# The Clustering Effects of Surfaces within the Tooth and Teeth within Individuals

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### **Abstract**

The objectives of this study were I) to provide an estimate of the value of the intraclass correlation coefficient (ICC) for dental caries data at tooth and surface level, 2) to provide an estimate of the design effect (DE) to be used in the determination of sample size estimates for future dental surveys, and 3) to explore the usefulness of multilevel modeling of cross-sectional survey data by comparing the model estimates derived from multilevel and single-level models. Using data from the United Kingdom Adult Dental Health Survey 2009, the ICC and DE were calculated for surfaces within a tooth, teeth within the individual, and surfaces within the individual. Simple and multilevel logistic regression analysis was performed with the outcome variables carious tooth or surface. ICC estimated that 10% of the variance in surface caries is attributable to the individual level and 30% of the variance in surfaces caries is attributable to variation between teeth within individuals. When comparing multilevel with simple logistic models,  $\beta$  values were 4 to 5 times lower and the standard error 2 to 3 times lower in multilevel models. All the fit indices showed multilevel models were a better fit than simple models. The DE was 1.4 for the clustering of carious surfaces within teeth, 6.0 for carious teeth within an individual, and 38.0 for carious surfaces within the individual. The ICC for dental caries data was 0.21 (95% confidence interval [CI], 0.204–0.220) at the tooth level and 0.30 (95% CI, 0.284–0.305) at the surface level. The DE used for sample size calculation for future dental surveys will vary on the level of clustering, which is important in the analysis—the DE is greatest when exploring the clustering of surfaces within individuals. Failure to consider the effect of clustering on the design and analysis of epidemiological trials leads to an overestimation of the impact of interventions and the importance of risk factors in predicting caries outcome.

**Keywords:** dental public health, caries, statistics, intra-class correlation coefficient (ICC), design effect (DE), multilevel modeling

## Introduction

Epidemiological data are often clustered (hierarchical or nested) in nature; a simple example of clustered data is where students are clustered within a class and classes clustered within schools. This situation is a 3-level data structure, the first level being the students, the second level being the classes, and the third level being the schools. In broader scenarios, clustering can be seen in any setting, for example, in social settings (e.g., individuals  $\rightarrow$  families  $\rightarrow$  neighborhoods) or in geographical settings (e.g., wards  $\rightarrow$  cities  $\rightarrow$  counties  $\rightarrow$  countries). In addition, in longitudinal studies or clinical trials, clustering appears due to aggregates of individuals or repeated measurement of the same subject (Masood, Yusof, et al. 2012a, 2012b; Fleming et al. 2013). However, in dental research, a special type of natural clustering is encountered, where surfaces are clustered within teeth and teeth clustered within individuals. However, frequently in dental research, the surface or tooth is taken as the unit of analysis and the clustering structure of surfaces  $\rightarrow$  teeth  $\rightarrow$  individuals is ignored, and thus each surface or

tooth is treated as an independent observation. This independence of observations treats 5 teeth from 20 patients (i.e., 100 observations) as equivalent to observations of 1 tooth from 100 patients. However, outcomes such as caries experience are likely to be more closely correlated within

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A supplemental appendix to this article is published electronically only at http://jdr.sagepub.com/supplemental.

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clusters than between them. For example, the magnitude of caries risk is likely to be more comparable for different teeth within the same individual than would be the case between separate individuals (Hannigan and Lynch 2013).

When the within-cluster correlation or intraclass correlation coefficient (ICC) is very small (i.e., observations within the cluster are almost independent), the impact of the clustering on analysis can be ignored. However, where the ICC is high, the impact of clustering is likely to be much greater. Therefore, the degree to which statistical analysis should be modified as a result of clustering can be assessed by examining the estimated within-cluster correlation or ICC of different clusters. The ICC measures the similarity among outcome observations within the same cluster compared with that among observations in different clusters. The information contributed by each cluster in data analysis is inversely proportional to the ICC of the observations (Kerry and Bland 1998; Eldridge et al. 2006). Clustering of data has 2 important implications for the design and analysis of studies: a design effect (DE) whereby the sample size calculation is adjusted to account for clustering and the analytical methods selected to adjust estimates for clustering effects (Fleming et al. 2013).

