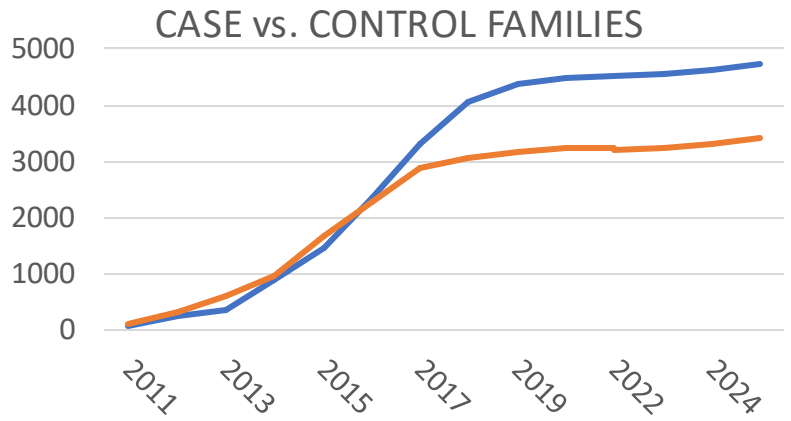
International Family Study- Executive Summary

The International Family Study (IFS) is an ongoing case–control study with supplemental parental trio data led by investigators at the University of Southern California, a large research university, and Children's Hospital Los Angeles, the affiliated pediatric hospital, in collaboration with Operation Smile (OS). It is designed to examine genetic, environmental, lifestyle, and sociodemographic risk factors of orofacial clefts in low- and middle-income countries. Many of these cases are treated only through not-for-profit organizations and are therefore difficult to locate, document, and characterize through other data sources. The study is currently active in 5 countries: Guatemala, Honduras, Madagascar, Malawi, and the Philippines, and previously collected data from the Democratic Republic of the Congo (DRC), Morocco, and Vietnam.

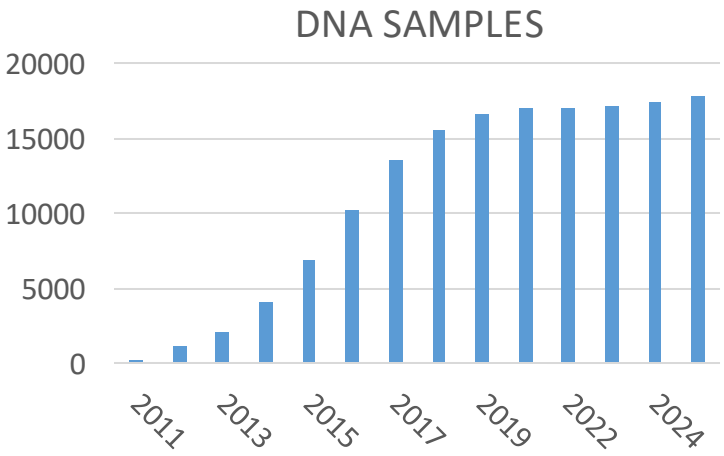
8,138 FAMILIES INCLUDED

Mothers and fathers answer a wide variety of questions surrounding potential risk factors. These represent both case families affected by cleft conditions and controls.



17,895 DNA SAMPLES

Saliva samples are collected during medical missions by a team of trained volunteers. The samples capture DNA of the mother, father & child.



The IFS is the largest case–control study with a supplementary biobank, regionally sampled controls, and child–parent trios for exploration of etiologic questions around NSOFCs in a diverse group of LMICs with extensive population-wide recruitment. This information can inform public health interventions and education to potentially prevent disease in populations where care is sparse, and where children are most likely to feel the detrimental, lifelong medical and social effects of cleft. Modifiable, patient-centric solutions, such as providing a clean-burning cookstove, will be critical for efforts to decrease the burden of this malformation globally and improve lives around the world.

Recent Highlights

Published a study of case trios from Madagascar using whole- exome sequencing to explore previously unknown genetic loci for cleft. This study highlights new potential regions of risk and the unique genetic makeup of Malagasy individuals.

Acting on the finding that exposure to smoke from cooking increases cleft risk by 50%. This led to Operation Smile exploring partnerships with clean cookstove organizations around the globe to promote safe cooking.

Publishing a manuscript exploring the role of chemical exposures on the risk of cleft. The preliminary findings from this project were presented at the International Cleft Congress 2022.

Partnering with new institutions to publish more findings and expand on the knowledge of the study

Future Directions

Sequence 1500 cases and controls from Nicaragua, and Honduras to perform the first large- scale Hispanic genome- wide association study for cleft lip and/ or palate.

Harmonize and clean our full environmental database so it can be a global resource for cleft researchers, doctoral students, and others to ensure we learn as much as possible from the data.

Conduct gene- environment interaction analyses using novel statistical approaches to better understand the combined effects of different environmental exposures and genetic profiles.

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