Journal of Clinical Periodontology
Official Journal of The European Federation of Periodontology
Founded by the British, Dutch, French, German, Scandinavian, and Swiss Societies of Periodontology

J Clin Periodontol 2009; 36: 190–197 doi: 10.1111/j.1600-051X.2008.01365.x

Journal of Clinical Periodontology

Tooth loss and osteoporosis: the osteodent study

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Nicopoulou-Karayianni K, Tzoutzoukos P, Mitsea A, Karayiannis A, Tsiklakis K, Jacobs R, Lindh C, van der Stelt P, Allen P, Graham J, Horner K, Devlin H, Pavitt S, Yuan J. Tooth loss and osteoporosis: the osteodent study. J Clin Periodontol 2009; 36: 190–197. doi: 10.1111/j.1600-051X.2008.01365.

Abstract

Aim: To determine the cross-sectional association of the osteoporotic status of patients with the number of their teeth, with and without taking into account age and/or smoking.

Material & Methods: At four centres, the study recruited 665 females aged 45–70 years and the number of teeth was counted for 651 subjects. Bone density was measured at the total hip, femoral neck and lumbar spine.

Results: The mean number of teeth in the osteoporotic subjects was 3.3 fewer than normal subjects and 2.1 fewer if those with no teeth were excluded. The association between osteoporosis and having <6 or having <28 teeth remained significant after adjusting for age, smoking and centre with p-values of 0.016 and 0.011, respectively. A single regression model for tooth count with normal errors would not fit all the data. By fitting mixture regression models to subjects with tooth count >0, three clusters were identified corresponding to different degrees of tooth loss. The overall effect of osteoporosis was as follows: -1.8 teeth before and after adjusting for smoking, -1.2 teeth after adjusting for age, and -1.1 teeth after adjusting for both age and smoking.

Conclusions: We have established a significant association between osteoporosis and tooth loss after adjusting the effect for age and smoking.

Key words: bone mineral density; osteoporosis; tooth loss

Accepted for publication 17 November 2008.

Osteoporosis is one of the commonest of chronic diseases and is a disease in which bone becomes porous and more susceptible to fracture. It is estimated that one in three postmenopausal women and one in five men over the age of 50 years are affected (European Parliament Osteoporosis Interest Group and EU Osteoporosis Consultation Panel 2005). Osteoporosis is a disease that has provoked considerable interest amongst dentists in the context of its possible impact upon periodontal disease, residual alveolar ridge resorption and implant success rates (Hildebolt 1997). In recent years, research has also tried to determine whether dental radiographic evidence of osteopenia may be used as a way of identifying individuals at risk of having osteoporosis (White 2005).

The aetiology of tooth loss is multifactorial, but one particular focus of interest has been whether osteoporosis is a contributory factor. Various researchers have addressed this question, in studies of varying qualities. The weight of the evidence suggests that there is a significant relationship between the number of teeth present and skeletal bone mineral density (BMD) (Krall et al. 1994, 1996, Taguchi et al. 1995, 1999, Drozdzowska et al. 2006), although two studies did not demonstrate relationships (Earnshaw et al. 1998, Taguchi et al. 2004). Similarly, the majority of studies comparing tooth number in osteoporotic and normal subjects showed a smaller number in the former group (Kribbs 1990, Mohammad et al. 2003, Bodic et al. 2005, Yoshihara et al. 2005), although conflicting results have also been reported (May et al. 1995, Mohammad et al. 1997).

From 2003 to 2005, the OSTEODENT multicentre research project was carried out with the aim of identifying the value of a range of dental radiographic and clinical indices for osteoporosis diagnosis in women. As part of this study, subjects underwent a ''gold standard'' assessment of osteoporosis status using dual energy X-ray absorptiometry (DXA), collection of medical and lifestyle information, and a panoramic dental radiographic examination. This large dataset has offered an opportunity to conduct studies beyond the original focus of the OSTEODENT project. The aim of the study reported here was, therefore, to determine whether the osteoporosis sta-

Conflict of interest and source of funding statement

The authors declare that they have no conflicts of interests.
This work was supported by a research and technological development project grant from the European Commission FP5 ''Quality of Life and Management of Living Resources'' (QLK6-2002-02243).

tus of perimenopausal and postmenopausal women was predictive of their number of teeth, independent of their age or smoking status.

