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Cerebral Palsy And The Hispanic-Immigrant Paradox In California Births From 2000-2015

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Abstract

Background: Cerebral palsy (CP) affects approximately 3 out of 1000 children in the United States (U.S.),[1] and while previous studies have shown significant racial disparities in CP outcomes, the Hispanic population is understudied despite it being the fastest growing minority group in the U.S. Data shows poorer health outcomes in cancer, neonatal morbidity, and other perinatal outcomes among U.S.-born Hispanic women compared to their foreign-born counterparts. This analysis aimed to investigate whether incidence of CP in Hispanic women's offspring differed by the mother's birthplace.

Methods: Linked California birth certificate and California Department of Developmental Services (DDS) records between 2000-2015 were used for this analysis. Non-Hispanic mothers were excluded from the main analysis, resulting in a cohort of 4,233,966 births containing 5,476 CP cases. A sub-analysis of only Mexican mothers included 3,514,470 births and 4,515 CP cases. Multivariable logistic regression models adjusted for sex, birth year, mother's age and education, father's age, trimester of prenatal care onset, parity, and multiple births were used to estimate odds ratios (ORs) for CP diagnosis by maternal nativity. Stratification analysis was performed for child's sex, CP subtype and CP location.

Results: CP was 12% more likely to occur in the offspring of U.S.-born Hispanic mothers compared with the offspring of foreign-born Hispanic mothers (OR = 1.12; 95% CI: 1.05 – 1.19). Similar results were found for Mexican mothers (OR = 1.13; 95% CI: 1.05 – 1.21) where odds of CP diagnosis was greater among U.S.-born mothers. Stratification showed that this increased likelihood was greater in unilateral CP over bilateral CP and stronger among female offspring than male offspring. Lastly, increased odds of CP diagnosis in offspring of U.S.-born mothers was only present in the spastic CP type.

Conclusions: In line with previous research into other health outcomes, CP was more likely to be diagnosed in the offspring of Hispanic women born in the U.S. compared to offspring of foreign-born Hispanic women. This adds CP to the list of poorer pregnancy-related outcomes among Hispanic women born in the U.S. Future policymakers and investigators working with Hispanic populations should carefully consider how mothers' nativity might influence policy impacts and developmental disorder outcomes, especially for neurological disorders such as CP.

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Introduction

Cerebral palsy (CP) describes a group of neurological disorders that begin in infancy or early childhood and are attributed to lesions in the developing brain which permanently affect movement and muscle coordination.[1] CP affects approximately 3 out of 1000 children in the United States (U.S.).[2] While racial disparities in perinatal and infant outcomes in the U.S. have been documented between non-Hispanic Black and non-Hispanic White populations,[3] Hispanic populations have received less focus. Hispanics are one of the fastest growing ethnic groups in the U.S.,[4] and have been so since the 90s in California.[5] Therefore, understanding disparities in birth outcomes within the Hispanic community in California is crucial for implementing appropriate public health policies and goals for the Hispanic community in California and elsewhere.

Literature has identified both nativity and country of origin as important areas when studying perinatal health events among Hispanic population.[3] An "immigrant health paradox" found in the U.S. describes how, despite multiple risk factors including lower social economic status, first-generation immigrants have better outcomes in several health domains – including infant and maternal mortality rates – than individuals of the same race born in the U.S.[6] In addition, it has been suggested that the protective health advantage of foreign-born immigrants does not continue to benefit their offspring's future health.[3] Prior studies have also suggested it is important to consider country of origin as differences in improved birth outcomes have been observed between Caribbean and Central American versus Mexican and South American Hispanic immigrants compared with their U.S born counterparts.[6]

To our knowledge, no studies have investigated nativity subgroups among Hispanic women in the context of CP occurrence in offspring despite research showing differential offspring CP rates in subgroups of both non-Hispanic Black mothers and Asian mothers.[5,7] This analysis would fill this gap and provide more insight into the Hispanic-immigrant paradox. Various studies have described the Hispanic-immigrant paradox in cancer, neonatal morbidity, and even a resilience measure[8–10] but adding CP will expand the literature to include neurological diseases. Therefore, this analysis aims to investigate the Hispanic-immigrant paradox in CP by comparing foreign-born Hispanics to U.S.-born Hispanics and limiting the analysis to country-of-origin subgroups to provide a more complete picture of this phenomenon.

