

Editorial

# Organized, Population-based Cervical Cancer Screening Program: It Would Be a Good Time for Brazil Now

## *Programa de rastreamento populacional de câncer de colo uterino organizado: é um bom momento para o Brasil de hoje*

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Estimates indicate that around 16,000 new cases of cervical cancer were diagnosed in 2014 in Brazil. This cancer is the third most frequent in Brazil, the first in the North region, and the fifth in the South region of the country.<sup>1</sup> The Unified Health System (SUS), the public health care system of Brazil, has implemented several actions for qualifying cervical cancer screening, but there are challenges to be overcome, such as the large national territory and heterogeneous resources from every site.<sup>2</sup> Despite the efforts made by SUS, the current cervical cancer screening has shown many weaknesses. There is no doubt that regular screening of appropriate women for cervical cancer with the cytopathology test reduces mortality from cervical cancer.<sup>3</sup> However, appropriate policy and program organization remain essential to achieve a good balance between benefit and harm of any screening program. The knowledge of the potential of population-based cervical screening to reduce the burden of cervical cancer in the population is doubtless. However, as pointed out by Dillner et al,<sup>4</sup> this knowledge has not always been translated into effective national programs. To be effective, cervical cancer screening should be performed in an organized, population-based screening program with comprehensive quality assurance covering all steps in the screening process. An organized program should include quality assurance in monitoring cervical cancer screening performance. The European guidelines define such a performance through achieving: (1) an invitation coverage of at least 95% of the target women; (2) an examination coverage of at least 70% (85% is desirable); and (3) a participation rate of at least 70% (85% is desirable).<sup>5</sup>

The current recommendations for the SUS establish the cytology-based cervical cancer screening, conducted with a three-year interval after two consecutive annual negative

exams. The target population for cervical cancer screening comprised women aged 25 to 64 years, which represents around 55 million Brazilian women.<sup>6</sup> Although SUS is universal, ~25% of all Brazilians have private health; therefore, ~41 million women are dependent on the SUS as their health care provider. In the last decade, SUS conducted 9 to 11 million cytological exams per year.<sup>7</sup> If it maintains the recommended age group and three-year interval preconized, the SUS would be able to include 27 to 33 million women in the screening program, reaching almost 70–85% women as preconized for an organized population-based program for cervical cancer screening.<sup>4</sup>

In their Historical Analysis of the Brazilian Cervical Cancer Screening Program from 2006 to 2013, Costa et al<sup>8</sup> observed that the Pap test coverage rate in Brazil is below 70%. Data from the Ministry of Health from 2012 and 2013 showed that around 50% of the cytological tests in Brazil were conducted on an annual basis and only 10% within a three-year interval. Also, around 20% of the tests were conducted on women less than 25 years of age.<sup>9</sup> Regarding data from 2013, out of total 8,951,266 cytological tests, only 78.7% were conducted in women aged 25–64 years old. Around 16% of these tests were conducted in young women, aged less than 25 years or even younger than 20 years: it is well known that treatment procedures related to cervical lesion could be associated with a higher frequency of obstetric and neonatal morbidity. Also, for 46.9% of women, the interval since the last test was one year or less, and only 9.4% followed the frequency recommended in the Brazilian Cervical Cancer Screening Guidelines.<sup>10</sup>

These data about Brazil present some regional variability, but the general pattern tends to be homogeneous. An evaluation of the cervical of the cancer screening program in

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Campinas, a more economically developed region, showed 63.7% of the tests exceeded the parameters defined in SUS Guidelines, characterizing opportunistic screening, that is, most women have their cytological test when seeking health care for reasons other than cervical cancer screening.<sup>11</sup> A similar analysis for the municipality of Amparo showed that, between 2001 and 2007, 61.2% to 65.5% of cytological tests were conducted in excess, with a great number of women under the recommended age.<sup>12</sup> Although there was a decrease of 36% in invasive cervical cancer (with a significant increment of stage I compared with advanced disease) in the Hospital da Mulher Professor Doutor José Aristodemo Pinotti at Campinas State University, located in Campinas, from 2006 to 2013, cervical cancer screening remains largely opportunistic even in this region.<sup>13</sup> Although it is an arduous and complex task, Brazil could organize the cervical cancer screening program through the use of SUS card.