Higher ICC values necessitate an increase in the required sample size in a clustered survey to maintain power analogous to a nonclustered survey. This increase in sample size can be determined by the DE, which is related to the ICC. The DE must be considered in the planning of oral health studies to ensure adequate statistical power. The DE is the ratio of the sample size required for a clustered design to that required for a design with independent samples to achieve the same power. For example, to obtain equal statistical power, a clustered design with DE = 2 requires twice as many observations as a nonclustered design. To calculate the sample size needed for a study, the DE for the anticipated cluster sizes and ICC must be considered. In study designs with more than one level (e.g., 3 levels in surfaces  $\rightarrow$  teeth  $\rightarrow$  individuals) of clustering, separate estimates of ICC and DE can be calculated for each level of clustering and used sequentially to adjust the required sample size (Litaker et al. 2013).

Clustered dental data are often analyzed by using classic statistical techniques, which are mostly based on the assumption of independent observations. Because observations within clusters violate the assumption of independence, these methods may not be appropriate (Litaker et al. 2013). For example, using classic regression approaches in analyzing clustered data results in biased regression estimates and standard errors (Loc Giang et al. 2011; Mamai-Homata et al. 2012). Therefore, if there is a significant correlation between the observations (i.e., a high ICC), the possibility of a type I error increases (Burnside et al. 2007, 2013). One alternative is to ignore clustering by undertaking a separate analysis for each subject—such an approach reduces the number of

observations considerably in each analysis, leading to an increased risk of type II errors. The most appropriate method of analysis for clustered data is multilevel modeling, which accounts for the correlation between clusters by modeling intercepts and regression coefficients as random (Diez Roux 2002). Caries data naturally fall into a 3-level structure, with the individual participant as the top or level 3 unit, tooth as the level 2 unit, and surface as the level 1 unit. Multilevel models work by splitting the variance in outcome into components for each level of the model, so random effects at tooth and participant levels are estimated in the modeling process. These random effects are assumed to follow a normal distribution with a mean of 0 and a variance that is estimated in the modeling process. Simulation studies have shown that parameter estimates are fairly robust to violations of this assumption (Burnside et al. 2007).

To date, multilevel models have not been used for the analysis of caries data from epidemiological surveys, and thus the potential of multilevel modeling to enhance efficiency and understanding of the risk factors is unknown. Therefore, there are 3 objectives of this study: 1) to provide an estimate of the value of the ICC for dental caries data at the tooth and surface levels, 2) to provide an estimate of the DE to be used in the determination of sample size estimates for future dental surveys, and 3) to explore the usefulness of multilevel modeling of cross-sectional survey data by comparing the model estimates derived from multilevel and single-level models of the same data.

## **Methods**

Data from United Kingdom Adult Dental Health Survey 2009 (ADHS) were analyzed. A description of the ADHS is provided in the Appendix. The outcome variable was caries experience at the surface or tooth level. We recoded each tooth or surface as 0 for sound or 1 for carious or restored. Missing surfaces or teeth were excluded from the analysis as the reason for the missing surface or tooth was not known—assuming that they were missing as a result of caries would overestimate the ICC. This excluded 19,025 of 180,889 teeth (10.5%) and 98,612 of 904,400 surfaces (10.9%).

There are various methods available to calculate ICC for a binary outcome, as discussed by Wu et al. (2012) for randomized controlled trials and Fenn et al. (2004) for cross-sectional survey data. The ICC estimation from the random intercept logistic method suggested by Wu et al. has some limitations. In most cases, this method substantially overestimates the ICC values. Therefore, we used the formula suggested by Fenn et al. for cross-sectional survey data.

$$ICC = \frac{\sigma_b^2}{\sigma_x^2},$$

Equation 1 (Donald and Donner 1987; Fenn et al. 2004)

$$ICC = \frac{\sigma_b^2}{\pi(1-\pi)},$$

Equation 2 (Donald and Donner 1987; Fenn et al. 2004) where  $\sigma_b^2$  is the between-cluster variance of the outcome variable. For binary outcome measures,  $\sigma_x^2 = \pi(1-\pi)$ , where  $\pi$  is the average cluster-specific proportion.

