

The Effects of Paternal Factors on Offspring Dental Eruption

by

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Abstract

In a study conducted using rodents, it was found that a higher level of paternal physical activity prior to fertilization had a positive effect to decrease the offspring's predisposition for metabolic syndrome. In another study conducted using human subjects, an examination of 145 offspring-parent groups showed significant positive correlation between paternal height and weight and offspring bone mineral density and content. While there is an established body of research examining maternal factors and their effects on offspring, such as tooth development, there has been very little examination of the influence of paternal factors on offspring health outcomes, such as tooth development. The objective of this study is to determine if there exists any correlation between paternal body mass index (BMI) and offspring tooth development. It is hypothesized that an increased paternal BMI will be associated with decreased offspring tooth development. To answer this question, we have recruited women and their children, 0-6 years of age, to participate in the study. All maternal participants completed a modifiable physical activity questionnaire, which acquired information about both parents: age, BMI, education level, and physical activity. All child participants were seen at the ECU pediatric dental clinic for standard dental screenings and clinic measures were collected directly. We classified parent:child pairs into 2 groups: group with paternal BMI 18.5-24.9 as Normal weight (NW) group, and group with paternal BMI >25 as Overweight or Obese (OW/OB) group. All women completed consent for themselves and their child. Mothers also completed a questionnaire, and the children received standard dental care. Alpha level was set a priori at 0.05 and multiple t-tests were performed to determine differences between groups and regression analyses were completed to look for significant associations. We recruited 23 parent-child pairs. There are no significant differences between paternal BMI groups with child tooth development. There are consistent trends of positive correlation between paternal normal weight BMI with child tooth development. Conversely, there is consistently negative

correlation between paternal OW/OB (BMI) with child tooth development. These data suggest paternal BMI, an indicator of overall health of the father, is associated with child dental health. Further research is necessary to determine the extent of paternal health measures required to fully understand child tooth development and disease risk.

Chapter 1:

Background

While there has been significant research conducted examining the maternal health and lifestyle on offspring health outcomes, much less is known about the influence of paternal health on child outcomes. Understanding the paternal impacts on the growth and development of children can provide further insight into the health and disease prevention of future generations. One study, using rodents, found that increased paternal physical activity prior to fertilization has a positive association with offspring predisposition for metabolic syndrome. For example, offspring of fathers that exercised were more susceptible to increased adiposity, impaired glucose tolerance and insulin levels when fed a high fat diet, showed compared to offspring fed a high fat diet whose fathers did not exercise¹. In another rodent study, researchers found when fathers were fed a high fat diet their offspring had lower birth weight and lower overall growth from birth forward compared to offspring of fathers fed a control diet⁵. Furthermore, the offspring from high-fat diet fathers had a 10% deficit in body weight and significantly reduced muscular and adipose development at six months old. In a human study, paternal factors were also shown to be associated with offspring development. In an examination of 145 offspring-parent groups, significant positive correlation was found between paternal height and weight and offspring bone mineral density and content (BMD/C)². In another human study examining 278 human pregnancies, bone mass of fathers and offspring were measured using whole body dual-x-ray absorptiometry (DXA). A significant correlation was found between paternal whole body bone area and bone mineral content /density, and the corresponding measures in female offspring, but there was not a significance relationship between paternal measures and male offspring³. Altogether, these studies suggest a possible correlation between paternal health measures and offspring health.

Based on previous research, further study is warranted to determine paternal correlation with offspring health factors. Although a significant relationship between paternal measures and offspring bone growth has been shown, research has not analyzed dental development, which involves bone development along with signaling molecules, and neuronal development. With this in mind, it is unknown if there is also a correlation between paternal health measures and offspring dental development. This study aims to find a correlation between paternal health measures and offspring dental development. If a correlation exists, then this could help to educate parents on how to improve the dental health of their child.