Material and Methods

Six hundred and sixty-five women, aged 45–70 years, were recruited into the study in four European centres: Manchester (UK), Leuven (Belgium), Malmo (Sweden) and Athens (Greece). Local ethical approval for the study was obtained at each centre and all subjects gave informed consent before inclusion in the study. Of the 665 subjects, complete data for the osteoporotic status, age and number of teeth were known for 651 and the smoking status for 650 patients.

Subjects were recruited from the patient and staff pool in the vicinity of each institution, using local literature and publicity available at each centre. The group was mainly Caucasian, and insufficient numbers of other racial groups were present for analysis. This methodology tended to recruit a large proportion of health-conscious individuals without osteoporosis, so a stratified sampling procedure was used at one centre to recruit osteoporotic individuals from a metabolic disease clinic. This targeted recruitment involved separate ethics approval to approach patients with osteoporosis diagnosed within the last 6 months and, therefore, with minimal exposure to treatment medication. The final percentage of osteoporotic individuals in the whole sample was representative of other studies that have examined a similar female age group (WHO 1994).

Subjects were asked if they had ever smoked cigarettes and were scored 0 for never having smoked and 1 for having smoking experience. Many factors affect bone metabolism, but information about age and smoking status of each patient was collected because there is evidence that these factors have a strong influence on tooth retention.

The BMD of each subject was measured using DXA performed at three different sites, lumbar spine (L1 to L4), femoral neck and total hip, using DXA. The precision of DXA measurements for a variety of sites and devices has been found to have a range of coefficients of variation equal to 0.5–3% (Simpson & Truscott 2000). These scans were performed on either the Hologic QDR 4500, Hologic Discovery (Hologic Inc., Bedford, MA, USA) or the GE Lunar Prodigy (GE Lunar Corporation, Madison, WI, USA). Standardized *T*-scores were used (according to the WHO criteria for Caucasian women) to classify women in the sample as osteoporotic (*T*-score more than 2.5 SD below the young adult mean BMD) or normal/osteopenic (BMD *T*-score > -2.5 SD). In the data analysis, subjects were classified as osteoporotic if they had osteoporosis at any measurement site, and normal if otherwise.

Dental panoramic radiography was performed on each subject using digital and conventionally processed dental panoramic radiography films. The Leuven and Malmo centres used a Cranex DC3 machine (Soredex, Tuusula, Finland) whereas the Athens and Manchester centres used a Planmeca PM2002CC machine (Planmeca, Oy, Helsinki, Finland).

Tooth counting was done manually using a simple MATLAB® program (The MathWorks Ltd, Cambridge, UK) which displayed each of the images in a designated folder one at a time. For each image, the user was prompted to enter the numbers of incisor, canine, premolar and molar teeth, and the results were written to disc. The observer was blinded as to the patient's skeletal bone mineral status. Roots, impacted teeth and implants were excluded from the data analysis; for inclusion, each tooth had to have at least 3 mm of crown height. Occasionally, buried roots were present but were excluded, as in the study by Bollen et al. (2004). There was no instance of a person with a high caries rate and multiple roots.

Statistical analysis

The distribution of tooth count was studied by examining plots against age and histograms conditioning on osteoporotic status. A χ^2-test of independence was conducted to assess the association between osteoporosis and having a very low or very high tooth count, which was further analysed using logistic regression. Hypotheses of location shifts in the distribution of tooth count due to osteoporosis were tested using Wilcoxon rank sum tests and the amount of shift was determined using non-parametric tests of equal probability density functions.

The assumptions underlying standard multiple regression model building were not satisfied. Standard multiple regression models did not fit the data well, with small R^2 (i.e., percentage of variation in the outcome variable explained by the explanatory variables) and skewed distribution of residuals resulting in invalid conclusions. As a single regression model would not fit all the data, mixtures of regression models (Turner 2000) were fitted to the dependent variable, number of teeth, with subsets of age, smoking status and osteoporosis as explanatory variables. Mixture regression analysis may provide an insight into hidden subgroups in data not recorded, that further investigation may show as reflecting characteristics such as lifestyle and oral hygiene.

Results

The number of teeth was counted in 651 subjects, of whom 140 were osteoporotic. A histogram was produced in Fig. 1a showing proportions of 0, 1, 2, up to 32 tooth counts in the osteoporotic group (red) and in the normal group (blue). It was observed that the proportion of low tooth counts (<6) were higher and the proportion of high tooth counts (>27) were lower in the osteoporotic group (no tooth counts of 32), and that the distribution had excess 0s, a long tail towards 0 and was skewed to the left for both groups.

