Effective cervical cytology screening programmes in middle-income countries: The Chilean experience

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Abstract

Objective: To demonstrate that an effective cervical cancer screening programme based on the Papanicolaou (Pap) smear can be organized in a middle-income country, such as Chile. *Methods:* The cervical cytology screening programme in Chile is evaluated by comparing process measures and cervical cancer mortality before and after its reorganization in 1987. *Findings:* Two decades of opportunistic annual screening for cervical cancer from the mid-1960s to the mid-1980s did not reduce cervical cancer mortality in Chile. In 1987, a public health oriented program was launched, based on screening women aged 25–64 every 3 years, rather than the annual screening of low risk women attending family planning clinics that gathered mainly women less than 25 years of age. The reoriented program emphasized the optimization of existing resources, the timeliness of diagnosis and treatment, reliability of the Pap smear and low cost screening promotion strategies at the community level. More than 80% of women with abnormal Pap smears received prompt medical attention and 100% of the public laboratories were subject to external quality control. According to biannual national surveys, coverage by Pap smear screening in the target group rose from 40% in 1990 to 66% in 1996. The age adjusted cervical cancer mortality rate decreased from 12.8 in 1980 to 6.8 per 100,000 women in 2001. *Conclusions:* Improved organization of the national cervical cancer screening programme in Chile and more efficient use of existing resources resulted in a decrease of cervical cancer mortality.

Keywords: Cervix neoplasms; Diagnosis; Pathology; Cervix dysplasia; Vaginal smears; Cytodiagnosis; Cervical intraepithelial neoplasia; Mass screening; Organization and administration; National health programs; Quality assurance; Health care; Mortality; Trends; Chile

1. Introduction

Cervical cancer is the second most common cancer worldwide and the leading cause of cancer deaths among women in less developed countries. In Chile, it accounts for 9.5% of cancer deaths in women, only surpassed by deaths from cancers of the gall bladder, breast and stomach [1].

The best established screening method for cervical cancer is the Papanicolaou (Pap) smear [2]. Between 1965 and 1982 nationwide programmes in Finland, Iceland and Sweden demonstrated cervical cancer mortality reductions of 35–80%, comparing mortality rates before and after the introduction of organized screening programmes [3]. Effective screening programmes have been introduced in many industrialized countries. However, in developing countries Pap smear programmes have been mostly limited to offering the test to women attending primary health care and other health clinics (opportunistic screening). Nearly, all programmes in developing countries have no organized efforts to reach the high-risk women or to ensure that those found to have an abnormal smear receive effective follow-up and treatment. Existing programmes in these countries are failing to achieve a major impact [4,5].

The purpose of this paper is to demonstrate that an effective cervical cancer screening programme based on the Pap smear can be organized in a middle-income country such as Chile. Screening activities and the epidemiologic situation are described before and after the programme

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reorganization in 1987. Process measures, such as target age group coverage, timeliness of diagnosis and treatment, and reliability of the cytology diagnosis, document the pre- versus post-reorganization changes in the programme components. The overall impact of the reorganization is demonstrated by its effect on the proportion of cases with advanced disease, the rate of invasive disease and cervical cancer mortality.

2. Materials and methods

2.1. Evaluation design

The impact of the reorganized cervical cancer screening programme was evaluated by comparing process and outcome measures before and after the programme reorganization in 1987. Process measures included the percentage of Pap smears taken in target group (women aged 25–64), the timeliness of diagnosis and treatment of women with abnormal Pap smears and the quality of the Pap smears. These were evaluated using annual questionnaires. These surveys were sent from the Ministry of Health and the National Cytology Reference Laboratory to the health centres and the cytology laboratories, which collected information from their records at the primary, secondary and tertiary levels.

Compliance to screening was determined by calcula- ting the percentage of women age 25–64 years who had been screened at least once in their lifetime and the percentage screened within the last 3 years. This compliance information was obtained from a series of biannual national surveys Caracterización Socioeconó- mica Nac- ional (CASEN) conducted in 1990, 1992, 1994 and 1996. These surveys were stratified random samples from the entire population of Chile. The questions on screening were a small component of the surveys. After 1990 they collected information on Pap smear screening status and after 1992 they collected information on the reasons for screening non-compliance as reported by the women surveyed.

