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The Impact of The COVID-19 Pandemic on Cervical Cancer Screening: An Ecological Study on Pap Smears Test Conducted In Brazil.

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Abstract

Objective: To assess the impact of the COVID-19 pandemic on cervical cancer screening in the Brazilian Unified Health System (SUS).

Methods: This ecological study analyzes the repercussions of isolation during the pandemic on pap smear tests in women aged 25-64. Epidemiological information was obtained from the Cancer Information System database (SISCAN), integrated with the Department of Informatics of the Unified Health System (DATASUS). Statistical analysis was performed using SPSS V20, Minitab 16, and Excel Office 2010 software. The correlation between COVID-19 cases and the pap smears test was evaluated using the Pearson coefficient. The variation in the pap smears test between 2020 and 2021, compared to the pre-pandemic year of 2019, was calculated using the Two Proportions Equality Test.

Results: Between 2020 and 2021, 18,957,470 pap smear tests were performed for screening purposes in Brazil. The average reduction in 2020 was 42.73 % compared to 2019, with no statistically significant difference between the age groups of 25-64 years. There was a progressive decrease in screening tests, with the lowest rate in June, with only 75,281 tests collected, representing an 82.24 % reduction compared to the same period in 2019.

Conclusion: The COVID-19 pandemic led to a significant decrease in cervical cancer screening tests in the first months of the pandemic in 2020, particularly during the months with the highest confirmed cases of COVID-19. Only in 2021 did the number of pap smears test increase, showing a trend towards reaching the pre-pandemic period, despite having a higher number of confirmed COVID-19 cases than in 2020.

Keywords: Cervical cytology, Pap smear, Cervical cancer, COVID-19.

Introduction

Cervical cancer is most commonly diagnosed in women between the ages of 35 and 44, uncommon in those under 20. However, older women still have a risk and should undergo screening **[1]**. It is the third most common malignant tumor in the female population, excluding non-melanoma skin cancer, ranking behind breast and colorectal cancer. According to INCA, it is the fourth leading cause of cancer-related death in women in Brazil **[2]**.

It is estimated that for each year of the 2020-2022 triennium, 16,590 new cases of cervical cancer will be diagnosed in Brazil, with a calculated risk of 15.43 points per 100,000 women **[2]**.

Among the risk factors for developing cervical cancer, infection with the Human Papillomavirus (HPV) stands out. Although very common, it is not considered a disease in itself. Most cases occur transiently and are cleared by the body within 6 months to 2 years, especially in young women **[3]**.

Persistent infection with certain oncogenic types of HPV (particularly subtypes 16 and 18) leads to precancerous changes known as cervical intraepithelial neoplasia (CIN), which can progress slowly over 10 to 20 years until the development of actual cancer. More than 70 % of cases are related to these strains **[4]**.

In Brazil, the Ministry of Health recommends performing cervical cytology (pap smears test) annually for two consecutive years, starting at the age of 25, in patients who have already initiated sexualactivity. The test should be offered to anyone with a cervix, includingtrans men and non-binary individuals assigned female at birth. If thisscreening is negative for neoplastic lesions, it should be followed by a triennial collection. Pap smears test is recommended until the age of 64, and after that, if there have been two consecutive negative results in the past five years, screening can be discontinued **[2,5,6]**. According to the Brazilian Federation of Gynecology and Obstetrics Associations (FEBRASGO), sexually active young women and adolescents should receive guidance on contraception, sexually transmitted diseases, and safe sex practices. Screening in these cases should be initiated three years after the onset of sexual activity **[7]**.

FEBRASGO emphasizes that the discontinuation of screening should consider each patient's history, the frequency of tests, and the results of previous examinations. Postmenopausal women at low risk,

without a history of recent diagnosis and treatment of precursor lesions of cervical cancer and immunosuppression, can be excluded from screening at 70 years of age if they have had three regular exams in the last decade **[7]**.

To determine an age for ending screening, institutions rely on the fact that although over 20 % of cervical cancer cases are diagnosed in women over 65, the majority occur in those who have not been screened or have done so irregularly **[1,7]**.

In Brazil, as in other developing countries, screening follows an opportunistic pattern, meaning that women seek healthcare services for different reasons and are advised to undergo a pap smear test. As a consequence, 20 to 25 % of exams are performed outside the recommended age group, and approximately 50 % have intervals of one year or less **[5,7]**.