Multilevel logistic regression was used to produce an estimate of the ICC using a model that contains no explanatory variables, the so-called intercept-only model or null model. This model partitions the variance in the outcome variable into 2 independent components:  $\sigma_b^2$  and  $\sigma_w^2$ . Three null models—model N<sub>1</sub> (surfaces within a tooth), model N<sub>2</sub> (teeth within individual), and model N<sub>3</sub> (surfaces within individual)—were used to calculate the 3 ICC values using equations 1 and 2 (Diez Roux 2002). The sampling distribution of the variance estimates in multilevel logistic regression models is, in general, strongly asymmetric. Therefore, the standard error (SE) may be a poor characterization of the distribution, and confidence intervals (CIs) derived from the SE are likely to be unrepresentative of the data (Wu et al. 2012). Given this difficulty, we estimated the 95% CI of the ICC and DE by using "bootstrapping"—a technique for generating a description of the sampling properties of empirical estimators using random sampling with replacement from the original data set (Hox 2010).

The relationship between DE, cluster size, and ICC is represented in the following equation:

$$DE = 1 + (m-1).ICC$$
,

Equation 3 (Fenn et al. 2004)

where DE is the design effect, and m is the average number of respondents per cluster, or average cluster size.

First, we performed an analysis for teeth clustered within individuals; the outcome variable was caries at the tooth level and took the value 0 if the tooth did not have caries and 1 if it had caries. The first model, model 0, was a simple logistic regression with no multilevel structure. This model was fitted only as a baseline for comparison with later model 1. The next model, model 1, was the 2-level model, allowing clustering of the teeth within individuals (Gilthorpe et al. 2000).

Second, the analysis of surfaces within teeth and teeth within individuals was performed; the outcome variable was caries at the surface level, which took the value 0 if the surface did not have caries and 1 if it had caries. Model 0 was a simple logistic regression with no multilevel structure and formed the point of comparison for model 1, model 2, and model 3. Model 1 and model 2 were 2-level models, model 1 incorporated clustering of the surface within teeth, and model 2 incorporated clustering of the surfaces within individuals. Finally, model 3 was a 3-level model allowing clustering of the surface within teeth and teeth within individuals (Gilthorpe et al. 2000).

All analyses were performed with R software; for multilevel analysis, the lme4-package of R software was used (Bates et al. 2014). For each model, a set of explanatory variables was included comprising age, sex, educational qualification, brushing, sugar intake, and use of fluoridated toothpaste. See the Appendix for the description of all these variables. All explanatory variables were modeled at the same level as the outcome variable in model 0 and model 0 since they were simple logistic regression models. However, in model 1, model 1, model 2, and model 3, the explanatory variables were modeled at the individual level (i.e., at level 2 in 2-level models and at level 3 in 3-level models). Regression estimates (β), SE, and level of significance were compared for all the models. Model fit was assessed by examining various fit indices: Akaike information criterion (AIC), Bayesian information criterion (BIC), deviance, -2 log-likelihood, and the chi-square test (Burnside et al. 2007, 2013).

# **Results**

A total of 6,469 dentate adults were examined for dental caries; 9 individuals had only 1 tooth and were therefore excluded from the clustered analyses. The final sample size included 6,460 individuals, 161,855 teeth, and 805,788 surfaces. The mean number of teeth per person was 25.0, with an average of 4.97 surfaces per tooth and 124.5 surfaces per individual. Table 1 gives the descriptive analysis of all variables at the individual, tooth, and surface levels.

Table 2 displays the ICC and DE for teeth within individuals, surfaces within teeth, and surfaces within individuals. All values of the ICC are greater than 0.1, with the highest ICC being that for surfaces clustered within the individual. The most obvious feature of the results is the inverse relation between cluster size and ICC. For larger cluster sizes, even small ICCs might be associated with a substantial DE that should not be ignored in designing studies. The ICC estimate shows that 21% of the variance can be attributed to variation between individuals, 10% of the variance in surface caries is attributable to the individual level, and 30% of the variance in surface caries is attributable to variation between teeth within individuals.

