expressed as values of proportions, rates, or mean scores. For additional variables, data were also obtained by state. Table 1 details the variables incorporated in the model, as well as their respective sources and time periods.

Descriptive statistics were used for the initial analysis, followed by a mixed-effects linear regression model selected to account for the longitudinal structure of the data that consisted of repeated measures for each state at different time points. This method enabled the analysis of unbalanced longitudinal data (measures obtained for each state that were observed at different times) in a hierarchical structure, incorporating the dependent variables, the variation matrix, and covariation (Fitzmaurice & Ravichandran, 2008). In the mixed-effects model, regression coefficients (β) are fixed effects but intercepts are random (Goldstein et al., 2002). The estimation of fixed effects, variance, and covariance components was done using the methods of maximum likelihood estimation and restricted maximum likelihood estimation (Verbeke & Molenberghs, 2000). The maximum likelihood method, by estimating the variance, assumes that there is no error in the mean estimate and, consequently, underestimates this kind of error. Restricted maximum likelihood estimation produces estimates unbiased for variances, eliminating the bias that exists in the mean estimate (Diggle & Kenward, 1994).

Regression coefficients (β) and 95% confidence intervals (95% CIs) were estimated. The inclusion of variables followed a hierarchical approach, according to the theoretical model

Table 1. Variables and Data Sources

Category	Indicator	Description	Source	Period
Confounders	Gini index	Measures different degrees of income inequality	IBGE: Brazilian Institute of Geography and Statistics	2002-2012
	Per capita household income, in Real (R$)	Sum of the monthly income of all household members divided by the number of residents		
	Life expectancy of woman	Average number of years of life expectancy for a female newborn		
	Population size (per 100 000)	Total number of residents		
	Population with more than 11 y of study	Proportion of population between 18 and 24 y, with 11 or more y of the study		2002-2012, except 2010
	Year	Year regarding the data collected		2002-2014
PHC structure	PHCT with sufficient structure to perform women's health	Percentage of PHCT with the minimum requirement items: speculums, gynecologic light and table	PHC surveys and PMAQ	2002, 2008, and 2012
	PHC coverage	Population covered by PHCT; number of Family Health Teams multiplied by 3450 and divided by the population	Ministry of Health	2002-2012
	Primary health care financing (R$/100.000)	Amount of public funds invested for all primary care activities	SAGE—Support Strategic Management Room	
PHC work process	PHCT performing colposcopy	Proportion of PHCT performing colposcopy examination	PHC surveys and PMAQ	2002, 2008, and 2012
	Follow-up of cervix high-grade lesions	Ratio between the number of women diagnosed with high-grade squamous intraepithelial lesion being tracked and the total number of women with a diagnosis of a high-grade squamous intraepithelial lesion	SISCOLO—Information system for cervical cancer	2008-2012
Outcome	Mortality due to cervical cancer	Number of deaths from cervix neoplasm (*ICD-10*: C53)	SIM—Mortality Information System	2002-2014

Abbreviations: *ICD-10*, *International Classification of Diseases, Tenth Revision*; PHC, primary health care; PHCT, primary health care team.

(Figure), which considers the influence of variables related to structural characteristics on work processes and the influence of work processes on health outcomes (Donabedian, 1992). Variables that were included in the adjusted model were grouped sequentially by constructs of socioeconomic context (first), structural characteristics of health services (second), and work processes (third). Variables were retained for the adjusted model if they reached a significance of .2 at each level of analysis. A cutoff of 5% was considered as the criterion for statistical significance ($\alpha = .05$). Multicollinearity among variables of the same block was tested. Because of the imbalanced nature of the panel, data were adjusted for population size, regardless of statistical significance. Moreover, considering that data from surveys were only available for 3 years (2002, 2008, and 2012), we performed additional analyses imputing data for the variables "PCT with adequate structural characteristics to perform women's health care" and "PCT performing colposcopy." The multiple imputation technique of linear regression was used, including all model variables as predictors. Finally, we compared the results with and without imputation. This procedure was used to measure potential bias due to missing data. Analyses were carried out using Stata 12.0 (StataCorp LP, 2011).

RESULTS

Cervical cancer mortality rates varied among states over the period analyzed (see the table in Supplemental Digital Content 1, available at: http://links.lww.com/JACM/A75). Over this time, 6 states (Rondônia, Espírito Santo, São Paulo, Paraná, Rio Grande do Sul, and Mato Grosso do Sul) experienced a reduction in standardized cervical cancer mortality rates. In other states, mortality rates increased, ranging from a 2.68% rise in Minas Gerais to a 194% rise in Amapá. States located in the less developed North and Northeast regions underwent the greatest observed increase in mortality rates.

