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Breast cancer age at diagnosis patterns in four Latin American Populations: A comparison with North American countries

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ABSTRACT

Background: In the Latin America countries (LAC), one in five breast cancer (BC) cases occur in women younger than 45 years, almost twice the frequency seen in developed countries. Most BC cases in younger women are premenopausal and are generally more difficult to detect at early stages and to treat than postmenopausal cancers. We employ data from four high quality population-based registries located in LAC and assess the extent to which the higher frequency of BC occurring in younger women is due to a younger population structure, compared to that of developed countries. Next, we analyze secular and generational trends of incidence rates in search for additional explanations.
Methods: Using data from the International Agency for Research on cancer, between 1988 and 2007, the age distribution of BC incident cases for registries located in Brazil, Colombia, Costa Rica, Ecuador is compared to that of USA and Canadian registries, both before and after removing differences in population age structure. An age-period-cohort modelling of incidence rates is also conducted in all compared registries to identify secular and generational effects.
Results: BC incident cases in the LAC registries present, on average, at an earlier age than in the USA and Canadian registries and for 2003–2007, between 20 and 27% of cases occur in women aged 20–44. About two thirds of the difference in age distribution between LAC and USA registries is attributable to the younger age distribution in the LAC base populations. The USA registries show the highest age-specific BC incidence rates of all compared aggregated registries, at all ages. However, in all the LAC registries incidence rates are rapidly increasing, fueled by a strong birth cohort effect. This cohort effect may be explained by important reduction in fertility rates occurring during the second half of the 20th century, but also by a greater exposure to other risk factors for BC related to the adoption of life styles more prevalent in developed countries.
Conclusion: The younger age at presentation of BC incident cases seen in the analyzed LAC registries, and possibly in many Latin American countries, is not only attributable to their relatively young population age structure but also to the low incidence rates in older women. As more recently born cohorts, with greater exposure to risk factors for postmenopausal BC, reach older age, incidence rates will be more similar to the rates seen in the USA and Canadian registries. There is a need for additional research to identify determinants of the higher BC rate among younger women in these countries.

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1. Introduction

Breast cancer is the most frequent cancer among women worldwide [1]. Breast cancer has a high burden of morbidity and mortality for pre-menopausal women, whose disease, characterized by more aggressive tumors [2], may be particularly difficult to detect at early stages and to treat [3,4]. It is estimated that 20% of Latin American breast cancer cases occur in women younger than 45 years, compared to 12% in higher-income countries [5]. Reasons for this higher proportion remain largely unexplored. The leading hypothesis is that the concentration of breast cancer among younger women in Latin America is attributable to the younger age distribution of their populations compared to developed countries. However, age at presentation may also be influenced by the prevalence of risk factors for breast cancer, and by the breast cancer screening and education policies in place in a given country. The relative distribution of risk factors and access to screening may also vary by age and birth cohort.

In this paper, we analyze data from four high quality population-based registries in Brazil, Colombia, Costa Rica, and Ecuador and compare them with cancer registry data from the US and Canada. First, we estimate the difference in age at presentation observed among these populations, and the proportion of this difference that can be attributed to the differences in population age structure that exist between them. We then analyze the secular and generational trends of incidence rates across registries in search for additional explanations.

2. Materials and methods

Female breast cancer incidence data analyzed here are taken from the 2014 release of the CI5plus database [6] which contains annual counts of newly diagnosed cancer cases and population for 89 population based cancer registries, located in 41 countries. Analyses are restricted to the most recent 20-year available time period (1988–2007). We focus our analysis on the only 4 Latin American registries included in CI5plus (Brazil-Goiania, Colombia-Cali, Ecuador- Quito and Costa Rica) and compare their breast cancer incidence trends with aggregated all-race data from 3Canadian registries (Manitoba, Nova Scotia and Saskatchewan) and from 21 USA registries (San Francisco-California, Los Angeles-California, Connecticut, Atlanta-Georgia, Iowa, Detroit-Michigan, New Mexico, New Jersey, New York State, Utah, Seattle-Washington, Hawaii and SEER-9 registries), also included in CI5plus and with complete information for the study period. We also analyze breast cancer incidence data for Hispanic women from the Los Angeles Cancer Registry since this population group is more similar, both culturally and racially, to Latin American than to the all-race USA registry populations.

In the Latin American registries, the proportion of microscopically verified breast cancer cases ranged between 85 (Ecuador-Quito) and 97% (Brazil-Goiania) during the period 1993-1997 [7], rising to 94–98% during the period 2003–2007 [8]. In contrast, for the aggregated USA and Canadian registries, this proportion has ranged between 98 and 99% for the same time periods. The proportion of breast cancer cases registered exclusively from death certificates has been relatively low in the aggregated four Latin American registries (2% in 1993–1997 and 1.6% in 2003–2007), but higher than in the USA and Canadian registries (less than 1% in both periods).