Table 3 shows the values of  $\beta$ , SE( $\beta$ ) for models 0, and model 1, and the ratio of coefficients and SE for model 0, model 1. Both models show a significant positive relationship of caries with older age, being female, higher educational qualification, and high sugar intake. Significant negative relationships exist between caries and brushing frequency, as well as fluoride usage. The relationship between caries and fluoride usage was not significant in the multilevel analysis for the category of 1,000 to 1,300 parts per million (ppm). If we consider only those results where  $P \le 0.01$ , the relationship becomes insignificant for all the fluoride categories. Comparing the multilevel model with

Table 1. Descriptive Analysis of Data at Individual, Tooth, and Tooth Surface Levels.

	Individual (n = 6,469), n (%)	Teeth (n = 161,855), n (%)	Surfaces $(n = 805,788), n (\%)$		
Age, y					
16 <del>-44</del>	2,837 (43.86)	79,606 (49.18)	396,397 (49.19)		
45–64	2,355 (36.4)	57,678 (35.64)	287,114 (35.63)		
65 and older	1,277 (19.74)	24,571 (15.18)	122,277 (15.17)		
Sex					
Male	2,961 (45.77)	73,795 (45.59)	367,242 (45.58)		
Female	3,508 (54.23)	88,060 (54.41)	438,546 (54.42)		
Educational qualification					
No	1,499 (23.17)	31,999 (19.77)	159,151 (19.75)		
Yes	4,966 (76.77)	129,766 (80.17)	646,192 (80.19)		
Brushing frequency					
<once a="" day<="" td=""><td>181 (2.80)</td><td>3,897 (2.41)</td><td>19,354 (2.40)</td></once>	181 (2.80)	3,897 (2.41)	19,354 (2.40)		
Once a day	1,450 (22.41)	34,617 (21.39)	172,365 (21.39)		
≥Twice or more a day	4,823 (74.56)	122,994 (75.99)	612,340 (75.99)		
Sugar intake					
Low	3,256 (50.33)	81,099 (50.11)	402,109 (49.90)		
High	3,213 (49.67)	80,756 (49.89)	403,679 (50.10)		
Toothpaste fluoride concentra	tion, ppm				
≤550	996 (15.40)	24,562 (15.18)	122,267 (15.17)		
1,000-1,300	1,061 (16.40)	26,591 (16.43)	132,404 (16.43)		
1,350–1,500	4,351 (67.26)	109,434 (67.61)	544,819 (67.61)		
Carious tooth					
No	4,543 (70.2)	106,863 (66.02)	_		
Yes	1,926 (29.8)	54,992 (33.98)	_		
Carious surface	, ,	, ,			
No	4,543 (70.2)	<del>_</del>	667,478 (82.84)		
Yes	1,926 (29.8)	_	138,310 (17.16)		

<sup>—,</sup> blank.

Table 2. ICC and Design Effect for Various Oral Health-Related Outcome Variables.

	$Model\;N_{_{I}}$	Model $N_{_2}$	Model $N_3$		
Outcome	Carious tooth = Yes/No	Carious surface = Yes/No	Carious surface = Yes/No		
Clustering	Individual	Tooth	Individual		
Number of individuals	6,469	_	6,469		
Number of teeth	161,855	161,855	_		
Number of surfaces	<del>_</del>	805,788	805,788		
Average cluster size	25.0	4.97	124.5		
Individual-level variance (SD)	0.047 (0.216)	_	0.029 (0.170)		
Tooth-level variance (SD)	<u>-</u>	0.015 (0.121)	<u> </u>		
Residual variance (SD)	0.179 (0.423)	0.104 (0.323)	0.104 (0.323)		
Average proportion (π)	0.34	0.17	0.11		
ICC (95% CI)	0.21 (0.204-0.220)	0) 0.10 (0.063–0.159) 0.30 (0.284–			
DE (95% CI)	6.04 (5.89–6.30)	1.40 (1.24–1.59)	38.0 (36.85–39.11)		

Cl, confidence interval; DE, design effect; ICC, intraclass correlation coefficient; SD, standard deviation; —, blank.

the simple logistic model, values of  $\beta$  were 4 to 5 times lower and the SE( $\beta$ ) 2.3 times lower in multilevel models. All the fit indices suggested that the multilevel models were a better fit than the standard regression models.