From 2002 to 2012, the Gini index decreased from 0.57 to 0.52, indicating a reduction in income inequality, a pattern that was observed throughout the whole country. Per capita household income also increased during the period analyzed; however, there was a heterogeneous effect across regions. Life expectancy at birth also rose nationwide. Furthermore, the percentage of the population with more than 11 years of formal education increased (see the table in Supplemental Digital Content 2, available at: http://links.lww.com/JACM/A76). Health indicators related to PC also improved. Financing increased 3-fold over the period. PCTs equipped with

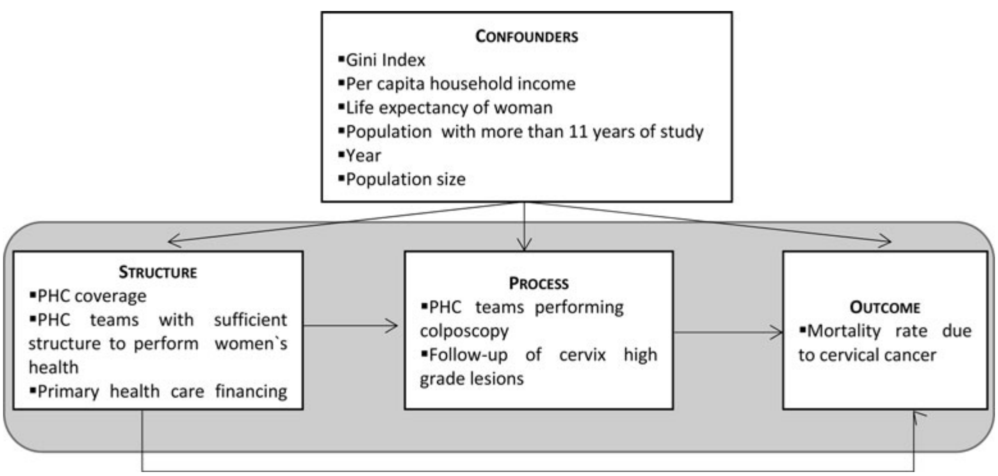

Figure. Theoretical model of predictors of mortality rates by cervical cancer for Brazil. PHC indicates primary health care.

adequate infrastructure dedicated to women's health care jumped from 64% in 2002 to 79% in 2012. However, this trend was not uniform, as some states experienced a decrease over the same period. The percentage of the population covered by PC services aligned with the same upward trend, reaching 62% in 2012. Roraima was the only state that showed a decline in coverage (see the table in Supplemental Digital Content 3, available at: http://links.lww.com/JACM/A77). The collection of samples for colposcopy by PCTs also rose nationwide. The percentage of monitoring for high-grade lesions, which began to be recorded in 2008, decreased by 2012, as evident in declining follow-up rates (see the table in Supplemental Digital Content 4, available at: http://links.lww.com/JACM/A78).

In the unadjusted analyses, the variables that were found to have a significant positive association ($P < .001$) with cervical cancer mortality rates were the percentage of the population with more than 11 years of formal education ($P < .001$), per capita household income ($P = .011$), female life expectancy at birth ($P < .001$), time ($P < .001$), PC investment ($P = .014$), and PC coverage ($P < .001$). In contrast, Gini index was found to be negatively associated with age-standardized cervical cancer mortality rates. Variables related to work processes were not found to be significantly associated with cervical cancer mortality rates. In the adjusted model, cervical cancer mortality rates were significantly higher in states with lower per capita household income ($\beta = -.006$; $P < .001$), with lower population sizes ($\beta = -.01$; $P = .025$), with lower PC investment ($\beta = -.0002$; $P = .027$), and with a lower proportion of PCTs that perform colposcopy ($\beta = -.14$; $P = .036$). Even after adjustments were made, mortality rates continued to be positively associated with time ($\beta = .30$; $P < .001$), indicating an increase in mortality rates over time (Table 2).

The results after imputation for observations missing in the surveys were similar to those without imputation. Investment in PC remained the only variable in the block of structural characteristics significantly associated with the outcome. In the block of work processes in PC, performing follow-up of cervical high-grade lesions remained unassociated with the outcome ($B = -0.02$; 95% CI, -0.04 to 0.007). However, the proportion of PCTs performing colposcopy stopped being associated with cervical cancer. The proportion of PCTs performing colposcopy continued to have a negative regression coefficient ($B = -0.081$; 95% CI, -0.17 to 0.01) but lacked statistical significance ($P = .087$). These results suggest no significant biases due to missing observations in the surveys throughout the temporal series.

DISCUSSION

This study had the principal objective of examining whether infrastructure available and work processes of PHCT influence the mortality by cervical cancer, adjusting for socioeconomic confounders. It can be observed that these characteristics influenced cervical cancer mortality rates. Furthermore, per capita household income and population size were the contextual variables found to be the best predictors of risk of mortality due to cervical cancer.