Three of the Latin American registries (Brazil-Goiania, Colombia-Cali, Ecuador-Quito) have catchment areas covering the metropolitan areas of cities with important rural immigration over several decades. The Costa Rica cancer registry has national coverage [7,8]. Annual growth rates for the base populations of Latin American registries ranges between 1.6 and 2.1% during the analyzed period, whereas the corresponding figures for the aggregated USA and Canadian registries are 0.8 and 0.1%, respectively. In addition, over the study period, in the Latin American registries base populations only between 6.8 and 8.9% of the population is 60 and older, compared to 17.5 and 19.8% of persons in the same age group in the USA and Canadian registries, respectively. In contrast, the base population for the Hispanic women from the Los Angeles Cancer Registry has annual growth rates and a proportion of persons 60 and older that are more similar to the Latin American registries (3.6% and 7.6%, respectively).

We excluded breast cancer incident cases occurring in women under 20 years of age because they represent 1.2 per 10,000 cases in the entire analyzed registries. Between the ages of 20 and 74, 5-year age groups were used in our analyses and a closing age group of 75 and older was used because three Latin American registries lacked more detail in their population counts.

Statistical analyses were carried-out to evaluate the age distribution of breast cancer incident cases and its changes overtime, as well as the levels and time trends of incidence rates in all compared registries.

The age distribution of incident cases is initially compared among registries by the mean age at diagnosis and the proportion of cases occurring in young women (aged 20–44), most of whom are premenopausal and have therefore a distinct etiology and clinical course than their older counterparts. To analyze trends in these measures yearly data are collapsed into 5-year periods. 95% Confidence intervals for the ratio of the proportion of cases occurring in young women, among specific registries, were obtained through the formula proposed by Rothman [9].

To assess the extent to which the age distribution of breast cancer incident cases among the compared populations was explained by differences in their base population age structures, we calculated the expected number of breast cancer incident cases if all compared populations had the same age structure observed in the aggregated USA registries for a specific time period, through the following formula:

$$\mathrm{EIC}_{a,p} = \mathrm{IR}_{a,p}(\mathrm{P}_{a,\mathrm{USA}})\left(\frac{\Sigma\mathrm{IC}_p}{\Sigma\mathrm{IC}_{a,\mathrm{USA}}}\right)$$

Where $EIC_{a,p}$ is the expected breast cancer incident cases in age group a for population p,$IR_{a,p}$ is the observed breast cancer incidence rate in the age group a in population p, $P_{a,USA}$is the CI5plus population in the aggregated USA registries in the age group a, $\Sigma\mathrm{IC}_\mathrm{p}$ is the total number of incident cases observed in population p and $\Sigma\mathrm{IC}_{\mathrm{a,USA}}$ is the total number of incident cases observed in the aggregated USA registries.

In addition, we calculated the proportion of the overall differences in the age distribution of breast cancer incident cases, between the Latin American registries and the aggregated USA registries that could be explained (AP) by differences in their age distribution through the following formula:

$$AP = 1 - \frac{\Sigma abs(EP_{a,p} - OP_{a,\,\mathrm{USA}})}{\Sigma abs(OP_{a,p} - OP_{a,\,\mathrm{USA}})}$$

Where $EP_{a,p}$ is the expected proportion of breast cancer incident cases in age group a, for population p, $OP_{a,USA}$ is the observed proportion of incident cases in the age group a in the aggregated USA registries and $OP_{a,p}$ is the observed proportion of breast cancer incident cases in age group a, for population p.

Age-specific breast cancer incidence rates were summarized through the cumulative risk of developing breast cancer between the ages of 20 and 74 years [10].

Age (a), period (p) and cohort effects (c) for the natural logarithm of the incidence rates (λ) were estimated using the following Poisson regression model developed by Holford [11]:

$$Ln(\lambda_{a,p,c}) = \mu + [\beta_a + \beta_p]a' + [\beta_p + \beta_c]c' + \alpha_a + \pi_p + \gamma_c$$

Where a' and c' are the curvature components of the age and cohort effects, respectively, $\left[\beta_p + \beta_c\right]$ is the 'net drift parameter' and indicates the overall direction in which the mortality trend is moving, and α, π and γ are the parameters describing the age, period and curvature trends, respectively. The net drift parameter was extracted using Holdford's naive average. The model was fitted so that age effects are presented as death rates for the reference cohort.

This model was fitted in each registry, using the annual information from 1988 through 2003. Natural splines with 7 parameters for the age, period and cohort terms were incorporated into the modeling to reduce random variation due to the use of such detailed tabulations.

Most of the analyses were carried out using version 12 of the STATA statistical software [12]. Holford's model was fitted using the implementation provided by Carstensen [13] for the R Statistical Package [14].

