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Age at menopause and determinants of hysterectomy and menopause in a multi-ethnic community: The Hilo Women's Health Study



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ABSTRACT

Objectives: A lifespan approach was used to evaluate age at menopause, and determinants of surgical and natural menopause, in the multi-ethnic community of Hilo, Hawaii.

Study design: Participants aged 40–60 years (n = 898) were drawn from a larger, randomly generated sample recruited by postal questionnaires. Median age at natural menopause was computed by probit analysis. Logistic regression analysis was applied to examine determinants of hysterectomy, and Cox regression analysis was used to examine risk factors for an earlier age at menopause.

Main outcome measures: History of hysterectomy, age at menopause.

Results: Frequency of hysterectomy was 19.2% at a mean age of 40.5 years. The likelihood of hysterectomy increased with older ages, lower education, mixed ancestry, having been overweight at age 30, and married 20 years prior to survey. Median age at natural menopause was 53.0 years. Smoking and not being married 10 years before survey were associated with an earlier age at menopause.

Conclusions: Median age at menopause was later than the national average. Ethnicity and education were determinants of hysterectomy, but not associated with age at natural menopause. Events later in the lifespan (e.g., smoking and not being married 10 years prior to the survey) were more important than earlier events (e.g., childhood residence) in relation to age at menopause. The timing of weight gain and marital status appear to be important in relation to surgical menopause, and the timing of marital status appears to be important in relation to the timing of natural menopause.

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1. Introduction

Ages at surgical or natural menopause are associated with long term consequences for health during the post-reproductive years. For example, earlier ages at hysterectomy with bilateral oophorectomy are associated with an elevated risk of cardiovascular mortality [1,2], and a later age at natural menopause is associated with a higher risk of breast cancer [3,4]. A later age at natural menopause is also associated with increased longevity [5,6] and lower all-cause mortality [7].

The state of Hawaii boasts the longest life expectancy in the nation, with a mean life expectancy of 80.5 years [8] vs. a national average of 78.7 years [9]; thus, median age at menopause in Hawaii

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may also be later, relative to the median ages of 51–52.5 years in the United States [10–12]. The purpose of this study was to establish the median age at natural menopause in Hilo, Hawaii, as well as the determinants of surgical and natural menopause among this multi-ethnic population. Confirming determinants in this population contributes to our knowledge about risk for health concerns in Hawaii so that women can be targeted for screening and other preventative measures.

Variation in age at menopause, both within and across populations, is related to differences in genes, early environment, adult lifestyle, and reproductive history. Estimates for heritability in age at menopause vary from 31 to 85% [13–16]. A number of studies have demonstrated a relationship between early ages at menopause and adverse early life events, such as severe caloric restriction during early childhood [17], low weight gain during early childhood [18,19], socioeconomic disadvantage [20], or infectious disease burden [21]. Early ages at menopause are also associated with smoking [10,22], nulliparity [10,23], low levels of education [11], being single or otherwise unmarried [24], and low BMI at midlife [22,23].

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Ethnicity has been associated with age at menopause in some studies, but not others. In the longitudinal Study of Women's Health Across the Nation (SWAN), Japanese ancestry was at first significantly associated with a later age at natural menopause compared to non-Hispanic whites (51.8 years vs. 51.4 years) [10]. The most recent study by SWAN researchers, using data from 1996 through 2007 (n=3253), found that Japanese participants had a later age at menopause than African-American, Chinese, and Hispanic participants in unadjusted results. However, after adjusting for smoking, self-reported health, education level, use of oral contraceptives, alcohol intake, employment, physical activity, and baseline weight, ethic differences were no longer significant [11]. An independent effect of race/ethnicity on the timing of natural menopause was shown in the Multiethnic Cohort Study of women aged 45-74 (n=95,704). After adjusting for smoking status, age at menarche, parity, and BMI, native Hawaiians had an earlier menopause than non-Hispanic whites (HR 1.05, 95% CI 1.01-1.09). Japanese-Americans experienced a later menopause than non-Hispanic whites (HR = 0.93, 95% CI 0.90-0.95) [23].

Ethnicity has also been associated with variation in rates of hysterectomy. In a 1977 study of menopause among women aged 35 to 60 in Hawaii, menopausal women of European descent were more likely to have undergone "surgery for female disorders" compared to Japanese-Americans (52% vs. 37%) [25]. More recently, SWAN results found that Asian-Americans reported a lower rate of hysterectomy compared with non-Hispanic whites [26]. In a study of California school teachers, Asians/Pacific Islanders were not more likely to have surgery for uterine fibroids than non-Hispanic whites [27].

