

# Contemporary United States Incidence of Oral Clefts: Geographic and Socioeconomic Considerations

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# INTRODUCTION

- The Center for Disease Control (CDC) estimates the incidences of cleft lip and palate (CLP), isolated cleft lip (ICL), and isolated cleft palate (ICP) as 1 in 1600, 1 in 2800, and 1 in 1700, respectively.<sup>1</sup> However, considering its multifactorial etiology, these estimates likely fail to capture the highly variable oral cleft (OC) incidence across a diverse US population.
- Due to large ethnic, racial, and SES diversity in the United States, international studies conducted in relatively homogenous populations may not be representative of the US population as a whole.<sup>2</sup>

### Objective:

- This study aims to better define the US incidence, identify the geographic variability, and clarify the impact of sociodemographic factors of OC by analyzing the largest and most diverse data set available in order to direct interventions aimed at promoting equitable care.

## METHODS

**Dataset:** Primary data analyzed in this study was sourced from Cosmo<sup>TM</sup>, a data collective that amalgamates and de-identifies data from over 180 participating institutions throughout the USA that utilize EPIC medical records. Cumulatively, this data accounts for over 169 million patients, spanning all 50 states, including rural and urban populations. Owing to its large sample size, this data closely reflects the demographics of the USA when compared to US Census data (Figure 1).

**Inclusion criteria:** Patients born between November 3<sup>rd</sup> 2012, and November 2<sup>nd</sup> 2022 were included in this study.

**Data collected:** Social Vulnerability Index (SVI) was used to identify social determinants of health among the included cohorts. SVI is derived using a combination of variables, which are broadly categorized into four CDC defined themes: minority/language, household composition, socioeconomic status, and housing/transportation.

### Analyses:

- Analysis was conducted both by OC cohort and, to control for potential confounding, by racial and ethnic subgroups.
- Incidence rates per 10,000 live births were calculated along with 95% confidence intervals.
- Univariate analysis was conducted to assess the associations between the above-mentioned variables and the eight OC cohorts ( $p < 0.05$ ).
- Cochrane-Armitage tests were used to evaluate for differences in trends of ordinal SVI variables ( $p < 0.05$ ).

## RESULTS

|                                            | Any Cleft | Any Cleft Palate | ICD Cleft Palate (Q 35.*) | Isolated Cleft Palate | Any Cleft Lip | ICD Cleft Lip (Q 36.*) | Isolated Cleft Lip | ICD Cleft Lip with Palate (Q37.*) |
|--------------------------------------------|-----------|------------------|---------------------------|-----------------------|---------------|------------------------|--------------------|-----------------------------------|
| Social Vulnerability Index (SVI) (Overall) | -         | -                | -                         | -                     | +             | +                      | -                  | +                                 |
| Household Composition (Theme)              | +         | +                | +                         | n.s.                  | +             | +                      | n.s.               | +                                 |
| % > 65 years-old                           | +         | +                | +                         | +                     | +             | +                      | +                  | +                                 |
| % < 17 years-old                           | +         | +                | n.s.                      | -                     | +             | +                      | n.s.               | +                                 |
| % Disabled                                 | +         | +                | +                         | +                     | +             | +                      | +                  | +                                 |
| % Single Parent Home                       | -         | -                | -                         | -                     | -             | -                      | -                  | -                                 |
| Housing / Transport (Theme)                | -         | -                | -                         | -                     | n.s.          | n.s.                   | -                  | -                                 |
| % Multi-Unit                               | -         | -                | -                         | -                     | +             | n.s.                   | n.s.               | -                                 |
| % Mobile Homes                             | +         | +                | n.s.                      | +                     | +             | +                      | +                  | +                                 |
| % Crowding                                 | +         | n.s.             | -                         | +                     | +             | +                      | +                  | +                                 |
| % No Vehicles                              | -         | -                | -                         | -                     | -             | -                      | -                  | -                                 |
| % Group Quarters                           | n.s.      | n.s.             | n.s.                      | n.s.                  | n.s.          | +                      | n.s.               | n.s.                              |
| Minority / Language (Theme)                | -         | -                | -                         | -                     | -             | -                      | -                  | -                                 |
| % Minority                                 | +         | +                | -                         | -                     | -             | -                      | -                  | -                                 |
| % Limited English Speaking                 | -         | -                | -                         | -                     | +             | n.s.                   | +                  | n.s.                              |
| Socioeconomic (Theme)                      | -         | -                | -                         | -                     | +             | +                      | n.s.               | +                                 |
| % Below Poverty                            | -         | -                | -                         | -                     | n.s.          | n.s.                   | -                  | +                                 |
| % Unemployed                               | -         | -                | -                         | -                     | n.s.          | n.s.                   | -                  | -                                 |
| % Without Highschool Diploma               | -         | -                | -                         | -                     | +             | +                      | -                  | +                                 |
| % Uninsured                                | n.s.      | n.s.             | -                         | -                     | +             | +                      | n.s.               | +                                 |