The emergence of a new type of coronavirus - Sars-CoV-2 - surprised the world in 2019. The first cases were reported to the WHO in December of that year. In early March 2020, the status of the new coronavirus infection in Brazil was changed to a pandemic due to its high infectivity.

With the pandemic in place, there were changes in the recommendations for cervical cancer screening in Brazil. In 2020, the Brazilian Society of Pathology and the Brazilian Society of Clinical Pathology/Laboratory Medicine published a joint note stating that, due to the Covid-19 pandemic, it was necessary to postpone non-urgent exams and procedures, including pap smears test **[8]**.

Methods

This ecological study aimed to compare the performance of cervical cancer screening through colposcopy in the years 2018 and 2019 (pre-pandemic) with that of the 2020-2021 biennium to determine the correlation of these data with the increase in the incidence of COVID-19 cases and the pandemic-related restrictions.

The epidemiological information was secondary and extracted from the Cancer Information System (SISCAN) database, part of the Department of Informatics of the Unified Health System (DATASUS). SISCAN is a free and easily accessible program that collects and disseminates health-related information.

The software packages SPSS V20, Minitab 16, and Excel Office 2010 were used for statistical analysis. The normality of the quantitative variables was tested using the Shapiro-Wilk test (N<30), a parametric test where N corresponds to the number of months evaluated during the biennium.

The correlation between confirmed COVID-19 cases and colposcopy exams in the 2020-2021 biennium was calculated using the Pearson correlation coefficient. The correlation coefficient (r) values were assumed to be weak for |0.10| to |0.40|, moderate for |0.40| to |0.60|, and vigorous for |0.60| to |1.00|.

The variations in pap smear tests performed between 2020 and 2021 compared to the pre-pandemic year 2019 were calculated using the Two-Proportion Equality test. 2018 was excluded from this analysis since the growth 2019 was only 2.9 %.

The study included pap performed on women aged 25 to 64, the period the Brazilian Ministry of Health (MS) recommended for screening. Follow-up exams after cancer treatment or those performed for control due to previous abnormal results were not included.

The confirmed cases of COVID-19 were obtained from an interactive panel on a SUS platform that provides epidemiological information on pandemic **[11]**. As this is an ecological study without directpatient participation, there was no need to submit the work to an ethics committee or include a term of informed consent.

Results

A total of 23,885,294 pap smear tests were performed in Brazil by the SUS between 2018 and 2021. Among these, 558,287 were performed for follow-up or repeat, while 18,743,022 were done for screening purposes, comprising only the age group of 25-64 years, according to the recommendations of MS **[2,5,6]**.

However, it is essential to note that postponing screening for too long can lead to cancer detection in more advanced stages, increasing the risk of mortality **[9]**.

In October 2020, the Ministry of Health issued guidelines for the resumption of cervical cancer screening, stating that screening should be resumed with priority given to women who were unable to perform the test during the pandemic, followed by women who are due for screening according to their age and the recommended interval **[10]**.

It is important to remember that the pandemic is not over yet, and caution is still necessary to avoid infection. Women due for screening should seek guidance from their healthcare provider on the best time to perform the exam and the safety measures to prevent Covid-19 transmission.

In summary, cervical cancer is a significant health problem in Brazil, and most cases are related to infection with certain strains of HPV. Cervical cytology is an effective screening method, and its implementation has reduced cervical cancer incidence and mortality rates. Screening recommendations vary depending on age, sexual activity, and previous results, and it is essential to follow the guidelines established by the Ministry of Health and professional associations. The Covid-19 pandemic has caused disruptions in the screening programs, but measures have been taken to resume screening while ensuring the safety of patients and healthcare professionals. This study aimed to evaluate the impact of the COVID-19 pandemic on cervical cancer screening in the Brazilian Public Health System (SUS).

Table 1 analyses the number of exams performed in the last 4 years. Considering a growth of 2.9 % between 2018 and 2019, it was expected that this growth would be maintained in the following years.

Figure 1 shows the number of exams performed, by age group, highlighting a lower rate of exams in 2020 and 2021 across all categories. Patients between 60 and 64 years old had the lowest rate of pap tests, regardless of the pandemic context.

