Trends in Cervical Cancer Mortality in the Americas

SYLVIA C. ROBLES,1 FRANKLIN WHITE,1 & ARMANDO PERUGA1

This article presents an assessment of cervical cancer mortality trends in the Americas based on PAHO data. Trends were estimated for countries where data were available for at least 10 consecutive years, the number of cervical cancer deaths was considerable, and at least 75% of the deaths from all causes were registered. In contrast to Canada and the United States, whose general populations had been screened for many years and where cervical cancer mortality has declined steadily (to about 1.4 and 1.7 deaths per 100,000 women, respectively, as of 1990), most Latin American and Caribbean countries with available data have experienced fairly constant levels of cervical cancer mortality (typically in the range of 5-6 deaths per 100,000 women). In addition, several other countries (Chile, Costa Rica, and Mexico) have exhibited higher cervical cancer mortality as well as a number of noteworthy changes in this mortality over time.

Overall, while actual declining trends could be masked by special circumstances in some countries, cervical cancer mortality has not declined in Latin America as it has in developed countries. Correlations between declining mortality and the intensity of screening in developed countries suggest that a lack of screening or screening program shortcomings in Latin America could account for this. Among other things, where large-scale cervical cancer screening efforts have been instituted in Latin America and Caribbean, these efforts have generally been linked to family planning and prenatal care programs serving women who are typically under 30; while the real need is for screening of older women who are at substantially higher risk.

The uterine cervix is the most common cancer site for females in Latin America and the Caribbean, where approximately 52,000 new cases occur annually. Overall in the Americas, where it is estimated that nearly 68,000 new cases occur annually (1), North America exhibits the lowest morbidity and mortality. Elsewhere in the Americas there is considerable variation, with cancer registry morbidity data showing relatively high incidences of cervical cancer in Brazil, Paraguay, and Peru compared to relatively low incidences in Cuba and Puerto Rico. With regard to mortality, the rates are relatively high in the English-speaking Caribbean, Chile, and Mexico and relatively low in Cuba, Puerto Rico, and Argentina (2). These differences between countries may be due to both different risk factor prevalences and different cytology screening practices.

A previous study that compared cervical cancer mortality in 1975 and 1985 in countries of the Americas found that mortality increased in 12 of 23 countries and decreased significantly only in North America (3). In the United States there was a steady decline among older women in both the incidence of invasive cervical cancer and cervical cancer mortality, but rates tended to stabilize among women under 40 (4). Overall there is strong evidence of decline in the U.S. A study covering the pe-

1 Program on Noncommunicable Diseases, Division of Disease Prevention and Control, Pan American Health Organization, Washington, D.C., U.S.A.
period 1947–1984 found cervical cancer rates to be consistently lower and declining among white women (5), while a more recent U.S. study documented 66% and 61% declines among American Indians and Hispanics, respectively (6).

Limited cytologic screening for cervical cancer was introduced in most countries in the late 1950s and early 1960s within the context of clinical practice. Broader efforts to organize a program in the Canadian province of British Columbia, which got underway in the 1950s, produced noteworthy declines in cervical cancer incidence and mortality over a 30-year period (7). More recently, over the past two decades, several countries have attempted to organize screening programs. Most of them have initiated activities through a centralized office, usually located within the Ministry of Health. Some degree of success has been reported, particularly in urban areas of medium- to high-income countries; but the common denominator is difficulty reaching the population at risk (8), that is, middle-aged women of low socioeconomic status.

The efficacy of cervical cytology at the individual level has been indicated by three case-control studies, which have found it to have a protective effect against invasive cervical cancer in the Latin American context (9–11). Nonetheless, true demonstration of effectiveness would require a collective approach in the form of an organized population-based program, the impact of which would be reflected in declining incidence and mortality trends.

Measurement of mortality trends may be difficult in some countries where the quality of death registration is not high. In the Americas, out of 25 countries for which mortality data are available, at least 20% of all deaths are not registered in nine; and in 15 over 10% of the registered deaths are attributed to "signs, symptoms and ill-defined conditions" (12). In general, under-registration of deaths and death certification inaccuracies tend to be higher among people over 65 years old and among women.

In contrast to cervical cancer mortality data, long-term incidence data are not available in Latin America and the Caribbean—either because cancer registries are relatively new or because they have not continued operating at the required level of quality. In addition, important changes in diagnostic criteria have occurred over the past 20 years, due to differences in cytologic and histopathologic classifications and the introduction of new technical procedures such as colposcopy. At least in principle, these changes have tended to have more impact upon incidence than upon mortality. Because of these limitations, we have chosen to describe only trends in mortality.

