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International Variability in Ages at Menarche, First Livebirth, and Menopause

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The occurrences and timing of reproduction-related events, such as menarche, first birth, and menopause, play major roles in a woman's life. There is a lack of comparative information on the overall patterns of the ages at and the timing between these events among different populations of the world. This study describes the variability in reproductive factors across populations in Europe, the Americas, Asia, Australia, and Africa. The study sample consisted of 18,997 women from 13 centers in 11 countries interviewed between 1979 and 1988 who comprised the control group in a World Health Organization international, multicenter case-control study of female cancers. All were surveyed with the same questionnaire and methodology. Overall, a typical woman in this study reached menarche at age 14 years and delivered her first live child 8 years later, at age 22. She was 50 years old at natural menopause and had had 36 years of reproductive life. The median ages at menarche varied across centers from 13 to 16 years. For all centers, the median age at first livebirth was 20 or more years, with the largest observed median (25 years) occurring in China. The median delay from menarche to first livebirth ranged from 5 to 11 years. Among the centers, the median age at natural menopause ranged between 49 and 52 years. In most populations, younger women had a first birth at a later age than did older women. This tendency was more accentuated in some populations. These results reveal, perhaps for the first time, the variability of reproductive histories across different populations in a large variety of geographic and cultural settings. Except for menopause, international variability is substantial for both biologically related variables (age at menarche) and culturally related variables (age at first birth). There is a generational effect, characterized by more variability of age at first birth and delay to first birth in the younger than in the older generations. *Am J Epidemiol* 1998;148:1195–1205.

menstruation; reproductive history; surveys

The occurrences and timing of reproduction-related events, such as menarche, first birth, and menopause, play major roles in a woman's life. In this context, it is striking that the variations in reproductive histories among different populations of the world are not well known.

International comparisons on a single reproductive variable (e.g., age at menarche, characteristics of the menstrual cycle, age at menopause) conducted through the 1970s appear in reviews by Gray and Doyle (1) and Richardson (2). It is generally accepted that the average age at menopause is about 51 years in industrialized countries (2, 3), but data are inconsistent for the developing world (3) because of methodological problems (4). There are also recent reviews of the epidemiologic literature about determinants of age at menarche and patterns of menstruation (5) and about age at menopause (6). In addition, while information on the timing of reproduction-related events can, in principle, be retrieved from many epidemiologic studies of breast cancer (e.g., Kelsey et al. (7)), published data usually report the information on reproductive events as categories rather than as continuous variables. Such categorized data are ill-suited for comparisons of distributions. In addition, definitions may differ across studies so that pooling the information from several published sources may be inappropriate. Thus, the overall timing of reproductive events has been described at the single population level (8, 9), but, to our knowledge, there is no published work comparing the timing of reproductive events from menarche to menopause between different populations.

An international comparison of the timing of reproductive events is important for epidemiology, since

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Abbreviations: IQR, interquartile range; P, percentile.

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many diseases (e.g., breast, ovarian, and uterine cancers and cardiovascular disorders) seem to be related to various characteristics of reproductive life. It is therefore of interest to determine whether the variability in disease incidence is consistent with that in reproductive life. It is also important for family planning and preventive counseling to establish the biologic limits of variability in reproductive histories related to the human genetic constitution and to identify the extent of the cultural and, therefore, modifiable influences on reproductive histories within these limits.

The objective of this study was to describe the variability in reproductive factors that have mainly biologic (ages at menarche and menopause, duration of reproductive life) or cultural (delay between menarche and first birth, age at first birth) determinants across populations in Europe, the Americas, Asia, Australia, and Africa surveyed with the same questionnaire and methodology.

MATERIALS AND METHODS

Study women

The study sample consisted of 18,997 women comprising the control group in a World Health Organization international, multicenter case-control study of female cancers. The study design and primary results have been previously reported based on data collected from 1979 to 1986 (10–13). The analyses performed for this report were based on the data from those control women plus the data collected on additional control women recruited for the World Health Organization study through 1988. A total of 13 populations ("centers") in 11 different countries (Australia, Chile, People's Republic of China, Colombia, the (former) German Democratic Republic, Israel, Kenya, Mexico, Nigeria, the Philippines, and three separate centers in Thailand) were studied.

The World Health Organization study control group consisted of women who had been admitted to other than obstetrics and gynecology hospital wards and who were free of medical conditions it was thought could possibly alter contraceptive practices (i.e., cardiovascular and circulatory diseases, diabetes, chronic renal disease, benign breast disease, cancer, chronic liver disease, and any obstetric or gynecologic condition). These women were selected from a large variety of different clinics within each center to avoid any link between their reproductive characteristics and their likelihood of being recruited into the World Health Organization study. The control women were of the same age and residential origin as the cases. These hospital control patients were interviewed, mostly in the hospital, by using a standardized questionnaire administered by trained female interviewers.

Reproductive variables, statistical analyses, and sample sizes

The main reproductive study variables (measured in years) were age at menarche, age at first livebirth, delay from menarche to first livebirth, age at (natural) menopause, and duration of reproductive life (time between menarche and (natural) menopause). Percentiles for each center and for the total study sample were used to summarize the observed distributions of the study reproductive variables: The median (or 50th percentile) was used as the measure of central tendency, and variability was assessed by the 10th, 25th, 75th, and 90th percentiles. Percentiles were deemed more informative than means and standard deviations because of the skewed distributions involved.