3. Results

The Latin American and Canadian registries reported considerably fewer breast cancer incident cases than the combined US registries (Table 1). In the Latin American registries the cumulative risk percent [20–74] of developing breast cancer, during 2003-2007, was between 24 and 57% lower than that observed in the combined USA registries. Hispanic women from Los Angeles had a 31% lower cumulative risk than the aggregated all-race USA registries. Over the analyzed period, all compared registries show increases in their cumulative risk but the increase is greater for the Latin American (31-81%) and the Los Angeles Hispanic registries (6%) than for the Canadian and US registries (1% in both cases). In the Latin American and the Los Angeles Hispanic registries, breast cancer incident cases are diagnosed, on average, at ages between 4.0 and 6.8 years younger than in the aggregated USA registries.

Over the study period, the proportion of breast cancer occurring in young women (aged 20-44) has ranged between 20 and 30%, both in the four Latin American registries and in Hispanic women from Los Angeles, roughly doubling the corresponding proportion observed in the combined USA and Canadian registries (Table 2). Except for the Brazil-Goiania registry, the proportion of cases occurring in young women has decreased between 1988 and 2007 in all compared cancer registries, with the Latin American and Canadian registries showing the highest decreases (about 20% over the study period).

The observed relative frequency, by age group, of breast cancer incident cases in the combined four Latin American registries shows important differences to the corresponding USA registries distribution, with the Latin American registries showing higher proportions of cases in younger women and lower proportions of cases in women 60 and older than the USA registries (Fig. 1). These differences have tended to decrease over the study period, but are still important in 2003-2007. Furthermore, although of lower magnitude, Latin American registries still present higher proportions of younger cases and lower proportions of older cases than the USA registries, after removing the differences in age distribution of the compared populations. About one third of the differences in the age distribution of incident cases seen between the Latin American and the USA registries is not explained by the fact that the population in the USA registries is older than in the Latin American ones (Supplemental Fig. 1). In addition, these findings are more or less replicated when specific Latin American registries are compared to the USA registries and are also seen in Hispanic women from Los Angeles.

According to the fitted Age-period-cohort model proposed by Holford, the USA registries show the highest age-specific breast cancer incidence rates of all compared aggregated registries, at all ages (Fig. 2, left panel). Rates for Hispanic women from Los Angeles are more similar to the rates seen in the combined Latin American registries. Among the Latin American registries, only the Brazil-Goiania registry shows rates that are similar to the combined USA registries rates at older ages (Fig. 2, right panel).

In all compared registries, breast cancer incidence rates show cyclic fluctuations over calendar time that are often not significantly different from unity at specific time points (Fig. 3). The average rate ratio for the whole calendar period is 1 in all analyzed registries; therefore no calendar time secular trend is evident in any case.

In contrast, all compared registries show birth cohort effects, albeit of varying magnitude (Fig. 4). The USA and Canadian registries have the smallest cohort effects, with incidence rates more rapidly increasing for women born between 1940 and 1945. For more recently born cohorts, incidence rates progressively increase in the USA registries, reaching a maximum in women born between 1975 and 1979, whereas for the Canadian women born after 1945, rates do not show an statistically significant increase ($p < 0.05$) (Fig. 4, left panel). As in the case of the all-race USA women, Hispanic women from Los Angeles also show a peak in breast cancer incidence starting about 1940, but a stronger cohort

Table 1
Breast cancer incident cases, person-time, cumulative risk and average age at diagnosis for women aged 20 and older observed in the Latin American, Canadian and USA cancer registries included in CI5Plus.

Cancer registry	2003–2007			Percent cumulative risk [20–74] in 2003–2007			Average age at diagnosis in 2003-2007	
	Total incident cases	Total person-years		Ratio with respect to USA registries	% change over the study period		Difference with respect to USA registries	% change over the study period
Brazil, Goiania	4,651	6,809,362	7.4	0.76	80.5	51.6	-6.8	0.8
Colombia, Cali	7,469	12,047,130	5.4	0.55	25.6	54.3	-4.1	1.8
Costa Rica	10,225	21,066,698	4.4	0.45	41.9	54.4	-4.0	1.5
Ecuador, Quito	3,526	8,364,531	4.2	0.43	31.3	53.9	-4.5	1.3
The four Latin American registries	25,871	48,287,721	5.0	0.51	42.9	53.7	-4.7	1.3
Los Angeles, Hispanics	16,699	22,013,948	6.8	0.69	6.2	54.0	-4.4	0.5
Canadian registries	36,455	22,787,800	8.6	0.88	1.2	60.1	1.7	-0.3
USA registries	1,101,53	633,728,445	9.8		1.0	58.4		-0.9

Table 2
Percent breast cancer incident cases occurring in younger women among compared registries.