Table 1: Pap smear tests performed in Brazil between 2018-2021.

	2018	2019	2020	2021	Total
Pap smear tests	6.819.071	7.045.257	3.996.293	5.949.673	23.885.294
Screening (25-64 years)	5.313.523	5.480.883	3.134.627	4.813.989	18.743.022

Source: DATASUS - SISCAN, accessed on 06/22/2022

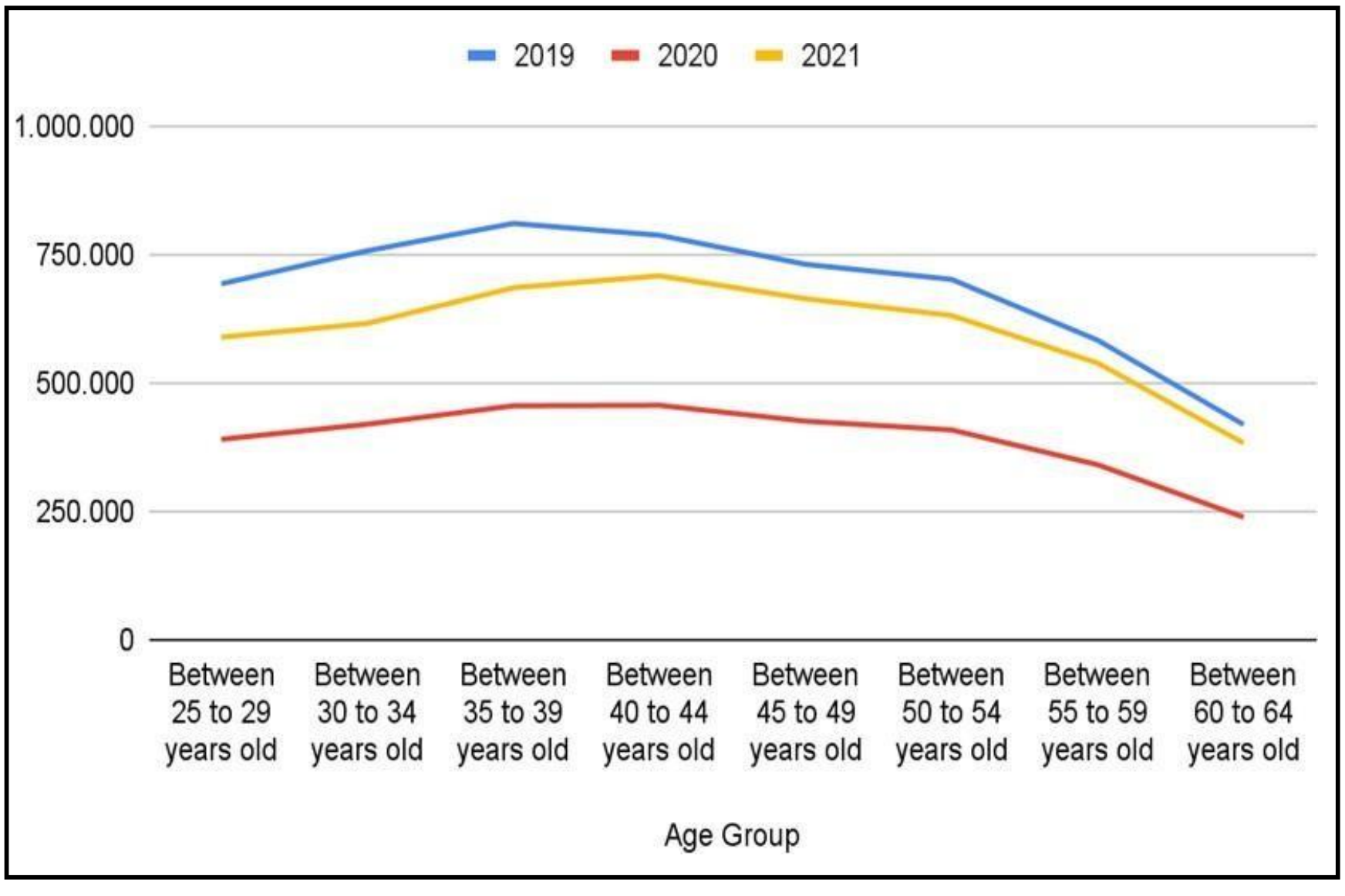

Figure 1: Pap semear test by age group in Brazil

Table 2 analyses the reduction in Pap smear tests performed between 2020 and 2021 compared to exams conducted in 2019, according to age group. A significant difference was observed in 2020 when restrictions and isolation were more severe than in 2021.