Since most cervical cancer occurs in developing countries, and since data on mortality are needed for program development, monitoring, and evaluation, careful assessment of such data’s quality is warranted. In this article we discuss issues and other considerations involved in the use of such data as well as the general cervical cancer situation prevailing in the Region of the Americas.

METHODS

Information on mortality and population was obtained from the Technical Information System of the Pan American Health Organization (PAHO). Member country mortality data by age, sex, and cause are available from 1960 onward. Detailed information about data availability by country is published periodically (12). The population estimates used are those employed by the United Nations, with rates age-standardized to those of the World Standard Population (13). Trends were estimated for those countries where data were available for at least 10 consecutive years with less than 30% underregistration. Further analyses were conducted only for countries
where changes in trends were observed. Rates of change in these trends were estimated using the least squares method, under the assumption that the logarithm of the observed rate varied linearly (14). No attempt was made to model age-cohort data, as the graphic display presented suffices for the purpose of making intercountry comparisons (15).

RESULTS

Table 1 shows data on age-adjusted cervical cancer mortality, underregistration of overall mortality, and the percentage of deaths attributed to "signs, symptoms, and ill-defined conditions" (International Classification of Diseases, Ninth Revision, categories 780–799) in 24 countries of the Americas. Only the United States and Canada appeared to have less than 2% underregistration, seven other countries appeared to have less than 10% underregistration, and the remaining countries had 10% or more. Belize, Guyana, Haiti, and a number of other Caribbean countries are not listed because the number of deaths was too small or because it was not possible to obtain estimates of underregistration. The proportion of deaths attributed to "signs, symptoms, and ill-defined conditions" was taken as an indicator of death certification accuracy; as may be seen, 13 countries reported that less

<table>
<thead>
<tr>
<th>Country</th>
<th>Mortality (age-adjusted) per 100 000</th>
<th>Underregistration of deaths (%)</th>
<th>Mortality ascribed to signs, symptoms, and ill-defined conditions (%)</th>
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<tbody>
<tr>
<td>Argentina</td>
<td>5.4 10.5 13.8 4.7 9.2 5.1 3.7 4.1</td>
<td>8.1 27.8 21.7 21.7 21.7 3.0 40.3 28.9</td>
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than 10% of all registered deaths were in this category.

Age-adjusted cervical cancer mortality trends from 1960 to 1993 in 14 countries of the Americas are shown in Figure 1. It may be seen that while Canada exhibited mortality similar to that of several Latin American countries in the 1960s, a steady decline has been evident since 1965. As a result, Canada currently enjoys the lowest rate in the Region (1.4 deaths per 100,000 women). In contrast, various Latin American and Caribbean countries with rates fairly similar to Canada's 1960 rate (Brazil, Colombia, Cuba, Guatemala, Uruguay, and Venezuela) saw their cervical cancer mortality fluctuate at a similar level over the 33-year period without showing significant downward trends.

Meanwhile, there were several other Latin American countries (Chile, Costa Rica, and Mexico) that exhibited higher mortality than the rest as well as a number of noteworthy changes over time. Costa Rica showed a decline from 1965 to 1973, after which mortality tended to stabilize at around 10 deaths per 100,000. The large variations observed from year to year are most likely a result of the small number of cases involved. On the average, Costa Rica reported nearly 118 deaths from cervical cancer annually over the period 1984–1993. In Mexico, cervical cancer mortality increased from 1965 onward, remaining fairly steady at around 14 deaths per 100,000 in recent years. Since 1975 Chile has reported a slightly declining trend, on the order of that seen in Canada; but cervical cancer mortality in Chile has remained much higher, in the area of 12 deaths per 100,000 women.

In order to further compare the trends in Chile and Canada, we charted these countries' age-specific mortality data for different birth cohorts (Figure 2). This allows one to view cervical cancer mortality patterns for each of six groups of women born in a given period of time. In Chile, no major age-specific differences were found between the different birth cohorts; but in Canada each of the first four cohorts exhibited considerably lower age-specific mortality than its predecessor, demonstrating progressively lower risks in successive cohorts as a result of cervical cancer screening.