**Table 3.** General SVI Data analysis, including all oral cleft patients. Red + indicates diseased group tended to exhibit greater association with increasing social determinant burden, Green - indicates non-diseased group tended to exhibit greater association with increasing social determinant burden. n.s. = no significant correlation.

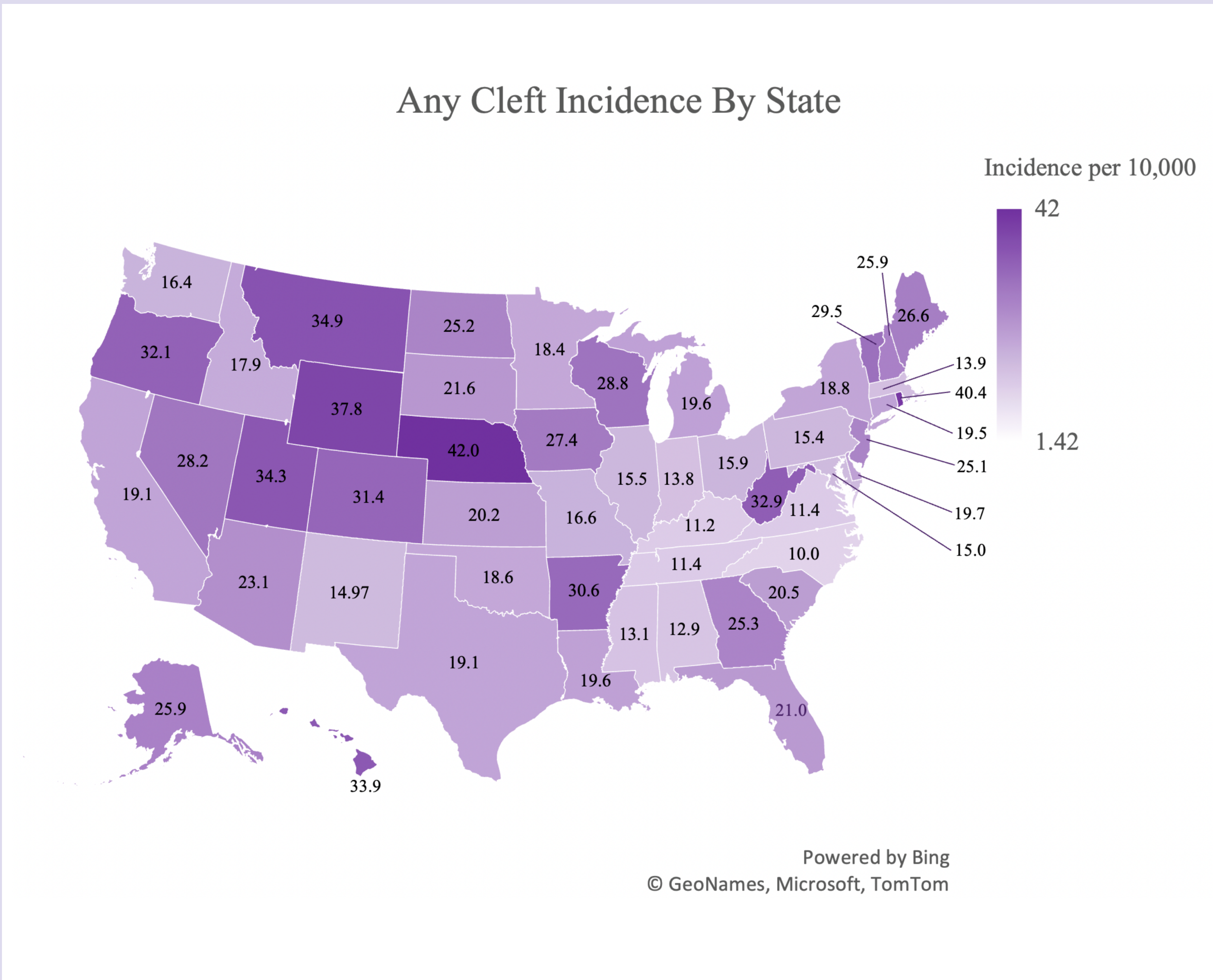


**Figure 2.** US Map with Incidence of all oral clefts by states.

| White Race                                 | Any Cleft | Any Cleft Palate | ICD Cleft Lip (Q 35. *) | Isolated Cleft Palate | Any Cleft Lip | ICD Cleft Lip (Q 36. *) | Isolated Cleft Lip | ICD Cleft Lip with Palate (Q37. *) |
|--------------------------------------------|-----------|------------------|-------------------------|-----------------------|---------------|-------------------------|--------------------|------------------------------------|
| Social Vulnerability Index (SVI) (Overall) | +         | +                | +                       | B.A.                  | +             | +                       | B.A.               | +                                  |
| Household Composition (Theme)              | +         | +                | +                       | B.A.                  | +             | +                       | B.A.               | +                                  |
| % > 65 years-old                           | +         | +                | B.S.                    | B.S.                  | +             | B.S.                    | +                  | B.S.                               |
| % < 17 years-old                           | B.S.      | +                | B.S.                    | B.A.                  | +             | +                       | B.S.               | +                                  |
| % Disabled                                 | +         | +                | +                       | +                     | +             | +                       | +                  | +                                  |
| % Single Parent Home                       | B.S.      | B.S.             | -                       | -                     | +             | B.S.                    | +                  | +                                  |
| Housing / Transport (Theme)                | +         | +                | +                       | B.A.                  | +             | +                       | B.S.               | +                                  |
| % Multi-Unit                               | -         | -                | -                       | -                     | -             | -                       | -                  | -                                  |
