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# Age, period, and cohort effects in adult lifetime asthma prevalence in California: an application of hierarchical age-period-cohort analysis



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#### ABSTRACT

*Purpose*: Using 27 years of survey data, the contributions of age, period, and cohort effects on the increase in adult lifetime asthma prevalence in California were examined.

Methods: Lifetime asthma diagnosis for adults was assessed in 1984–1992 and 1995–2011 through the California Behavioral Risk Factor Surveillance System, an annual, cross-sectional, population-based survey (n=144,100). Using date of survey and date of birth, we classified 18,305 adult respondents with lifetime asthma into 7 age groups, 6 periods, and 17 cohorts. Using hierarchical, cross-classified random effects models, birth cohort, period, and age patterns in adult lifetime asthma prevalence were analyzed. Results: After adjusting for sex, ethnicity, education, and smoking, age effects peak in young adulthood, flatten from 40 to 60 years old, and then decrease in older adulthood. A significant positive trend in asthma prevalence was observed in the two earliest survey periods (1984–1993; P value < .0001). Survey period trends appear to flatten beginning in 2004. Although the overall birth cohort effect was statistically significant, the magnitude of the effect for each birth cohort category was small (P value = .0005). Conclusions: We observed that strong age and period effects have been driving the increase in lifetime asthma prevalence in California over the past 3 decades.

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#### Introduction

Asthma affects nearly 5 million Californians [1]. No cure currently exists for asthma, although treatments exist to manage symptoms and control exacerbations. Since the early 1980s, the prevalence of asthma has been increasing in California and nationwide [1–3]. The relatively short time frame of the increase in asthma suggests that environmental and behavioral changes, perhaps combined with increased case identification (especially with mild cases), rather than purely genetic changes, are primarily responsible [2].

The causes of developing asthma are not fully understood but are likely complex and involve many factors. Specific causes cannot be identified for most cases. Studies have identified several factors that increase the likelihood of developing asthma. These include a family history of asthma or allergies; certain viral respiratory infections during early childhood; early exposure to secondhand tobacco smoke, traffic-related air pollution, house dust mites, cockroaches, indoor dampness, and mold [2,4-6]. Many other environmental and behavioral factors have been hypothesized to play a role in asthma incidence, including exposure to pesticides, volatile organic compounds, and plasticizers; increases in obesity; decreases in exercise and outdoor play; changes in microbial flora due to increased use of antibiotics; breastfeeding practices and the rate of cesarean births; and decreases in certain childhood environmental exposures and infections due to Western sanitation practices (known as the hygiene hypothesis) [2]. An age-periodcohort analysis can aid in understanding the already established temporal trend of increasing asthma prevalence. Since 1984, the California Behavioral Risk Factor Surveillance System (CA BRFSS) has systematically collected information on asthma among adults. This creates an exceptional opportunity for examining the influence of age, period, and cohort effects on asthma prevalence trends. Age

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effects represent changes in disease prevalence because of aging processes, including those due to biological and social factors. Trends associated with survey period or birth cohort would indicate that social or environmental factors play a role. Some of the hypothesized social and environmental factors that may drive period and cohort effects are policies that have affected air pollution levels; population-level changes in diet, physical activity, or tobacco use; changes in indoor air quality and allergens; and changes in clinical practice such as increased awareness and diagnoses of asthma or increased use of certain medications. Previous studies have found that these factors influence asthma prevalence and severity. However, it is unclear whether these influences would work through a period effect, which would mean having similar effects simultaneously across a population, or a cohort effect, which would mean affecting certain birth cohorts of people at certain developmental stages (e.g., during the second trimester) and appearing over time sequentially as each cohort ages. The aim of this study was to identify new insights into the monotonically increasing trend of rising asthma prevalence by examining the direct and unique influences of age, period, and cohort, as well as the synergistic effects of all three simultaneously.

#### Materials and methods

Study population

CA BRFSS is an ongoing, cross-sectional telephone survey of noninstitutionalized adults of age 18 years and older in California that provides representative data on health behaviors and outcomes. Methodological details have been published elsewhere [7]. For this analysis, we used nearly 3 decades of CA BRFSS data collected from repeated, annual cross-sectional surveys of representative samples of adults from 1984 to 2011 (n = 144,100).