In a "boxplot" (or "box and whisker" plot) of age at menarche, the median is depicted by the "center" line of the box, and the interquartile range (IQR) (distance from the 25th to 75th percentiles) is depicted by the length of the box; the "whiskers" (dotted lines extending from the top and bottom of the box) extend to the extreme values of the data or to a distance of 1.5(IQR), whichever is less, and the horizontal lines outside the whiskers indicate potential "outliers" (for normal or Gaussian data, almost all the data occur inside the whiskers).

In a "reproductive profile" plot (see Results), 95 percent nonparametric (or distribution-free) confidence intervals for the 10th, 50th, and 90th percentiles of age at menarche were calculated based on order statistics. (The 10th and 90th percentiles were preferred over the 5th and 95th percentiles because they could be estimated more precisely, given the sample sizes of the study centers.) The validity of these confidence intervals does not depend on any specific assumptions about the shape of the population distribution (14).

Age at menarche

Age at menarche was taken directly as recorded by the interviewer. In the analyses of this variable, 83 women who either reported never menstruating or whose menstruation status or age at menarche were recorded as unknown were excluded (net $n = 18,914$). (The same 83 women were also excluded from the analyses of all of the other reproductive variables.)

Age at natural menopause and duration of reproductive life

Most of the study women had not yet experienced either natural or artificial menopause at the time they

were interviewed. Therefore, the probability that the natural menopause of a study woman would occur beyond any given age was estimated by using censored data survival analysis techniques based on Kaplan-Meier (or product limit) methodology (15). A "competing risks" approach similar to that suggested by Krailo and Pike (16) was used. When available, corresponding asymptotic 95 percent confidence intervals for the Kaplan-Meier estimated 10th, 50th, and 90th percentiles were calculated and displayed in the "reproductive profile" plots (see Results). An analogous strategy was also used to estimate the probability that a study woman's duration of reproductive life would exceed any given time.

These Kaplan-Meier analyses of age at natural menopause and duration of reproductive life required information on menopausal status (i.e., censoring) that was not directly recorded during the interview. Instead, this information was estimated indirectly by using a classification algorithm applied to self-reported year of last menses, year of interview, year of birth (derived from self-reported age), and other relevant self-reported reproductive data (see below) that were directly recorded during the interview.

Most (83 of 142) of the missing data on age at natural menopause were due to missing data on age at menarche (see the previous section). Data on an additional 59 women were missing for some of the other reproductive variables (e.g., year of last menses, hysterectomy status, etc.) used to calculate menopausal status (net n = 18,855). There were also six missing values for age and five erroneous, negative, calculated values that could be attributed only to apparent errors in source data entry (net n = 18,844). The overall proportion of such errors (11 of 18,997) was otherwise remarkably small.

The logic and results of this classification algorithm are summarized briefly here. For all menarcheal study women, age at natural menopause was initially calculated as (year of last menses minus year of birth), regardless of censoring. Women who were actually classified as having undergone natural menopause (n = 2,949) were at least required to have had their last reported menses more than 1 year before their year of interview. Women who had undergone a hysterectomy, a double oophorectomy, or any operation/x-ray treatments preventing further menstrual periods at any time before or during their year of interview were classified as having had an artificial menopause (n = 968). In the survival analysis, their age at natural menopause was considered to be censored at the year of artificial menopause. For premenopausal (including a few pregnant and/or nursing) women (n = 14,927), their age at natural menopause was considered to be censored at the year of interview. Subsequently, using the same censoring classifications, duration of reproductive life was calculated as (age at natural menopause minus age at menarche).

Age at first livebirth and delay from menarche to first livebirth

The vast majority (18,988 of 18,997) of the study women provided complete interview data on age at first livebirth. There were 15,053 women who reported having had a livebirth and 3,935 who were nulliparous, either because their conceptions never resulted in a livebirth (n = 3,596) or because they had never been pregnant (n = 339). In the analysis, the age at first livebirth of a nulliparous woman was censored as her age at natural menopause if she had experienced a natural menopause, her age at artificial menopause if she had undergone an artificial menopause, or just her age if she was still premenopausal. Likewise, the censored delay from menarche to first livebirth for nulliparous women was calculated as the difference between their censored age at first livebirth and their age at menarche.

Censored data Kaplan-Meier techniques analogous to those described in the previous section were then used to estimate the distributions and percentiles of age at first livebirth and delay from menarche to first livebirth.

The sample sizes for age at first livebirth (net n = 18,894) and delay from menarche to first livebirth (net n = 18,892) reflected reductions due to missing data similar to, but less extreme than, those mentioned in the previous section. For example, missing values for menopausal status led to exclusions for nulliparous women, but not necessarily for those who were multiparous.

