Global Burden of Orofacial Clefts and the World Surgical Workforce

Appendix, Supplemental Digital Content 1

Cleft lip & cleft palate (orofacial clefts)

Case definition and associated health states

Orofacial clefts include isolated cleft lip, isolated cleft palate, and combined cleft lip and palate. The GBD case definition of orofacial clefts includes isolated cleft palate, which corresponds to ICD-10 codes Q35.2, Q35.3, Q35.5, Q35.6, Q35.7, Q35.8, and Q35.9, and cleft palate with or without cleft lip, which corresponds to ICD-10 codes Q36.0, Q36.1, Q36.9, Q37.1, Q37.5, Q37.8, and Q37.9.

These conditions can be surgically treated during the first few months or years of life, to alleviate some or all of the disease burden.

Thus, there were four main disability weights associated with orofacial clefting: an unrepaired, symptomatic orofacial cleft that is noticeable and causes stress (0.067, 95% uncertainty interval: 0.044-0.096), a speech problem due to an unrepaired cleft or sequelae of an orofacial cleft (0.051, 0.032-0.078), a repaired or incomplete orofacial cleft with lasting sequelae of an orofacial cleft (0.011, 0.005-0.021), or an asymptomatic or completely repaired orofacial cleft with no sequelae (zero).[1,2] We are unable to characterize the anatomic severity of any orofacial cleft. Thus, the disability weights do not reflect any specific characteristics of orofacial clefting and are instead based upon average orofacial clefting morbidity, based upon a systematic literature review.[3] We estimated that for the given prevalence reported in the birth defect registries, surveillance systems, and prior literature,[2] there was an equal distribution of mild disfigurement, moderate disfigurement, and mild disfigurement with speech problems.[2,4–7]

For example, consider a child born with an orofacial cleft in a country where they would have a life expectancy of 70 years. This child had their cleft repaired at age 1, which resulted in velopharyngeal insufficiency. They then had a speech procedure at age 7 which removed any sequelae of repair, and they went on to live until age 70 and died of a different cause. Their DALYs from orofacial cleft would be 0.133.

$$DALY = YLL + YLD = 0 + (0.067 \times 1) + (0.011 \times 6) = 0.133$$

Data Sources

Several data sources were used to estimate the prevalence and disease burden of orofacial clefting: literature prevalence, birth prevalence from international birth defects registries and surveillance systems, and inpatient hospital claims data. The global burden of disease team conducted a systematic review of all available literature to obtain information on the prevalence and disease burden of orofacial clefting.[1] All results of the systematic review were screened by abstract and then by full text in order to ensure accuracy of information and to exclude duplicate data from the birth registry data inputs.[2,3]

The international birth defect registries that were queried in this study were The International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR), The World Atlas Report, The European Surveillance of Congenital Anomalies (EUROCAT), China's Maternal and Child Health

Surveillance survey (MCHS), The National Birth Defects Prevention Network (NBDPN), and The Birth Defects Registry of India (BDRI).

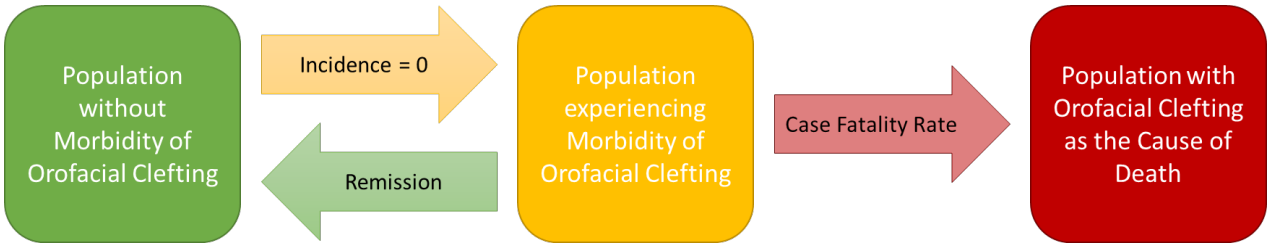
A total of 2,267 distinct data sources were used to model the data on orofacial clefting which represented 1,701 total site-years over 65 countries with available data. Each distinct data source can be found online using the Institute for Health Metrics and Evaluation interactive citation tool.[8]

Inpatient hospital and Marketscan claims data for orofacial clefting was prepped by the GBD team using the aforementioned ICD codes.

Modeling Strategy

All available data was input into an optimized Bayesian meta-regression tool, DisMod 2.1. This methodology has been previously published and extensively studies and validated.[2,9] To simplify and summarize, the DisMod 2.1 tool works as an incidence-prevalence-mortality model, as shown in the figure below.

Appendix Figure 1: Simplified schematic of the optimized Bayesian meta-regression tool, DisMod 2.1



In this example, we will focus on three populations: the population that is without morbidity of orofacial clefting, the population with morbidity of orofacial clefting, and the population who has died due to orofacial clefting. Incidence for orofacial clefting was set to zero, as orofacial clefting occurs at the time of birth and there should be no incident cases of orofacial clefting after birth, by definition. The population experiencing morbidity of orofacial clefting, are the prevalent cases. Prevalent cases were based upon the aforementioned data sources. Case fatality rate was also based upon the aforementioned data sources.

In the setting of orofacial clefting, remission is due to a surgical repair. Remission values were based on existing available literature and expert consensus between all of the GBD Orofacial Clefting Collaborators. The consensus and available literature estimated that around 75% of global orofacial clefts are repaired between the ages of three months and two years, another 5% may be repaired between the ages of five and 20 years, and a maximum of 5% of orofacial clefts are repaired between ages of 20 and 50 years. Thus, remission was set to zero for the first three months of life. For the ages of three months to two years remission ranged between 0 to 0.8, for ages two to five years remission ranged between 0 and 0.07, for ages five to 20 years remission ranged between 0 and 0.004, for ages 20 to 50 years remission ranged between 0 and 0.002, and remission was set to zero for ages 50 and above.

The DisMod tool was then used to variably input all possible values and combinations of remission over 10,000 trials until a best fit was found for all available numeric data. If data sources were known to include stillbirths in the reported birth prevalence, a covariate was used to adjust the data to ensure stillbirths were not included in our case definition of prevalence of orofacial clefting.

To determine the distribution of the health outcomes associated with orofacial clefting, we performed a systematic review on available literature on the long-term health outcomes of patients born with orofacial clefting. We estimated that for the given prevalence reported in the birth defect registries, surveillance systems, and prior literature,[2] there was an equal distribution of mild disfigurement, moderate disfigurement, and mild disfigurement with speech problems.[2,4–7]

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