Cancer registry	Percent breast cancer incident cases, aged 20–44				Ratio with respect to USA registries (95% C. I.)		Percent change over the study period (95% C. I.)
	1988–1992	1993–1997	1998–2002	2003–2007	1988–1992	2003–2007	
Brazil, Goiania	28.9	28.2	26.6	27.1	2.1 (1.8,2.3)	2.2 (2.1,2.4)	-6.3 (-19.0,8.4)
Colombia, Cali	26.5	23.8	22.7	20.2	1.9 (1.7,2.1)	1.7 (1.5,1.8)	-23.7 (-32.4,-13.9)
Costa Rica	25.4	23.8	20.9	19.8	1.8 (1.7,2)	1.6 (1.5,1.7)	-21.9 (-29.9,-12.9)
Ecuador, Quito	27.5	24.9	24.3	22.1	2.0 (1.7,2.2)	1.8 (1.6,2.0)	-19.7 (-32.0,-5.1)
The four Latin American registries	26.6	24.7	22.8	21.7	1.9 (1.8,2.0)	1.8 (1.7,1.8)	-18.5 (-23.6,-13.1)
Los Angeles, Hispanics	24.6	24.6	22.7	21.7	1.8 (1.6,1.9)	1.8 (1.7,1.9)	-12.0 (-18.9,-4.5)
Canadian registries	11.8	11.9	10.3	9.4	0.8 (0.8,0.9)	0.8 (0.7,0.8)	-20.4 (-26.9,-13.3)
USA registries	14.0	13.3	12.5	12.2			-12.7 (-13.9,-11.5)

effect afterwards. All four Latin American registries show very strong cohort effects, with more recently born cohorts having significantly higher incidence rates, but the strongest cohort effect is seen on the Brazil-Goiania registry with an exponential increase in incidence rates for women born after 1955 (Fig. 4, right panel). As in the case of the USA and Canadian registries, the Costa Rica and Colombia-Cali registries show an abrupt rise in rates for women born between 1945 and 1948, whereas a similar pattern is seen between 1948 and 1954 for the Ecuador-Quito registry.

4. Discussion

Good quality population based cancer registries, like the four whose breast cancer incidence data we analyze here, are scarce in Latin America. Despite the fact that these registries have small base populations, interesting findings are obtained regarding the reasons of the younger age distribution of breast cancer observed in them, particularly by making comparisons with the aggregated USA and Canadian registries, and with data for Hispanic women from the Los Angeles registry, available in CI5plus. However, caution must be exercised in extrapolating our results to the whole Latin American countries, since, according to GLOBOCAN estimates; breast cancer incidence varies substantially among countries in the region [5]. In addition, the analyzed USA and Canadian registries are not necessarily representative of the breast cancer incidence trends observed in these countries. Another caveat to interpreting our results concerns the sharp changes in incidence rates, over the analyzed time variables, namely age and

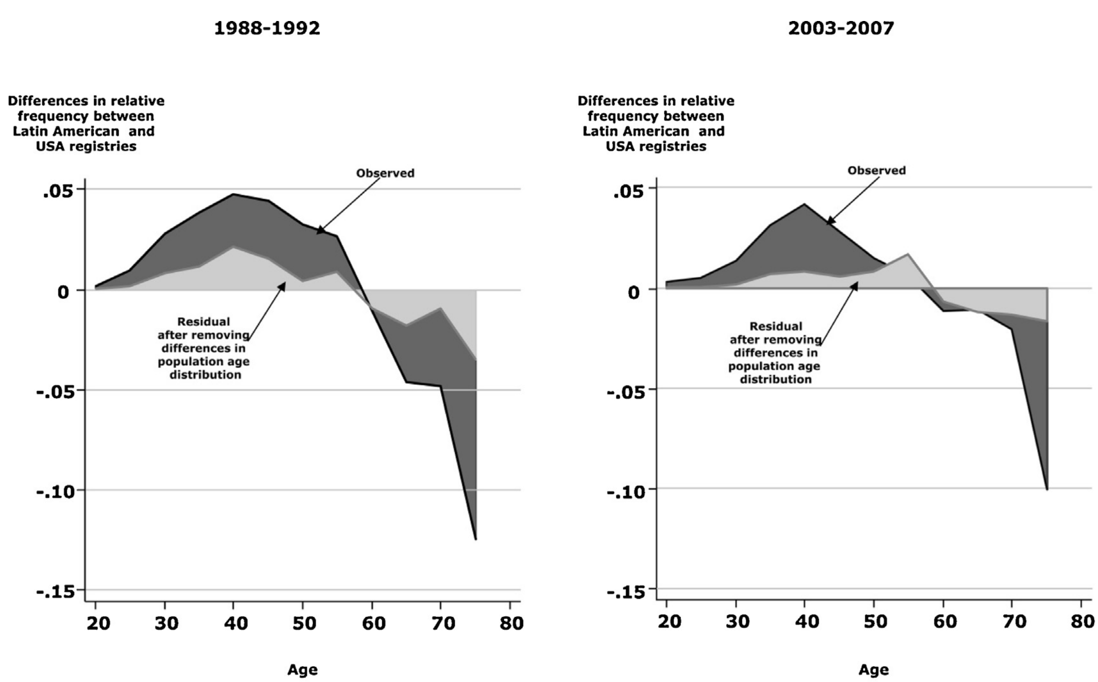

Fig. 1. Observed and residual differences in the relative frequency of breast cancer incident cases, between Latin American and USA registries, by age group, in two five-year periods.

