Proportion of orofacial clefts attributable to known risk factors differs for Hispanic and non-Hispanic White individuals

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Objective

To determine if risk factor profiles for orofacial clefts (OFCs) vary between Hispanic and non-Hispanic White (NHW) individuals.

Background

OFCs are a commonly diagnosed birth defect in the United States (US).

OFC prevalence varies by race and ethnicity in the United States (US); however, risk factors have been established in primarily NHW cohorts.

The effect of these exposures on the risk of OFCs in Hispanic populations has rarely been studied.

Methods

Study population: NBDPS participants who self-identified as Hispanic or NHW and delivered a non-malformed control infant (n=2,833 Hispanic and 6,209 NHW) or case infant with an OFC (n=961 Hispanic and 2,353 NHW) from 1997-2011.

Outcome classification: Cases were clinically verified and classified by phenotype – cleft lip (CL), cleft palate (CP), and cleft lip with palate (CLP).

Exposure measurement: We included established risk factors that had 3 or more published papers with most results reporting an odds ratio (OR) of 1.5 or greater. The 10 identified risk factors included:

- Binge drinking (>=4 drinks/setting)[1]
- Diet (prudent v. other)[2]
- Education (<12 years)
- Family history of OFC
- Infant sex
- Lack of folic acid (FA)[1]
- Secondhand smoke (SHS)[1]
- Smoking[1]
- Parity (>=2 pregnancies)
- Pregestational diabetes

Statistical analysis: We used average-adjusted population attributable fractions (aaPAFs) and 95% confidence intervals (CIs) to estimate the fraction of Hispanic and NHW cases attributable to each risk factor.
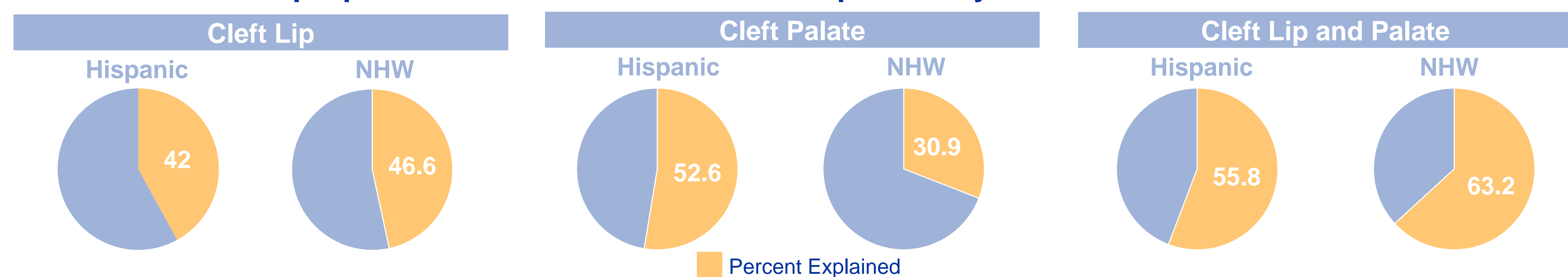
1. First 2 months of pregnancy
2. One year prior to pregnancy defined through a latent class analysis

Results

Largest modifiable average-adjusted population attributable fractions for orofacial clefts among NBDPS Hispanic and NHW participants from 1997-2011.

Cleft Lip		Cleft Palate		Cleft Lip and Palate	
Hispanic aaPAF (95% CI)	**NHW** aaPAF (95% CI)	**Hispanic** aaPAF (95% CI)	**NHW** aaPAF (95% CI)	**Hispanic** aaPAF (95% CI)	**NHW** aaPAF (95% CI)
Diet 9.9(0.0-31.6)	Diet 9.7(0.0-21.5)	Parity 14.0(7.0-18.5)	Diet 10.3(0.0-21.2)	Diet 14.1(0.0-29.3)	Diet 22.4(17.4-30.8)
SHS 4.4(0.0-8.5)	Smoking 1.6(0.0-4.4)	SHS 7.1(5.6-13.2)	Smoking 3.0(1.4-6.9)	Parity 6.5(3.2-14.3)	Lack of FA 22.4(17.4-30.8)
Lack of FA 4.0(1.7-7.5)	SHS 1.2(0.0-5.8)	Lack of FA 3.3(0.5-12.8)	SHS 0.9(0.0-4.5)	Education 4.7(0.0-8.0)	Smoking 4.9(2.2-8.2)

Total proportion of orofacial cleft cases explained by all identified risk factors.

Cleft Lip — Hispanic: 42; NHW: 46.6

Cleft Palate — Hispanic: 52.6; NHW: 30.9

Cleft Lip and Palate — Hispanic: 55.8; NHW: 63.2

Percent Explained

Main Findings

- The risk factor profile for OFCs varied between Hispanic and NHW individuals but some similarities were observed. Maternal diet, smoking, and secondhand smoke influenced OFC risk across most Hispanic and NHW phenotypes.

- The highest modifiable aaPAF for all cases was maternal diet, except for Hispanic CP (parity).

- The smoking aaPAF was larger for Hispanic CL compared to NHW CL, but smaller for CP and CLP. aaPAFs for secondhand smoke were larger for all Hispanic phenotypes compared to secondhand smoke for all NHW phenotypes.

- The total proportion of CL and CLP cases explained by our selected risk factors was larger for NHWs, but the total proportion of CP cases explained was noticeably larger for Hispanics.

Discussion

Current research suggests that smoking is one of the strongest risk factors for OFCs. Thus, the stronger effect of secondhand smoking (v. smoking) for Hispanic cases and smoking (v. secondhand smoking) for NHW cases warrants further research.

To our knowledge, this is the first OFC PAF analysis that includes maternal diet. Additional research is needed to confirm the strong relative effect of diet on OFC in both Hispanic and NHW populations.

Differences in Hispanic and NHW attributable risk profiles may aid in understanding observed differences in OFC prevalence. With confirmation, these findings could inform population-focused prevention strategies based on self-reported ethnicity.

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.