Estimating the effect of number of remaining teeth on social participation among older adults in Japan

\*Upul Cooray1, Georgios Tsakos2, Anja Heilmann2, Richard G Watt2, Kenji Takeuchi1, Katsunori Kondo4,5, Ken Osaka1 & Jun Aida3

1Department of International and Community Oral Health, Tohoku University Graduate School of Dentistry, Sendai, Japan

2Department of Epidemiology and Public Health, University College London, London, United Kingdom

3Department of Oral Health Promotion, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan

4Center for Preventive Medical Sciences, Chiba University, Chiba, Japan

5Center for Gerontology and Social Science, National Center for Geriatrics and Gerontology, Obu, Japan

### **\*Corresponding Author:**

Upul Cooray

Department of International and Community Oral Health, Graduate School of Dentistry, Tohoku University, Sendai, Japan

Address: 4-1, Seiryo-machi, Aoba-ku, Sendai, Miyagi, 980-8575, Japan

E-mail: [upul.cooray.15@ucl.ac.uk](mailto:upul.cooray.15@ucl.ac.ukp), Tel: +81-2-2717-7639

Abstract word count: 252

Total word count: 3063

Number of tables: 2

Number of figures: 3

Number of reference: 34

**Keywords**: Casual inference, Modified treatment policy, Targeted minimum loss-based estimation, Social participation, Older adults

## Abstract (word limit 250)

### Background

Participating in social activities and interacting with others in the community has numerous positive effects on older adults’ health and quality of life. We aimed to estimate the causal effect of number of teeth on social participation among older adults in Japan.

### Methods

Using longitudinal data (baseline=2010, follow-ups=2013 and 2016) from 24,872 participants of the Japan Gerontological Evaluation Study, we employed a longitudinal modified treatment policy approach to determine the causal effect of number of teeth on social participation. Corresponding statistical parameters were estimated using targeted minimum loss-based estimation (TMLE). Number of teeth (edentate, 1-9 teeth, 10-19 teeth, 20 teeth) was treated as a time-varying exposure and the estimates were adjusted for time-varying (income, self-rated health, denture use, marital status) and time-invariant (age, sex, baseline social participation) covariates.

### Results

After six years of follow-up, 48.4% reported less frequent social participation (< at least once a month). Causal odds ratios, calculated by contrasting counterfactual TMLE estimates at different levels of the exposure, showed a clear dose-response effect on social participation. When the exposure was shifted from being edentate to having 20 teeth, the likelihood of social participation increased by 30% (OR=1.30, 95%CI=1.23-1.38). A shift from the observed number of teeth to being edentate reduced social participation by 15% (OR=0.85, 95%CI=0.79-0.92).

### Conclusions

This study provided causal evidence that having a higher number of teeth and maintaining a functional dentition positively affects social participation among Japanese older adults, while being edentate or having relatively fewer teeth negatively affects social participation.

## Introduction

The term “social participation” refers to an individual’s involvement in activities that allow them to interact with others in their community or society in general.1 Social participation among older adults is an essential component of healthy ageing because it has numerous positive effects on both individuals and society.2 Previous studies have linked higher levels of social participation to higher life expectancy, better health-related quality of life, well-being, and functioning of older adults.3,4 Community-level health promotion and prevention activities such as physical activity, smoking and alcohol interventions, could also be facilitated through social engagement.5 On the other hand, a wide range of determinants, including health-related factors, influence older adults’ level of social participation.6

Teeth and oral health are important in different aspects of daily life, such as eating, speaking, smiling, and making facial expressions, all of which are essential for positive social interactions. Tooth loss is highly prevalent among older adults due primarily to a life-long accumulation of chronic dental conditions such as dental caries and periodontal diseases.7 Previous studies have consistently linked social and neighbourhood related factors such as social capital and social participation to oral health related outcomes among older adults.8–10 However, much less is known about the effect of oral health on participation in social activities. Experimental studies to evaluate the potential causal effect of the remaining number of teeth on social participation are not practically feasible, further complicated by the time varying nature of the exposure (number of teeth) and confounders. As an approach to overcome these problems for causal inference from observational data, the *longitudinal modified treatment policy* *(LMTP)* approach can be an ideal method.