The average reduction in 2020 was 42.77 %, without an evident difference when comparing all age groups. The most minor reduction was 41.47 % among patients aged 55-59 years, while the most significant drop was among women aged 30 to 34, at 44.57 %.

Figure 2 compares the monthly incidence of pap smear tests performed over the 3 years, observing a certain constancy throughout 2019, in remarkable contrast with 2020, in which there was a marked decrease after March when the country began to adopt more restrictive measures regarding the pandemic.

In the first quarter of 2020, the incidence of pap smear tests was equivalent to the same period of the previous year, being higher in March. Due to the upward curve in **Figure 2**, there is a presumption of a growth trend and overcoming the year 2019. However, after March, there was a progressive decrease in the performance of pap smear tests, with the lowest rate in June, with only 75,281 tests collected. A reduction of 82.24 % compared to the same period in 2019.

Table 2: Pap smear test - Comparative analysis by age group, between the years 2020 and 2021 in relation to 2019.

Age	Pap Smears Test			Variation		p-value
	2019	2020	2021	19/20	19/21	
25 - 29 years	701.844	395.424	595.850	- 43,66 %	-15,10 %	< 0,001
30 - 34 years	767.134	425.248	623.014	-44,57 %	-18,79 %	< 0,001
35 - 39 years	821.181	461.656	693.459	-43,78 %	-15,55 %	< 0,001
40 - 44 years	797.647	462.680	716.873	-41,99 %	-10,13 %	< 0,001
45 - 49 years	740.960	431.466	672.120	-41,77 %	-9,29 %	< 0,001
50 - 54 years	711.212	414.456	639.077	-41,73 %	-10,14 %	< 0,001
50 - 54 years	711.212	414.456	639.077	-41,73 %	-10,14 %	< 0,001
55 - 59 years	591.145	345.973	545.485	-41,47 %	-7,72 %	< 0,001
60 - 64 years	424.796	242.324	387.923	-42,96 %	-8,68 %	< 0,001