Chapter 2:

Review of Literature

The literature on the subject of parental factors affecting the offspring's growth and development is mostly focused on the maternal factors. For example, in a study that was a part of the Avon longitudinal study of parents and children, data from 7212 parent-offspring groups were examined. This study examined the possible relationship between maternal and paternal BMI and the offspring's growth measures, specifically total body less head (TBLH) bone measurement, and spine bone measurements, both derived from x-ray absorptiometry. Maternal and paternal BMI was calculated from self-reported values. The results showed that maternal BMI was positively correlated with offspring TBLH bone mineral density and content, as well as with spine bone mineral density and content, with SD values of boys, 0.19 (0.16, 0.23) and 0.15 (0.12, 0.19), respectively; girls, 0.23 (0.19, 0.26) and 0.19 (0.16, 0.23), respectively and spine bone mineral content and bone mineral density for boys, 0.20 (0.16, 0.24) and 0.18 (0.14, 0.22), respectively; girls, 0.22 (0.18, 0.26) and 0.21 (0.17, 0.25), respectively. The relationship between the offspring's growth factors and paternal BMI was similar, but not of statistical significance⁴. In another study on humans, data from the Southampton Women's Survey Study Group was analyzed to examine the relationship between paternal bone mass and the bone mass of their offspring. The objective of this study was to focus on the paternal side of the equation. 278 pregnancies from the group were examined, with paternal and offspring bone measures being taken using whole body dual x-ray absorptiometry. The measures were taken within 2 weeks post-partum. The results of the data analysis showed significant positive correlation between the offspring bone mineral content, bone mineral density, and bone mass, when compared with the same paternal measures, in female offspring. There was not significance for the same measures in the male offspring. From this data, it can be concluded that paternal bone measures are a strong predictor of the bone growth outcomes for female children, but more research needs to be done to develop significance for male offspring

³. In another study that looked at parental bone growth and its effect on offspring bone development, 145 parent-offspring groups were examined. This study focused specifically on the intrauterine growth of the offspring. Offspring bone measures were taken using dual x-ray absorptiometry. Maternal and paternal measures included birthweight (of the parents), height, weight, smoking participation, and exercise participation. The results showed a positive correlation between paternal height and both parents birth weights when compared with neonatal bone mineral content. It was also found that women who were smokers had offspring with lower bone mineral content and bone mineral density. Women who were thinner and had a faster walking pace also produced offspring with lower bone mineral content. These data suggest that both environmental and genetic factors have an effect on intrauterine bone development ². The effects of paternal adiposity on offspring's health outcomes were examined in a study that examined male Sprague-Dawley rats. Specifically, male rats were fed a high fat diet (HFD) or a control diet (CD) for a period of 12 weeks, before being mated with control-fed female rats. The offspring were examined post-partum at 8 and 12 weeks. The male offspring from the HFD fathers did not develop any glucose metabolism impairment, but they did exhibit a growth deficit. The HFD offspring showed lower birth weight, as well as a 10% lower body weight at 6 months and significantly smaller muscled and fat pads when compared to the CD offspring. It was concluded that a reduced secretion of growth hormones in the HFD offspring resulted in smaller animals, as well as impaired lipid metabolism in these offspring ⁵. In another study that used rodents, paternal pre-fertilization exercise as a predictor for offspring's health outcomes was examined. Male rodents were exercised for 12 weeks prior to mating. After examination of the offspring, it was found that the offspring from exerciser fathers had a more efficient metabolism than those that did not have physically active fathers. But, when fed a high fat diet, the offspring from the exercise group showed significantly increased adiposity, impaired glucose and insulin levels, and overall higher risk for metabolic syndrome. These results were not hypothesized, and could suggest a genetic adaptation to the environmental stresses endured by the exercised fathers.¹

Chapter 3:

Methods

This was a retrospective analysis of a prospective cohort study. Our study protocols are approved by East Carolina University (ECU) Institutional Review Board. Women must be between the ages of 18 and 40 years old when they were pregnant with their child; children must be six years of age or younger and seen as a patient at East Carolina University School of Dental Medicine Pediatrics Clinic were asked to participate in this study. All women completed consent for themselves and their child. Maternal and paternal data was collected using a modifiable physical activity questionnaire (MPAQ) completed by the mother. This questionnaire acquired information including maternal and paternal information, such as age, BMI, education level, and physical activity. Participants who used alcohol, tobacco, recreational drugs, or other medications (i.e. mental health medications) during the pregnancy with their child were not included in the study.