The case of Costa Rica provides a likely example of patterns ascribable to changes in reporting accuracy. The available data

Figure 1. Annual cervical cancer mortality in selected countries of the Americas, age-adjusted to the world population, 1960–1993. Source: PAHO/WHO.
Figure 2. Annual cervical cancer mortality by selected five-year birth cohorts in Canada and Chile, 1960–1990.

indicate that Costa Rica experienced an important decline in age-adjusted mortality from all causes between 1965 and 1983 (Figure 3), after which overall mortality continued to decline but at a slower pace. Also, beginning around 1982 there was a sharp drop in mortality from “signs, symptoms, and ill-defined conditions.” Mortality from all cancers (“malignant tumors” in the figure) apparently remained essentially unchanged throughout the 1965–1991 period, as did cervical cancer mortality; but deaths from all other uterine cancers exhibited a marked decline.

These patterns of cervical and other uterine cancer mortality could have been affected by better reporting and improved medical care in such a way as to mask a downward trend in cervical cancer mortality. Specifically, if a malignant tumor is widely disseminated and undifferentiated, it may be difficult to determine whether the primary tumor originated in the cervix or the endometrium, in which case the cause
Figure 3. Mortality from all causes and selected causes (including cervical cancer) among women in Costa Rica, 1965–1991.

of death is reported as being a malignant tumor of the uterine corpus or uterus (unspecified). As an increasing number of women receive medical attention, the cancer may be detected earlier and is more likely to be correctly diagnosed. Under these circumstances, it is possible that deaths previously attributed to cancer of the corpus uteri or uterus (unspecified) are now being more precisely reported as due to cervical cancer.

To control for this possibility, annual mortality from all uterine cancer (International Classification of Diseases, Ninth Revision, categories 179–182) was established for six age groups, and the annual rate of change for each group was calculated for 1961–1991 (Table 2). Significant declines were found to have occurred in all age groups except the one over 74 years old, which showed annual increases averaging 6.8%. The 35–44 year age group experienced the largest average mortality decline, −5.8% per annum. Within this context, it should be noted that cancer of the body of the uterus is rare among women under 50; thus, the declining mortality trend among younger women in Costa Rica is likely due to reduced cervical cancer mortality, a trend masked by improvements in health care and reporting accuracy. The fact that mortality from all malignant tumors did not exhibit important changes in this period may be explained partly by increased mortality from cancers at other sites, such as the breasts.

As previously noted, sharply contrasting cervical cancer trends have been found in Mexico and the United States. When the increasing Mexican mortality is examined by age group (Figure 4), the increase appears to occur almost entirely among


<table>
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<tr>
<th>Age group (in years)</th>
<th>Average annual rate of change (%)</th>
<th>Standard error (%)</th>
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<tbody>
<tr>
<td>25–34</td>
<td>−2.4</td>
<td>0.64</td>
</tr>
<tr>
<td>35–44</td>
<td>−5.8</td>
<td>0.60</td>
</tr>
<tr>
<td>45–54</td>
<td>−3.0</td>
<td>0.47</td>
</tr>
<tr>
<td>55–64</td>
<td>−1.3</td>
<td>0.42</td>
</tr>
<tr>
<td>64–74</td>
<td>−3.4</td>
<td>0.51</td>
</tr>
<tr>
<td>≥75</td>
<td>+6.8</td>
<td>0.72</td>
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women who are at least 50 years old. In younger Mexican age groups (30–34 and 40–44), mortality remained virtually unchanged over a 25-year period. In contrast, the marked decline in cervical cancer that occurred in the United States was reflected in sharply reduced cervical cancer mortality for all age groups except the 30–34 group (Figure 4). In each of these groups a sharp decrease was observed, and even in the 30–34 group some gains were registered, though cervical cancer mortality in this age group tended to stop declining around 1975.

Table 3 shows the average annual rate of change of cervical cancer mortality in 1960–1993 by age group, as indicated by available data from Canada, Chile, Mexico, and the United States. Marked decreasing trends for all age groups can be seen in the United States and Canada, with the declines being sharpest in the three middle-aged groups (40–64 years). In Chile, mortality decreased significantly among women 30–34 years old (by an average of 2.2% per year), but by less (around 1% per year) in the 40–44 and 50–54 groups, and even less in the 60–64 group, while rising slightly (by 0.7% per year) in the oldest group. In Mexico, average cervical cancer mortality increased in all age groups, the increase being especially marked (3.5% per year) in the oldest (70–74) group.