An improvement in sociodemographic indicators over time was accompanied by a statistically significant inverse association with cervical cancer mortality rates. The principal findings of our study were similar to those found in the literature (Müller et al., 2011; Pereira-Scalabrino et al., 2013). Precarious socioeconomic conditions were highlighted as factors that increased susceptibility to cervical cancer (Coker et al., 2006; Shanta et al., 2000; Tadesse, 2015). Regardless of socioeconomic trends, mortality rates, both unadjusted and adjusted, did not significantly change over the analyzed time period for some states. This disconnect has been observed in other studies in which socioeconomic improvements, even in the absence of screening programs, are inversely associated with mortality rates (Bermudez, 2005; Pereira-Scalabrino et al., 2013; Sankaranarayanan et al., 2001).

A recent evaluation of trends in cervical cancer incidence and mortality between 2003 and 2012 in high-, middle-, and low-income

Table 2. Association Between Sociodemographic Confounders, Structure, and Work Process in PHC (2002-2012), With Mortality Rate Due to Cervical Cancer (2002-2014), Brazil[a]

	Mortality Rate									
	Unadjusted					Adjusted				
	Fixed Effect			Random Effect		Fixed Effect			Random Effect	
Variables	**β**	**95% CI**	**P**	**β**	**Residue**	**β**	**95% CI**	**P**	**β**	**Residue**
Contextual									2.18	1.63
Gini index	**−8.77**	**−15.27 to −2.28**	**.008**	2.58	1.72					
Population >11 y of the study (%)	**.07**	**0.04 to 0.10**	**<.001**	2.77	1.70	0.05	−.02 to 0.11	.151		
Per capita household income—R$	**.002**	**−0.001 to 0.004**	**.011**	2.81	1.71	**− 0.006**	**−0.01 to −0.003**	**<.001**		
Life expectancy of woman	**.38**	**0.22 to 0.54**	**<.001**	3.21	1.65					
Population size (per 100 000)	−.01	−0.02 to 0.001	.081	2.55	1.97	**− 0.01**	**−0.02 to −0.002**	**.025**		
Time, y	**.19**	**0.14 to 0.24**	**<.001**	2.78	1.81	**0.30**	**0.16 to 0.43**	**<.001**		
Structure of PHC services										
Financing of PHC—R$ (per 100 000)	.0001	0.00003-0.0002	.014	2.98	1.93	**− 0.0002**	**−0.0004 to −0.0003**	**.027**	2.15	1.62
PHC Coverage	.05	0.03-0.07	<.001	2.66	1.66					
PHCT with the minimum requirement items	.03	−0.008 to 0.07	.129	3.27	2.29					
Work process in PHC									2.56	1.87
PHCT performing colposcopy	.06	0.02-0.09	.002	3.42	2.18	**− 0.14**	**−0.27 to −0.009**	**.036**		
Follow-up of cervix high-grade lesions	−.02	−0.04 to −0.003	.023	3.43	1.46	− 0.009	−0.05 to 0.03	.164		

Abbreviations: β, regression coefficient. 95% CI, 95% confidence interval; P, type I error probability (α); PHC, primary health care.

[a]Bold numbers mean statistically significant variables.

countries identified that mortality rates are declining in high-income countries and increasing in low- and middle-income countries (Torre et al., 2015). These findings corroborate mortality trends in our study.

The association between demographic indicators and mortality patterns can be justified in part by the fact that women at lower socioeconomic levels face barriers to accessing health services and are therefore less likely to participate in screening and other early detection programs (Currin et al., 2009). Furthermore, women with less education, lower income, and precarious living situations have an increased chance of high-risk sexual behavior, associated with a higher probability of contracting HPV infection, as well as a greater chance of persisting with HPV infection and the occurrence of invasive lesions (Pereira-Scalabrino et al., 2013).

Trends evidenced by this study support the need for social investment, capacity building to improve sociodemographic indicators, as a possible approach to addressing cervical cancer mortality rates. It is worth noting that even after the insertion of intermediate (structure of health centers) and proximal (work processes) blocks of variables, per capita household income remained significantly associated with lower cervical cancer mortality rates; this is highlighted as an important contribution of this study.

Various studies have emphasized lack of access to health services, especially in the case of population screening, as one of the factors that increases the risk of death due to cervical cancer (Ramondetta et al., 2015; Robles et al., 1996). Therefore, these studies recommended the implementation of cervical cancer screening as part of ensured PHC scope in developing countries (Bobdey et al., 2015).