Testing the association between osteoporosis and tooth count

A contingency table (Table 1) was constructed with osteoporosis status in rows and whether a subject had fewer than six teeth in columns. A χ^2-test of independence was significant ($\chi^2 = 16.78$ on 1 df, $p < 0.001$), which showed an association between osteoporosis and having fewer than six teeth.

A second contingency table (Table 2) was constructed with osteoporosis status in rows and whether a subject had 28 or more teeth in columns. A χ^2-test of independence was significant ($\chi^2 = 14.24$, on 1 df, $p < 0.001$), which showed an association between osteoporosis and having fewer than 28 teeth. Increasing the threshold to 29, 30 and 31 increased the *p*-value to 0.011, 0.052 and 0.080, respectively.

Using logistic regression, the association between osteoporosis and having few (<6) or not quite a full complement of teeth (<28) remained significant after adjusting for age, smoking and centre with *p*-values of 0.016 and 0.011, respectively.

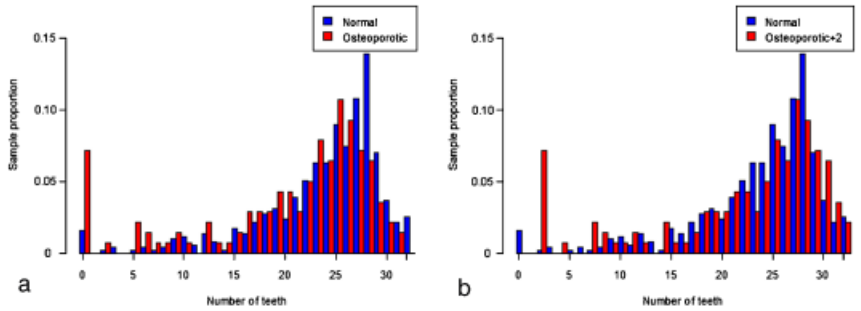

Fig. 1. (a) Histogram of tooth count for osteoporotic group (red) and that for normal group (blue). (b) Histogram of tooth count +2 for the osteoporotic group and tooth count for normal group.

Table 1. Cross tabulation of osteoporotic status with number of teeth (<6 or ⩾6 teeth)

	<6 Teeth	⩾6 Teeth	Total
Osteoporotic	14	126	140
Normal	12	499	511
Total	26	625	651

Table 2. Cross tabulation of osteoporotic status with number of teeth (<28 or ⩾28 teeth)

	⩾28 Teeth	<28 Teeth	Total
Osteoporotic	19	121	140
Normal	150	361	511
Total	169	482	651

Testing location shift

Close examination of the histogram in Fig. 1a showed that if the extreme left tail of the distribution was ignored, the distribution for the osteoporotic group may be a shifted version of that for the normal group. The sample medians of 23 and 25 suggested a location shift by two teeth. Figure 1b shows what would happen to the histogram if two extra teeth were added to this group – it would be a reasonable match between the two distributions over the range 8–32. A Wilcoxon rank sum test on a location shift by two teeth was not significant ($p = 0.587$) based on teeth count from 6 to 30 from the osteoporotic group and those between 8 and 32 from the normal group. For comparison, test results on location shifts by 0, 1 and 3 teeth were respectively significant ($p = 0.001$), non-significant ($p = 0.243$) and borderline significant ($p = 0.051$).

Identifying possible confounding variables

The osteoporotic group apparently had, on average, lower tooth counts than the normal group, but the difference may not be entirely attributable to osteoporosis. The possibility of confounding by smoking and age is considered below.

There were about the same number of smokers as non-smokers among the normal subjects (252 *versus* 258), and among the osteoporotic subjects (75 *versus* 65). The mean number of teeth among subjects who smoked was 22.34 (SE = 0.394). Formally, this was not significantly different (z-score of -1.94, $p = 0.053$) from the mean tooth count of 23.38 (SE = 0.367) for subjects who did not smoke. The median tooth count was 25 for both smokers and non-smokers. Excluding subjects with no teeth, the conditional means were 23.19 (SE = 0.323) and 23.83 (SE = 0.327), respectively, for smokers and non-smokers, which were not significantly different ($p = 0.166$). Smoking was, therefore, not a confounding factor in the effect of osteoporosis on tooth count which was confirmed in regression analysis.