Outcome measures included the reduction in the proportion of cases of invasive cancer of the cervix with advanced-staged disease (a short term measure), the reduction in incidence of invasive cervical cancer (a medium term measure) and the reduction in cervical cancer mortality (a long term measure). Information regarding the cases of invasive cancer was obtained by the annual questionnaire survey from the health centres, and because individual patient registration of cases was fully imple- mented in only some health centres, this information should be regarded with caution. However, the mortality and population data are reliable and were obtained from the National Center of Statistics. Incidence and mortality rates were age standardized to the 1982 Chilean population to facilitate time trend comparisons.

2.2. The programme before and after 1987

Cervical screening activities in Chile started in 1965 with the implementation of National Public Health System (NPHS) cytology laboratories, cervical pathology clinics and a policy of taking Pap smears every year from women attending the maternal and child care units at the primary health care level. The screening programme was mainly oriented to low income women served by NPHS, and thus concentrated on young women at low risk for cervical cancer. The NPHS covered 70% of the population and consisted of 29 health services, each serving a geographic area and administering its own budget.

Up to 1986 there was no supervision of cervical screening activities from the Ministry of Health and very little mon- itoring or evaluation by the health services. Only 10% of the women over 15 years old were being screened annually. In 1986, the Ministry of Health of Chile, assisted by WHO, in- itiated development of a National Cancer Control Programme with cervical cancer as one of its priorities. In 1987, a National Cervical Cancer Screening Programme with a public health orientation was launched following the guidelines of WHO [6].

In 1987, the health professionals in charge of the prog- rammes of health services nationwide in Chile were reluctant to apply the Ministry of Health's approach to focus cervical cancer screening on women aged 25–64 every 3 years. Consequently, the reorganization focused its effort and resources in a demonstration area, the Metropolitan Region of Santiago, the capital of Chile. Seven years later the programme was expanded to the rest of the country. In 1997, cervical cancer screening was officially included among the 10 national health priorities of the Ministry of Health.

The main programme goals were the reduction in cervix cancer mortality by 50% and the screening of 80% of women aged 25–64 every 3 years. The principal strategies included: (a) coordination, monitoring and evaluation at the national, regional and community levels, (b) timeliness and quality of diagnosis and treatment of women with abnormal Pap smears, (c) ensuring the reliability of the Pap test by monitoring the taking of Pap smears and by a quality control programme for the cytology laboratories and (d) promotion of cervical screening with Pap smears every 3 years in the target age group. The decision to concentrate on women 25– 64 years old was based on the fact that the age specific mortality rates were high enough to be of major public health concern for women as young as 35–39 years of age but that no mortality was observed under 25 years of age [7].

2.3. Implementation of the reorganized programme

The strategy adopted in the Metropolitan Region and later applied to the rest of the country was early involvement of the health authorities and a series of training workshops for health professionals concerned with the programme at each level of care. The conduct of workshops assisted by a physician skilled in education and health communication.

These workshops aimed at changing the established practices of health professionals by using a methodology resulting from a combination of the problem identification and solving approach and a variant of the problem based learning approach in medical education. The main areas of intervention were a personal (consistency, optimism, flexibility and good interpersonal relations) and a collective strategy. The collective strategy focused on achieving specific objectives based upon a systemic overview, critical mass, teamwork, efficient use of resources, a project planned with creative input from the local team, and quality information optimally circulated. This process resulted in a highly motivated multidisciplinary team that was able to gradually implement the strategies and monitor and evaluate them using existing resources.

Population-based registries were not available. Nevertheless an information system monitoring the women entering the programme was implemented and included case registries at every level of the health system. This permitted adequate coordination among primary health care centres, cytology laboratories, colposcopy clinics and gynaecological services. It also served as a basis to ensure the timeliness of diagnosis and treatment procedures for women with abnormal Pap smears and the quality control of cytologic diagnosis [8].