Lifetime asthma diagnosis was assessed on CA BRFSS from 1984 to 1992 and 1995 to 2011. The question used to assess asthma diagnosis changed at several points during these periods but is similar across years, so responses are comparable.

"Age" was defined by participant age at time of interview  $(18-24,\ 25-34,\ 35-44,\ 45-54,\ 55-64,\ 65-74,\ and\ \ge 75\ years)$ , except in regression models, when age was included as continuous. We included quadratic  $(age^2)$  and cubic  $(age^3)$  terms for age because generalized additive models indicated a cubic shape for the distribution. "Period" was defined as a 5-year period within the entire survey period from 1984 to 2011, with five periods of 5 years each and one period of 2 years (2009-2011). "Cohort" was defined as the birth year, calculated by subtracting the age when the survey was completed from the year of the survey. Cohort was grouped into 5-year birth cohorts, except for the earliest cohort, which includes 25 years due to small sample size of adults with asthma, yielding 17 cohorts of 5-year intervals each, 1914–1993, and one cohort of 25 years, 1887–1913.

Additional covariates were included as fixed effects to control for confounding and to isolate the direct effects of age, period, and cohort in regression models: sex (male vs. female), self-identified race African American or black vs. not), smoking status (current, former, never), and education (less than high school vs. high school or higher), as a proxy for socioeconomic status.

#### Statistical analysis

Age-standardized lifetime asthma prevalence was calculated overall and according to age, period, and cohort. Hierarchical age-period-cohort (HAPC) models developed for repeated cross-sectional surveys [8–10] were used to fit cross-classified random effects nonlinear regression models using a binomial distribution

with a log link [11] (see Supplemental material A for model details). Because of overdispersion in the data, we added a multiplicative dispersion parameter (random \_residual\_). Models were specified to take into account the embedded nature of participants in CA BRFSS surveys within a time period by birth cohort cross-classified matrix (Table 1).

All analyses were weighted to the California population according to California Department of Finance 2010 population estimates. Statistical analyses were calculated using survey procedures in SAS, version 9.2. HAPC analysis was conducted using PROC GLIMMIX (SAS Institute Inc., Cary, NC), which was adapted for use with complex survey data. The JoinPoint Regression program, version 4.2.0, was used to calculate JoinPoint regressions in the sensitivity analysis (National Cancer Institute, Bethesda, MD). We considered any *P* values less than .05 to be statistically significant.

#### Sensitivity analysis

In the HAPC analysis, we were unable to adjust for the complex survey design of CA BRFSS by including primary sampling unit and strata variables because of software limitations. Therefore, these models could underestimate the standard errors. To compare the standard errors and *P* values in the HAPC analysis with an analysis that accounted for the full complex survey design, we used SAS survey procedures to calculate age-standardized lifetime asthma prevalence and standard errors by birth cohort and survey period. Then, we used JoinPoint regression to calculate the average percent change (APC) and *P* values for trend for each survey period within each birth cohort and compared to results from the HAPC analysis.

#### Results

Trends in asthma prevalence

Adult asthma prevalence has been steadily increasing in California from 1984 to 2011, from 7% in 1984–1988 to 14% from 2009–2011 (Table 2). Asthma prevalence has been increasing among both men and women, and trends are similar among these two groups, with the exception that women have consistently higher prevalence over time (Fig. 1).

Age-period-cohort effects

In models with age included as an individual-level fixed variable and cohort and period included as level-2 random effects variables, significant age, period, and cohort effects were observed.

After adjusting for sex, race, education, and smoking, age effects peak in young adulthood, flatten from 40 to 60 years old, and then decrease in older adulthood (Fig. 2). Log odds of having been ever diagnosed with asthma are highest among the youngest adults in our sample, adjusting for sex, race, education, and smoking.

Significant period and cohort effects were observed (P < .001; Table 3). Effects of period and cohort were similar in the model adjusted for individual-level demographics (age, sex, race, and education; data not shown) and in the model adjusted for cigarette smoking.

Significant trends in period (P < .0001) and cohort (P = .0005) effects were also noted, reported as random effects variance components in Table 3. A significant positive trend in asthma prevalence was observed in the two earliest survey periods (1984–1993; Fig. 3). From 1994 to 2004, the positive trend continues but is not as steep. Survey period trends appear to flatten beginning in 2004. Although the overall birth cohort effect was statistically significant, the magnitude of the effect for each birth cohort category was small

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