LMTP is a recently developed non-parametric alternative that can be used to define causal effects.11 The literature for causal inference based on binary exposures is extensive.12 However, dichotomisation of the exposure using a arbitrary cut-off point leads to loss of information on the exposure and hinders the ability to observe any “dose-response” effect on the outcome. LMTP, on the other hand, allows us to quantify the effect of a treatment that changes the observed level of exposure in each individual to a new level11. In other words, this framework can be adapted to quantify counterfactual outcomes for questions such as, “What would have happened to the prevalence of social participation if everyone in the study population increased or decreased their number of teeth by a certain amount?”, and “What if everyone in the study population lost their teeth?”. Furthermore, the corresponding statistical parameters for LMTP can be estimated using sophisticated doubly-robust statistical estimators, such as the targeted minimum loss-based estimation (TMLE) with Super Learner, which allows for the use of flexible machine learning predictions avoiding parametric modelling assumptions.13,14

This study estimates the effect of the number of remaining teeth on social participation among older adults while taking the time-varying nature of variables into account. LMTP was used to dynamically shift the observed level of exposure (number of remaining natural teeth) to new levels in order to investigate its effect on social participation among functionally independent older adults in Japan over a 6-year period. We hypothesised that as the number of teeth increases, social participation improves, and as the number of teeth decreases, social participation declines among older adults.

## Methods

### Data

Data from the Japan Gerontological Evaluation Study (JAGES) was used in this study.15 JAGES is an on-going nationwide cohort study for functionally independent older adults in Japan aged 65 years or over. For this analysis, data from the 2010 survey as the baseline and two subsequent follow-up surveys (2013 and 2016) were used. A total of 52,053 functionally independent individuals participated in the baseline survey, and 24,872 individuals responded to all three waves (i.e., 2010, 2013, and 2016). During the 6 years of follow-up 4,611 died, 8,099 became ineligible as they became functionally dependent, and 14,471 were lost to follow-up due to other reasons (study flow chart in Figure 1). A comparison of baseline characteristics by participants' follow-up status (i.e., died/ became ineligible/ lost to follow-up/ or remained) is reported in Supplementary Table S1.

### Outcome variable

Social participation in 2016 was the outcome in this study. JAGES recorded the frequency of social participation (“nearly every day”, “twice or thrice a week”, “once a week”, “once or twice a month”, “a few times/year”, “never”) for various social activities. We assessed the frequency of participation in any of the following activities: hobby groups, sports clubs, senior citizens’ clubs, residence groups, or volunteer groups. Participation in any of the aforementioned activities once a month or more frequently (vs. less frequently or never) was defined as indicative of social participation (1=participation, 0=non-participation).16

### Exposure

The number of remaining natural teeth at the time of the surveys in 2010 and 2013 was used as a time-varying exposure in the analysis. The self-reported number of teeth was recorded using the response to the question, “How many natural teeth do you currently have?” (Instructions: capped/crowned teeth should be counted as “natural teeth”). The responses of participants were recorded in four categories (i.e., 20 teeth/ 10-19 teeth/ 1-9 teeth/ no teeth).

### Covariates

Because the number of teeth was evaluated as a time-varying exposure in this study, both time-invariant and time-variant covariates were taken into account. As time-invariant covariates, age (range 65–99 years), sex (male/female), and social participation in 2010 (outcome at the baseline) were adjusted for. Equalised annual household income (million yen), self-rated health (very good/ good/ fair/ poor), denture use (yes/ no), and marital status (married/ single, widowed or divorced) were used as time-varying covariates (measured in 2010 and 2013).

### Statistical analysis

The hypothesised temporal connections between study variables are shown in the directed acyclic graph (Figure 2). Descriptive analysis provided the characteristics of participants stratified by the outcome (social participation in 2016). Then, to specify the impact of number of teeth on counterfactual outcomes, the observed level of number of teeth of each individual was shifted to several new levels mimicking multiple hypothetical interventions. The following hypothetical scenarios were created by shifting the observed exposure to detect any dose-response associated with the outcome:

1. “all participants having ≥20 teeth in 2010 and in 2013,” (i.e., ideal counterfactual scenario where all the participants having a minimal functional dentition)17

2. “all participants having 10-19 teeth in 2010 and in 2013,”

3. “all participants having 1-9 teeth in 2010 and in 2013,”

4. “all participants being edentate in 2010 and in 2013,” (i.e., worse counterfactual scenario where all older adults were edentate)

5. “observed level of number of teeth category in 2010 and in 2013” (i.e., originally observed level in 2010 and in 2013).