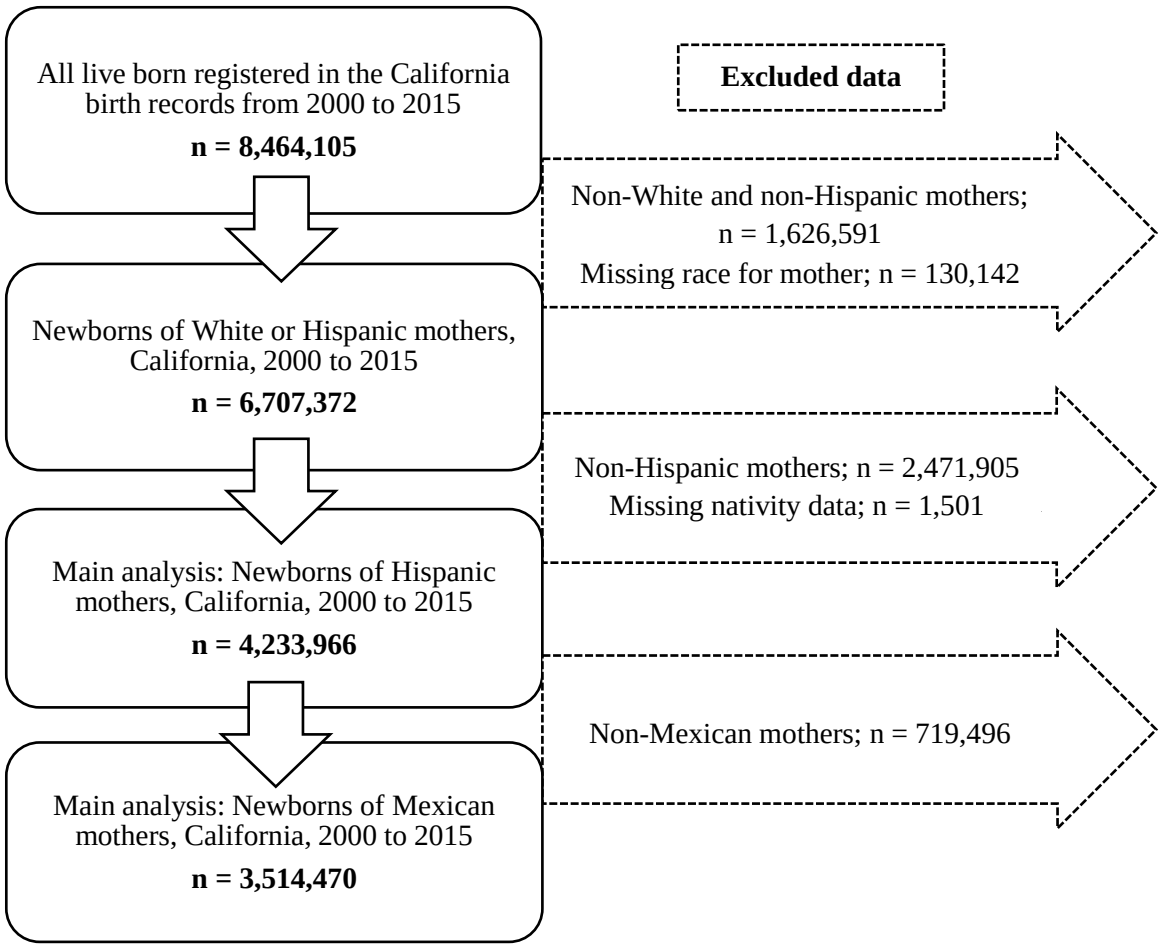
Methods

Collection and analysis of this data was reviewed and approved by the institutional review boards (IRBs) of the University of California, Los Angeles (IRB #15-001651), Yale University (IRB #2000028297), and the California Committee for the Protection of Human Subjects (Project #12-10-0861).