Despite this, we were not able to identify studies that had evaluated the influence of different elements of structure and work processes on cervical cancer mortality rates. In our study, just infrastructure available for PHC (financing) and proportion of coverage for the collection of colposcopy samples was inversely associated with cervical cancer mortality rates after the adjusted model. Early detection of cervical cancer, together with treatment of intraepithelial lesions, is associated with a reduction of up to 90% in cervical cancer (Benjamin et al., 2014), as well as a significant decline in mortality rates (de Mendonça et al., 2008). However, for such results to be achieved, it is essential that screening coverage reaches a greater percentage of the eligible population.

According to Denny (2012), coverage rates for screening programs need to reach 85% in order to make an impact on cervical cancer mortality rates to be achieved, which remains unfulfilled in Brazil (Müller et al., 2011), with FHS coverage at 62% nationwide in 2012. Furthermore, there are PCTs that reportedly do not collect samples for preventive cytopathology. Coverage for this type of examination in Brazil is still precarious (Barbosa et al., 2016; Müller et al., 2011), circumstances further supported by our study's findings, since the collection of samples for cytopathology screening was found to have a slight negative association with cervical cancer mortality rates and FHS coverage was not found to have an association. Specifically, regarding women's health, PMAQ aims to improve structural characteristics and adequacy of work processes, especially in relation to prevention of cervical cancer. Unfortunately, PMAQ data are only updated through the first cycle of the evaluation, and a longer time period would be better suited for understanding the long-term effects of monitoring initiatives.

PHC could assume a protagonist role in the development of actions around prevention and treatment of cervical cancer. Because of its work closer to health system users, PHC can catalyze screening procedures, promoting early detection, increasing treatment possibilities, and improving patient quality of life (Weinstein et al., 2009). In this sense, our study's findings help support these observations, as it was possible to link PHC investment to a reduction in cervical cancer mortality rates. The subject of financing was the target of specific policies that quintupled the amount of funds invested in PHC throughout the 10-year period, including investments from PMAQ. Furthermore, it was possible to identify a relationship between states with PHCT that collected samples for colposcopy and a decrease in cervical cancer mortality rates, which reinforces the potential contributions to be made at the level of PHC.

This study did not find a statistically significant relationship between certain indicators (FHS coverage, adequate infrastructure, and the proportion of women with cervical lesions followed up) and cervical cancer mortality rates. This absence of significant findings could be partially explained by the fact that the proportion of the population covered by FHS falls short of the 85% goal recommended by Denny (2012), or suboptimal work processes such as low professional capacity in oncological care, the inability of health facilities to meet demand, and the difficulties of municipal and state administrators to coordinate between levels of care (Benjamin et al., 2014). There is a potential lag effect that needs to be taken into account related to health policy, especially for chronic long-term diseases such as cancer. However, we have a 12-year study that makes it possible to identify some predictors to reduce the Brazilian mortality rate due to cervical cancer. The regular basis of assessment defined by PMAQ will produce better circumstances to evaluate PHCT performance once the lag effect will decrease with new monitoring cycles.

Improvement in the structure of cervical cancer screening and prevention programs needs to address these challenges related to work processes in order to achieve both an increased coverage of health services and a greater quality of preventive and curative care delivered. The evidence produced in this study suggests that PHC can contribute to minimize cervical cancer mortality rates, and there is still much to be done to realize these potential results. Our study provides an innovative contribution to articulating time-series data, involving socioeconomic characteristics and health services, in relation to the evolution of mortality patterns for all Brazilian states.

Limitations of this study stem from lack of indicators for certain time points over the examined period. However, the use of mixed linear effects regression allowed the incorporation of unbalanced data over time, keeping missing variables in the analysis for some years. Even so, sensibility analysis was realized. Unfortunately, the software used does not support estimates for standardized associations when independent variables are in different units. Nevertheless, the independent variables with a high discrepancy were adjusted, for example, financing. Additional limitations were the impossibility of disaggregating data to lower levels such as PHCT coverage area, which could reduce the possibility of ecological fallacy. Cervical cancer notifications and cancer staging data are not available in Brazil and so it is not possible to take this into account in the analysis.

In the future, with continued monitoring of PCT performance, it will be possible to overcome the methodological limitations of the present study and better investigate the effects of PC actions on cervical cancer mortality rates. PMAQ is an important initiative through which to work because of its focus on regular evaluation to inform quality improvements. PMAQ is likely to contribute positive results to preventive initiative in PC, including increased adherence to cervical cancer protocols and improved physical infrastructure. Considering our findings, the development of programs similar to PMAQ that link performance to financial investments could decrease the mortality due to cervical cancer. Therefore, initiatives such as PMAQ should be fostered with the objective of decreasing cervical cancer mortality rates.

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