To estimate the social participation with the shifted (and the observed) exposure, we used TMLE.11,14 In TMLE, the probability of the exposure conditional on covariates (exposure model), and the conditional probability of the outcome given exposure and covariates (outcome model) were estimated to obtain an unbiased estimation of the counterfactual outcomes.14,18 If either the exposure model or the outcome model was consistently estimated, unbiased estimates could be obtained (hence doubly-robust).19 To increase the likelihood of robust specification of exposure and outcome models, Super Learner, an ensemble method that uses weighted combinations of multiple machine learning algorithms was used.20–22 Within Super Learner, generalized linear models (*glm*), extreme gradient boosting models, and neural nets were used as candidate algorithms.23,24 Then, the TMLE estimate for the ‘ideal’ counterfactual scenario (i.e., everyone having at least a functional dentition at each time point) was used as a reference to calculate causal odds ratios (OR) and 95% confidence intervals (95% CI) for the other scenarios. Additionally, the same procedure was followed to calculate ORs and 95% CIs using the TMLE estimate for the observed level of number of teeth as the reference. To check the robustness of TMLE estimates, an analysis without using Super Learner (using *glm*) was also conducted. All estimates were appropriately controlled for the aforementioned time-variant and time-invariant covariates. E values for the estimates were calculated to report the impact of unmeasured confounders. Furthermore, information on censoring was included in models to reduce bias due to attrition of the study population.

For the imputation of missing data in covariates, we used random forest multivariate imputation by chained equations (MICE). In imputing complex epidemiologic data, random forest MICE has been shown to produce less biased parameter estimates and better confidence interval convergence compared to parametric MICE.25 Analyses were performed using five imputed datasets and the results were pooled using Rubin’s rules. MICE was implemented using mice R package.26 The distribution of missingness among covariates in relation to outcome and exposure are reported in Supplementary Figures S1 and S2 . A supplementary complete case analysis was conducted to check the robustness of results with imputed data. The lmtp R package was used to compute TMLE estimates with Super Learner for each scenario.27 Main R codes used to generate our results are provided in Supplementary material. All the other codes used in analyses can be found at https://github.com/upulcooray/social-participation. All the analyses were conducted in R studio using R version 4.1.2 for x86\_64, linux-gnu.

## Results

Baseline characteristics of participants stratified by the outcome variable are presented in Table 1. In the 2016 follow-up, 12,252 (48.4%) people reported social participation less frequently than at least once a month. Baseline characteristics associated with less frequent social participation in 2016 were older age, lower income, poor self-reported health, being edentate, and lower social participation at baseline.

Table 2 provides the causal ORs (95%CIs) calculated by comparing TMLE estimates for social participation at various levels of exposure (number of teeth categories). After a six-year follow-up, having a relatively lower number of teeth had a negative effect on social participation and having a relatively higher number of teeth had a positive effect. When the TMLE estimate for the observed level of exposure was used as the reference, a change from the observed number of teeth category to an edentate state was associated with a 15% reduction (OR= 0.85, 95%CI= 0.79-0.92) in the likelihood of social participation. A shift from the observed number of teeth category to having 20 or more teeth had a positive impact on social participation with an OR= 1.11, 95%CI= 1.08-1.15 . When the counterfactual outcome of being edentate was used as the reference, a clear positive dose-response effect of having more natural teeth on social participation was observed (Figure 3). The highest improvement of the likelihood of social participation (30%) was observed when the exposure was shifted from being edentate to having 20 or more teeth (OR= 1.30, 95%CI= 1.23-1.38). Even a minor change in number of teeth, such as going from edentate to having one to nine teeth, was associated with a 10% increase (OR= 1.10, 95%CI= 1.00-1.19) in the likelihood of frequent social participation. Age, sex, baseline social participation, and a range of time-varying confounders (annual household income, self-rated health, dental prosthesis use, and marital status) were adjusted for in all reported estimates. Furthermore, the reported estimates were obtained by allowing exposure to vary during the follow-up period and accounting for participant censoring.

Figures 3-a and 3-b show the clear dose-response in point estimates as well as the robustness of the results regardless of the use of Super Learner. TMLE estimates obtained with Super Learner appeared to be slightly more conservative, therefore, these estimates are reported in Table 2. The findings of the supplementary complete case analysis were consistent with the findings of the main analysis (Supplementary Table S2 and Supplementary Figure S3).