Procedures

Women participants were recruited for the study by in-person recruitment while they were waiting in the pediatric dental clinic or via an emailed questionnaire, if we were not in the clinic when they came for their child's appointment. Once eligibility is determined (child less than or equal to 6 years of age), then the study was explained in detail. Participants signed informed consent for enrollment, and completed the modifiable physical activity questionnaire (MPAQ), while the dentist was seeing their child.

Questionnaire

The Modifiable Physical Activity Questionnaire (MPAQ) was used to assess maternal physical activity levels prior to enrollment and after delivery in order to a) determine activity levels of participants prior to the start of their respective exercise training protocol and b) verify the amount and type of exercise completed outside of the study protocol throughout pregnancy (i.e. control group not exercising aside from stretching or normal activities of daily living). This questionnaire applies to physical, occupational, and leisure-time activities taking place over the past 12 months and was chosen based on its validity and reliability of use in pregnant populations as well as its ability to adequately assess activity levels.^{30,54}

Child Dental Clinic Measures

The offspring data were collected directly at the ECU Pediatric Dental clinic, via standard dental procedures. Some of the standard measures include mixed tooth count, Decayed Missing Filled Teeth (DMFT) to Decayed Missing Filled Surfaces (DMFS) ratio, and overall periodontal health (perio health). Mixed tooth count is defined as the total number of erupted teeth in the child's mouth, including both primary teeth and secondary teeth, if present. DMFT/DMFS is a measure of the disease progression of dental caries. Molars are classified as having 5 surfaces, while frontal teeth are classified as having four surfaces. The ratio of DMFT/DMFS is considered to be a more accurate prediction of caries prevalence than either measure alone.

The paternal group categories were defined using guidelines standard BMI cut-offs for the 2 groups: group with paternal BMI 18.5-24.9 as Normal weight (NW) group, and group with paternal BMI >25 as Overweight or Obese (OW/OB) group. All women completed consent for themselves and their child. Mothers also completed a questionnaire, and the children received standard dental care. Alpha level was set a priori at 0.05 and multiple t-tests were performed to determine differences between groups and regression analyses were completed to look for significant associations.

Data Analysis

The primary outcome measure of the study was offspring dental measures and how they were influenced by Paternal BMI. Paternal data was obtained from the MPAQ filled out by the women. Body Mass Index was calculated as weight in kilograms divided by height squared, in centimeters. Once paternal BMI was calculated, each paternal: child pair was classified based on paternal BMI. National standards were used for BMI classification: normal weight (NW; BMI=18.5-24.9) and overweight/obese (OW/OB; BMI>24.9). Once dichotomized, the child dental measures were analyzed using multiple T-tests. Significance level was set at $\alpha < 0.05$.

Chapter 4:

Results

Parent Demographics. We recruited 74 parent:child data for the study. Some of the questionnaires had incomplete paternal data, and were excluded. Therefore we analyzed 23 parent-offspring groups (12 NW and 11 OW/OB) for this study. There fathers were separated by their BMI (Table 3) Maternal Demographics between the different groups based on maternal BMI (Table 1).

Child Demographics. All child participants were in good health and free of chronic conditions. There are no significant differences between groups in child demographics for age and BMI (Table 2).

Child Dental Measures. There were no differences in tooth count between paternal BMI groups (Table 3). No significant correlation was found when paternal BMI was compared to offspring tooth eruption. Although there was no statistical significance, there was a slight positive correlation ($r=0.31$) between the NW paternal group and offspring tooth eruption (Figure 1). In contrast, the OW/OB paternal group showed slightly negative correlation ($r=-.000001$) with tooth eruption (Figure 2).