Study Sample

Data was retrieved from California birth certificate records and the California Department of Developmental Services (DDS), which provides services at 21 regional centers to children with cerebral palsy living in California.[11] The California Vital Statistics Birth files were linked to the DDS files via probabilistic linkage of CP diagnoses (success rate 86.3%) based on child's first name, last name, date of birth, sex, and both mother's and father's first name, last name, and date of birth.[1] The self-reported primary race of the mother was used to restrict the preliminary analyses to White and Hispanic mothers (n = 6,707,372), and the main analyses were further focused on Hispanic mothers only (n = 4,233,966) and Mexican mothers only (n = 3,514,470) using the self-reported ethnicity data (Fig 1.) The main analyses also excluded mothers with missing nativity data which is a main predictor of interest in analyses of the Hispanic cohorts.

Fig 1. Study sample subsets analyzed for CP outcome



Outcome Classification

The DDS defines CP as a group of non-progressive lesions or disorders in the brain occurring during intrauterine life or the perinatal period and characterized by paralysis, spasticity, or the abnormal control of movement or posture that is manifest before 2 or 3 years of age. These disorders are usually manifested during early childhood and may be due to developmental anomalies of the central nervous system or injury of the brain during intrauterine life, the perinatal period, or within the first few months of life.[12] The primary outcome in this analysis was any CP diagnosis as defined by the DDS. Sub-types of CP (spastic/hypertonic, ataxic, dyskinetic, and others including hypotonic and mixed types) as well as the distribution of affected limb movement (unilateral or bilateral) were analyzed in secondary analyses.

Covariates

Confounders were identified by literature review.[12–16] Mother's age and education, sex of the child, trimester of prenatal care onset, parity, multiple births, and father's age were extracted from the California data birth certificates. The exact birth year was also included to account for population changes and potential birth cohort effects. Both maternal and paternal age were stratified into four categories: <18, 18-25, 26-34, ≥35 years old. Mother's education was stratified into three categories: no high school diploma, high school diploma and any college. Parity was stratified into four categories: 1, 2, 3, ≥4 children. Known CP risk factors such as preterm birth, birthweight, gestational age, mode of delivery, and birth complications likely lie within the causal pathways and act as mediating factors thus they are not included as confounders.

Statistical Analysis

Multivariable logistic regression was performed to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for CP in the offspring according to maternal race/ethnicity or nativity status. Given the low prevalence of CP, all ORs we estimated would be a close approximate to the measure of risk ratios. We conducted a preliminary analysis on offspring born to mothers self-identified as Hispanic compared to non-Hispanic White as the reference to understand the differences between the two groups. In our main analysis of Hispanic mothers only, we compared maternal foreign-born status to U.S.-born as the reference. We repeated this analysis in Mexican mothers only to investigate whether birthplace affects CP outcomes in all Hispanic countries of origin. In each analysis, we adjusted for sex, birth year and mother's age (Model A), and additionally included education, father's age, trimester of prenatal care onset, parity, and multiple births (Model B). Father's age was included in Model B after a sensitivity check, ensuring collinearity between father's and mother's age did not impact the model stability. In secondary analyses, we examined whether the results differ by child's sex, by CP sub-types (Spastic, Ataxic, Dyskinetic, or others including hypotonic and mixed), or by CP location (unilateral, bilateral). Analyses were performed using SAS statistical package (version 9.4; SAS Institute Inc, Cary, NC).

Results

For the live births records we included in California between 2000-2015, 4,233,966 children were born to Hispanic mothers and 2,471,905 to non-Hispanic White mothers. Among the Hispanic mothers, 2,393,229 (56.5%) were born outside of the U.S., and 1,840,737 (43.5%) were born in the U.S. The U.S.-born mothers were more likely to be younger, more educated and have fewer children. (Table 1). A total of 3,514,470 (83.0%) of Hispanic mothers were identified as Mexican, and similarly 57.9% of Mexican mothers were foreign-born. (Table 1).