Table 4 describes the results of the multivariate regression analysis of caries at the surface level, showing a simple logistic regression (model  $0_s$ ), a 2-level multilevel model where surfaces were clustered within individuals (model

**Table 3.** Multivariate Regression Analysis of Carious Teeth as an Outcome Variable, Showing Results of Simple Logistic Regression (Model  $0_t$ ), Multilevel Model (Model  $I_t$ ) (Level I = Tooth; Level 2 = Individual), and Ratio of Regression Coefficients ( $\beta_r$ ) and Standard Error (SE).

	$Model\ 0_{_{_{t}}}$		Mode	el I <sub>t</sub>	Ratio of Model 0, Model 1,				
	β	SE	β	SE	$\beta_r$	SE			
Fixed Effect					<u> </u>	· ·			
Age, y									
16 <del>–44</del>	Reference group								
45–64	1.15	0.012***	2*** 0.245 0.0054***		4.7	2.2			
65 and older	1.38	0.016***	0.294	0.0070***	4.7	2.3			
Sex									
Male	Reference group 0.10 0.011*** 0.019 0.005*** 5.3								
Female	0.10	0.011***	0.019	0.005***	5.3	2.2			
Education qualification									
No		Reference group							
Yes	0.14	0.014***	0.034	0.0061***	4.1	2.3			
Brushing frequency									
<once a="" day<="" td=""><td></td><td></td><td>Reference</td><td>e group</td><td></td><td></td></once>			Reference	e group					
Once a day	-0.238	0.040***	-0.056	0.017**	4.3	2.3			
≥Twice or more a day	-0.226	0.039***	-0.054	0.017**	4.2	2.3			
Sugar intake									
Low			Reference	e group					
High	0.06	0.011***	0.015	0.0047**	4.0	2.3			
Toothpaste fluoride concenti	ration, ppm								
≤550	• • • • • • • • • • • • • • • • • • • •		Reference	e group					
1,000-1,300	-0.056	0.019**	-0.014	0.0085	4.0	2.2 <sup>a</sup>			
1,350-1,500	-0.064	0.015***	-0.015	0.0068*	4.2	2.2 <sup>b</sup>			
Random Effect									
Individual	_	_	0.02956	0.171					
Residual	_		0.1787	0.422					
Model Fit									
AIC	192,825		189,089.1						
BIC	192,924.9		189,208.9						
Deviance	193	2,805	189,065.1						
–2 Log-likelihood	<b>–96</b> ,	402.52	<b>-94,53</b>	2.56***					

AIC, Akaike information criterion; BIC, Bayesian information criterion; —, blank.

 $1_s$ ), a 3-level multilevel model where surfaces were clustered within teeth and teeth were clustered within individuals (model  $2_s$ ), and the ratio of regression coefficients ( $\beta_r$ ) and standard error (SE $\beta_r$ ). All models again showed a significant positive relationship between having carious surfaces and older age, being female, higher educational qualification, and high sugar intake. Similarly, both models found a significant negative relationship between caries at the surface level and brushing frequency and fluoride usage. However, if we consider only  $P \le 0.01$ , the relationship between caries at the surface level and fluoride intake becomes insignificant.

# **Discussion**

The first aim of this report was to investigate the degree to which caries experience is correlated between teeth in the same mouth and across surfaces on the same tooth. A significant amount of the variability in caries experience at the surface level was explained by being on the same tooth—caries on the surfaces of the same tooth is more highly correlated than surfaces from different teeth. Similarly carious teeth in the same individual are more highly clustered than caries in different individuals. Thus, caries levels in the same individual or the same tooth are more correlated than

<sup>&</sup>lt;sup>a</sup>Significantly different at  $P \leq 0.05$ .

<sup>&</sup>lt;sup>b</sup>Significantly different at  $P \le 0.01$ .

 $<sup>*</sup>P \le 0.05. **P \le 0.01. ***P \le 0.001.$ 

**Table 4.** Multivariate Logistic Regression Analysis of Carious Surfaces as an Outcome Variable, Showing Results of Simple Logistic Regression (Model 0), 2-Level Multilevel Model (Model 1) (Level I = Surfaces; Level 2 = Individual), 3-Level Multilevel Model (Model 2) (Level I = Surfaces; Level 2 = Tooth; Level 3 = Individual), and Ratio of Regression Coefficients ( $\beta$ ) and Standard Error (SE).