Promotion strategies to invite women to screening were implemented step-by-step, carefully synchronised with health centres for the adequate provision of care. These strategies included motivation of female health care providers to be screened, offering screening to women in the target group attending primary health care centres and development of community strategies to reach older women who cease to attend health care centres once their reproductive time has finished. No national mass media campaigns were included due to a lack of resources. In the last few years women in need of repeat cytology after 3 years were identified through the primary health care registries and were either reached by a letter of invitation or by volunteers visiting them at home.

Between 1987 and 1997 financial support for the programme was less than US$ 3.6 million. Initially this support was by small grants from WHO. In 1993, a World Bank grant was obtained, consisting of US$ 1.0 million for upgrading equipment at the secondary level. Since 1994 the Ministry of Health has provided an average of US$ 270,000 each year, largely for support of the community-based health promotion activities.

2.4. Cytology

In concert with introduction of the new strategies of the National Cervical Cancer Screening Programme, a national system of cytology laboratories was implemented between 1990 and 1994. The main objective of this system was to optimize the diagnostic reliability of cytology laboratories by improving internal quality assurance and providing adequate external quality control. Components of this system included a network of 22 cytology laboratories and a National Cytopathology Reference Laboratory. To date this system has focused on the public laboratories which process about 65% of all the Pap smears reported nationwide.

Software for the cytology laboratories was developed to facilitate the operation and evaluation of these laboratories, as well as the surveillance of activities performed by other components of the screening program such as quality of smears taken at the primary health care units, follow up of cases with abnormal cytology reports, periodic control of cases with normal cytology, and information on new cases being incorporated into the screening program. This software has been implemented in all laboratories of the national system [9].

The Bethesda System [10,11] was the basis for the cytopathology terminology, but the classification system was modified, as is often necessary, to fit the local situation in Chile. For example, there was local concern regarding possible infection by HPV and the potential for over-diagnosis. Cytological reports of low grade SIL were divided into two groups: those with minimal atypia, suggesting only HPV infection, and those with more intense nuclear alterations in mature squamous cells favouring a diagnosis of CIN I. Low grade SIL cases of the first group were followed with a repeat cytology 1 year later and those in which cytological atypia persisted were referred to colposcopy clinics for additional diagnostic procedures. Those cases in which low grade SIL cytology favoured CIN I were referred directly for additional diagnostic workup.

The quality of cytologic specimens was evaluated using the proportion of Pap smears reported as "unsatisfactory" or "satisfactory but limited by absence of metaplastic and endocervical cells" (transformation zone components). This information was available for each smear taken in every primary health care unit of the screening program nationwide. The correlation between cytopathology and histology served as the standard for internal quality assurance. External quality control was performed by the National Cytopathology Reference Laboratory through annual surveys on overall performance of cytology laboratories, including cyto-histo-logic correlation in cases for which biopsies were performed following an abnormal cytologic report or because of clinical indications. In addition, sets of slides representing different diagnostic categories were circulated among all laboratories and concordance of diagnoses with those of the reference laboratory was evaluated. Continuous education and site visits to the laboratories were also a part of the reference laboratory's responsibilities.

3. Results

3.1. Percentage of women aged 25–64 years with Pap smears

In 1986, the majority of Pap smears were for the annual screening of women less than 40 years of age and about 40%

of all Pap smears were for women less than 25 years of age. Ten years later, after the reorganization process, 80% of all Pap smears were focused on screening women in the target group, 25–64 years of age, every 3 years and only 20% were for women below the age of 25 years. There was no increase in resources. The same number of cytology tests (about 600,000 per year) was enough to meet the programme needs.

3.2. Follow-up of women with abnormal Pap smears

Before 1988 there was no organized patient follow-up. In most health centres less than 60% of the women with an abnormal Pap smear (CIN I and higher grade lesions) were referred to a colposcopy clinic and only 30% of them attended within a month. After training of the health care professionals and implementation of the follow-up system for the primary and secondary levels this situation improved remarkably. In 1995–1997, about 98% of women with abnormal Pap smears reached the colposcopy clinics and in 80% of those cases the referral was done in a timely manner.