Table 1. Demographic characteristics of the Hispanic study cohort by maternal self-reported nativity, California, 2000-2015

Characteristics	Foreign-born Hispanic Mothers (N = 2,393,229)	U.S.-born Hispanic Mothers (N = 1,840,737)
	N (%)	N (%)
Child's Sex		
Male	1,219,986 (51.0)	939,523 (51.0)
Female	1,173,192 (49.0)	901,177 (49.0)
Maternal Age (years)		
<18	611,68 (2.6)	119,196 (6.5)
18-25	814,365 (34.0)	910,660 (49.5)
26-34	1,118,129 (46.7)	662,296 (35.6)
35+	399,512 (16.7)	148,562 (8.1)
Paternal Age (years)		
<18	11,228 (0.5)	38,587 (2.3)
18-25	523,855 (23.5)	657,290 (39.7)
26-34	1,060,532 (47.6)	706,953 (42.7)
35+	633,783 (28.4)	252,497 (15.3)
Maternal Education		
no high school diploma	1,349,703 (57.7)	439,824 (24.2)
high school diploma	588,744 (25.2)	666,768 (36.7)
any college	401,649 (17.2)	708,593 (39.0)
Parity		
1	685,897 (28.7)	766,607 (41.7)
2	718,356 (30.0)	542,246 (29.5)
3	544,595 (22.8)	302,902 (16.5)
4+	442,888 (18.5)	227,677 (12.4)
Multiples		
Singleton	2,344,082 (98.0)	1,796,070 (97.6)
Multiple	49,147 (2.1)	44,666 (2.4)
Prenatal Care Onset		
No prenatal care	10,137 (0.4)	14,892 (0.8)
1st trimester	1,941,242 (82.5)	1,471,913 (81.5)
2nd trimester	327,822 (13.9)	268,405 (14.9)
3rd trimester	72,689 (3.1)	52,020 (2.9)
Year of Birth		
2000-2005	1,029,489 (43.0)	584,853 (31.8)
2006-2010	809,103 (33.8)	601,167 (32.7)
2011-2015	554,637 (23.18)	654,717 (35.6)

There were 5,476 cases of CP among Hispanic mothers. Among these, 3,099 (56.6%) were offspring of foreign-born mothers and 2,37 (43.4%) were offspring of U.S.-born mothers. Preliminary analysis showed that CP was 10% more likely to occur in the offspring of Hispanic mothers (OR = 1.10; 95% CI: 1.04 – 1.16) than the offspring of White mothers after controlling for the full set of potential confounding factors (Table 2). Among Hispanic mothers, CP was 12% more likely to occur in the offspring of those who were born in the U.S. compared with the offspring of foreign-born mothers in the fully adjusted model (OR = 1.12; 95% CI: 1.05 – 1.19). Similar results were found for Mexican mothers where the OR for child's CP among U.S.-born compared to foreign-born mothers was 1.13; (95% CI: 1.05 – 1.21) (Table 2).

Table 2. Odds Ratio (OR) and 95% confidence interval (CI) for cerebral palsy in the offspring according to maternal race/ethnicity and nativity

	Hispanic vs. Non-Hispanic White Mothers[a]			**U.S.-born vs. Foreign-born Hispanic Mothers[b]**			**U.S.-born vs. Foreign-born Mexican Mothers[b]**		
Total CP Cases	N = 8,418			N = 5,476			N = 4,515		
	OR	**95% CI**		**OR**	**95% CI**		**OR**	**95% CI**	
Crude	1.09	1.04	1.14	1.00	0.95	1.05	1.02	0.96	1.08
Model A[c]	1.12	1.07	1.18	1.07	1.01	1.13	1.10	1.04	1.17
Model B[d]	1.10	1.04	1.16	1.12	1.05	1.19	1.13	1.05	1.21

[a]Reference = Non-Hispanic White mothers

[b]Reference = Foreign-born mothers

[c]Adjusted for sex, birth year and mother's age.