Source: DATASUS - SISCAN, accessed on 06/22/2022

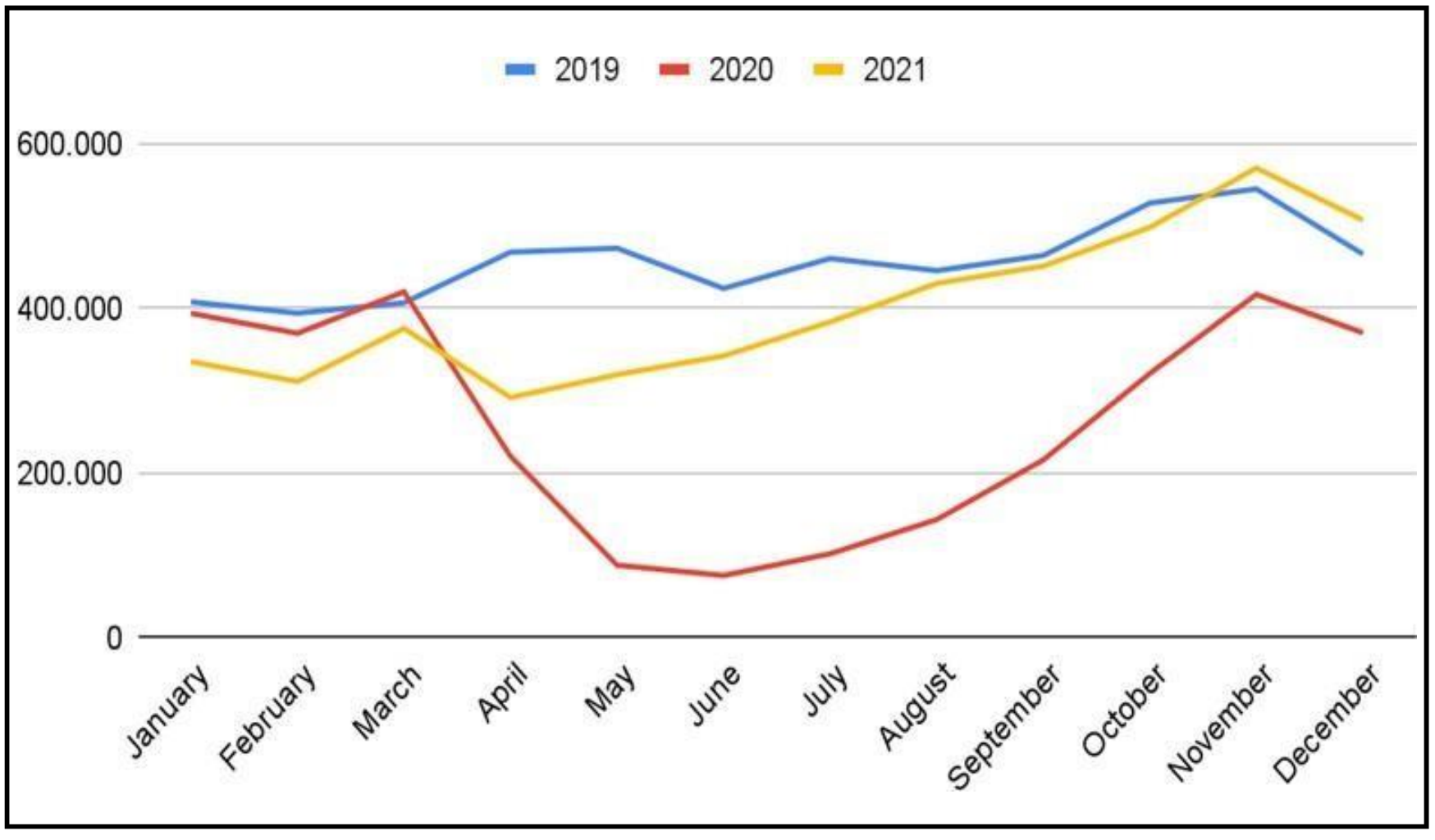

Figure 2: Monthly pap smear test performed in Brazil, between 2019 - 2021.

Pearson's correlation was used to analyze Covid cases, and the number of pap smear tests performed in Brazil from 2020 to 2021, as shown in **Table 4**.

Figure 3 compares the COVID-19 confirmed casa in Brazil between 2020 and 2021 and the pap smear test performed in the same period. We can observe that COVID-19 increased between April 2020 and August 20202 and an import reduction in the number of pap smear tests performed.

All three correlations were negative, indicating that the higher the number of COVID cases, the lower the number of exams performed. However, only in the year 2021 is this correlation considered statistically significant, with $r = -0.878$ ($p < 0.001$), classified as Strong, while for the year 2020, $r = -0.409$ (p-value = 0.187), was ranked as Moderate. For the biennium, the correlation was $r = -0.217$ (p-value = 0.308), evaluated as Weak. This is shown in **Figure 4**.