The mean age for the osteoporotic group (59.24, SE = 0.51) was significantly higher ($p < 0.001$) than that of the normal group (53.76, SE = 0.25). Among the younger subjects (age <57.5 years), the effect of osteoporosis was two teeth as measured by the median tooth count, and among older subjects (age ⩾57.5) the difference in median tooth count was 1. Thus, age may be a confounding variable and the effect of age was adjusted for in regression analysis.

Adjusting for age by mixture regression

The distribution of tooth count had a wide range from 0 to 32 with a long tail towards 0 and a left skew which remained the case when conditioning on age or osteoporosis status. Based on our assessment of Fig. 2, we concluded that a single regression model with normal errors would not fit all the data, requiring a mixture of regression models to be fitted.

Mixture regression is also known as latent class regression (Wedel & DeSarbo 1995), where a latent variable represents several unobserved classes and there is a generalized linear regression model for each class or cluster. Using the R package Mixreg (Turner 2006), three clusters were identified in the data (excluding the 0s) as described by three linear regression models of tooth count on age and osteoporosis status. Each subject originates from one of three normal populations according to probabilities π_1, π_2 and π_3 which add up to 1, and each distribution has a conditional mean on age and osteoporosis in a linear form. The parameters were estimated by maximum likelihood via the EM algorithm (Turner 2000). Each data point was assigned to the class with the largest conditional probability. The results are shown in Fig. 3 with labels 1–3 in font sizes proportional to the posterior probabilities, and the fitted linear regression line for each cluster is superimposed.

Details of the fitted regression models are given in Table 3. The effect of osteoporosis was not significant in clusters 2 ($p = 0.16$) and 3 ($p = 0.06$), while it was significant in cluster 1 ($p = 0.03$). For cluster 1 which corresponded to high tooth counts (mean = 27) and covered 55.7% of the study population, osteoporosis accounted for nearly one (0.85) less tooth on average after adjusting for age. Increasing age was associated with reduced numbers of teeth except for cluster 3 ($p = 0.64$) where the difference in mean tooth count due to osteoporosis was $9.5 - 7 = 2.5$.

The regression lines may not appear the best fit for each cluster but the cluster memberships are estimated and thus not definitive. The same equations can be obtained by weighted least squares regression using posterior probabilities as weights. For each data point there were three fitted values, one from each regression equation, and thus three residual values. The residuals were standardized for diagnostic purposes. Figure 4 shows fitted values against observed values of tooth counts, standardized residuals against age and against fitted values, and a normal quantile plot for the standardized residuals. Ignoring the small dots, which represent small posterior probabilities, and concentrating on the larger symbols (Turner 2000) we found no overwhelming evidence against model adequacy.

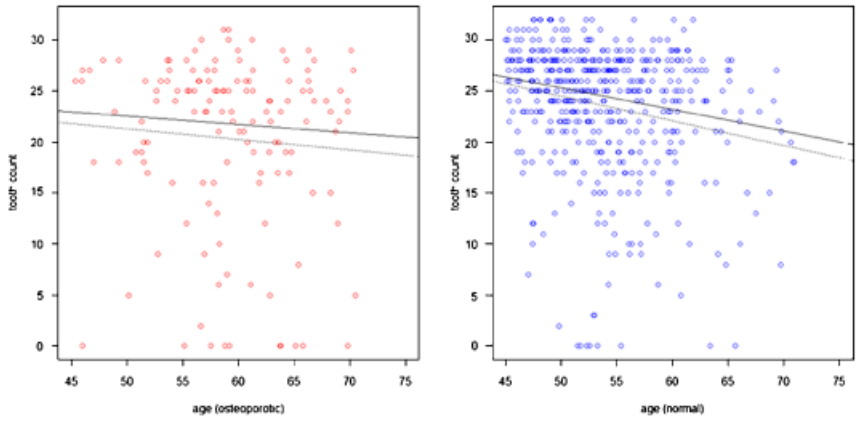

Fig. 2. Plots of tooth count against age for osteoporotic (red) and normal subjects (blue) with least squares (lower) and robust (higher) regression lines superimposed. The robust estimator (Huber 1981) calculated using the rim package (Venables and Ripley, 2002) was less affected by data points with low tooth counts.