Regression analysis found paternal BMI is associated with offspring tooth count when controlling for maternal exercise participation. The highest average tooth count came from offspring whose fathers were classified as NW, and whose mothers were classified as exercisers; therefore, paternal BMI and maternal exercise explain 56% of child tooth dentition. The lowest average tooth count was displayed by offspring with OW/OB fathers and non-exerciser mothers; similarly, paternal BMI and maternal lack of exercise explain 84% of child tooth dentition (Figure 3). When comparing mixed tooth count as a function of age, the children in the NW group had a more

significant trend toward a higher tooth count when compared to the OW/OB group of children (Figure 4). With regards to disease risk as a function of age, there was significant difference between the NW and OW/OB groups (P 0.03). Children from the NW group showed a significant positive trend, while those from the OW/OB group showed a slightly negative trend.

Table 1: Maternal Demographics

	NW	OW/OB
Age	30.25 ± 3	30.89 ± 6
Height	64.88 ± 1	61.93 ± 4
Pre Preg. weight	154.6 ± 16	165.57 ± 20
# Pregnancy	1.5 ± 0.5	2.4 ± 2
# Children	1.0 ± 0	1.67 ± 0.3

Table 2: Child Demographics

	NW	OW/OB
Age	4.17 ± 1.5	5 ± 1.2
BMI	15.42 ± 1.0	16.51 ± 1.7

Table 3: Paternal Demographics

	NW	OW/OB	P-Value
BMI	20.25 ± 1.7	20.72 ± 1.4	0.48
Age	27.17 ± 10.9	29.78 ± 7.2	0.33

Table 4: Child Oral Measures

	NW	OW/OB	P-Value
Mixed Tooth Count	18.94 ± 4.9	20.42 ± 1.1	0.21
Risk Assessment Score	2.82 ± 0.6	2.42 ± 0.7	0.19
DMFT	8.13 ± 4.3	4.73 ± 5.1	0.14
DMFS	19.88 ± 16.7	7.55 ± 10.2	0.06
DMFS:DMFT	2.33 ± 1.9	0.84 ± 0.8	0.03