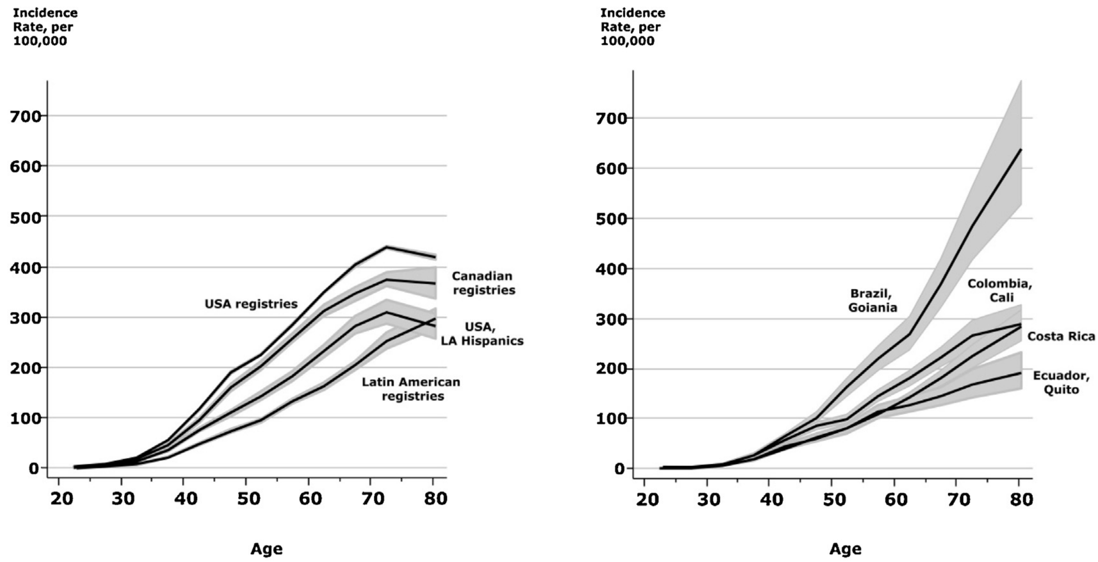

Fig. 2. Estimated breast cancer incidence rates, for cancer registries from Latin America, USA and Canada, obtained by fitting the Age-period-cohort model proposed by Holford [11]. Gray areas correspond to 95% confidence bands for the incidence rates.

birth cohort, seen for the Brazil-Goiania registry which may partially be the result of improved diagnostic and detection services since the early 1990s [7].

Breast cancer incident cases in the four Latin American registries, but also in the Hispanic women from the Los Angeles registry, present on average at an earlier age than in the USA and Canadian registries. In addition, for 2003–2007, between 20 and 27% of cases occur in women aged 20-44 in the analyzed Latin American and Hispanic registries, almost doubling the frequency seen in USA and Canadian registries. Earlier reports, often based on hospital-based or treatment-provider information, have shown an earlier age at breast cancer presentation in Colombia, Mexico and other low and middle income countries than that observed in high income countries [15–19].

Only two thirds of the difference in age distribution between Latin American and USA registries is attributable to the younger age distribution in the Latin American base populations. After eliminating differences in age distribution, the Latin American registries still show a higher proportion of cases at younger ages and a lower proportion at ages 60 and older than women in the aggregated USA registries. The relative lack of older breast cancer cases in Latin American registries could be the result of lower access to mammographic screening in these populations, as mammography is more effective for women at older ages, with less dense breasts [20,21]. However, lower detection through mammography would only have a marginal effect on the lower proportion of older breast cancer cases we observe in the Latin American registries, since most breast cancer cases are eventually detected, although at later stages.

A more plausible explanation for the residual differential distribution of breast cancer incident cases by age, between the Latin American and the USA registries, lies in a differential pattern of age specific incidence rates among them. Results from our age-period-cohort modelling of incidence rates indicate that, while the