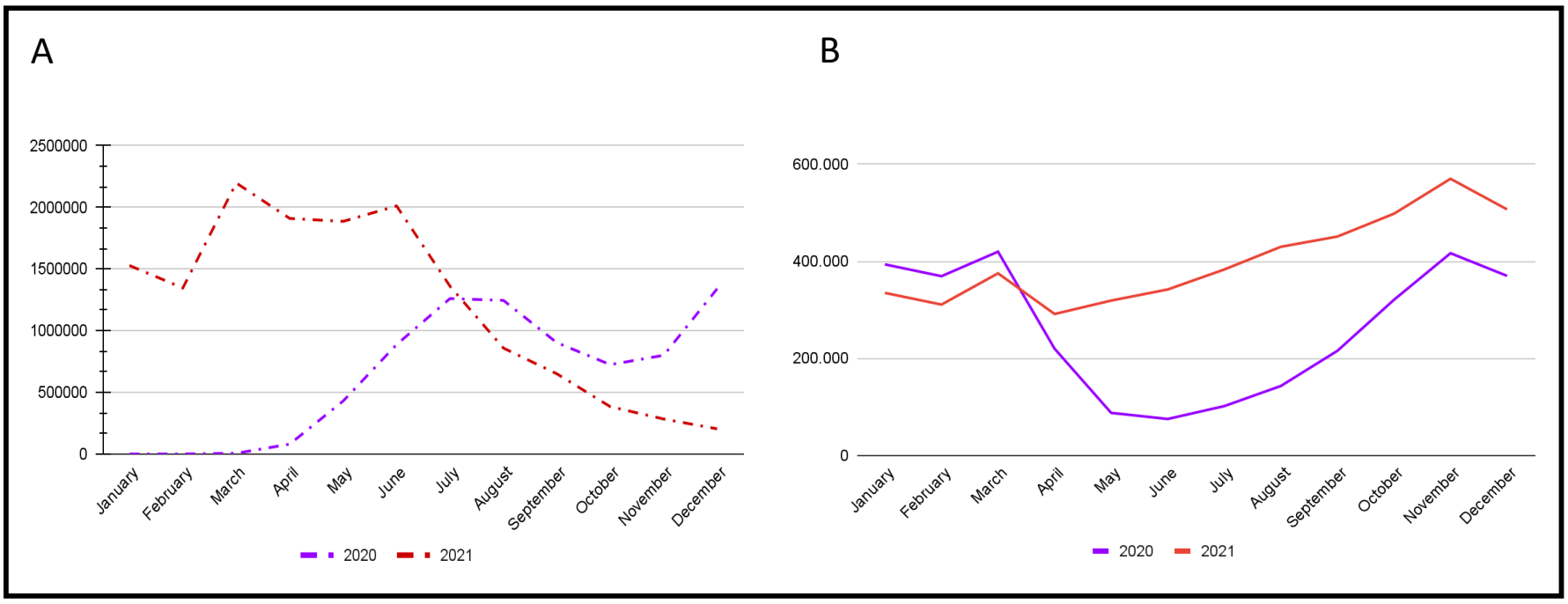

Figure 3: A – Confirmed cases of COVID-19 in Brazil between 2020 and 2021. B – Pap smear test performed between 2020 and 2021.