RESULTS

Table 1 presents the sample sizes and age distributions (medians, percentiles, ranges) of the 18,997 study sample women (age range, 15–64 years) interviewed between 1979 and 1988 stratified by center. Israel (n = 2,106) and the three Thai centers (Siriraj (n = 3,174), Chulalongkorn (n = 2,566), and Chiang Mai (n = 2,861)) contributed the largest study samples. The median age was 40 years overall, but the median ages ranged from 33 years (Chile and Kenya) to 46 years (Chiang Mai, Thailand).

Age at menarche

The median age at menarche was 14 years overall. It varied across centers from 13 to 16 years (table 2). More than 90 percent of the women had their men-

TABLE 1. Interview years, sample sizes, and age distributions for study women in 13 international centers, 1979–1986

Center	Interview years	No.*	Age distribution	
			Median	(Range†)
Australia	1980–1983	905	38	(17, 23, 30, 48, 53, 64)
Israel	1979–1987	2,106	40	(17, 27, 33, 47, 50, 54)
German Democratic Republic	1981–1986	1,223	45	(25, 35, 41, 49, 52, 56)
Chile	1979–1985	1,243	33	(15, 20, 26, 43, 49, 60)
Colombia	1981–1983	235	36	(16, 23, 28, 47, 52, 57)
Mexico	1979–1986	1,670	38	(15, 23, 30, 44, 49, 55)
Philippines	1979–1984	1,270	41	(15, 26, 33, 47, 50, 54)
People's Republic of China	1981–1987	816	44	(18, 26, 32, 51, 53, 58)
Siriraj, Thailand	1979–1987	3,174	39	(17, 22, 30, 46, 50, 57)
Chulalongkorn, Thailand	1979–1987	2,566	39	(18, 25, 32, 46, 50, 57)
Chiang Mai, Thailand	1979–1988	2,861	46	(15, 26, 35, 53, 57, 63)
Kenya	1980–1986	757	33	(17, 20, 25, 42, 49, 55)
Nigeria	1980–1982	171	37	(16, 24, 30, 42, 46, 50)
All centers		18,997	40	(15, 24, 32, 47, 52, 64)

* Total sample sizes shown include six women with missing age data.
† P, percentile; range = minimum, P10, P25, P75, P90, maximum, where *Px* = *x*th percentile.

TABLE 2. Median (P10, P25, P75, P90)* years of age at menarche, age at first livebirth, and delay from menarche to first livebirth for study women in 13 international centers, 1979–1986

Center	Menarche		First livebirth†		Delay to first livebirth†	
	Age (years)	(Range)	Age (years)	(Range)	No. of years	(Range)
Australia	13	(11, 12, 14, 15)	24	(18, 21, 29, NA‡)	11	(5, 8, 16, NA)
Israel	13	(11, 12, 14, 15)	22	(18, 20, 26, 32)	9	(5, 7, 13, 20)
German Democratic Republic	14	(12, 12, 15, 16)	22	(18, 20, 26, NA)	9	(4, 6, 13, NA)
Chile	13	(11, 12, 14, 15)	22	(17, 19, 27, 36)	9	(4, 6, 14, 23)
Colombia	13	(11, 12, 14, 15)	20	(16, 18, 24, 31)	7	(3, 4, 11, 18)
Mexico	13	(11, 12, 14, 15)	20	(16, 18, 24, 31)	7	(3, 4, 11, 18)
Philippines	14	(12, 13, 15, 16)	23	(17, 20, 30, NA)	10	(3, 6, 16, NA)
People's Republic of China	15	(13, 14, 16, 17)	25	(20, 23, 28, 33)	10	(4, 7, 13, 18)
Siriraj, Thailand	15	(13, 14, 16, 17)	24	(18, 20, 31, NA)	9	(3, 5, 17, NA)
Chulalongkorn, Thailand	15	(13, 14, 16, 17)	24	(18, 20, 32, NA)	9	(3, 5, 17, NA)
Chiang Mai, Thailand	16	(13, 14, 17, 18)	22	(18, 20, 26, 36)	6	(2, 3, 10, 23)
Kenya	15	(13, 14, 16, 16)	20	(16, 18, 22, 28)	5	(2, 3, 8, 11)
Nigeria	15	(13, 14, 16, 18)	21	(17, 19, 27, NA)	6	(2, 3, 8, NA)
All§	14	(12, 13, 15, 17)	22	(18, 19, 27, NA)	8	(3, 5, 14, NA)

* P, percentile, where *Px* = *x*th percentile.
† Kaplan-Meier estimates for age at first livebirth and delay to first livebirth.
‡ NA, not available.
§ Total numbers were 18,914 for age at menarche, 18,894 for age at first livebirth, and 18,892 for delay to first livebirth.

arche between ages 11 years (lowest observed, percentile (P) 10)) and 18 years (highest observed, P90).

Further details on the distributions of age at menarche are shown in the boxplots in figure 1. The Chilean woman who reported having had her menarche at age 28 years was pathologic, but such extreme observations have no influence on the median or other percentiles. There was a clear shift of distributions toward later age at menarche among women from Asia (the Philippines, China, and Thailand) and Africa (Kenya and Nigeria) compared with women from the Americas (Chile, Colombia, Mexico), Australia, Israel, and Europe (German Democratic Republic). In addition, the IQR spread between the 25th and 75th percentiles was 2 years in most centers (3 years in Chiang Mai, Thailand and the German Democratic Republic). The biologic extremes were at ages 8 and 28 years.