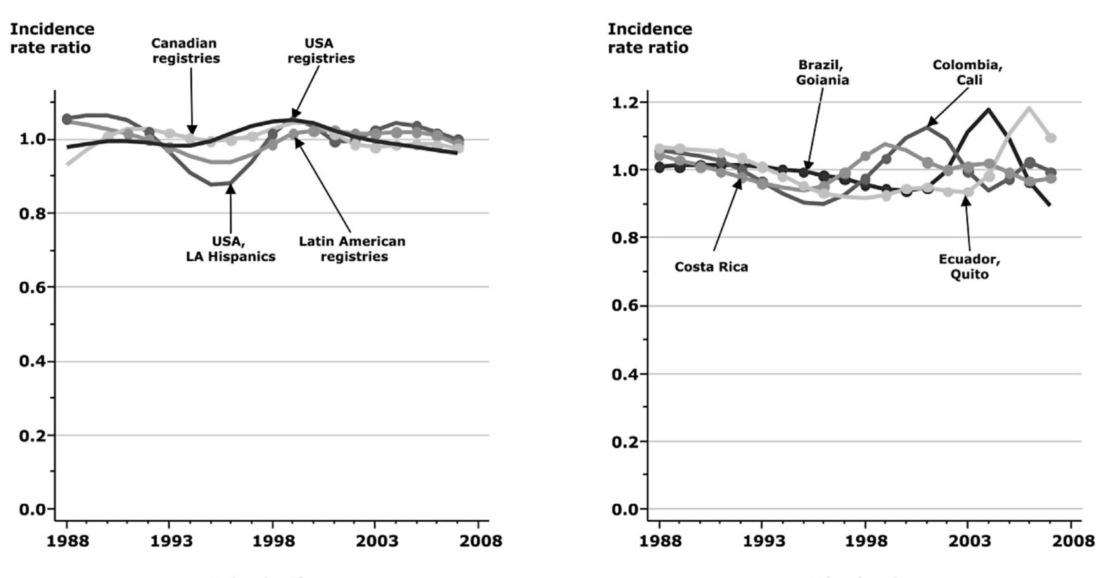

Fig. 3. Estimated period effects, on breast cancer incidence rates, for registries from Latin America, USA and Canada, obtained by fitting the Age-period-cohort model proposed by Holford [11]. Dots represent time points where the incidence rate ratios are not significantly different from unity, at $p < 0.05$.

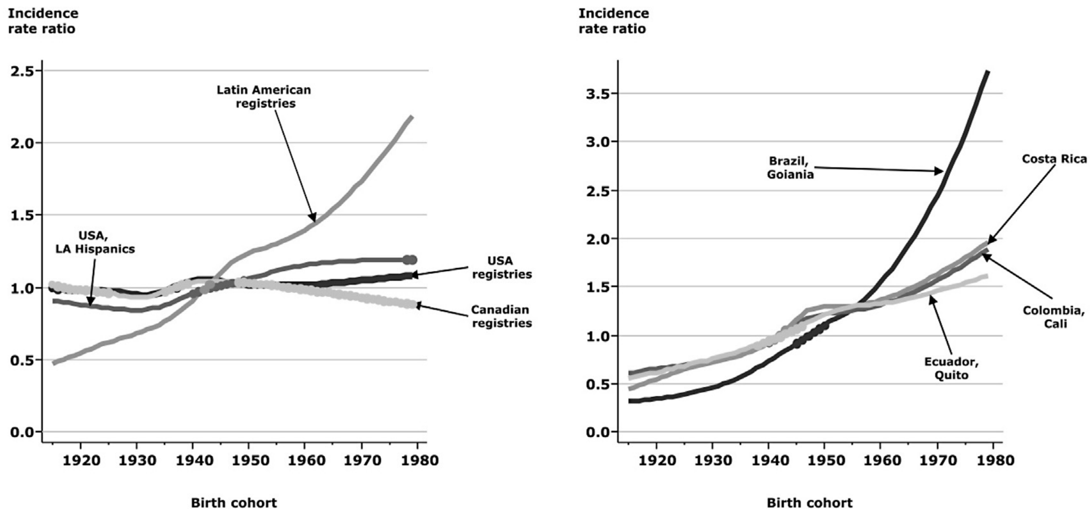

Fig. 4. Estimated birth cohort effects, on breast cancer incidence rates, for registries from Latin America, USA and Canada, obtained by fitting the Age-period-cohort model proposed by Holford [11]. Dots represent time points where the incidence rate ratios are not significantly different from unity, at $p < 0.05$.

incidence rates for the aggregated USA registries are higher than in the Latin American registries, at both younger and older ages, the absolute differences in these rates are higher at older ages. In addition, the lower the cumulative risk is in a Latin American registry, the higher the absolute differences are in the incidence rates, with respect to the aggregated USA registries at older ages.

Over the study period, breast cancer incidence rates have been growing more rapidly in the four Latin American registries and in Hispanic women from the Los Angles registry than in the aggregated Canadian and USA registries, as a consequence of stronger cohort effects in the first. All compared registries show a peak in incidence for women born during the period 1940 (USA and Canadian registries) through 1948 (Ecuador-Quito), which probably reflects the introduction of effective birth control methods, including hormonal contraceptives, occurring at different times. Declining fertility produces important changes in exposure to endogenous hormones, an important risk factor, especially for postmenopausal breast cancer [22]. The strong cohort effect seen in the Latin American registries may well be the result, at least partially, of the declining fertility rates of Latin American women seen during the second half of the 20th century, and, in the following decades, it will likely result in an epidemic of postmenopausal breast cancer in this region, as women born after 1970 approach older age (Supplemental Fig. 2).