| % Mobile Homes                             | +         | +                | +                       | +                     | +             | +                       | +                  | +                                  |
| % Crowding                                 | +         | +                | B.A.                    | -                     | +             | +                       | B.S.               | +                                  |
| % No Vehicles                              | -         | B.S.             | -                       | -                     | B.S.          | B.S.                    | B.S.               | B.S.                               |
| % Group Quarters                           | +         | +                | +                       | +                     | +             | B.S.                    | +                  | +                                  |
| Minority / Language (Theme)                | -         | -                | -                       | -                     | B.S.          | +                       | -                  | B.S.                               |
| % Minority                                 | -         | -                | -                       | -                     | B.S.          | +                       | -                  | +                                  |
| % Limited English Speaking                 | -         | -                | -                       | -                     | B.S.          | B.S.                    | -                  | -                                  |
| Socioeconomic (Theme)                      | +         | +                | +                       | B.A.                  | +             | +                       | B.S.               | +                                  |
| % Below Poverty                            | +         | +                | B.S.                    | B.A.                  | +             | +                       | B.S.               | +                                  |
| % Unemployed                               | +         | +                | B.S.                    | B.A.                  | +             | +                       | B.S.               | +                                  |
| % Without Highschool Diploma               | +         | +                | B.S.                    | -                     | +             | +                       | B.S.               | +                                  |
| % Uninsured                                | B.S.      | +                | B.S.                    | -                     | +             | +                       | B.S.               | +                                  |