Age at first livebirth

By age 22 years, about half of the study women had had a first livebirth (table 2). In most centers, the median age was above 20 years. The largest observed

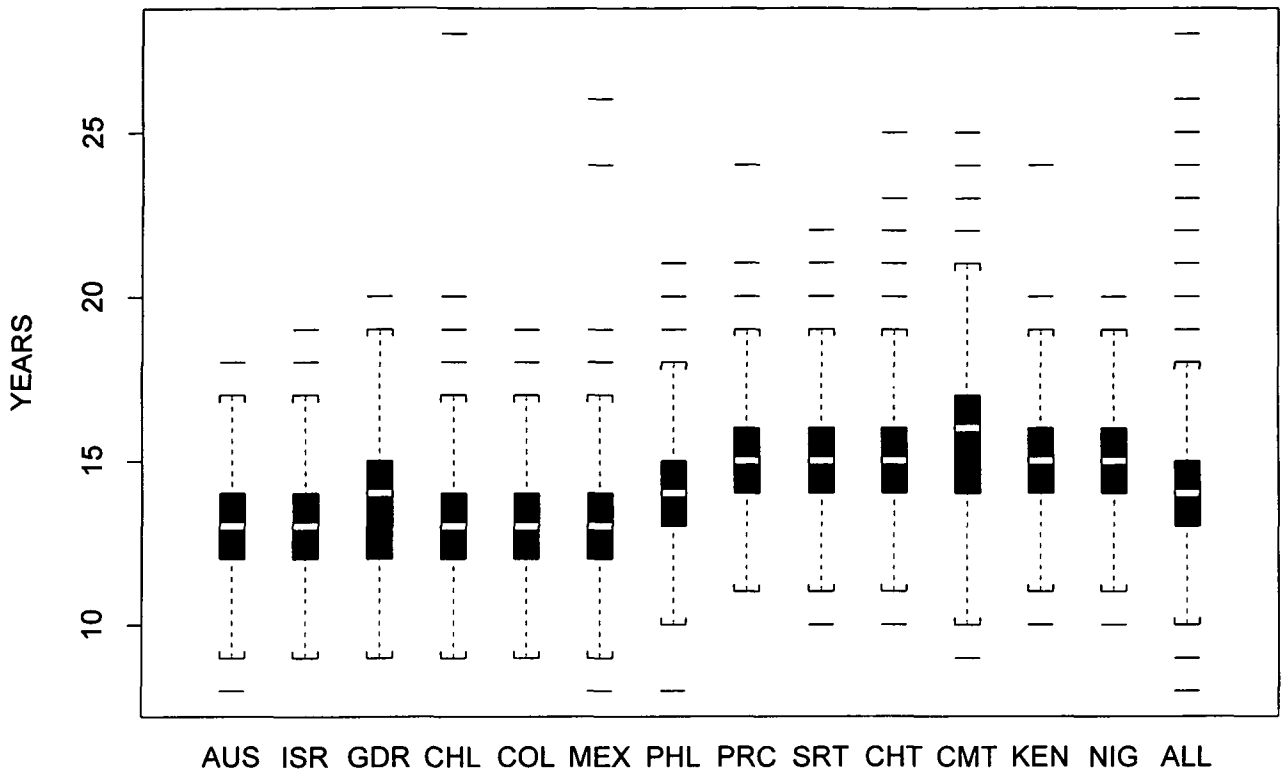

FIGURE 1. Boxplot distribution of age at menarche for study women in 13 centers in 11 countries interviewed between 1979 and 1988. AUS, Australia; ISR, Israel; GDR, (former) German Democratic Republic; CHL, Chile; COL, Colombia; MEX, Mexico; PHL, the Philippines; PRC, People's Republic of China; SRT, Siriraj, Thailand; CHT, Chulalongkorn, Thailand; CMT, Chiang Mai, Thailand; KEN, Kenya; NIG, Nigeria; ALL, all centers.

median (25 years) occurred in China. The relatively more urban Thai centers (Siriraj and Chulalongkorn) and Australia had the next highest median ages at first livebirth (24 years). The lowest median ages at first livebirth (20 years) occurred in Colombia, Mexico, and Kenya. The median for Nigeria (21 years) was also below the overall median of 22 years.

The effect of including versus excluding the approximately 20 percent censored data because of nulliparity in these analyses was obtained by comparing the Kaplan-Meier estimated percentiles with those estimated solely from the women who had a livebirth (data not shown). The Kaplan-Meier estimates in table 2 were generally from 1 to 2 years higher than, but otherwise consistent with, the estimates obtained after excluding the nulliparous women.

Delay from menarche to first livebirth

The median of the individual differences between age at menarche and age at first livebirth ranged considerably, from 5 to 11 years between the centers (table 2). The lowest medians occurred in the two African centers (5 and 6 years) and the more rural Chiang Mai Thai center (6 years). The highest medians occurred in Australia (11 years) and the Philippines and China (10 years).