However, over the past several decades, women in the Latin American region have also been subject to increasingly westernized lifestyles, associated with higher breast cancer incidence, for instance, greater alcohol and tobacco consumption, a change in dietary habits with increasing saturated fat consumption and a greater exposure to environmental agents [23]. The growing prevalence of obesity seen in Latin America [24–26] and the consequent greater prevalence of excess abdominal fat, a risk factor for postmenopausal breast cancer [27], may also contribute to the strong cohort effect that we observed in the Latin American registries.

There is a need for more epidemiological studies to evaluate the etiological role of genetic, lifestyle and environmental risk factors in Latin America and this should be an important area for future research [28].

5. Conclusions

The younger age at presentation of breast cancer incident cases seen in the analyzed Latin American registries, and possibly in many Latin American countries, is not only attributable to their relatively young population age structure but also to the low incidence rates in older women. As more recently born cohorts, with greater exposure to risk factors for postmenopausal breast cancer, reach older age, incidence rates will be more similar to the rates seen in the USA and Canadian registries. This trend, coupled with population ageing, will make that in the coming decades the distribution of breast cancer by age in most countries of Latin America will be more similar to the distribution seen today in the USA and Canada. In the meantime, the high prevalence of breast cancer cases occurring at younger ages will continue to be an important challenge in terms of prevention, early detection, treatment and survivor care [29–33] for most countries on the Latin American region, highlighting the need for more research in these areas.

Authorship contribution's

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.canep.2015.10.004.