[d]Adjusted for sex, birth year, mother's age and education, father's age, trimester of prenatal care onset, parity, and multiple births.

Of all CP cases, 2,884 (53.2%) were spastic CP, 256 (5.1%) were ataxic CP, 149 (2.8%) were dyskinetic CP, and 2,110 (38.9%) fell under Mixed or hypotonic. After stratifying by CP Type, spastic CP was 21% more likely in offspring of Hispanic mothers born in the U.S. than offspring of Hispanic mothers born outside of the U.S. (OR = 1.21; CI: 1.11 – 1.33). Other types of CP were also more likely in U.S.-born Hispanic mothers, but those estimates' 95% confidence intervals crossed the null (Table 3). Both unilateral (OR = 1.35; CI: 1.11 – 1.64) and bilateral CP (OR = 1.18; CI: 1.06 – 1.31) were more likely in offspring of women born in the U.S. (Table 3). Lastly, female offspring (OR = 1.14; CI: 1.03 – 1.25) of Hispanic women were slightly more likely to have CP than male offspring (OR = 1.10; CI: 1.01 – 1.20).

Table 3. Odds Ratio (OR) and 95% confidence interval (CI) for cerebral palsy in the offspring according to maternal nativity in Hispanic mothers, stratified by type, location, and child's sex

		U.S.-born vs. Foreign-born (reference) Hispanic Mothers								
		Crude			Model A[a]			Model B[b]		
	n (%)	OR	95% CI		OR	95% CI		OR	95% CI	
Type										
Spastic	2,884 (53.2)	1.08	1.00	1.16	1.15	1.07	1.24	1.21	1.11	1.33
Ataxic	276 (5.1)	0.89	0.70	1.13	1.00	0.78	1.28	0.95	0.71	1.27
Dyskinetic	149 (2.8)	1.00	0.73	1.39	1.10	0.79	1.54	1.01	0.69	1.48
Other/Mixed/ Hypotonic	2,110 (38.9)	0.91	0.83	0.99	0.97	0.89	1.07	1.03	0.92	1.14
Location										
Unilateral	596 (21.3)	1.23	1.05	1.44	1.30	1.10	1.54	1.35	1.11	1.64
Bilateral	2,200 (78.7)	1.03	0.95	1.12	1.11	1.02	1.21	1.18	1.06	1.31
Sex										
Male	3036 (55.4)	1.00	0.93	1.07	1.08	1.00	1.16	1.10	1.01	1.20
Female	2440 (44.6)	1.00	0.92	1.08	1.06	0.98	1.16	1.14	1.03	1.25

[a]Adjusted for sex, birth year and mother's age.

[b]Adjusted for sex, birth year, mother's age and education, father's age, trimester of prenatal care onset, parity, and multiple births.

Discussion

In this California cohort study, we found that among cohorts of Hispanic only and Mexican only mothers, the risk for CP in their offspring was higher if the mothers were born in the U.S. compared to if they were born abroad. These observed associations were slightly stronger for Spastic CP and unilateral subtypes but were similar in male and female offspring. This study also confirmed that the offspring of Hispanic mothers have a higher risk for CP compared to non-Hispanic White mothers.

Increased risk of CP in the offspring of Hispanic women compared to offspring of White women is consistent with literature demonstrating increased risk of adverse birth outcomes, such as low birthweight, preterm birth, and small for gestational age in Hispanic mothers compared to non-Hispanic White mothers,[17] as well as when comparing offspring of foreign-born Hispanic women compared with their U.S.-born counterparts.[17] There were some inconsistencies in findings when assessing nativity in specific subgroups of Hispanic and birth outcomes.[6] Our results in California were consistent for Mexican mothers which were the largest Hispanic subgroup. Studies assessing whether there would be differences among other Hispanic groups, such as the Caribbean and Central American women,[6] warrant further research.