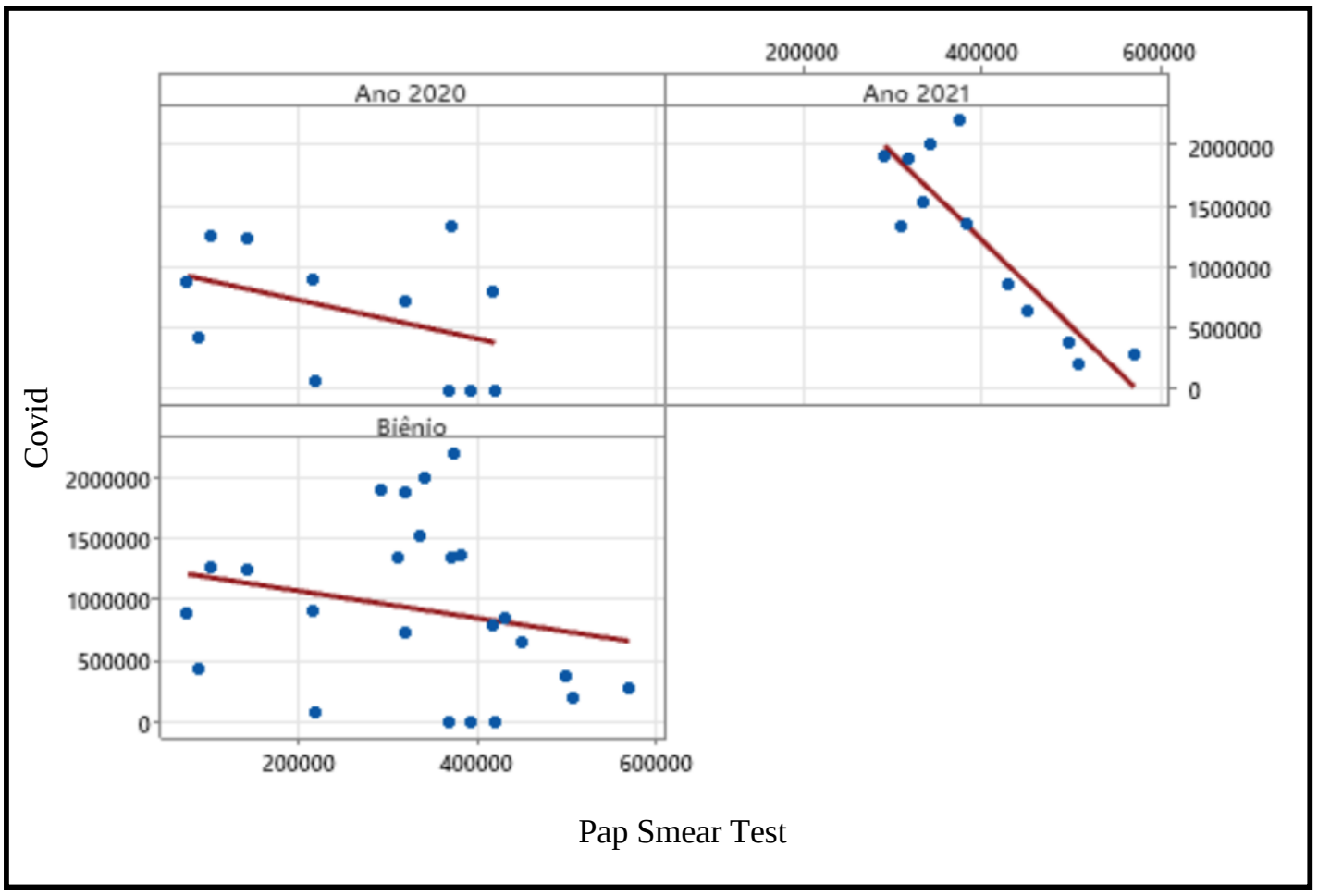

Figure 4: Correlation between Covid-19 cases and performed pap smear test exams.

Table 4: Pearson correlation - Comparison between Covid-19 cases and Pap Smear tests performed.

Years	Corr (r)	p-valor
2020	-0,409	0,187
2021	-0,878	< 0,001
Biennium	-0,217	0,308

Discussion

During the first semester of the pandemic, there were no effective measures against Sars-CoV2, and the number of cases increased exponentially, leading the health system to suspend non-urgent medical activities. In the acute phase of the pandemic, SUS management reallocated human and financial resources for the assistance of patients diagnosed with COVID-19 **[11,12]**.

This reallocation of resources led to a shortage of supplies for diagnostic tests, scarcity of PPE, and restricted circulation of people to avoid contamination by COVID-19. In many countries, one of the first guidance measures was to interrupt contact tracing, making the impact of the pandemic more significant in the first months of 2020 **[13]**.

There was again an increase in cases in November of the same year, with the emergence of a new strain of the virus leading to a second wave of infection. In that month, the performance of pap smear tests,

which was increasing, presented values similar to the pre-pandemic months.

Despite the significa nt increase of 53.3 % in exams performed in 2021 compared to the previous year, when compared to 2019, there is still a reduction of 12.17 % in the period from 2019 to 2021 ($p<0.001$) - **Table 3**. This was statistically different from 2019 to 2020, in which there was a reduction of 42.81 % in exams performed.

Table 3: Pap Semear Test monthly comparative analysis between the years 2020 and 2021 in relation to 2019.

Age	**Pap Smears Test**			**Variation**		**p-value**
	2019	2020	2021	19/20	19/21	
January	407.618	393.752	335.051	-3,40%	-17,80%	< 0,001
February	393.863	369.444	310.956	-6,20%	-21,05%	< 0,001
March	406.473	369.444	375.370	-9,11%	-7,65%	< 0,001
April	468.096	220.044	291.549	-52,99%	-37,72%	< 0,001
May	472.767	87.847	319.230	-81,42%	-32,48%	< 0,001
June	423.951	75.281	342.111	-82,24%	-19,30%	< 0,001
July	460.430	101.777	383.259	-77,90%	-16,76%	< 0,001
August	445.575	143.241	430.024	-67,85%	-3,49	< 0,001
September	463.994	215.678	451.112	-53,52%	-2,78	< 0,001
October	527.633	320.766	498.139	-39,21%	-5,59%	< 0,001
November	544.811	416.778	570.148	-23,50%	4,65%	< 0,001
December	465.672	370.098	507.040	-20,52	8,88%	< 0,001
Total	5.580.883	3.134.627	4.813.989	-42,81%	-12,17%	< 0,001

Source: DATASUS - SISCAN, accessed on 06/22/2022

The highest number of Covid-19 cases was recorded in March 2021, and there was no longer a decrease in cervical cancer screenings, probably because vaccination campaigns began in this same period. In both 2020 and 2021, there was a peak in pap smear test screenings in October, which may be due to the international campaign of Pink October. The population is encouraged to seek health services for mammograms, with pap smear tests also being collected.

