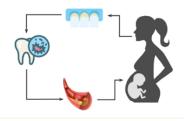




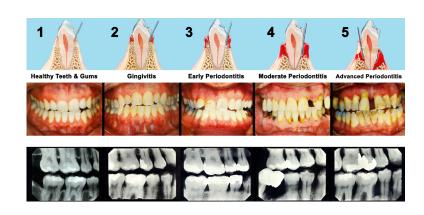
Does the treatment of maternal periodontal disease can reduce the risk of preterm birth and low birth weight?

Baurice Nafack

June 30, 2023



What is Periodontal Disease?



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Periodontal Disease and Factors Affecting Preterm Low Birth Weight

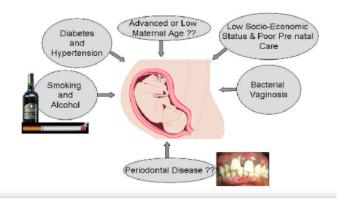


Figure: Schematic image of the various factors affecting preterm low birth weight deliveries

Periodontal Disease and Preterm Birth

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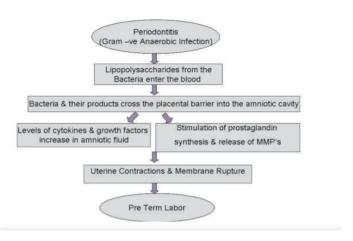


Figure: An algorithm for periodontal examination and treatment of pregnant women.

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- Pregnant women with PD are at a higher risk of preterm birth compared to alcohol consumption or smoking.
- Researchers discovered that preterm mothers exhibited higher rates of supporting tissue loss around the teeth, a greater proportion of sites with deep pockets, and unhealthy oral bacteria compared to full-term mothers.
- Mothers with periodontitis had significantly lower birth weights in comparison to mothers with good oral health or those experiencing bleeding gums without pathological pockets.

Problem Statement

 Several interventional studies have been conducted to investigate the potential impact of periodontal treatment on pregnancy outcomes, considering periodontal diseases as a risk factor for preterm birth (PB).

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- However, the results from these studies have been somewhat contradictory, leading to different conclusions.
- Some case-control studies suggest that periodontal treatment can improve both periodontal conditions and pregnancy outcomes, while others indicate no significant effect.

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• A meta-analysis (the statistical combination of results from two or more separate studies) was conducted to conclude periodontal diseases treatment is associated with preterm birth.

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- The hazard ratio of treatment groups compared to control groups indicates that treating periodontitis in pregnant women improves periodontal disease and is considered safe. However, the treatment does not result in a significant reduction in preterm birth rates, low birth weights, or fetal growth restrictions.

- A meta-analysis (the statistical combination of results from two or more separate studies) was conducted to conclude periodontal diseases treatment is associated with preterm birth.
- The hazard ratio of treatment groups compared to control groups indicates that treating periodontitis in pregnant women improves periodontal disease and is considered safe. However, the treatment does not result in a significant reduction in preterm birth rates, low birth weights, or fetal growth restrictions.
- These divergent results have contributed to the overall uncertainty surrounding the benefits of periodontal disease treatment in reducing the rate of preterm birth.

• In our study, we will analyze the data using a new approach called meta-learning.

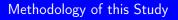
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- Estimate individual treatment effects using a meta-learner.
- Identify people who could have a positive reaction to the treatment and who shouldn't.



• Determine what features are important for predicting whether the treatment will be effective for the pregnant woman.

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- We will find the conditional treatment effect (CATE) for different groups of people.

T-learners and S-learners will be used for estimating the conditional average treatment effect (CATE) in the causal inference setting.

• The conditional average treatment effect (CATE) is defined as:

$$\tau(x) := \mathbb{E}[Y(1) - Y(0) \mid X = x]. \tag{1}$$

If we define the response under control and the response under treatment as

$$\mu_0(x) := \mathbb{E}[Y(0) \mid X = x],
\mu_1(x) := \mathbb{E}[Y(1) \mid X = x],$$
(2)

then we can write the CATE as:

$$\tau(x) = \mu_1(x) - \mu_0(x). \tag{3}$$

T-learner

The T-learner consists of 2 steps:

• Use observations in the control group to estimate the response under control, $\hat{\mu}_0(x)$.

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- Use observations in the control group to estimate the response under control, $\hat{\mu}_0(x)$.
- use observations in the treatment group to estimate the response under treatment, $\hat{\mu}_1(x)$.
- Estimate the CATE by $\hat{\tau}_T(x) = \hat{\mu}_1(x) \hat{\mu}_0(x)$.