3.3. Reliability of cytologic reports

The National Cytopathology Reference Laboratory began its activities in 1993; thus, the information presented covers the period from 1993 to 1997. A total of 2,876,074 Pap smears were reported by the 22 laboratories during this period. The number of smears and their respective proportion in each diagnostic category is presented in Table 1.

The proportion of unsatisfactory specimens was fairly uniform, 3–4%, during the study period. However, Pap smears reported in the "satisfactory but limited" category showed a steady decline from 21.7 to 10.1%, reflecting an improvement in the quality of specimen collection.

The percentage of positive smears declined from 2.4% in 1993 to 1.7% in 1995 and 1997 (Table 1). This was accompanied by almost a doubling of the proportion of high grade squamous intraepithelial lesions relative to the overall number of squamous intraepithelial lesions (SIL) cases, from 20.5% in 1993 to 35.7% in 1997, most likely a result of concentrating screening activities upon the higher risk women.

Accuracy of cytologic diagnosis was monitored through the correlation of cyto-histologic and biopsy results for cases on which biopsies were performed after a positive or atypical cytologic report. During the study period a biopsy was performed on 7840 women with a cytological diagnosis of high grade SIL and on 1208 women with a cytological report of cancer. In 79% of cases with a cytological diagnosis of high grade SIL, the biopsy report was high grade SIL or cancer and in 93% of cases with a cytological report of cancer, the histological diagnosis was cancer or high grade SIL.

During the study period, 7915 women with a cytological report of low grade SIL were biopsied. The histopathological diagnosis reported on these cases shows a 70% agreement between cytological and histological diagnosis. For 11% the biopsy was normal, for 19% the biopsy revealed high grade SIL and for 0.6% the diagnosis was cancer. This 20% cytological under-diagnosis for this category influenced the decision of the national committee

Table 1
Cytologic reports by diagnostic category of the national cytology laboratory system

Cytologic diagnosis	1993	1994	1995	1996	1997	Total
Normal, satisfactory	391385	455805	487443	438796	500067	2273496
	(71.8)[a]	(75.0)	(82.1)	(82.5)	(83.6)	(79.0)
Satisfactory, but limited[b]	118492	112763	73138	58341	60284	423018
	(21.7)	(18.6)	(12.3)	(11.0)	(10.1)	(14.7)
Unsatisfactory	17854	23096	18562	18882	22594	100988
	(3.2)	(3.8)	(3.1)	(3.6)	(3.8)	(3.5)
ASCUS/AGUS[c]	3943	3995	4233	5016	5259	22446
	(0.7)	(0.7)	(0.7)	(0.9)	(0.9)	(0.8)
Low grade SIL[d]	10208	8301	6262	6781	6269	37821
	(1.9)	(1.4)	(1.1)	(1.3)	(1.0)	(1.3)
High grade SIL	2625	3041	3283	3346	3476	15771
	(0.5)	(0.5)	(0.6)	(0.6)	(0.6)	(0.5)
Carcinoma	437	495	562	494	546	2534
	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)
Total	544944	607496	593483	531656	598495	2876074
Percentage with a positive cytology[e]	(2.4)	(1.9)	(1.7)	(2.0)	(1.7)	(2.0)
High grade SIL as percentage of SIL	(20.5)	(26.8)	(34.4)	(33.0)	(35.7)	(29.4)

[a] Figures in parentheses are percentages.
[b] Satisfactory, but limited by absence of metaplastic and endocervical cells.
[c] Atypical squamous cells of undetermined significance (ASCUS)/atypical glandular cells of undetermined significance (AGUS).
[d] Squamous intraepithelial lesions (SIL).
[e] Positive cytology is a low or high grade SIL or carcinoma.