There was also marked variability of spread in delay between the centers. For example, the estimated IQR was only 5 years in Kenya and Nigeria compared with 12 years in the two more urban Thai centers (Siriraj and Chulalongkorn). Generally, the distributions were skewed upward; the apparent "outliers" (data not shown) represented the relatively small (perhaps increasing; see Generation Effects) numbers of women in each center who had had their first livebirth after age 40 years.

The Kaplan-Meier censored data estimated percentiles of delay from menarche to first livebirth were from 1 to 2 years larger than the corresponding estimates based exclusively on the approximately 80 percent of women who had had a livebirth (data not shown).

Age at natural menopause

The median age at natural menopause was estimated to be 50 years overall, and the median ages at menopause ranged moderately between 49 and 52 years among the centers (table 3). Although all five percen-

TABLE 3. Median (P10, P25, P75, P90)* years of age at menopause and duration of reproductive life (age at menopause – age at menarche) for study women in 13 international centers, 1979–1986

Center	Menopause†		Reproductive life†	
	Age (years)	(Range)	Duration (years)	(Range)
Australia	51	(45, 48, NA‡, NA)	38	(31, 35, 40, NA)
Israel	NA	(46, 49, NA, NA)	NA	(32, 36, NA, NA)
German Democratic Republic	NA	(46, 49, NA, NA)	38	(32, 35, NA, NA)
Chile	50	(41, 46, 52, NA)	37	(28, 34, 39, NA)
Colombia	50	(41, 47, NA, NA)	36	(28, 34, 39, NA)
Mexico	51	(44, 47, NA, NA)	39	(31, 34, NA, NA)
Philippines	50	(44, 47, NA, NA)	37	(30, 33, NA, NA)
People's Republic of China	49	(45, 47, NA, NA)	34	(29, 32, NA, NA)
Siriraj, Thailand	51	(45, 48, NA, NA)	36	(29, 33, NA, NA)
Chulalongkorn, Thailand	52	(45, 48, NA, NA)	38	(30, 33, NA, NA)
Chiang Mai, Thailand	49	(40, 45, 52, 55)	32	(24, 28, 36, 40)
Kenya	50	(43, NA, NA, NA)	36	(28, 32, NA, NA)
Nigeria	NA	(41, NA, NA, NA)	NA	(27, 30, NA, NA)
All§	50	(44, 47, 55, 58)	36	(28, 32, 44, 45)

*P, percentile, where Px = xth percentile.
† Kaplan-Meier estimates.
‡ NA, not available.
§ Total numbers were 18,844 for age at menopause and for duration of reproductive life.

tiles listed in table 3 were reasonably estimated for the study women overall, in most of the centers, the sample women were too young for the 75th and 90th percentiles to be determined (also see table 1).

Duration of reproductive life (time from menarche to natural menopause)

In the total study sample, the median of the individual differences between age at menarche and age at menopause was 36 years (table 3). Heterogeneity in duration across centers was moderate, with 32 years (Chiang Mai, Thailand) being the lowest and 39 years (Mexico) being the highest median durations. In most centers (as well as overall), fewer than 10 percent of the women had a duration of reproductive life shorter than 28 years. The exceptions were Chiang Mai, Thailand (P10 = 24 years) and Nigeria (P10 = 27 years). Despite the fact that the 90th percentile was estimable in only a single individual center (P90 = 40 years for Chiang Mai), the overall study sample estimated P90 was 45 years.

Generation effects

To assess possible heterogeneity in the timing of reproductive events across generations, the analyses of all five reproductive variables were repeated separately by center for sample women who were age 15–29, 30–39, 40–49, and 50–64 years at the time of their interview.

Within each center, the percentiles of age at menarche were almost identical among the study women in all four age subgroups (data not shown). Moreover, the (limited but) comparable portions of the Kaplan-Meier estimated distributions of age at menopause and duration of reproductive life for the women in the older age subgroups were also almost identical to those for the women in the younger age subgroups within centers (data not shown). These stratified analyses spoke against generation effects for the biologically determined reproductive variables.

On the contrary, evidence of generation effects was found for the culturally determined variables, age at and delay to first livebirth, in most of the study centers. Specifically, in the Australian, Israeli, Asian (the Philippines, China, and the three Thai centers), and African (Kenya and Nigeria) centers, there was a clear tendency for the two youngest subgroups of women to be older at and to delay longer until their first livebirth compared with their older counterparts (see medians in table 4). This tendency was not evident in the German Democratic Republic or American (Chile, Colombia, Mexico) centers. Moreover, the four corresponding age subgroup-stratified boxplots of the medians of each of these variables across centers showed clear decreasing (or nonincreasing) trends in the variability of the ages at first livebirth (figure 2) and delays to first livebirth with older age (not shown).