Instead of having two models for the response as a function of the covariates X, the S-learner has a single model for the response as a function of X and the treatment W:

$$\mu(x,w) := \mathbb{E}[Y^{obs} \mid X = x, W = w]. \tag{4}$$

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$$\mu(x, w) := \mathbb{E}[Y^{obs} \mid X = x, W = w]. \tag{4}$$

The S-learner consists of 2 steps:

• Use all the observations to estimate the response function above, $\hat{\mu}(x, w)$. Estimate the CATE by

$$\hat{\tau}_{S}(x) = \hat{\mu}(x, 1) - \hat{\mu}(x, 0)$$
 (5)

Data Description

The dataset consists of 823 participants, each with 171 variables.

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- The treatment group received nonsurgical periodontal treatment before 21 weeks gestation, and the control group received it after delivery.
- Throughout the study, all participants attended monthly follow-up visits until delivery.
- During these visits, the treatment group received periodontal therapy, oral hygiene instruction, and tooth polishing, while the control group received brief oral exams.

Preterm Birth Definition

 Preterm birth is defined as delivery before 37 weeks of gestation.

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- Birthweight is dichotomized as "low" or "high" at the 2500 g defined by the World Health Organization's definition for low birth weight.

Missing Data Sources and Data Cleaning

- BMI: Body Masse index
- Vn: visit at n.
- Cal: Clinical attachment.
- avg: whole-mouth average
- Calc: Calculus index
- % : fraction of site
- PD : pocket depth
- BOP bleeding on probing
- > m : > = mmm

columns	missing values pourcentage
ВМІ	8.845209
Birthweight	0.614251
V3 %BOP	16.216216
V3 GE	16.216216
V3 PD avg	16.216216
V3 %PD>4	16.216216
V3 %PD>5	16.216216
V3 CAL avg	16.216216
V3 %CAL>3	16.216216
V3 Calc I	16.216216
V5 %BOP	19.041769
V5 %PD>4	19.041769
V5 %PD>5	19.041769
V5 %CAL>2	19.041769
V5 %CAL>3	19.041769

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 A significant amount of missing data can be attributed to missed visits, human error, and other practical problems.

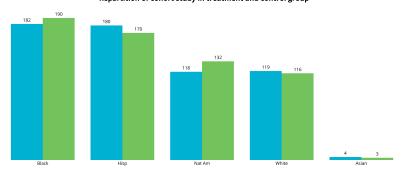
Missing Data Sources and Data Cleaning

- A significant amount of missing data can be attributed to missed visits, human error, and other practical problems.
- Lost to follow-up: 9 individuals.
- We use MissForest to handle missing. For each variable with missing values, MissForest employs a random forest model trained on the observed data to predict the missing values.

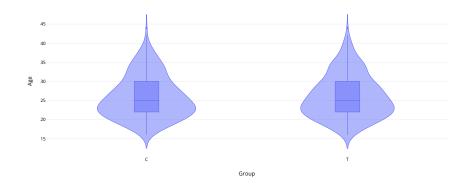
Repartition of cohort study in treatment and control group

Group

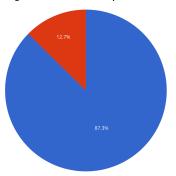
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Data Vizualization



Percentage of Preterm Births Compared to Normal Births



	mean outcome	size outcome	
Group			
С	0.130542	406	
т	0.122549	408	
All	0.126536	814	

Figure: Conditional probability estimates for Preterm Birth

• Relative Risk = 0.92 < 1, 95%CI(0.67, 1.38). The treatment has a small impact and is likely to do good. The risk of a bad outcome is decreased.

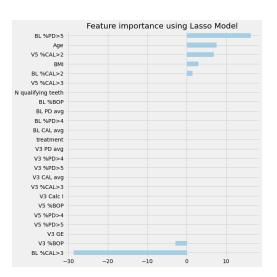
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Figure: Conditional probability estimates for Preterm Birth

- Relative Risk = 0.92 < 1, 95%CI(0.67, 1.38). The treatment has a small impact and is likely to do good. The risk of a bad outcome is decreased.
- We will further investigate this hypothesis using the meta-algorithm.

Features Selection with LassoCV for Birthweight Prediction

- Best $\lambda = 284.43$
- We use the default parameter of the package with a 5-folder.



Sources of Bias

In our study, potential bias can arise during:

 Missing value imputation, feature selection, group labelling across different visits, and ML training. In our study, potential bias can arise during:

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- Missing value imputation, feature selection, group labelling across different visits, and ML training.
- Feature selection (24 chosen out of 48) and labelling biases during different visits are additional sources of bias that need consideration in our study.
- Um-balanced label.

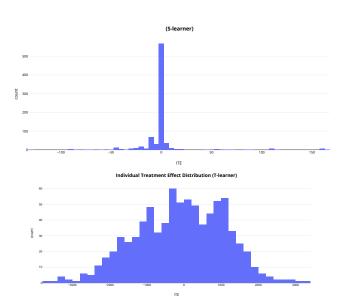
Model use for prediction

• For T-learner: the backbone model is the Linear regression

- For S-learner: the backbone model is the XGBoost regressor.
- For preterm birth; we use the XGBClassifier to train a S-learner.