Table 2
Percentage of Chilean women aged 25–64 years who stated they had a Pap smear within the last 3 years according to type of health insurance[a]

Years	Chile overall	Public	Private
1990	51	49	63
1992	58	55	68
1994	65	62	74
1996	66	63	74

[a] *Source:* Chilean national survey (CASEN).

to maintain the referral of these cases for additional diagnostic procedures.

3.4. Compliance with screening in the target age group

The national survey (CASEN) in 1996 showed that 79% of women aged 25–64 years of age had a Pap smear at least once in their lifetime and 66% had a Pap smear within the last 3 years (see Table 2). Only 3% of the women surveyed failed to provide information on their screening status. The percentage of women aged 25–64 years having a Pap smear within 3 years increased from 51% in 1990 to 66% in 1996. The public system had a lower coverage than the private system but proportionally the public system achieved a greater relative increase.

The compliance with screening within 3 years increased from 58% in 1992 to 66% in 1996. Table 3 shows that the largest increase in compliance from 1992 to 1996 was seen in the 35–54 year age group, which had been specifically emphasized by the programme. However, the compliance rate for all age groups was still below the goal of 80%. The main reasons for non-compliance given by women aged 35–64 in the CASEN survey of 1996 were negligence (49%), afraid of the test (18%), do not care (14%), unaware of the Pap test (11%) and did not know how to get the Pap test (2%).

3.5. Stage distribution and incidence rates of invasive carcinoma of the cervix

According to data provided by the health centres, the proportion of women with stage I cervical cancer progressively increased from 30.4% in 1990 to 39.0% in 1996. Correspondingly, the proportion with more advanced

Table 3
Percentage of Chilean women aged 25–64 years who stated they had a Pap smear within the last 3 years by age group[a]

Age group	1992	1994	1996
25–29	58.1	63.7	61.6
30–34	66.6	72.2	71.3
35–39	65.1	72.5	71.9
40–44	60.2	70.6	71.4
45–49	58.4	65.1	67.5
50–54	51.1	64.9	62.7
55–59	46.1	51.6	54.0
60–64	34.7	43.6	45.0

[a] *Source:* Chilean national survey (CASEN).

Table 4
Incidence of invasive carcinoma of the cervix in 1996, age specific rates per 100,000 women, Metropolitan Region vs. the remainder of Chile[a]

Age group	Metropolitan Region	Remainder of Chile
15–24	1.3	1.3
25–34	11.4	14.3
35–44	25.5	32.2
45–54	32.3	49.9
55–64	26.3	44.6
>64	45.2	45.5

[a] *Source:* Miller [12].

disease declined over this same time period; from 28.8 to 23.0% for those with stage III disease and from 6.5 to 4.0% for those with stage IV disease.

The incidence rate of invasive cervical cancer in the age group emphasized by the programme was considerably lower in the Metropolitan Region as compared to the rest of the country, suggesting the effects of the longer programme implementation in the Metropolitan Region [12] (Table 4). However, ecologic fallacy is a possibility as there could be differences in risk factors between the Metropolitan Region and the rest of the country.

4. Mortality rate

The age adjusted mortality rate for cervical cancer decreased from 13.1 per 100,000 women in 1970 to 11.1 in 1986 to 6.8 in 2001 (Fig. 1). Between 1970 and 1986 there was a 15% reduction, 1% per year. Between 1986 and 2001 there was a 39% reduction, 2.6% per year. The rate of reduction of cervical cancer mortality appears to have been greater during the past 15 years.

5. Discussion

We have demonstrated that it is feasible to implement a Pap smear-based screening programme in a middle-income country that can effectively reduce cervical cancer mortality. This investigation confirms and extends the state-level approach of Paraná State in Brazil, which showed a reduction of cervical cancer deaths from 297 in 1998 to 188 in 2002 following an enhancement of Pap smear coverage from 43 to 86% [13].