## Discussion

To estimate the impact of the number of remaining teeth on social participation among older adults in Japan, we used an analytic approach that allowed us to estimate the effects of different levels of exposure over time while controlling for time-variant covariates. The estimates were obtained using a doubly-robust estimator (TMLE) in combination with a machine learning-based ensemble (Super Learner). To the best of our knowledge, this is the first study to estimate the effect of number of remaining natural teeth on social participation. Our findings show that having a relatively higher number of teeth during the follow-up period had a positive effect on social participation among older adults. In addition, a decrease in the observed number of teeth had a negative impact on social participation. These findings support our hypothesis and consistent with previous related research.

Previous studies, however, were based on cross-sectional data and used the number of teeth as the outcome variable.8,10 However, this association can be bi-directional and the effect of number of teeth on social participation has not been researched. Using longitudinal data and causal inference, this study added evidence related to the importance of maintaining an adequate number of teeth for frequent social participation among older adults. Given the consistent evidence that social participation improves older adults’ health and well-being, mechanisms that leads to increased levels of social participation should be promoted and encouraged. In this context, our findings emphasise the importance of older adults retaining a greater number of teeth, not only for obvious benefits on oral functions such as mastication and speech, but also to have better social relationships and thus reap the benefits associated with social participation.

The mechanism that explains our findings is straightforward and intuitive. Teeth play an important role in social interactions such as smiling, speaking, eating, and maintaining facial aesthetics.28 As a result, tooth loss would naturally lead to a reluctance to engage in social activities. A recent cross sectional study by Koyama et al.29 examined the association between the number of teeth and social isolation among older adults using data from Japan and England. They found that having fewer teeth was significantly associated with being socially isolated in both countries. Although Koyama et al. investigated a different outcome (i.e., social isolation), the mechanism between the number of teeth and social isolation may be similar to that of current study. We believe that our study’s estimates, which were based on longitudinal data and a robust causal inference methodology, add compelling evidence to the link between oral health and social participation/interactions.

This study has several strengths. We employed a powerful yet underutilised LMTP approach to define causal effects without needing to dichotomise the number of teeth variable. The LMTP approach naturally satisfied the positivity assumption30 (i.e., all people had a non-zero probability of obtaining a specific exposure level) in defining causal effects since it could shift each individual’s observed number of teeth level to any defined level at any time point. Furthermore, by using doubly robust TMLE to estimate the corresponding statistical parameters, we were able to minimise parametric modeling assumptions.11 Traditionally, causal estimates could only be obtained by contrasting conterfactual outcomes at the exposure’s extremes (due to forced binary exposures). In this study, for example, a traditional method would have only allowed us to estimate the difference between the counterfactual outcomes of being edentate versus having teeth, or having 20 or more teeth versus having less than 20 teeth. However, using LMTP/TMLE to estimate counterfactual outcomes across the entire spectrum of exposure, we were able to detect a gradual increase in social participation at each level of improvement in the number of teeth (Figure 3-a). Additionally, the TMLE estimate under the observed level of number of teeth could be contrasted against counterfactual outcomes under hypothetical exposure levels to estimate the expected change in mean population outcome for each one of these scenarios (Figure 3-b).

Our analysis has several limitations, some of which may lead to biased estimates. First, the variables were self-reported, therefore prone to measurement and classification errors. Previous studies in Japan, however, demonstrated the validity of the self-reported number of teeth measure.31,32 Second, causal inference for time-varying exposure necessitates no unmeasured confounding assumption at each time point (conditional exchangeability assumption)33. Therefore, despite adjusting for multiple time-varying and time-invariant confounders, as well as baseline levels of social participation, the possibility of unmeasured confounding cannot be completely ruled out (E-values for all point estimates are reported in Table 2 to reflect the potential effect of unmeasured confounding).34 Third, we used panel data with older participants who took part in all three waves of the JAGES. Therefore, we had considerable attrition of our sample population within six years (n=52,053 at baseline to n=24,872 in 2016 follow-up). To minimise bias due to attrition, we included censored participants’ information in our analysis to obtain estimates controlled for censoring. Additionally, we examined the baseline characteristics and found that censoring was associated with a lower number of teeth at baseline (Supplementary Table 1). As having fewer teeth had a negative impact on social participation, any selection bias caused by attrition would have resulted in an underestimation of the effect of number of teeth on social participation. Future research should focus on aspects our study was unable to address due to lack of available data. We were unable to assess the quality of social interactions, which is just as important in obtaining the health benefits associated with social participation. Furthermore, we had no information on the location of missing teeth in the mouth. Missing anterior teeth could have a greater impact on facial aesthetics and speech, whereas missing posterior teeth (molars and premolars) could have a greater impact on masticatory function. Such information could further help refine interventions to improve oral health and contribute to higher levels of social participation.