**DISCUSSION AND CONCLUSIONS**

Cervical cancer mortality has not declined in Latin America as it has in developed countries, particularly Canada and the United States. In Chile, declines in mortality did occur among younger women in 1960–1993, but these were not so large as those registered in Canada and did not pertain to older age groups. Chile has reported low underregistration of deaths, and the proportion of deaths attributed to "signs, symptoms, and ill-defined conditions" has remained reasonably steady in recent times (4.9% in 1972, 5.6% in 1992). Therefore, it seems unlikely that more pronounced actual declines have been masked by improved reporting and diagnosis, as appears to have been the case in Costa Rica (16).

Another factor that may be influencing cervical cancer mortality is increasing rates of hysterectomy, for which reason it has been argued that adjustments to denomi-
Table 3. Average annual percentage rates of change in cervical cancer mortality, by age group, in Canada, Chile, Mexico, and the United States, 1960–1993.

<table>
<thead>
<tr>
<th>Age group (in years)</th>
<th>Canada</th>
<th>Chile</th>
<th>Mexico</th>
<th>United States</th>
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<tbody>
<tr>
<td>30–34</td>
<td>-3.0</td>
<td>-2.2</td>
<td>+1.3</td>
<td>-2.8</td>
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<tr>
<td>40–44</td>
<td>4.7</td>
<td>-1.1</td>
<td>+0.8</td>
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<tr>
<td>50–54</td>
<td>5.6</td>
<td>-1.0</td>
<td>+1.9</td>
<td>-3.8</td>
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<tr>
<td>60–64</td>
<td>-4.6</td>
<td>-0.4</td>
<td>+1.6</td>
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<tr>
<td>70–74</td>
<td>2.9</td>
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nators (indicating the number of women at risk) may be necessary (17). There are currently no data directly indicating the importance of this factor in Latin America; but if hysterectomy rates were high enough to make a substantial difference, we should be seeing a trend toward lower cervical cancer mortality than expected, when in fact there were no significant overall changes of this kind.

In Mexico, where cervical cancer mortality has been rising, the rise has been concentrated mainly in older age groups. This is the converse of the situation in the United States, where declines occurring in all age groups have been especially marked in older groups (see Figure 4). While it is not clear whether the high rates among older women in Mexico might be an artifact of improved diagnosis, the existence of such higher rates in Mexico has been affirmed by a 10-year mortality analysis that found a significant increasing trend among women 74 years of age and older (18). This study also noted variations between states and found that 71% of the cancers involved were diagnosed at advanced stages.

Our results suggest that in some Latin American countries decreasing cervical cancer mortality trends may be disguised. There are two possible reasons for this: first, cervical cancer mortality is likely to be decreasing among young women (under age 40) at the same time that it is increasing among older women; and second, as already noted, declines could be masked by improvements in death registration and the accuracy of death certification. Regarding the first point, rising trends among elderly women, very clear in Mexico, were also observed in Chile and Costa Rica. These differentials between young and old may result from concentrating screening efforts on young women while failing to reach older women at higher risk. Regarding the second point, data from the Cali Cancer Registry in Colombia, the longest-standing population-based registry in Latin America (19), suggest that the incidence of invasive cervical cancer is decreasing in the area covered by this registry, although it is not certain that this trend is occurring in the rest of Latin America.

Clearly, there is a need for further country-by-country studies on cervical cancer incidence and mortality trends, as well as for studies clarifying the role of potential artifacts. We did not analyze trends for all countries, limiting ourselves to trends in three countries with the highest rates that exhibited noteworthy changes over time; nor did we obtain information from countries where a large proportion of all deaths were unregistered. The situation in these latter countries should be explored, because lack of death registration goes along with low national income and poor living conditions, which makes the population more susceptible to risk factors and more likely to have high rates of cervical cancer. For
example, while Honduras reported the lowest cervical cancer mortality in the Region (see Table 1), it appears that some 46.6% of all deaths in the country were unregistered. Moreover, an independent study on causes of mortality among Honduran women 15–49 years old found that 12% of all the deaths studied could be classified as due to "cancer of the uterus" (20), which clearly suggests a higher rate of cervical cancer mortality than the one reported through routine death registration.

Usually, trends are described graphically. The magnitude of change over a given unit of time is accurately represented by displaying the rate of change; and while use of the least squares method (to estimate the slope of the curve and thus the rate of change) assumes that the logarithms of the rates are linear, this method is relatively simple and easy to understand. However, for age-period-cohort models or geographic age-specific comparisons, when it is unlikely that the assumption of linearity will hold, it is necessary to use more sophisticated methods that permit inclusion of interaction terms within the model. In the study reported here, stratification by age made it possible to examine differences between age groups, which is important because cervical cancer risk varies with age, and screening practices tend to focus on particular age groups, not necessarily those at highest risk. For the purpose of program monitoring, it may be desirable to follow changing incidence and mortality trends by monitoring tracer age groups that are especially sensitive to the effects of screening and where screening should be targeted. Within this context it should be noted that the traditional age-standardized rates can mask changes that are of low magnitude but of public health significance.