	Model 0 <sub>s</sub>		Model I <sub>s</sub>		Model 2 <sub>s</sub>		Ratio of Model 0 / Model I s		Ratio of Model 0 / Model 2 s	
	β	SE	β	SE	β	SE	$\beta_{r}$	SE <sub>r</sub>	$\beta_r$	SE <sub>r</sub>
Fixed Effect										
Age, y										
16-44					Reference	e group				
45–64	1.20	0.007***	0.157	0.004***	0.169	0.004***	7.6	1.8	7.1	1.8
65 and older	1.45	0.009***	0.197	0.005***	0.230	0.005***	7.4	1.4	6.3	1.4
Sex										
Male					Reference	e group				
Female	0.10	0.006***	0.012	0.004**	0.012	0.004***	8.3	1.5	8.3	1.5
Education qualification										
No .					Reference	e group				
Yes	0.15	0.008***	0.026	0.004***	0.013	0.005**	5.8	2.0	11.5	1.6
Brushing frequency										
<once a="" day<="" td=""><td></td><td></td><td></td><td></td><td>Reference</td><td>e group</td><td></td><td></td><td></td><td></td></once>					Reference	e group				
Once a day	-0.29	0.021***	-0.052	0.012***	-0.053	0.012***	5.6	1.8	5.5	1.8
≥Twice a day	-0.28	0.021***	-0.049	0.012***	-0.056	0.012***	5.7	1.8	5.0	1.8
Sugar intake										
Low					Reference	e group				
High	0.09	0.006***	0.014	0.004***	0.016	0.0036***	6.4	1.5	5.6	1.7
Toothpaste fluoride cor	ncentratio	n, ppm								
≤550					Reference	e group				
1,000-1,300	-0.08	0.010***	-0.014	0.006*	-0.013	0.006*	5.7	1. <b>7</b> ª	6.2	1.7 <sup>a</sup>
1,350-1,500	-0.07	0.008***	-0.013	0.005**	-0.012	0.005*	5.4	1.6	5.8	1.6ª
Random Effect										
Individual		_	0.0182	0.1349	0.0191	0.138	_	_	_	_
Tooth		_	_	_	0.0147	0.121	_	_	_	_
Residual		_	0.1188	0.3447	0.1038	0.322	_	_	_	_
Model Fit										
AIC	68	8,820	583	,111.5	477	,469.3	_	_	_	_
BIC	688,935.7		583,250.6		477,619.9		_	_	_	_
Deviance	688	3,799.8	583	,087.5		,443.3	_	_	_	_
–2 Log-likelihood		4,399.9		1,543.8		8,721.6	_		_	_

AIC, Akaike information criterion; BIC, Bayesian information criterion; —, blank.

dental caries measured in different individuals or different teeth. These findings have significant implications for the modeling of dental caries, in that ignoring within-individual or within-tooth correlation could result in biased regression estimates and standard errors. The regression models with and without consideration of the intraclass correlation compared in this study quantify the extent of this bias in estimates of regression statistics (Gunsolley et al. 1994; Chuang et al. 2005).

The effect of clustering on sample size requirements can be substantial, especially for large cluster sizes. Failure to account for clustering typically leads to an underestimation of the required sample size. If the cluster size is large, even low values of ICC have a considerable impact, for example, in the case of surfaces clustered in an individual. It is also important to note that for dichotomous variables such as caries experience (yes or no), the ICC varies with the prevalence of the outcome, tending to increase with higher prevalence (Litaker et al. 2013). Therefore, the DE values identified in this study should be considered in the light of the prevalence of the carious tooth and carious surfaces in this sample (Table 1), as suggested by Gulliford (2005).

The ICC is a portable parameter that can be compared across studies since it does not depend on the cluster size or

<sup>&</sup>lt;sup>a</sup>Significantly different at  $P \le 0.01$ .

 $<sup>*</sup>P \le 0.05$ .  $**P \le 0.01$ .  $***P \le 0.001$ .

on the numbers of clusters. The DE, on the other hand, is affected by the sample design and is strongly dependent on cluster size (Fenn et al. 2004). Therefore, not only DE but also ICC should be considered for accurate sample size calculation for future studies (Litaker et al. 2013).

