AAOF Final Report

<u>Type of Award:</u> Biomedical Research Award

<u>Name(s) of Principal Investigator(s):</u> Christina Nicholas

<u>Title of Project:</u> Obesity, oral inflammation, and timing of dental development

<u>Period of AAOF Support:</u> 7/1/2018 – 6/30/2023

<u>Amount of Funding:</u> $29,350

Summary/Abstract of Completed Project (250 words maximum)

Children with obesity have been documented to show accelerated timing of dental development and may also show accelerated facial skeletal growth. Any potential mechanism relating obesity with early dental development has yet to be elucidated. This study examined the hypothesis that oral inflammation, as a byproduct of obesity-induced systemic inflammation, may play a role. Secondarily, we examined patient-reported diet via Food Frequency Questionnaires to address this potential alternative association. We failed to find a statistical association between oral inflammation and timing of dental development. We saw an association between obesity and gingival bleeding during prophylaxis (an indicator of inflammation; p=0.03) but not between obesity and levels of pro-inflammatory cytokines. In examining our dietary data, we were able to demonstrate that although BMI was associated with timing of dental development, self-reported macronutrient intake was not (Cardona Salazar et al., 2021). There is clear need for additional research in this area, to help identify potential causative mechanisms for the association between high BMI and accelerated dental development.

1. Were the original, specific aims of the proposal realized?

Yes, we were able to examine the association between our primary variables (obesity, oral inflammation, dental development). Our first Specific Aim (SA1) hypothesized that children with obesity would show higher levels of pro-inflammatory cytokines and biomarkers associated with induced osteoclastic activity. While we saw an association between general indicators of oral inflammation (bleeding during prophylaxis; p=0.03) and obesity there was no association between our cytokine biomarkers and obesity. We hypothesize that these somewhat contradictory results may be either related to sample size or to issues with our cytokine analyses. Delays due to the COVID-19 pandemic meant we had to analyze the cytokine samples in separate batches several months apart, and we have noted that our cytokine outputs do not seem consistent across the three batches.

Our second specific aim (SA2) had two subaims. SA2.1 hypothesized that early dental maturation in children with obesity would be associated with levels of pro-inflammatory cytokines. We failed to see a statistical association between inflammation and eruption timing. SA2.2 hypothesized that early dental maturation and greater oral inflammation would be associated with diet quality. We again failed to find an association between these variables. While initial regression analyses revealed a statistical association between obesity and total fat consumption (p=0.01), this association was not present in our more sophisticated path analysis which controlled for a wider range of variables. Similarly, initial regression analysis indicated an association between total caloric intake and timing of dental development (p=0.003), but this association again vanished when submitted to the more rigorous path analysis.

2. Were the results published?

To date, we have published one paper from data generated by the AAOF-funded project (Cardona Salazar et al., 2021). This paper examines dental development in relation to diet and obesity. AAOF support was recognized in the Acknowledgements. We have future plans to publish additional data regarding oral health status in children with obesity; final analysis of these data are currently under way.

3. Have the results of this proposal been presented?

We have presented results from this study at multiple national/international conferences. Final slides or the "Acknowledgements" section of the posters have include acknowledgement of AAOF funding. Due the AAOF cohort also serving as the cohort for a spin-off study regarding microbiome in children with obesity, AAOF funds were also acknowledged in presentations on this topic.