Nonetheless, these efforts would bring little improvement if the cytology quality is not assessed. Tobias et al,<sup>14</sup> in the article entitled "Quality indicators of cervical cytopathology exams of public service in Minas Gerais State, Brazil," indicated the need to evaluate the performance of cytopathology laboratories that provide services to the SUS. The authors collected their data from the Cervical Cancer Information System (SISCOLO). According to Costa et al,<sup>8</sup> the SISCOLO is an important tool for improving the Brazilian opportunistic cervical cancer program, as it contains a significant amount of data regarding Pap smear tests that can be used to calculate quality indicators. Through these data, it is possible to identify fragilities and strengths and to evaluate indicators to adjust the course of action.

Tobias et al<sup>14</sup> concluded that most of the laboratories that provides service for SUS in the state of Minas Gerais presented quality indicators outside the parameters recommended by the Ministry of Health. Those findings are not restricted to Minas Gerais state. Costa et al<sup>8</sup> also observed that the index of positivity was maintained at levels below those indicated by international standards in all the states in Brazil. They observed that the prevalence of cell alteration, which characterizes the sensitivity of the screening process for detecting lesions, was below those recommended by the Brazilian guidelines (3–10%). They also pointed out that these indexes are significantly below those observed in developed countries, which have already achieved control of cervical cancer incidence, such as Norway (4.9%)<sup>15</sup> or the USA (6.8%).<sup>16</sup> Costa et al<sup>8</sup> also found that, although there was an increased rate of rejected exams from 2009 to 2013, they observed very low frequencies of unsatisfactory cases over the study period, which partially contradicts the low rate of positive cases. In Brazil, the prevalence rates of cytological results with alteration vary significantly with the region, probably due to the cytological test quality variability.<sup>17</sup> The cytological test for cervical cancer screening is a procedure that depends on the actions of health care professionals and, therefore, shows high performance variability.

Franco et al<sup>18</sup> evaluated factors associated with false-negative cervical cytopathological results. They found that

a small number of isolated atypical cells, present only in part of the smear, and the presence of blood and inflammatory process are frequently associated with false negative results in cytological smear. These factors are largely related to the collection conditions; therefore, the lesion cannot be adequately represented in the Pap smear. Among the complex chain of events in a cytology screening program, there are important steps beyond the collection and processing of the sample in the laboratory. Costa et al<sup>8</sup> observed that the percentage of rejected tests significantly increased in recent years (2010–2013). Part of these results is explained by the lack of care in handling, transportation and identification of samples, which underscores the importance of focusing not only on sample collection but also on all of the steps between sample collection and sample analysis. Another important pre-analytical indicator is the presence of epithelial cells from the transformation zone (TZ): although the results showed that the percentage of TZ cells was close to the Brazilian National Cancer Institute reference value, it significantly decreased over the years, which may be a consequence of problems related to sample collection.

According to European guidelines for quality assurance in cervical cancer screening, revised in 2015, the HPV primary testing is suitable in an organized, population-based program for cervical cancer screening. This statement has the highest level of scientific evidence and this intervention is strongly recommended.<sup>5</sup> Currently, the understanding is that there is necessary infrastructure to exploit the potential of HPV-based screening for improved cost-efficiency within organized invitational screening programs.<sup>4</sup> Additionally, the compliance with surveillance and optimal management of HPV-positive women after primary HPV screening is of key importance.<sup>19</sup> Despite the advantage of the DNA-HPV tests in achieving high laboratory quality control and reproducibility, an organized screening is still necessary.

Tobias et al<sup>14</sup> data seriously highlight the need for education activities involving all levels of health care agents to improve the national cervical cancer screening program. As long as the distance between the knowledge of the benefit of the effective organized programs and the opportunistic national program persists in Brazil, any effort to improve the quality of any screening method, either cytological or HPV detection, is unlikely to significantly impact mortality from cervical cancer.

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