Following its reorganization in 1986 the National Cervical Cancer Screening Programme of Chile has a number of important achievements. A trained and motivated network of health professionals in the public system who contribute actively to the programme has been organized. Facilities and procedures have been developed for the diagnosis and treatment of abnormalities and these have ensured timeliness and compliance to follow-up for the vast majority of the cases.
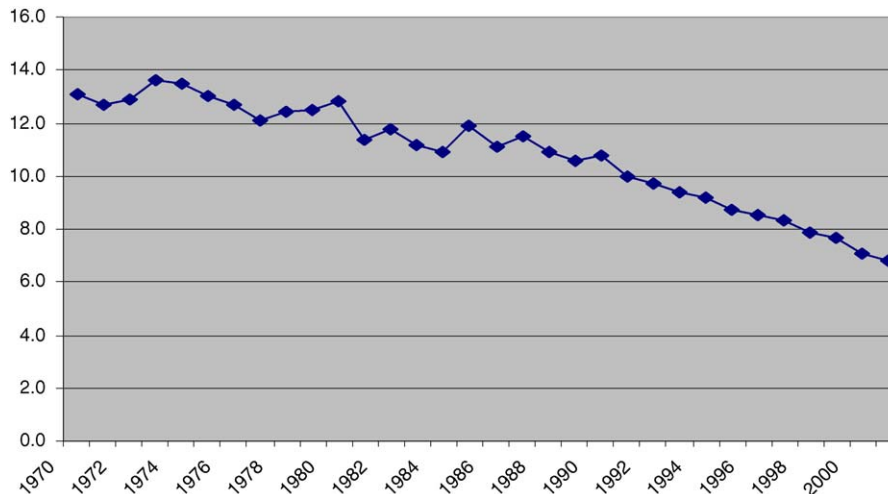
Fig. 1. Mortality from cervical cancer, Chile 1970–2001. (Age standardized mortality rate per 100,000 women using the 1982 Chilean population as standard). *Source*: Ministry of Health, Chile.

Continuous training of health professionals taking the Pap smears and a quality control programme for the cytology labs, introduced in 1995, improved the reliability of the Pap test in the public system. Focusing on Pap smear screening every 3 years in the 25–64 year age group has permitted a gradual increase of compliance to screening with no major increase in resources. CASEN surveys report that the majority of non-compliant women aged 35–64 years have been informed about the Pap test and know how to get it done. The incidence of invasive cancer appears to be less in the Metropolitan Region than in the remainder of the country for the age group upon which the programme concentrated. Cervical cancer mortality rates have been decreasing, apparently largely due to the effects of the programme. However, the declines in incidence and mortality may also have been helped by changes in reproductive patterns in the country, particularly in relation to reduced parity and delayed child-bearing.

In spite of this progress there are still important challenges for this programme. The programme needs to improve the information system by developing population-based registries for determining coverage and ensuring full follow-up and by implementing an individual patient case registry for pre-invasive and invasive cancers. The programme also should allocate adequate resources for research studies aimed at overcoming cultural barriers for improving compliance, especially in older women, including private laboratories in the quality control programme, and integrating services with other women's health promotion and prevention programmes. To avoid over-treatment and waste of valuable resources, the management guidelines for abnormal PAP smears should be revised, especially concerning referral of LSIL to biopsy. There is evidence that the majority of the abnormalities would regress without biopsy and the remainder can be picked up on a repeat smear in 6 months [14].

The National Cervical Cancer Screening Programme of Chile has shown substantial progress since 1987 due to an improved organization, more efficient use of resources, application of low cost promotion strategies to increase compliance to screening and provision of quality control procedures. The significant decrease in mortality rates in the last 15 years may be attributed to a certain extent to this reorganized programme. In order to continue the reduction in mortality, special efforts have to be made to reach women over 35 years old who are reluctant to attend the health care centres mainly due to cultural barriers.

Cytology screening remains the standard approach for cervical cancer screening. Effective programmes should be implemented, especially in middle-income countries where cervical cancer is an important public health problem and cytology screening is feasible. New approaches for low resource settings, such as the visual inspection with acetic acid, may be suitable as a supplementary approach in a few years if early positive results are confirmed by ongoing investigations [4].

Acknowledgements

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