Figure 1: Normal Paternal BMI vs. Child Tooth Count

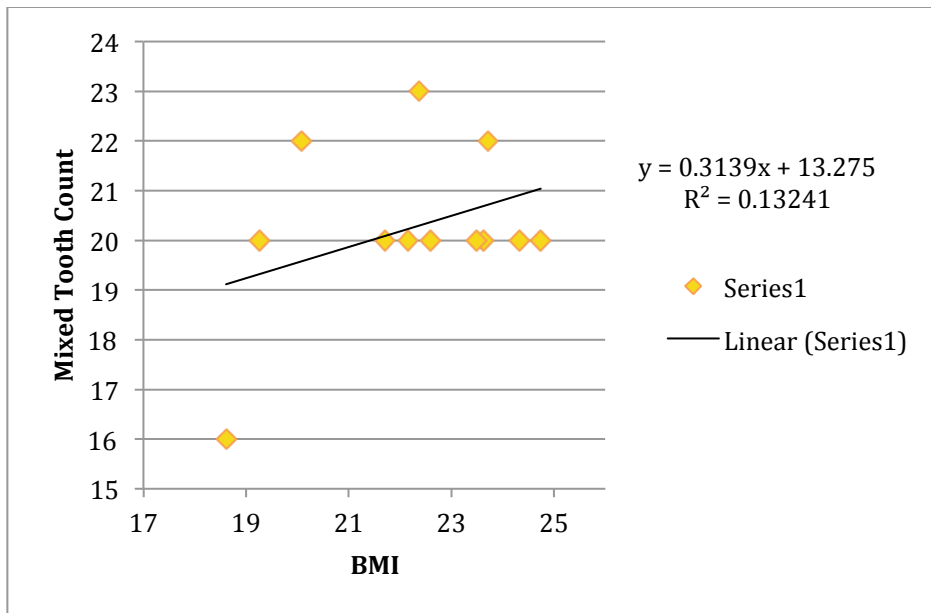


Figure 2: OW/OB Paternal BMI vs. Mixed Child Tooth Count

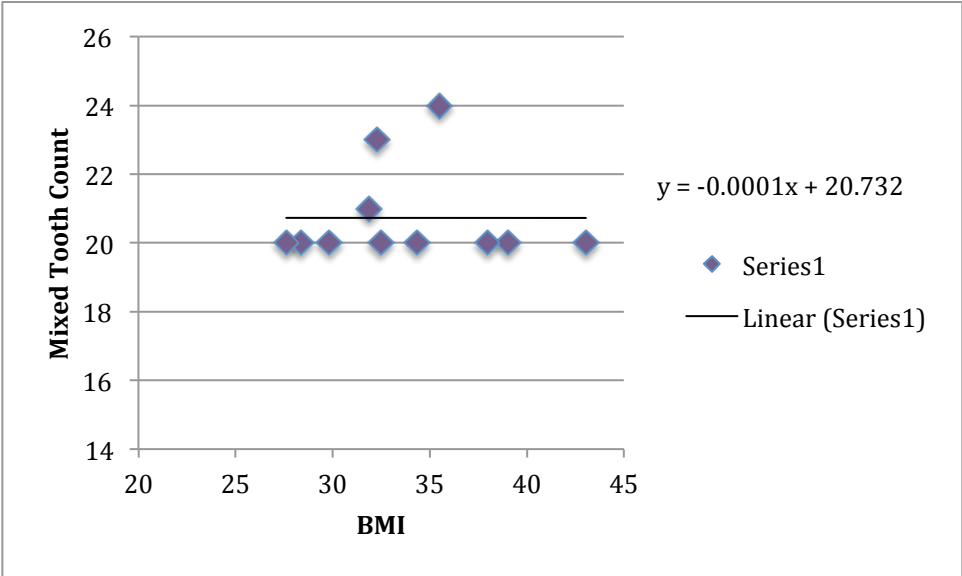


Figure 3: Mixed Tooth Count as a Function of Maternal Exercise Participation

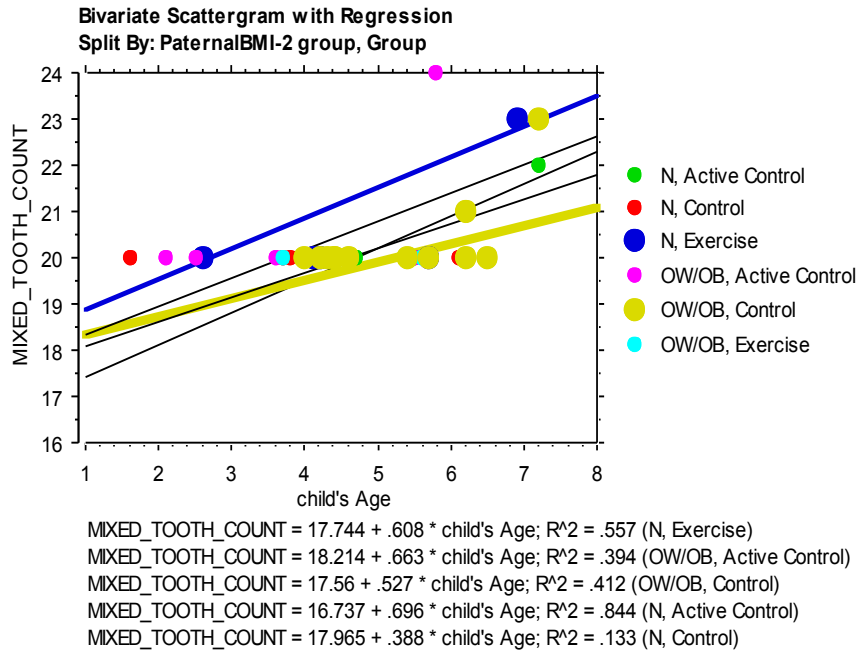


Figure 4: Mixed Tooth Count As a Function of Age

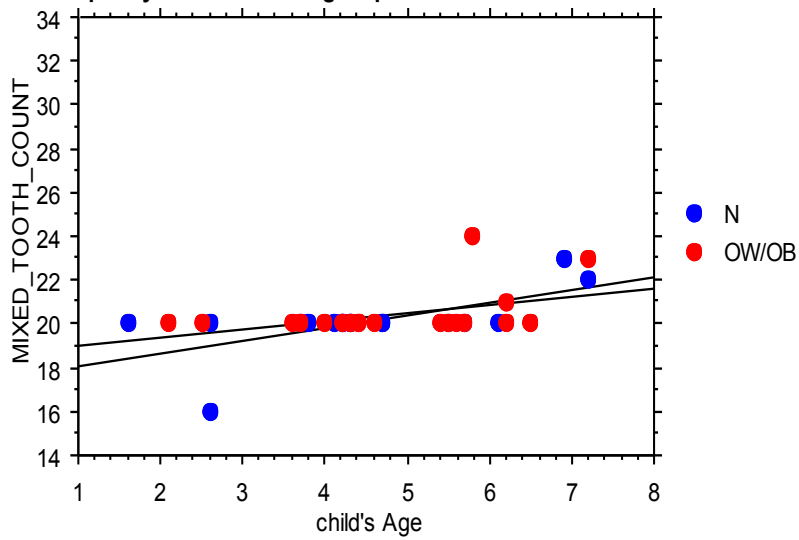
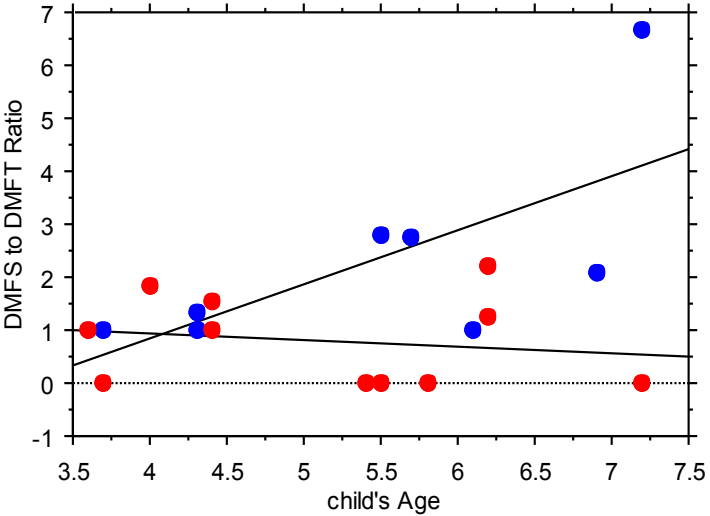


Figure 5: Disease Risk as a Function of Age



Chapter 5

Discussion:

This study aims to find a correlation between paternal health measures and offspring dental development. The data suggest that paternal BMI is linked to offspring dental outcomes. Pooled data show that there is a positive relationship between paternal BMI and offspring tooth count for the NW group. This is in contrast to the hypothesized outcome, since it was expected that an increased BMI would result in a decrease in offspring tooth eruption. This correlation was supported by a study conducted on humans that showed a significant positive relationship between paternal height and weight and offspring's bone mineral density and content.

When Examining the OW/OB group, there was a negative correlation between BMI and offspring tooth count. This result is in following with the hypothesis, although the negative trend was not statistically significant, it is an indicator of an existing relationship. This correlation is supported by a study conducted on rats. In this study, fathers who were fed a high fat diet (which can be correlated to a high BMI) produced offspring who showed significantly lower birth weight and length⁵. This can be related to the negative relationship observed between increasing paternal BMI and decreasing offspring tooth count.