| Stack Race                                 |      |      |      |      |      |      |      |      |  |
|--------------------------------------------|------|------|------|------|------|------|------|------|--|
| Social Vulnerability Index (SVI) (Overall) |      |      |      |      |      |      |      |      |  |
|                                            | B.S. | +    | +    | B.S. | B.S. | B.S. | B.S. | B.S. |  |
| Household Composition (Theme)              | +    | +    | +    | B.S. | +    | B.S. | B.S. | +    |  |
| % > 65 years-old                           | +    | +    | +    | +    | B.S. | B.S. | B.S. | B.S. |  |
| % < 17 years-old                           | B.S. | B.S. | B.S. | B.S. | +    | +    | B.S. | +    |  |
| % Disabled                                 | B.S. | B.S. | B.S. | B.S. | B.S. | B.S. | B.S. | B.S. |  |
| % Single Parent Home                       | B.S. | B.S. | B.S. | B.S. | B.S. | B.S. | -    | B.S. |  |
| Housing / Transport (Theme)                | B.S. | B.S. | +    | +    | -    | B.S. | B.S. | B.S. |  |
| % Multi-Unit                               | -    | -    | -    | B.S. | B.S. | B.S. | B.S. | B.S. |  |
| % Mobile Homes                             | +    | +    | +    | +    | +    | +    | +    | +    |  |
| % Crowding                                 | B.S. | B.S. | B.S. | B.S. | B.S. | B.S. | B.S. | B.S. |  |
| % No Vehicles                              | B.S. | B.S. | B.S. | B.S. | -    | -    | -    | B.S. |  |
| % Group Quarters                           | B.S. | B.S. | B.S. | +    | B.S. | -    | B.S. | B.S. |  |
| Minority / Language (Theme)                | B.S. | B.S. | B.S. | B.S. | B.S. | B.S. | +    | B.S. |  |
| % Minority                                 | B.S. | B.S. | B.S. | -    | B.S. | B.S. | B.S. | B.S. |  |
| % Limited English Speaking                 | B.S. | B.S. | B.S. | B.S. | B.S. | B.S. | B.S. | B.S. |  |
| Socioeconomic (Theme)                      | B.S. | +    | +    | B.S. | B.S. | B.S. | B.S. | B.S. |  |
| % Below Poverty                            | B.S. | B.S. | B.S. | B.S. | B.S. | B.S. | B.S. | B.S. |  |
| % Unemployed                               | B.S. | B.S. | B.S. | B.S. | B.S. | B.S. | B.S. | B.S. |  |
| % Without Highschool Diploma               | B.S. | B.S. | B.S. | B.S. | B.S. | B.S. | B.S. | B.S. |  |
| % Uninsured                                | +    | +    | +    | B.S. | +    | +    | B.S. | +    |  |