This study has shown a substantial difference between the estimated power of multilevel models and classic regression analysis. Traditional regression analysis is known to overestimate the beneficial effects of interventions where clustering is present (Shaffer et al. 2013; Masood and Reidpath 2014). In this analysis, we used fluoridation and frequency of brushing as examples of preventive measures: simple regression analysis ascribes a nearly 6 times greater beneficial effect to such interventions than 2- or 3-level multilevel analysis. It was interesting to see that if we require more precise results with a P value of 0.01, then the preventive effect of fluoride becomes insignificant in multilevel models. Similarly, traditional analysis also overestimates the effect of risk factors; in this analysis, the effect of sugar consumption on dental caries was nearly 6 times higher in the classic logistic regression than in the 2- and 3-level multilevel analysis (Chuang et al. 2001; Masood, Masood, et al. 2012). Although this was not an objective for this study, it is important to discuss the unexpected positive relationship between educational qualification and caries. There could be 2 possible reasons for this relationship: 1) the educational qualification was coded as "yes" or "no," which might not capture the education effect well, and 2) the outcome was whether or not the tooth or surface was sound or carious/restored. Education may be related to restoration via use of dental services.

There may be a number of reasons why an investigator or health care provider would be interested in the multilevel analysis of caries data, especially for preventive agents or treatments at different levels. Multilevel modeling offers the advantage of allowing greater understanding of the patterns of caries development within the mouth since it allows estimates to be made of the relative variance at individual, tooth, and surface levels (Burnside et al. 2007). Therefore, investigators who are interested in exploring the effect of their intervention in more detail may wish to consider the use of multilevel modeling (Burnside et al. 2013). The ability to quantify relative treatment effect sizes at the tooth level may be important when dental caries presents more commonly on different tooth types, for example, the relative benefit of fluoride varnish on molars and incisors. Investigators may also need to measure the comparative benefit at the surface level, or level 1 (e.g., being able to determine whether a preferential benefit is found on fissures compared with smooth surfaces).

It should be noted that although the results are based on a large sample size, the data set comprises a sample of the population of UK adults with a particular disease level, and the results may vary in populations with higher or lower levels of caries. Younger age groups will certainly show different patterns due to the different teeth present, deciduous teeth in very young children, and a mixture of deciduous and permanent teeth in older children. The finding of differing probabilities of caries according to differing tooth types, with molars most susceptible, is well established (Reidpath et al. 2014). The current work indicates that the advantages of multilevel modeling in dental caries may lie in a greater understanding of the data structure and within-mouth patterns of caries development, rather than a reduction in required sample sizes (Hannigan and Lynch 2013). In addition to the hierarchy reported here, further levels of clustering exist in this data set, such as individual  $\rightarrow$  neighborhood  $\rightarrow$  district  $\rightarrow$  county. Data on these clusters were not available in the data set owing to confidentiality issues. Another limitation was the inability to include survey design features in this analysis. Multilevel analysis for logistic regression models incorporating survey design features is not currently available (Thomas Lumley, developer of the survey package in R-project, personal communication [StataCorp 2013]).

### Conclusion

This study has provided estimates of the ICC for dental caries data: 0.21 (95% CI, 0.204–0.220) at the tooth level and 0.30 (95% CI, 0.284–0.305) at the surface level. The DE used for sample size calculation for future dental surveys will vary on the level of clustering, which is important in the analysis—the DE is greatest when exploring the clustering of surfaces within individuals. In such instances, clustering will have a considerable effect on the required sample size. Failure to consider the effect of clustering on the design and analysis of epidemiological trials leads to an overestimation of the impact of interventions and the importance of risk factors in predicting caries outcome.

# **Author Contributions**

M. Masood, contributed to conception, design, data acquisition, analysis, and interpretation, drafted and critically revised manuscript; Y. Masood, contributed to design, data analysis, and interpretation, drafted and critically revised manuscript; T.J. Newton, contributed to data interpretation, critically revised manuscript. All authors gave final approval and agree to be accountable for all aspects of the work.

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