## Conclusions

Our findings provide robust causal evidence that having a higher number of teeth, and in particular maintaining a functional dentition, positively affects social participation among Japanese older adults, while being edentate or having relatively fewer teeth negatively affects their social participation. This emphasises the importance of incorporating tooth loss prevention into interventions aimed at increasing social participation among older adults. Our findings also indicated that increasing the number of teeth leads to improved social participation, highlighting the potential impact of effective dental prosthetic treatments to restore missing teeth.

## References

1. Levasseur M, Richard L, Gauvin L, Raymond É. Inventory and analysis of definitions of social participation found in the aging literature: Proposed taxonomy of social activities. *Social science & medicine*. Elsevier; 2010;**71**(12):2141–2149.

2. Golinowska S, Groot W, Baji P, Pavlova M. Health promotion targeting older people. *BMC Health Services Research*. Springer Science; Business Media LLC; 2016 Aug;**16**(S5).

3. Wanchai A, Phrompayak D. Social participation types and benefits on health outcomes for elder people: A systematic review. *Ageing International*. Springer Science; Business Media LLC; 2018 Nov;**44**(3):223–233.

4. Dahan-Oliel N, Gelinas I, Mazer B. Social participation in the elderly: What does the literature tell us? *Critical Reviews™ in Physical and Rehabilitation Medicine*. Begel House Inc.; 2008;**20**(2).

5. Saito M, Aida J, Kondo N, et al. Reduced long-term care cost by social participation among older japanese adults: A prospective follow-up study in JAGES. *BMJ Open*. BMJ; 2019 Mar;**9**(3):e024439.

6. Cornwell EY, Waite LJ. Measuring social isolation among older adults using multiple indicators from the NSHAP study. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*. Oxford University Press (OUP); 2009 Jun;**64B**(Supplement 1):i38–i46.

7. Griffin SO, Jones JA, Brunson D, Griffin PM, Bailey WD. Burden of oral disease among older adults and implications for public health priorities. *American Journal of Public Health*. American Public Health Association; 2012 Mar;**102**(3):411–418.

8. Takeuchi K, Aida J, Kondo K, Osaka K. Social participation and dental health status among older japanese adults: A population-based cross-sectional study. Glogauer M, editor. *PLoS ONE*. Public Library of Science (PLoS); 2013 Apr;**8**(4):e61741.

9. Rouxel P, Tsakos G, Demakakos P, Zaninotto P, Chandola T, Watt RG. Is social capital a determinant of oral health among older adults? Findings from the english longitudinal study of ageing. Divaris K, editor. *PLOS ONE*. Public Library of Science (PLoS); 2015 May;**10**(5):e0125557.

10. Aida J, Kuriyama S, Ohmori-Matsuda K, Hozawa A, Osaka K, Tsuji I. The association between neighborhood social capital and self-reported dentate status in elderly Japanese–the Ohsaki Cohort 2006 Study. *Community Dent Oral Epidemiol*. 2011 Jun;**39**(3):239–249.

11. Dı́az I, Williams N, Hoffman KL, Schenck EJ. Nonparametric causal effects based on longitudinal modified treatment policies. *Journal of the American Statistical Association*. Informa UK Limited; 2021 Sep;1–16.

12. Höfler M. Causal inference based on counterfactuals. *BMC Medical Research Methodology*. 2005 Sep 13;**5**(1).

13. Laan MJ van der, Rose S. Targeted learning in data science. Springer International Publishing; 2018.

14. Schuler MS, Rose S. Targeted Maximum Likelihood Estimation for Causal Inference in Observational Studies. *American Journal of Epidemiology*. 2016 Dec 9;**185**(1):65–73.

15. Kondo K, Rosenberg M, WHO. Advancing universal health coverage through knowledge translation for healthy ageing: Lessons learnt from the japan gerontological evaluation study. World Health Organization; 2018.