Individual Treatment Effect (ITE)

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• The average treatment effect (ATE) for birthweight in this study using T-learner is -97.41 and -0.71 using the S-learner.

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- The CATE using T-leaner for individuals under the age of 25 in the control group is, is -457.04, whereas, for those over 25, it is 954.84.

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- The CATE using T-leaner for individuals under the age of 25 in the control group is, is -457.04, whereas, for those over 25, it is 954.84.
- The CATE for both the control grand treatment groups using S-leaner are -1.20 and -0.57

CATE

• For individuals over 25 in the treatment group using s-learner, the CATE is 1.22 , while for those under 25 is -2.12.

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- For individuals over 25 in the treatment group using s-learner, the CATE is 1.22, while for those under 25 is -2.12.
- The CATE for black individuals using the s-learner is 1.39, whereas, for white individuals, it is 15.14. The treatment has a positive effect on both groups.
- The average treatment effect for preterm birth using an S-learner is 0.005.

Observation

 According to S-leaner, the treatment of maternal periodontal disease does not decrease the risk of preterm birth and low birth weight.

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- T-leaner indicates that the treatment positively impacts birthweight, increasing it by 521.86.

 S-leaner indicates that the treatment positively impacts people over 25 and negatively impacts those under 25.

- According to S-leaner, the treatment of maternal periodontal disease does not decrease the risk of preterm birth and low birth weight.
- T-leaner indicates that the treatment positively impacts birthweight, increasing it by 521.86.
- The treatment benefits individuals under and over 25 years of age in the treatment group while showing a negative effect on those under 25 years of age in the control group. while positively impacting those over 25 in the control group.
- S-leaner indicates that the treatment positively impacts people over 25 and negatively impacts those under 25.

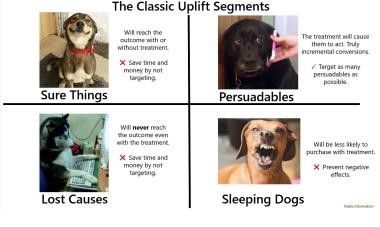
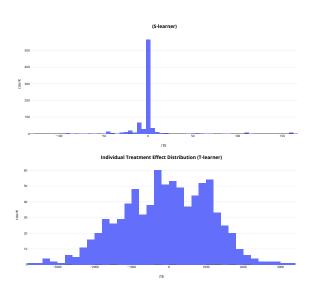


Figure: Grouping of cases according to their response to treatment

Individual Treatment Effect (ITE) and uplift Cutoff



Uplift Segment

	mean	size
	ITE	ITE
segment		
no_impact	-2.672143	780
persuadable	108.394592	23
sleeping-dog	-89.335983	11
All	-0.705027	814

	mean	size
	ITE	ITE
segment		
no_impact	-73.410925	804
persuadable	3203.936334	2
sleeping-dog	-3335.056157	8
All	-97.413956	814

a) S-learner segment

b) T-learner segment

The cutoff ITE is as follows:

• -50 and 50 for s-learner and -3000 and 3000 for T-leaner based on the histogram.

Uplift Segment

• T-learner:

• Inside the sleeping dog for the segment (8 individuals), 3 people are in the treatment group (2 people under age 25 and 1 over 25) and 5 in the control group (3 people over age 25 and 2 under 25).

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• T-learner:

- Inside the sleeping dog for the segment (8 individuals), 3 people are in the treatment group (2 people under age 25 and 1 over 25) and 5 in the control group (3 people over age 25 and 2 under 25).
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S-learner:

• Inside the sleeping dog for the segment (11 people), 6 people are in the treatment group (3 people under age 25 and 3 over 25) and 5 in the control group (2 people over age 25 and 3 under 25).

• T-learner:

- Inside the sleeping dog for the segment (8 individuals), 3 people are in the treatment group (2 people under age 25 and 1 over 25) and 5 in the control group (3 people over age 25 and 2 under 25).
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S-learner:

- Inside the sleeping dog for the segment (11 people), 6 people are in the treatment group (3 people under age 25 and 3 over 25) and 5 in the control group (2 people over age 25 and 3 under 25).
- Inside the persuadable group (23): 13 people are in the treatment group (6 people under age 25 and 7 over 25) and 5 in the control group (3 people over age 25 and 6 under 25).

Conclusion

• Treating "persuadable" individuals improves periodontal conditions and pregnancy outcomes significantly.

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 to as "sleeping dogs") is also important to ensure accuracy and avoid
 negative effects of the treatment on those individuals.
- Implementing these insights allows researchers to make informed decisions and allocate treatment more efficiently, resulting in improved patient outcomes.



Bibliography I

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