1. **Nicholas, CL**, Whyms, PS, Naqvi, A, Alrayyes, S, Thalji, G. 2023. Childhood obesity, oral inflammation, and timing of dental development. American Association of Orthodontists.
2. Kramer, I, Alrayyes, S, Wu, C, Naqvi, A, **Nicholas, CL**. 2023. Childhood obesity and oral health: inflammation and dental maturation. American Association of Pediatric Dentistry.
3. Whyms, P, Kramer, I, Truskoski, D, Silver, C, Valverde Estepa, A, Naqvi, A, Alrayyes, S, Thalji, G, Williams, S, Campos Riversa, M, Pinto, N, **Nicholas, CL**. 2023. Food insecurity, diet, and oral health in Chicago children. *J Dent Res*. 102A: 1215.
4. Whyms, P, Naqvi, A, Truskoski, D, Valverde Estepa, A, Alrayyes, S, Williams, S, Silver, C, Awadalla, S, **Nicholas, CL**. 2021. Childhood obesity's influence on the oral microbiome and oral health. *Am J Phys Anthropol*. 174S: 112-113.
5. Whyms, P, Truskoski, D, Silver, C, Valverde Estepa, A, Naqvi, A, Alrayyes, S, Thalji, G, Williams, S, Divaris, K, Campos Rivera, M, **Nicholas, CL.** 2021. Associations Between Childhood Obesity, Diet, and Oral Health. *J Dent Res* 100A: 0680.
6. Silver, CM, Naqvi, A, Valverde Estepa, AM, Alrayyes, S, Wu, CDR, **Nicholas, CL.** 2021. High BMI Children Show Increased Levels of Oral Inflammation. American Association of Pediatric Dentistry.
7. Whyms, P, Naqvi, A, Williams, S, Alrayyes, S, Truskoski, D, **Nicholas, CL**. 2020. An Examination of Food Insecurity, Obesity, and Pediatric Oral Health. *J Dent Res* 99A: 3124.
8. Truskoski, D, Alrayyes, S, Thalji, G, Naqvi, A, Wu, C, **Nicholas, CL**. 2020. The Influence of Oral Inflammation on Timing of Dental Eruption. American Association of Pediatric Dentistry.

4. To what extent have you used, or how do you intend to use, AAOF funding to further your career?

This AAOF grant has been instrumental in furthering my research career. Based upon our pilot data, we were able to secure a grant from the UIC Center for Clinical and Translational Studies ($60,000) to add a microbiome component. Our pilot data, especially the Cardona Salazar publication, was also fundamental in establishing my team's preparedness and expertise in dental age estimation. This has recently led to a new National Institute of Justice grant ("DENTAGE: A multi-component dental age

estimation method"; 2023-25). Through this grant, we will seek to develop an updated, contemporary baseline for dental age estimation, benefitting orthodontic and pediatric dentistry research as well as forensic dentistry practice.

5. Accounting for project, i.e., any left-over funds, etc.

Remaining (unspent) budget: **$6942.24**

	Original Budget	Revised Budget*	Actual Spend	Difference (from Original Budget)
Personnel	$0	$0	$0	$0
Supplies	$18410	$17292	$12944.76	$5465.24
Services	$3940	$1500	$0	$3940
Equipment	$0*	$4568	$4568	-$4568
Other	$7000	$7000	$4895	$2105
TOTALS	$29350	$29350	$22407.76	**$6942.24**

*On 8/19/22 we submitted a Revised Budget Request for a change of budget to allow for a purchase of a Periotron machine, which was approved by AAOF. We had previously been borrowing a Periotron (used to measure gingival crevicular fluid volume) from the Department of Periodontics but they began a new large-scale study which meant it was no longer possible to access their machine.

Explanation of differences in cost:

Supplies: The main discrepancy was our estimated cost for multiplex assay kits. We were able to secure a discount for purchasing multiple kits at once, bringing the total cost to $10,127.55 (vs. an estimated $15925). There were also minor differences in estimated costs for laboratory supplies, including: the need to purchase additional Periopaper strips (additional cost $259.9) and a slight increase in the rates for analysis of the Block Food Frequency Questionnaires due to inflation (additional cost $309). We also spent slightly less than anticipated (approx. $236) on other miscellaneous laboratory supplies.

Services: We budgeted for the costs for our central core to run the multiplex assay analyses. A postdoc in a collaborator's lab was able to run these analyses for us, saving the estimated cost of $3250. We also did not end up incurring self-pay costs for panoramic radiographs.

Equipment: We purchased a Periotron with associated software ($4568), per the Revised Budget Request approved by the AAOF.

Other: The main discrepancy in Other costs was a decrease in spending related to travel for presentation of this work at a conference. Our results were presented at AAO in Chicago in 2023, therefore the only incurred cost was registration ($495) due to the lack of travel expenses. Due to challenges and delays in data collection related to the pandemic, our final recruited number of participants was n=88, reducing our spending on participant incentives from an estimated $5000 to an actual spend of $4400.