16. Shiba K, Torres JM, Daoud A, et al. Estimating the Impact of Sustained Social Participation on Depressive Symptoms in Older Adults. *Epidemiology*. 2021 Jun 21;**32**(6):886–895.

17. Gotfredsen K, Walls AWG. What dentition assures oral function? *Clinical Oral Implants Research*. 2007 Jun;**18**:34–45.

18. Van Der Laan MJ, Rubin D. Targeted maximum likelihood learning. *The international journal of biostatistics*. De Gruyter; 2006;**2**(1).

19. Laan MJ van der, Gruber S. Targeted minimum loss based estimation of causal effects of multiple time point interventions. *The international journal of biostatistics*. De Gruyter; 2012;**8**(1).

20. Laan MJ van der, Polley EC, Hubbard AE. Super learner. *Statistical Applications in Genetics and Molecular Biology*. Walter de Gruyter GmbH; 2007 Jan;**6**(1).

21. Rose S, Rizopoulos D. Machine learning for causal inference in biostatistics. *Biostatistics*. Oxford University Press (OUP); 2019 Nov;**21**(2):336–338.

22. Schomaker M, Luque-Fernandez MA, Leroy V, Davies MA. Using longitudinal targeted maximum likelihood estimation in complex settings with dynamic interventions. *Statistics in Medicine*. Wiley; 2019 Aug;**38**(24):4888–4911.

23. Venables WN, Ripley BD. Modern applied statistics with s. Fourth. New York: Springer; 2002.

24. Chen T, Guestrin C. XGBoost: A scalable tree boosting system. *Proceedings of the 22nd ACM SIGKDD international conference on knowledge discovery and data mining*. New York, NY, USA: Association for Computing Machinery; 2016.

25. Shah AD, Bartlett JW, Carpenter J, Nicholas O, Hemingway H. Comparison of Random Forest and Parametric Imputation Models for Imputing Missing Data Using MICE: A CALIBER Study. *American Journal of Epidemiology*. 2014 Jan 12;**179**(6):764–774.

26. Buuren S van, Groothuis-Oudshoorn K. mice: Multivariate Imputation by Chained Equations inR. *Journal of Statistical Software*. 2011;**45**(3).

27. Williams NT, Díaz I. Lmtp: Non-parametric Causal Effects of Feasible Interventions Based on Modified Treatment Policies. 2020.

28. Steele JG, Sanders AE, Slade GD, et al. How do age and tooth loss affect oral health impacts and quality of life? A study comparing two national samples. *Community Dentistry and Oral Epidemiology*. 2004 Apr;**32**(2):107–114.

29. Koyama S, Saito M, Cable N, et al. Examining the associations between oral health and social isolation: A cross-national comparative study between Japan and England. *Social Science & Medicine*. 2021 May;**277**:113895.

30. Petersen ML, Porter KE, Gruber S, Wang Y, Laan MJ van der. Diagnosing and responding to violations in the positivity assumption. *Statistical Methods in Medical Research*. 2010 Oct 28;**21**(1):31–54.

31. Matsui D, Yamamoto T, Nishigaki M, et al. Validity of self-reported number of teeth and oral health variables. *BMC Oral Health*. 2016 Jul 15;**17**(1).

32. Ueno M, Ohara S, Inoue M, Tsugane S, Kawaguchi Y. Association between education level and dentition status in Japanese adults: Japan public health center-based oral health study. *Community Dentistry and Oral Epidemiology*. 2012 Apr 27;**40**(6):481–487.

33. Hernan MA. Estimating causal effects from epidemiological data. *Journal of Epidemiology & Community Health*. 2006 Jul 1;**60**(7):578–586.

34. VanderWeele TJ, Ding P. Sensitivity Analysis in Observational Research: Introducing the E-Value. *Annals of Internal Medicine*. 2017 Jul 11;**167**(4):268.

## List of figure and table legends:

Figure 1. Flow of participants during the 6 year follow-up

Figure 2. Directed acyclic graph showing hypothesised temporal associations between study variables

Figure 3. Shows the variation of estimates with and without Super learner. (3-a) shows odds ratios and 95% confidence interval when the reference was TMLE estimate related to edentate state. (3-b) shows shows odds ratios and 95% confidence interval when the reference was TMLE estimate related to observed number of teeth state.

Table 1.

Table 2.