Of note, Paternal BMI had a varying effect on offspring disease risk. For offspring in the NW group, there was a strong positive trend for disease risk as a function of age. Contrarily, in the OW/OB group, offspring showed a negative trend for disease risk as a function of age. There was significant difference in disease risk between these groups ($P=0.03$). This outcome is in contrast to what was expected, since the fathers who were in a less-healthy BMI classification produced children with a significantly lower risk for caries. It would be expected that the NW fathers would produce children with an improved disease risk relationship.

There are definite limitations to the method of this study. Although our maternal and paternal information is self-report, we have used a questionnaire that is validated for use up to 6 years post-partum. Due to the nature of the variables being examined, there is a potential for other

variables to be influence the outcomes of the data. One of these hidden variables could be paternal nutrition. This could have an effect on offspring development both directly, and indirectly, since children often mirror their parents eating habits, which could affect their disease risk. Another limitation is the sample size. With only 23 subjects, we do not have a large enough sample to power our analysis. A larger subject group would provide the ability to draw generalizable conclusions and applications for future study.

When compared to data gathered from other studies, the results are not unique. In another study, paternal BMI was shown to have a positive relationship with the child's bone development. Fathers with higher BMI produced children with increased bone mineral density and bone mineral content, as well as increased overall bone mass. This can be closely compared to the development of the child's teeth, therefore supporting the positive correlation observed in this study between paternal BMI and the child's tooth development. The findings from this study were also supported by the results of a study using subjects from a separate study. Looking at the maternal side, maternal BMI was positively correlated with offspring bone development. A higher maternal BMI was also shown to result in children with greater growth measurements. As with the previously mentioned study, these data suggest that bone, and therefore tooth, development is affected by the parents BMI. It should also be considered that the fathers BMI is not the only factor that is affecting the offspring's bone development. As mentioned before, there are likely other factors that were not examined in this study that could result in positive correlation with paternal BMI, with the possibility being that paternal BMI is not actually the effector. In a study focusing on paternal bone mineral content and bone density, it was shown that fathers with a higher bone mineral content and density produced children with the similar outcomes. This suggests that possibly paternal BMI is linked to the fathers own bone development, and therefore this results in an effect on the offspring. Given that paternal BMI has also been linked to genetic adaptation in their offspring in rats, the majority of the previous research supports the hypothesis that paternal BMI is an effector of the dental development for the child.

Conclusion:

In conclusion, the data gathered from this study support the idea that there is a link between paternal factors and offspring's dental outcomes. Paternal BMI was shown to have a positive effect on offspring tooth count for NW fathers, but a negative effect on offspring tooth eruption for OW/OB fathers. Paternal BMI was also shown to have a negative effect on offspring's disease risk. This information is important, because it is vital that fathers are provided with any information that is available that may have an effect on the development of their child. Providing this information to potential fathers prior to conception may influence them to change their habits in order to provide a better outcome for their child's development. More research will be required to examine the non-significant relationships observed between paternal BMI and tooth count, as well as to further establish a connection between paternal BMI and offspring disease risk.

Bibliography:

1. Murashov AK, Pak ES, Koury M, et al. Paternal long-term exercise programs offspring for low energy expenditure and increased risk for obesity in mice. *FASEB J*. 2016;30(2):775-784.
2. Godfrey K, Walker-Bone K, Robinson S, et al. Neonatal bone mass: influence of parental birthweight, maternal smoking, body composition, and activity during pregnancy. *J Bone Miner Res*. 2001;16(9):1694-1703.
3. Harvey NC, Javaid MK, Poole JR, et al. Paternal skeletal size predicts intrauterine bone mineral accrual. *J Clin Endocrinol Metab*. 2008;93(5):1676-1681.
4. Macdonald-Wallis C, Tobias JH, Smith GD, Lawlor DA. Relation of maternal prepregnancy body mass index with offspring bone mass in childhood: is there evidence for an intrauterine effect? *Am J Clin Nutr*. 2010;92(4):872-880.
5. Lecomte V, Maloney CA, Wang KW, Morris MJ. Effects of paternal obesity on growth and adiposity of male rat offspring. *Am J Physiol Endocrinol Metab*. 2017;312(2):E117-E125.