Reproductive profiles from menarche to menopause

The types of data presented on a variable-by-variable basis in tables 2 and 3 can be plotted on a

TABLE 4. Generation effects for age at and delay to first livebirth for study women in 13 international centers, 1979–1986

Center	Median age at first livebirth (years)*				Median delay to first livebirth (years)*			
	19–29	30–39	40–49	50–64	15–29	30–39	40–49	50–64
Australia	27	24	22	23	14	12	9	10
Israel	24	23	22	22	11	10	9	8
German Democratic Republic	22	21	22	23	9.5	8	9	9
Chile	22	21	22	23	9	8	9	9
Colombia	20	20	20	20	7	7	6.5	6
Mexico	21	20	20	20	8	6	6	7
Philippines	25	24	23	23	12	10	9	9
People's Republic of China	29	27	23	23	14	12	8	7
Siriraj, Thailand	28	24	23	22	13	9	8	7
Chulalongkorn, Thailand	29	25	23	22	16	10	8	7
Chiang Mai, Thailand	25	22	21	22	11	7	5	5
Kenya	21	19	19	18	6	4	4	4
Nigeria	24	21	20	21	9	6	5	3

* Kaplan-Meier estimates.

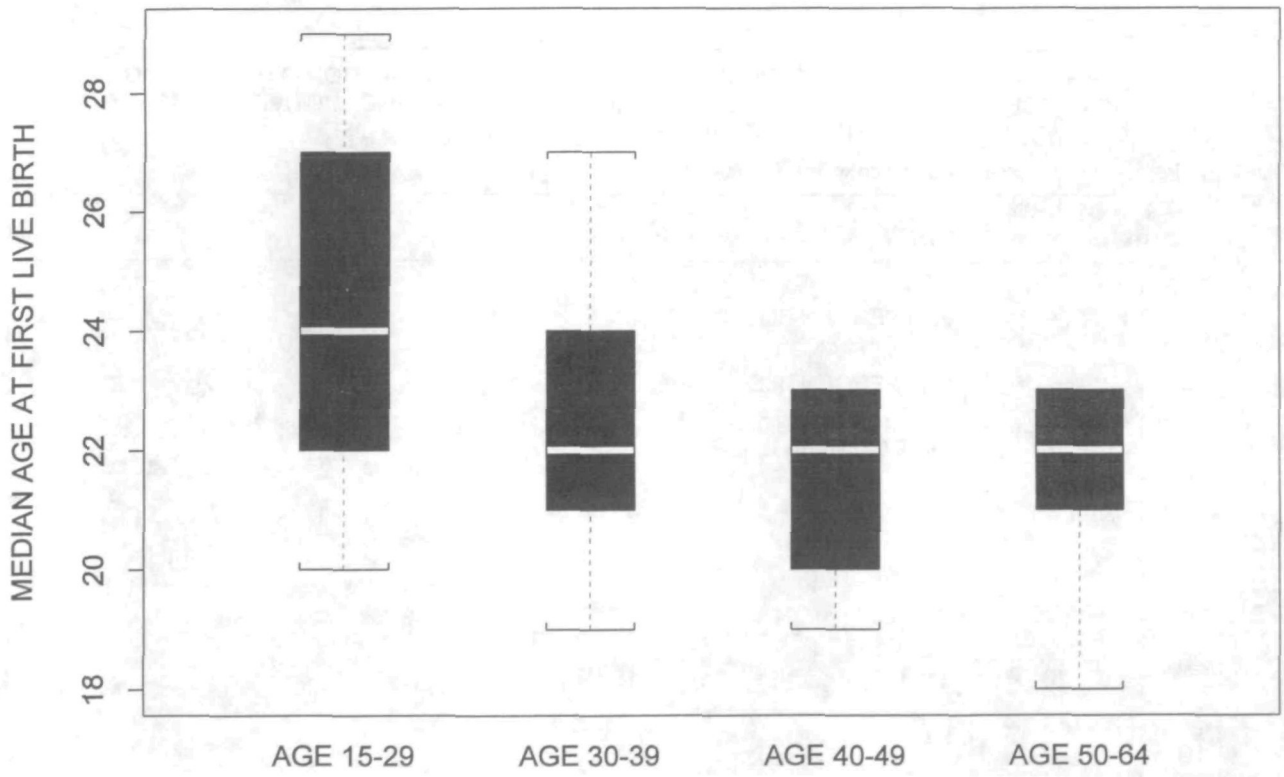

FIGURE 2. Boxplot distributions of median age at first livebirth for study women in 13 centers stratified by four age-at-interval subgroups, 1979–1988.

single graph indicating the sequence of reproductive events in a woman's lifetime (her "reproductive profile").

For example, figures 3 and 4 present the reproductive profiles for the study sample women from Australia and Chiang Mai, Thailand, respectively, which represent two extreme cases. A typical ("median") Australian woman has her menarche at age 13 years and, after a delay of 11 years, a first birth at age 24 years with, eventually, a (natural) menopause at age 51 years, implying 38 years of reproductive life. In contrast, a typical Thai woman from Chiang Mai has her menarche at age 16 and delivers a live child 6 years later at age 22 years, eventually experiencing natural menopause at age 49 years, having had 32 years of reproductive life. Thus, compared with the Australian woman, the Thai woman has half the delay between menarche and first livebirth and has a reproductive life that is 6 years shorter.