| Hispanic Ethnicity                         |      |      |      |      |      |      |      |      |
|--------------------------------------------|------|------|------|------|------|------|------|------|
| Social Vulnerability Index (SVI) (Overall) | B.S. | B.S. | B.S. |      | A    | C+   | B.S. | A    |
| Household Composition (Theme)              | B.S. | B.S. | B.S. | B.S. | D    | D    | B.S. | D    |
| % > 65 years-old                           | B.S. | B.S. | B.S. | B.S. | B.S. | B.S. | B.S. | B.S. |
| % < 17 years-old                           | D    | D    | D    | D    | D    | D    | B.S. | D    |
| % Disabled                                 | B.S. | B.S. | B.S. | B.S. | B.S. | B.S. | D    | B.S. |
| % Single Parent Home                       | -    | -    | -    | -    | B.S. | B.S. | B.S. | B.S. |
| Housing /Transport (Theme)                 | B.S. | B.S. | B.S. | -    | D    | B.S. | B.S. | D    |
| % Multi-Unit                               | -    | -    | -    | -    | -    | -    | B.S. | -    |
| % Mobile Homes                             | D    | D    | D    | D    | D    | D    | B.S. | D    |
| % Crowding                                 | B.S. | B.S. | B.S. | -    | D    | D    | B.S. | D    |
| % No Vehicles                              | -    | -    | -    | -    | -    | -    | B.S. | -    |
| % Group Quarters                           | B.S. | B.S. | B.S. | B.S. | B.S. | B.S. | B.S. | B.S. |
| Minority / Language (Theme)                | -    | -    | -    | -    | B.S. | B.S. | -    | B.S. |
| % Minority                                 | -    | -    | -    | -    | B.S. | B.S. | B.S. | D    |
| % Limited English Speaking                 | -    | -    | -    | -    | B.S. | B.S. | B.S. | B.S. |
| Socioeconomic (Theme)                      | D    | D    | B.S. | B.S. | D    | D    | B.S. | D    |
| % Below Poverty                            | B.S. | B.S. | -    | -    | D    | D    | B.S. | D    |
| % Unemployed                               | B.S. | B.S. | -    | -    | D    | D    | B.S. | D    |
| % Without Highschool Diploma               | B.S. | B.S. | D    | -    | D    | D    | B.S. | D    |
| % Uninsured                                | B.S. | B.S. | B.S. | B.S. | D    | B.S. | B.S. | D    |

**Table 4.** Subgroup Analyses of SVI Data analysis. Cohorts of White, Black and Hispanic patients are analyzed separately, to control for the effect of race. Red + indicates diseased group tended to exhibit greater association with increasing social determinant burden. Green - indicates non-diseased group tended to exhibit greater association with increasing social determinant burden. n.s. = no significant correlation.



## DISCUSSION

- Our data represents approximately 38% of the newly born population of the United States during the period studied. Our data found higher incidences of ICP (1 in every 971 babies) and CLP (1 in every 1,398 babies) than the previously published data (1 in every 1,700 and 1 in every 1,600 babies, respectively).<sup>1</sup> However, we found a lower incidence of ICL (1 in every 4,978 babies) than previous estimates (1 in every 2,800 babies).<sup>1</sup>
- No difference was found in the incidence of OC between metropolitan (>50k), micropolitan (10k-50k), and rural/small town (<10k) towns (Table 2). This contradicts a previous study conducted in the state of Washington between 1989 and 2014 found that infants born to mothers in rural settings had an increased odds (OR of 1.12, include SE or standard deviation) of having a cleft compared to infants born to mothers in urban settings even after adjusting for race and ethnicity.<sup>3</sup> Previous studies have also found that environmental exposures associated with more urban areas, such as ambient air pollutants, positively correlated with OC development.<sup>4,5</sup>
- Interestingly, our data indicates that speaking a non-English language as a primary language in the household is protective against OC, and to the knowledge of the investigators, this metric has not been previously studied. However, it has been demonstrated that cultural outreaching has been demonstrated to improve health outcomes.<sup>6,7,8,9</sup>

## CONCLUSIONS

- This study examines the largest cohort of oral cleft patients reported to date and reports the contemporary US OC incidence rates, which demonstrate an increase in incidence from previous estimates.
- The incidence of cleft palate appears to vary across ethnic populations, in contrast to previous reports.
- Importantly, we found that percent below the poverty line was most strongly correlated with OC, reinforcing the consequences of social determinants of health. These findings can help to counsel expectant families and direct future research.

### Future directions + limitations:

- In an effort to protect patient privacy, data analyzed in this study was only available when reported in aggregate, and thus patient level data could not be individually assessed, precluding multivariate analyses which would have better clarified the relative significance of each social determinant.
- SVI data is associated with a patient's home zip code, and thus may not directly reflect the social determinant of each individual patient.
- Future analyses should validate the findings of this study using individual-level data, such as patient-reported questionnaires.

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