References

[1] IARC. Latest world cancer statistics. Global cancer burden rises to 14.1 million new cases in 2012: Marked increase in brest cancers must be addressed. Press Release N. 223. Dec 12, 2013. Available at: http://www.iarc.fr/en/media-centre/pr/2013/pdfs/pr223_E.pdf Accessed on 07/28/2015.
[2] R. Bhikoo, S. Srinivasa, T. Yu, D. Moss, A.G. Hill, Systematic Review of Breast cancer Biology in Developing Countries (Part 1): Africa, the Middle East, Eastern Europe, Mexico, the Caribbean and South America, Cancers (Basel) 3 (2011) 2358–2381.
[3] S. Tfayli, R. Temraz Abou Mrad, A. Shamseddine, Breast cancer in low- and middle-income countries: an emerging and challenging epidemic, J. Onco.l 2010 (2010) 490631 Epub 2010 Dec 15.
[4] F.M. Knaul, A. Bhadelia, J. Gralow, H. Arreola-Ornelas, A. Langer, J. Frenk, Meeting the emerging challenge of breast and cervical cancer in low- and middle-income countries, Int. J. Gynaecol. Obstet. 119 (2012) S85–S88.
[5] J. Ferlay, I. Soerjomataram, M. Ervik, R. Dikshit, S. Eser, C. Mathers, M. Rebelo, D. M. Parkin, D. Forman, F. Bray, GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet], International Agency for Research on Cancer, Lyon, France, 2013 Available at: http://globocan.iarc.fr, accessed on: 07/29/2015..
[6] IARC. CI5plus. Cancer Incidence in Five Continents Time Trends. Available at: http://ci5.iarc.fr/CI5plus/Pages/download.aspx. Accessed on 7/28/2015.
[7] D.M. Parkin, S.L. Whelan, J. Ferlay, L. Teppo, D.B. Thomas (Eds.), Cancer Incidence in Five Continents, Vol. VIII, IARC Scientific Publications No. 155, IARC, Lyon, France, 2002.
[8] F. Forman, D.H. Brewster, B. Gombe Mbalawa, M. Piñeros, R. Steliarova-Foucher, J. Ferlay (Eds.), Cancer Incidence in Five Continents, Vol. X, IARC Scientific Publications No. 164, IARC, Lyon, France, 2014.
[9] Modern Epidemiology, in: K.J. Rothman (Ed.), first ed., Little Brown, Boston, 1986, pp. 164.
[10] N.E. Breslow, N.E. Day, Statistical Methods in Cancer Research, Volume II-The Design and Analysis of Cohort Studies, IARC Scientific Publications No. 82, IARC, Lyon, France, 1987, pp. 57–58.
[11] T.R. Holford, Age-Period-Cohort analysis, in: P. Armitage, T. Colton (Eds.), Encyclopedia of Biostatistics, second ed., Wiley, London, 2008, pp. 111–127.
[12] StataCorp, Stata Statistical Software, Release 12, College Station, Texas, 2012.
[13] B. Carstensen, Age-period-cohort models for the Lexis diagram, Stat Med. 26 (2007) 3018–3045.
[14] R Development Core Team, R: A Language and Environment for Statistical Computing, R Foundation for Statistical Computing, Vienna, 2004.
[15] S. Rodríguez-Cuevas, C.G. Macías, D. Franceschi, S. Labastida, Breast carcinoma presents a decade earlier in Mexican women than in women in the United States or European countries, Cancer 91 (2001) 863–868.
[16] S. Holgado, M. Sanchez Segura, A. Vinuales, V. Audi, F. Arrieta, D. Gonzalez, M. Jimenez, C.E. Lorente, R. Audi, A.C. d. Elias, J.J. Zarba, Breast cancer in young women in a northern province of Tucuman, Argentina, J Clin Oncol. 29 (Suppl) (2011) .
[17] C.J. Uribe-Pérez, M. Álvarez-Serrano, G. Montañez-Rizo, Incidencia de cáncer de mama en mujeres menores de 40 años en el Área Metropolitana de Bucaramanga, 2000–2004, MedUNAB. 13 (2010) 81–84.
[18] H. Najjar, A. Easson, Age at diagnosis of breast cancer in Arab nations, Int. J. Surg. 8 (2010) 448–452.
[19] C. Villarreal-Garza, C. Aguila, M.C. Magallanes-Hoyos, A. Mohar, E. Bargalló, A. Meneses, E. Cazap, H. Gomez, L. López-Carrillo, Y. Chávarri-Guerra, R. Murillo, C. Barrios, Breast cancer in young women in Latin America: an unmet, growing burden, Oncologist 18 (2013) 1298–1306.
[20] F.M. Knaul, G. Nigenda, R. Lozano, H. Arreola-Ornelas, A. Langer, J. Frenk, Breast cancer in Mexico: a pressing priority, Reprod. Health Matters 16 (2008) 113–123.
[21] World Cancer Research Fund/American Institute for Cancer Research, Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective, AIRC, Washington DC, 2007.
[22] A.I. Phipps, C.I. Li, Endogenous hormones, in: C.I. Li (Ed.), Breast Cancer Epidemiology, first ed., Springer, New York, 2009, pp. 73–87 Chapter 4.
[23] P. Porter, Westernizing women's risks? Breast cancer in lower-income countries, N. Engl. J. Med. 358 (2008) 213–216.
[24] S. Barquera, I. Campos-Nonato, L. Hernández-Barrera, M. Flores, R. Durazo-Arvizu, R. Kanter, J.A. Rivera, Obesity and central adiposity in Mexican adults: results from the Mexican National Health and Nutrition Survey 2006, Salud Publica Mex. 51 (2009) S595–S603.
[25] A.K. Arbex, D.R. Rocha, M. Aizenberg, M.S. Ciruzzi, Obesity epidemic in Brazil and Argentina: a public health concern, J. Health Popul. Nutr. 32 (2014) 327–334.
[26] V. Cuevas, C. Alvarez Olivos, The emerging obesity problem in Latin America, Expert Rev. Cardiovasc. Ther. 7 (2009) 281–288.
[27] K.D. Henderson, J. Prescott, L. Bernstein, Physical Activity and Anthropometric Factors, in: C.I. Li (Ed.), Breast cancer Epidemiology, first ed., Springer, New York, 2009, pp. 137–151 Chapter 7.
[28] Institute of Medicine (U.S.), Committee on Breast cancer and the Environment: The Scientific Evidence, Research Methodology, and Future Directions, Board on Health Care Services, Board on Health Sciences Policy. Breast cancer and the environment: a life course approach, 2011.
[29] C.D. Lehman, C.I. Lee, V.A. Loving, M.S. Portillo, S. Peacock, DeMartini W.B, Accuracy and value of breast ultrasound for primary imaging evaluation of symptomatic women 30-39 years of age, AJR Am. J. Roentgenol. 199 (2012) 1169–1177.
[30] J. Frenk, Sensibilizacióndetección temprana y combate a los prejuicios. Claves de la lucha contra el cáncer de mama, Salud Pública 51 (Suppl. (2)) (2009) 135–137.
[31] F.M. Knaul, E. González-Pier, O. Gómez-Dantés, D. García-Junco, H. Arreola-Ornelas, M. Barraza-Llorens, R. Sandoval, F. Caballero, M. Hernández, M. Juan, D. Kershenobich, G. Nigenda, E. Ruelas, J. Sepulveda, R. Tapia, G. Soberón, S. Chertorivski, J. Frenk, The quest for universal health coverage: achieving social protection for all in Mexico, Lancet 380 (2012) 1259–1279.
[32] F.M. Atun, Innovative financing: Local and global opportunities, in: J.R. Knaul, R. Gralow (Eds.), Closing the Cancer Divide: An Equity Imperative, Harvard University Press, Cambridge, MA, 2012 Chapter 8.
[33] N. Justo, N. Wilking, B. Jönsson, S. Luciani, E. Cazap, A review of breast cancer care and outcomes in Latin America, Oncologist 18 (2013) 248–256.