The results of this study may also be due to differential diagnoses rates between mothers born inside and outside of the U.S. Mothers born in the U.S. may be more likely to diagnose their children with CP due to greater interaction with the healthcare system, lack of language barrier and lower stigma and greater visibility of developmental disorders in the U.S. On the other hand, mothers born outside of the U.S. may be more susceptible to other CP risk factors due to less interaction with the healthcare system. Other perinatal risk factors of CP, including parental ages,[12] mode of delivery,[16] maternal infection,[14] smoking,[14] and injury during pregnancy,[18] and exposure to environmental pollutants,[1] might also contribute to disparities of CP in California. For example, injury during pregnancy and exposure to environmental pollutants may disproportionately affect Hispanic women due to greater occupational exposure and poorer working conditions in this population. However, whether these risk factors differentially affect foreign versus U.S.-born mothers is unclear and requires further investigation. Lastly, migration may also select for healthier women under the “healthy migrant effect,” resulting in artificial increased overall health in immigrants compared to U.S.-born individuals.

Proposed Mechanisms

Multiple mechanisms have been suggested for the Hispanic-immigrant paradox including social network, acculturation, duration of stay in the U.S. and selective return.[19,20] However, studies of these mechanisms have resulted in no conclusive evidence. Social networks have been shown to have an effect on birth weight, but not differentially by race or nativity.[20] Meanwhile, acculturation, duration of stay and selective return had minimal effects.[19] Other social determinants of health such as at-home maternity practices may be involved in a mechanism, but

they are understudied and difficult to measure. Currently, there is no consensus on a mechanism that adequately explains the Hispanic-immigrant paradox.

Strengths and Limitations

There are several strengths and limitations to this analysis. The size and length in time of the data allows for more precise estimates and robust subgroup analysis. In addition, given that it is sourced from California birth certificates, the sample is likely representative of California's population and is more complete than a self-reported dataset. However, the data was also limited in that some predictors of interest were either not collected in birth certificates (income) or too rare or inaccurate to analyze (maternal infection). Risk factors such as maternal smoking and BMI were also not collected until 2007 and thus not included in the analysis. Therefore, future analyses of the relationship between nativity and CP in Hispanic subgroups should focus on the collection and inclusion of these risk predictors and mediators.

Misclassification of race and nativity is also possible because they are self-reported and recorded in the birth certificates. The increase of interracial marriage and mixed-race individuals in the childbearing age population could also contribute to further misclassification. Lastly, this study is limited by the classification of CP under the DDS registry. Although the DDS service centers are widespread in California, it may under-ascertain cases where symptoms are mild enough to not require DDS services, and also the CP cases born in California who leave the state and are diagnosed elsewhere.[5] However, this should be a small fraction of CP cases and it is expected that DDS captures 75-80% of all CP cases in California.[21] In addition, it is less likely for children with disadvantaged backgrounds to be registered with DDS, which could affect the results of this analysis. Considering these factors, DDS likely underestimates the incidence of CP and outcome misclassification could induce small effect on the estimated associations.

Public Health Implications

This study stands out in public health literature due to its focus on a Hispanic-only cohort. Given the large proportion of immigrants in the United States' Hispanic population, finding that the offspring of U.S.-born Hispanic women have significantly higher odds of cerebral palsy, future public health plans and practitioners should strongly consider how policies and protocols may differentially affect the pregnancies U.S.-born versus foreign-born Hispanic women. In addition, all researchers working with Hispanic or predominantly Hispanic populations should consider controlling for and stratifying by nativity in their analyses. Lastly, when developing research questions and statistical models, scientists in the field of neurological disorders should investigate whether CP risk factors and possible confounders differentially influence health outcomes for U.S.-born and foreign-born mothers and their infants.