In general, Latin American countries tend to exhibit large within-country differences in cervical cancer incidence and mortality (12, 21–23). The completeness and accuracy of such incidence and mortality data tend to differ for different population groups, nor is there uniform provision of health services or access to cervical cancer screening. It is difficult to document the cervical cancer burden in the least-developed geographic areas or subpopulations, partly because of poor data quality, but also because lack of accessibility to health services precludes poor women from being diagnosed, not to mention having an opportunity to receive adequate treatment. In contrast, well-off areas or subpopulations can access health care services more easily and have more medical technology available to them for diagnosis and treatment, which in turn reduces morbidity and mortality. This situation is aggravated by the fact that the incidence of cervical cancer tends to be higher among those of low socioeconomic status. We now know that some types of human papillomavirus may be a necessary cause, although not a sufficient one, for development of cervical carcinoma (24, 25); other risk factors, such as high parity and smoking (26), may help to trigger progression of the disease, while dietary factors such as intake of beta-carotene (27, 28) and vitamin C (29) may have protective effects. These risk factors tend to be more prevalent in population groups with low socioeconomic status, which also are likely to have poor dietary intake of vitamins.

Although not all changes in cervical cancer mortality can be attributed directly to screening, early studies in developed countries demonstrated a correlation between declining mortality and screening intensity (30). More specifically, it has been found that declines in incidence and mortality have tended to be greater among age groups and birth cohorts subject to screening, whereas little change has been observed among women not enrolled in a screening program (31). Apparently as a consequence of screening in 12 European countries (32), cervical cancer's incidence declined more between 1962–1967 and
1978–1982 in women 35–55 than it did in any other age group. These and other data suggest that the direct benefit from an organized screening program can typically be observed mostly among middle-aged women who remain in the program (33, 34).

Self-selection may be playing a role in this, because women at lower risk may be more apt to participate. In addition, the effectiveness of screening is determined partly by the sensitivity of cytology and by the likelihood that women with a positive test will receive a complete diagnostic workup and appropriate treatment (35). All this makes it important that organized screening programs be able to reach women at risk, maintain attendance rates, and provide the mechanisms needed to ensure appropriate followup (36). Experience in the Nordic countries has demonstrated that, in the best situations, the incidence of cervical cancer following a negative Pap smear may be reduced by up to 90% (37). There will always be some women in whom the preinvasive lesions cannot be detected; for example, some women may have adenocarcinoma of the endocervix, which is hard to detect through cervical cytology (38).

Lately, in developed countries, cervical cancer incidence and mortality among women under 40 have been observed to level off or even to increase. These trends have been attributed to improved diagnostic precision (39), emergence of adenocarcinoma of the cervix in women under 35 years old (40, 41), and lifestyle changes in the younger generation that have a bearing on the prevalence of risk factors, such as use of oral contraceptives (42); both of the latter could be a problem in America.

In most Latin American and Caribbean countries, efforts to introduce cervical cancer screening and reach large numbers of women have been linked to family planning and prenatal care programs. Women who seek these services are young, commonly in their 20s, and at lower cervical cancer risk than older women. Screening these women is not cost-effective, partly because of the low incidence of cervical neoplasia in this age group and partly because the age distribution of the female population in Latin America resembles a pyramid with a large base. Thus, there are a large number of women under 30 years old; and if screening resources are concentrated on them, there may not be enough to screen older women at higher risk who usually have less access to health services (43).

As already noted, if cervical cancer screening is properly conceived and executed, it can have a pronounced impact on cervical cancer incidence and mortality. Moreover, it can also yield other benefits. Timely treatment for cervical cancer can improve a woman’s quality of life and enable her to remain or enroll in the workforce. In addition, women who are screened are more likely to receive medical examinations and be subject to other clinical preventive measures (44). Thus, the cervical cancer screening provided by an organized program may also provide an opportunity to increase health care access for women who are not in their prime reproductive years. If this can be achieved in Latin America and the Caribbean, reductions in disease incidence and mortality due not only to cervical cancer but also to other causes are likely to occur.

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