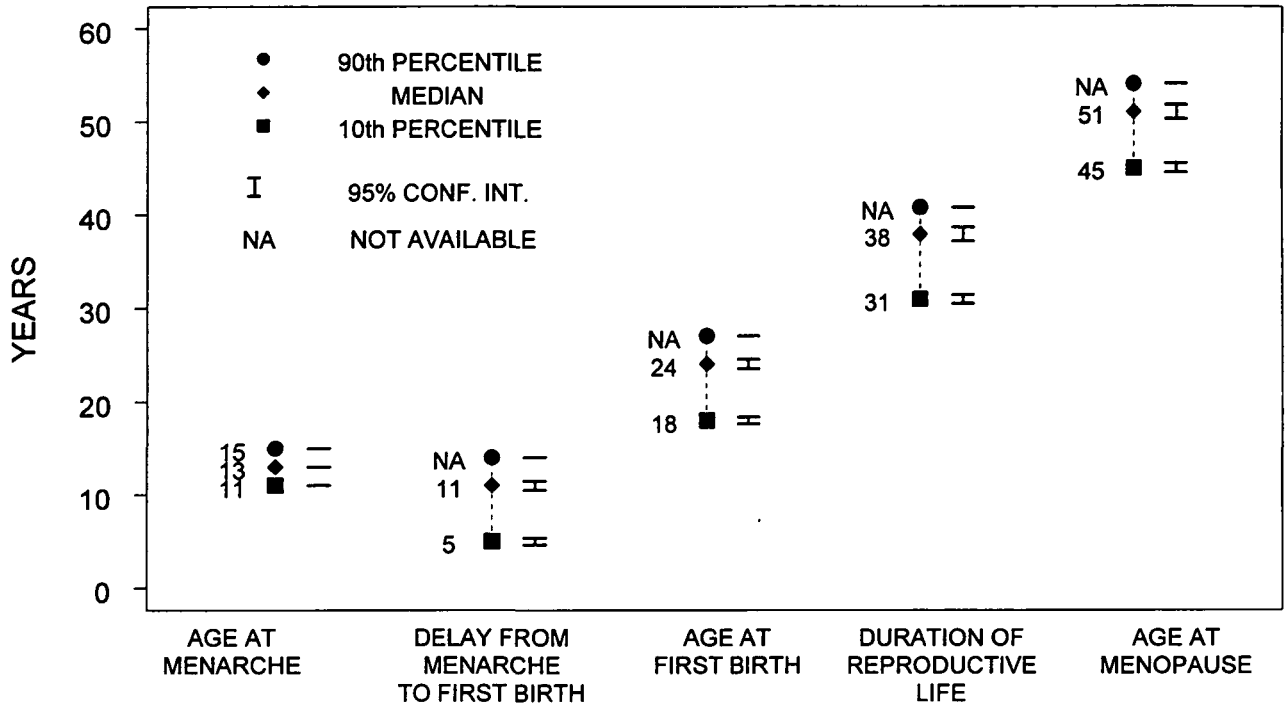

FIGURE 3. Reproductive profile of Australian women, 1980–1983.