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Appendix

Appendix 1. Demographic characteristics of the preliminary analysis study cohort by maternal self-reported nativity, California, 2000-2015

Characteristics	Non-Hispanic White Mothers (N = 2,471,905)	Hispanic Mothers (N = 4,235,467)
	N (%)	N (%)
Child's Sex		
Male	1,268,690 (51.3)	2,160,309 (51.0)
Female	1,203,198 (48.7)	2,075,070 (49.0)
Maternal Age (years)		
<18	26,257 (1.1)	180,436 (4.3)
18-25	595,979 (24.1)	1,725,615 (40.7)
26-34	1,277,765 (51.7)	1,781,045 (42.1)
35+	571,855 (23.1)	548,278 (13.0)
Paternal Age (years)		
<18	7,082 (0.3)	49,828 (1.3)
18-25	353,355 (15.0)	1,181,423 (30.4)
26-34	1,115,514 (47.5)	1,768,015 (45.5)
35+	874,131 (37.2)	886,551 (22.8)
Maternal Education		
no high school diploma	158,980 (6.5)	1,790,001 (43.1)
high school diploma	551,965 (22.7)	1,255,880 (30.2)
any college	1,722,105 (70.8)	1,110,539 (26.7)
Parity		
1	1,065,709 (43.2)	1,452,971 (34.3)
2	829,469 (33.6)	1,260,978 (29.8)
3	364,297 (14.8)	847,745 (20.0)
4+	209,339 (8.5)	670,804 (15.9)
Multiples		
Singleton	2,367,587 (95.8)	4,141,635 (97.8)
Multiple	104,318 (4.2)	93,831 (2.2)
Prenatal Care Onset		
No prenatal care	12,143 (0.5)	25,133 (0.6)
1st trimester	2,160,031 (88.6)	3,414,084 (82.1)
2nd trimester	224,604 (9.2)	596,401 (14.3)
3rd trimester	42,072 (1.7)	124,764 (3.0)
Year of Birth		
2000-2005	994,538 (40.2)	1,615,167 (38.1)
2006-2010	758,659 (30.7)	1,410,594 (33.3)
2011-2015	718,708 (29.1)	1,209,706 (28.6)

Appendix 2. Demographic characteristics of the Mexican study cohort by maternal self-reported nativity, California, 2000-2015

Characteristics	Foreign-born Mexican Mothers (N = 2,035,448)	U.S.-born Mexican Mothers (N = 1,479,022)
	N (%)	N (%)
Child's Sex		
Male	1,037,518 (51.0)	755,133 (51.1)
Female	997,882 (49.0)	723,858 (48.9)
Maternal Age (years)		
<18	55,609 (2.7)	99,605 (6.7)
18-25	711,424 (35.0)	740,550 (50.1)
26-34	940,906 (46.2)	525,603 (35.5)
35+	327,459 (16.1)	113,244 (7.7)
Paternal Age (years)		
<18	10,172 (0.5)	31,741 (2.4)
18-25	461,840 (24.3)	537,796 (40.4)
26-34	905,231 (47.7)	567,418 (42.6)
35+	522,410 (27.5)	195,012 (14.6)
Maternal Education		
no high school diploma	1,195,737 (60.1)	367,297 (25.1)
high school diploma	496,194 (24.9)	544,297 (37.3)
any college	298,904 (15.0)	549,444 (37.6)
Parity		
1	570,754 (28.1)	611,045 (41.3)
2	602,924 (29.6)	436,455 (29.5)
3	470,849 (23.2)	246,676 (16.7)
4+	389,679 (19.2)	183,935 (12.4)
Multiples		
Singleton	1,994,704 (98.0)	1,443,972 (97.6)
Multiple	40,744 (2.0)	35,049 (2.4)
Prenatal Care Onset		
No prenatal care	9,049 (0.5)	11,988 (0.8)
1st trimester	1,637,398 (81.9)	1,183,046 (81.3)
2nd trimester	288,681 (14.4)	217,808 (15.0)
3rd trimester	64,736 (3.2)	41,636 (2.9)
Year of Birth		
2000-2005	890,650 (43.8)	521,764 (35.3)
2006-2010	687,527 (33.8)	489,637 (33.1)
2011-2015	457,271 (22.5)	467,621 (31.6)