The Pearson correlation measured how closely the variables were linked. When applying this technique, it was observed that the higher the Covid cases, the lower the screenings performed. However, this was only statistically significant in 2021, with $r = -0.878$ ($p < 0.001$). For the two years, the correlation was evaluated as weak, with $r = -0.217$ (p-value = 0.308).

Similar reductions in cervical cancer screening during the pandemic were observed internationally. A retrospective observational study in Ontario, Canada, evaluated pap smear tests in the first six months of the pandemic **[15]**. There was a 92.3 % decrease in the number of pap smear tests performed for the worst month, April, in the first semester of the pandemic. This result is similar to those obtained in Brazil, with the worst reduction rate in June, with 82.24 % of Pap smears collected.

In the United States, as in Canada, a reduction in pap smear tests during isolation was evident, with the worst nadir in April. A study in California revealed a 78 % reduction in patients between the ages of 21 and 29. Among those over 30, the decline was 82 % **[16]**. There were no significant changes observed between age groups, as in Brazil.

In the United States, a comparative analysis was also performed to estimate the impact of the suspension of cervical cancer screening, including cytology, surveillance, colposcopy, and excisional treatment. By 2027, the number of cervical cancer diagnoses is expected to increase by 5 to 7 per million women screened in a 6-month interruption. Considering a suspension of 24 months, the increase could be from 38 to 45 cases per million **[17]**.

In England, tracking is organized, with women receiving triennial calls to undergo exams. A study in that country estimated that a 6-month interruption would increase cervical cancer incidence by 630 new cases in one screening cycle. If patients wait not only 6 months but a whole new process to undergo screening, the chance of developing cancer is 7 times higher, with the age group of 40 to 49 being at higher risk due to not having been covered by the vaccination program **[13]**.

In Australia, screening is done every 5 years through the molecular test to detect oncogenic HPV subtypes. A 2020 study did not quantify a significant short-term loss in the screening rate of its population, given the longer screening interval **[18]**.

It is important to emphasize that in Brazil, cervical cancer screening is opportunistic, with no public policy to call patients for pap smear tests as in other countries. Currently, in public health, we not only return to usual activities from the pre-epidemic period but also deal with the backlog of residual activities pending. The longer these individuals wait to return to screening, the greater the possibility of inadequate follow-up. In this case, with patients' return to health units,

we may observe more aggressive lesions and a greater chance of late diagnosis **[19]**.

The pap smear tests test is an important screening tool for cervical cancer. Its decrease during the 2020-2021 biennium resulted from prioritizing health service resources to confront COVID-19. These resources include personnel, distribution of PPE, laboratory exams, emergency care, isolation ward beds, and ICU beds. Dealing with an unknown disease required a reduction in people's circulation to contain the spread of the virus.

The year 2022 is marked by the return to usual activities, with the challenge of adopting well-coordinated measures to prioritize the care of patients who have missed their screening exams.

A strategy to solve this problem would be to develop policies for actively searching patients who have not undergone screening exams, encouraging them to resume healthcare services, or even those patients who may have experienced the exam and, even with HPV-induced lesions diagnosis, have not followed up properly.

It is necessary to implement awareness campaigns for the importance of screening and establish a reorganization of the network for early detection of cancer. Implementing a strategy for stratifying patients whose screening is outside the recommended periodicity, making cervical cancer screening more organized, centralized, and thus more effective **[20]**.

Conclusions

It was observed that the performance of screening exams for cervical cancer showed a significant decrease during the period, with higher confirmation of COVID-19 cases in the early months of the pandemic in 2020. Only in June of that year did the collection of pap smear tests begin to increase. It was only in 2021 that there was an increase in the number of cervical cancer screening exams being performed, showing a tendency to reach levels similar to those seen before the pandemic, despite having a higher number of confirmed COVID-19 cases than in 2020.

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