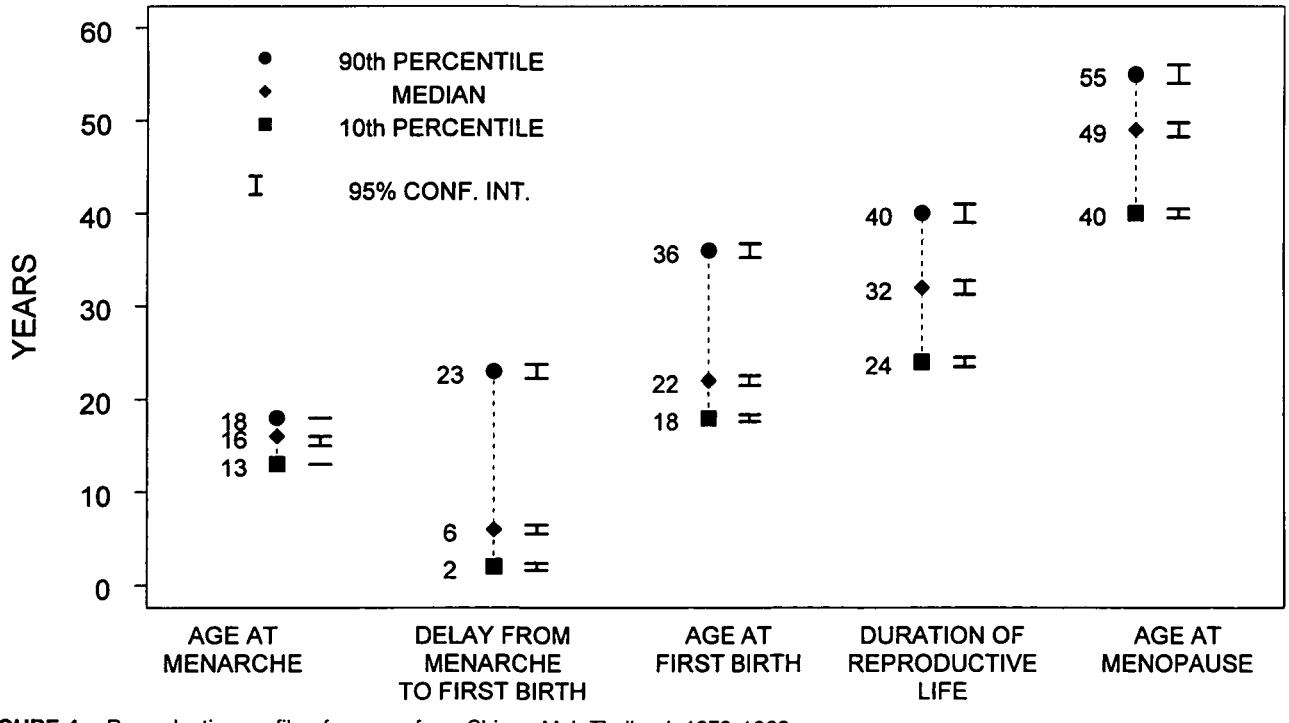

FIGURE 4. Reproductive profile of women from Chiang Mai, Thailand, 1979–1988.

DISCUSSION

These results indicate the extent of the variability of reproductive histories across different populations in a large variety of geographic and cultural settings. The ranges of observed timing of reproductive events are revealed, perhaps for the first time. Except for menopause, international variability is substantial and may

affect both biologically related variables, such as age at menarche, and culturally related variables, such as age at first birth.

Overall, a typical woman in this study had her menarche at age 14 years and delivered her first live child 8 years later, at age 22 years. She was 50 years old at natural menopause and had had 36 years of reproductive life.

There were some geographic variations in age at menarche, which tended to occur later among women from Asia or Africa in comparison with women from more Westernized regions. This strongly suggests that cultural or environmental factors can be influential. For example, the very high age at menarche in the rural Thai area of Chiang Mai could reflect urban-rural differences. This explanation seems at least as plausible as that of recall bias (i.e., Chiang Mai had the oldest sample women, with median age of 46 years).

Moreover, with the exception of China, where the timing of births and the number of children permitted per family are subject to governmental strictures, the longest delays from menarche to first birth tended to occur in the more Westernized countries (such as Australia and Israel), while the shortest delays occurred in the African countries (Kenya and Nigeria) and the more-rural Chiang Mai center in Thailand. This type of finding, along with the observed variability in ages at first birth, may reflect differences in marital customs related to, for example, the median age at marriage, especially in the more rural areas.

It is also important to consider the possible limitations of the present results. The study sample consisted of relatively young women (median age, 40 years). Therefore, not all of the study women had completed their reproductive histories. This would not have been a problem for assessing the distribution of age at menarche, or even of age at and delay to first livebirth, assuming the latter two distributions could be reasonably estimated solely from the usually large majority of women who had had a livebirth. However, for age at and delay to first birth, the censored data of nulliparous women were incorporated in the Kaplan-Meier analyses to address this potential problem. Likewise, for estimating age at menopause and duration of reproductive life (where the problem would be greatest), this issue was also addressed by using a survival analysis approach.

In general, such censored data analysis techniques yield valid overall estimates of the median age at event (e.g., age at menopause) within a given center if it can be assumed that there is no generation effect, i.e., that the experience of the older sample women reflects the future experience of the younger sample women in a given center. This assumption appeared reasonable for age at menopause and duration of reproductive life: Comparable portions of the Kaplan-Meier estimated distributions of these variables for the older sample women appeared to vary little from those of the younger sample women across the centers. The latter findings, along with no observed generation effect for age at menarche, speak for the validity of the overall estimates of the medians for the three mainly biologic reproductive variables within centers. Much the same could be argued regarding the validity of the overall median estimates of the more culturally determined variables, age at and delay to first livebirth, for the four study centers in which no generation effect was found. However, for the other nine study centers in which clear generation effects were observed, the validity of the overall median estimates of age at and delay to first livebirth remains more problematic.

Another possible matter for concern about the validity of the data involves potential differentials in reproductive history recall by the sample women in the various centers. Reproducibility studies have shown that US women have a precise recall of the major reproductive events (17, 18). However, it is unclear whether similar results would be obtained in less-developed countries.

Furthermore, selection bias may also be a problem because the study sample women were hospital controls, and access to hospital care may be more frequent for women of higher socioeconomic status than for other women. In less-developed countries, women who are more affluent are more likely to live in urban areas, and their way of life may more closely resemble that of Western women. On the other hand, women with diseases thought to alter contraceptive practices were not eligible, since these were originally controls for a case-control study on steroid contraceptive usage (10–13). In addition, life habits related to ages at reproductive events (e.g., smoking, diet, drinking) of women hospitalized may differ from those of the rest of the population. The net bias resulting from these multiple potential sources of selection on international variability remains unpredictable from the secondary analyses performed here because the specific data required to measure it were not collected in the original case-control study.

Our results are relevant for epidemiology, clinical medicine, and public health. International comparisons may provide some insight into the geographic variability of some reproductive history-related diseases, such as breast cancer in women.

Population-based information can help the clinician to identify how typical the reproductive history of a patient is compared with that of her community of

origin. From a public health perspective, monitoring of the timing of reproductive events may be a useful instrument to assess the impact of intervention strategies aimed at changing practices related to family planning and contraception.

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