Hilo, on the Big Island of Hawaii, was once a port associated with a sugar cane industry that attracted thousands of workers of different ethnicities to Hawaii [28]. Hilo is now a multiethnic community of 46,165 residents. Japanese-Americans are the largest ethnic group (21%), followed by European-Americans (19%), Native Hawaiians (11%), and Filipinos (7%). Thirty-two percent of people classify themselves as members of two or more ethnic groups (2010 census). This population provides the opportunity to study different ethnic groups residing in the same general locality, although there are socioeconomic and cultural differences, e.g., in diet and activity patterns [29]. Hilo is also of interest because of a previous study that showed a high frequency of hysterectomies. In a study of ambulatory blood pressure among Japanese-American and European-American school teachers (n=120), 66% of the 47 postmenopausal participants (29 Japanese-Americans and 18 European-Americans) had undergone a hysterectomy, 15 with ovaries left intact and 16 with ovaries removed [30].

The purpose of this study was to consider age at menopause in the multi-ethnic community of Hilo, HI, and to examine determinants of surgical and natural menopause. This study applied a lifespan approach [31,32] to examine early life events (e.g., where women grew up – Hawaii, U.S. mainland, not U.S.), level of education, and later life events such as smoking habits and marital status. In a lifespan perspective, biological and socio-cultural trajectories are intertwined across time [33–35], and every point in the lifespan can be studied as both predictive of later aging and the result of cumulative processes [36].

Age at hysterectomy and age at natural menopause are both influenced by biological and socio-cultural variables. For example, a twin study carried out in the UK found similar estimates of heritability for hysterectomy (0.59, 95% CI 0.43–0.72) and for the main indications for hysterectomy, fibroids (0.69) and menorrhagia (0.55) [15]. In a more recent study, the decision to undergo a hysterectomy was associated with fibroids and uterine bleeding, and also with the importance of sexual relationships and attitudes, e.g., whether the uterus is "useless" to women who have completed

childbearing [37]. A lower level of education and income has also been associated with increased rates of hysterectomy [38].

Age at natural menopause is determined by the number of undeveloped eggs present in ovaries at birth and the rate of loss of ovarian follicles across the lifespan [39,40]. We do not have birth weight to assess possible effects of maternal health on the number of undeveloped eggs present at birth; therefore, we focus on determinants that may influence the rate of loss of ovarian follicles across the lifespan. In addition to identifying determinants of age at surgical and natural menopause, we are interested in when, during the lifespan, such variables may have had an influence.

2. Methods

2.1. Study sample

For this study, women aged 40-60 (n=898) were drawn from the larger Hilo Women's Health Study. This study involved two phases: a postal survey about general health and menopause, and a follow up clinical study of hot flashes and blood pressure among a subsample of 200 women. The current analysis is based on the postal survey.

Eight-page health questionnaires were mailed to property lots in Hilo based on tax map key numbers chosen by random assignment (see Sievert et al. for further details) [41]. Surveys were mailed to 7207 households, and 1824 surveys were completed and returned for a household return rate of 28.5%. All women gave written informed consent and the study was approved by the University of Hawaii Human Studies Program.

To determine ethnicity, women were asked to check off all groups "that are included in your background" from a list of ethnicities, and were asked to include the percentage of each ethnicity where this was known. For these analyses, ethnicity was categorized into 4 groups: European-American, Japanese-American, Mixed, and Other. The category European-American was made up of women who claimed 100% European ancestry on the guestionnaire. The category Japanese-American was limited to women who claimed 100% Japanese ancestry. Although Hawaiian Japanese-Americans are primarily third and fourth generation, and native English-speakers, the Japanese-American community in Hawaii has intermarried less than other ethnic groups [42]. Therefore, a high proportion of women with 100% Japanese ancestry is present [41]. In the mixed ancestry group, the majority indicated Hawaiian (60%) and/or European (66%) ancestry. Mixed ancestry also included Chinese (43%), Japanese (25%), Filipino (23%), Hispanic (12%), Native American (12%), Korean (4%), Pacific Islander (4%), and African-American (2%) backgrounds. Women were categorized as "Other" if they described their background as 100% one ethnicity besides European or Japanese.

2.2. Variables of interest

Body mass index (BMI) at time of survey was calculated from self-reported height and weight. Past BMI was calculated from recalled, self-reported weight at ages 20, 30, and 40 in combination with self-reported height at time of survey. For multivariate models, BMI was categorized as underweight/normal ($<25 \text{ kg/m}^2$), overweight ($25-30 \text{ kg/m}^2$), and obese ($>30 \text{ kg/m}^2$).

Variables examined in relation to ages at surgical and natural menopause included: age at time of survey; ethnicity; where a woman grew up (Hawaii, U.S. mainland, not U.S.); level of education (some or completed high school, some or completed two year or four year college, some or completed postgraduate degree); financial comfort (struggling, OK, comfortable, well-off); marital status at time of survey, marital status 10 years ago, marital status 20

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