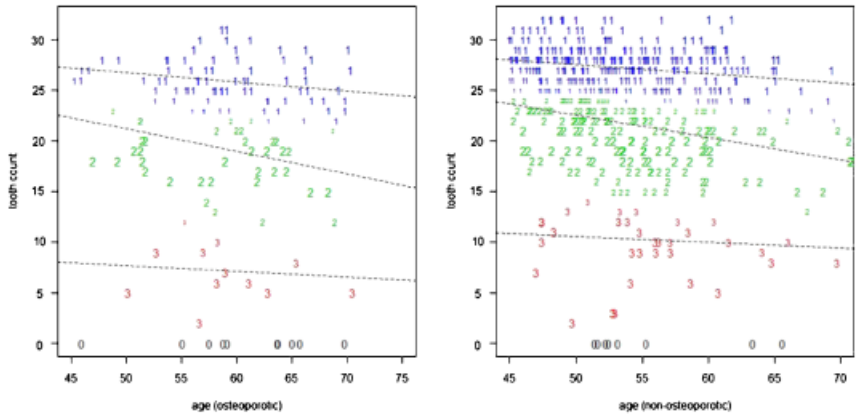

Fig. 3. Mixture regression model with the fitted linear regression line for each of the three clusters superimposed. Each data point was assigned to the class with the largest conditional probability with labels 1 to 3 in font sizes proportional to the posterior probabilities.

Table 3. Regression coefficients (Est) for independent variables in each of the three clusters with associated standard errors (SE)

	Cluster 1 ($\pi_1 = 0.557$)			Cluster 2 ($\pi_2 = 0.367$)			Cluster 3 ($\pi_3 = 0.076$)		
	Const	Age	**Op(1)**	Const	Age	**Op(2)**	Const	Age	**Op(3)**
Est.	32.07	− 0.09	**− 0.85**	33.59	− 0.22	**− 1.37**	13.33	− 0.06	**− 2.84**
SE	1.46	0.03	**0.38**	3.54	0.07	**0.98**	7.06	0.12	**1.50**
p	0.00	0.00	**0.03**	0.00	0.00	**0.16**	0.06	0.64	**0.06**

Op (1), Op (2) and Op (3) represent regression coefficients of osteoporosis (Op) for each cluster using the predictor variables in the table. Each subject originates from one of three normal populations according to probabilities π_1, π_2 and π_3, which add up to 1.
Const: constant, *p*: level of probability. The bold numerals emphasize the important numbers in this table. These important numbers refer to osteoporosis.

Using posterior probabilities as weights, the three fitted values were combined into one, which is the estimated conditional mean. These are plotted in Fig. 5 against observed values. The mixture regression models explained the data very well with a pseudo-R^2 value of 88.5%. However, they have limited predictive power for cluster memberships/tooth counts.

The additive mixture regression model with only main effects (no interaction) was satisfactory, suggesting that effect modification was not important. Adding interactions between age and osteoporosis allowed different gradients within each cluster but resulted in a non-significant increase ($p = 0.33$, df = 3) in log-likelihood value from − 1875.024 to − 1873.314. Adding main effect terms for smoking (and excluding one subject with missing smoking status data) did not result in a significant increase ($p = 0.35$, df = 3) in log-likelihood value (from − 1872.759 to − 1871.131) either.

We combined data from all four centres in order to have a sufficiently large dataset. Although the model (Table 3) did not include the recruitment centre as a variable, it fitted data from each centre very well (Fig. 6).

The effects of osteoporosis in each cluster were summarized in Table 3, from which an overall effect can be calculated by averaging the effects for each cluster using cluster probabilities as weights. The overall effect of osteoporosis was found to be − 1.8 teeth before and after adjusting for smoking, − 1.2 teeth after adjusting for age, and − 1.1 teeth after adjusting for both age and smoking. These results agreed well with the location shift of two teeth found earlier and confirmed the necessity to adjust the effect of osteoporosis by age, but not by smoking.

The mixture of regressions with normal errors are at best a good approximation as strictly speaking tooth count is a discrete random variable and there was some evidence of non-linear dependence on age. Alternative models with binomial or Poisson errors (parametric or semi-parametric, with or without incorporating zero inflation) can be fitted under the somewhat unrealistic assumption of independent loss at constant rate and with knowledge of the amount and duration of tooth loss, but the normal mixture regression was by far the best interpretable model.

Discussion

Osteoporosis and periodontitis are both chronic diseases presenting several similarities. Both involve bone resorption, with common risk factors such as age, smoking, systemic disease and dietary factors. Calcium absorbed from the diet is difficult to measure in large populations, but supplementary calcium and vitamin D, aimed at preventing osteoporosis, has also been shown to reduce tooth loss (Krall et al. 2001). Oestrogen therapy also protects both

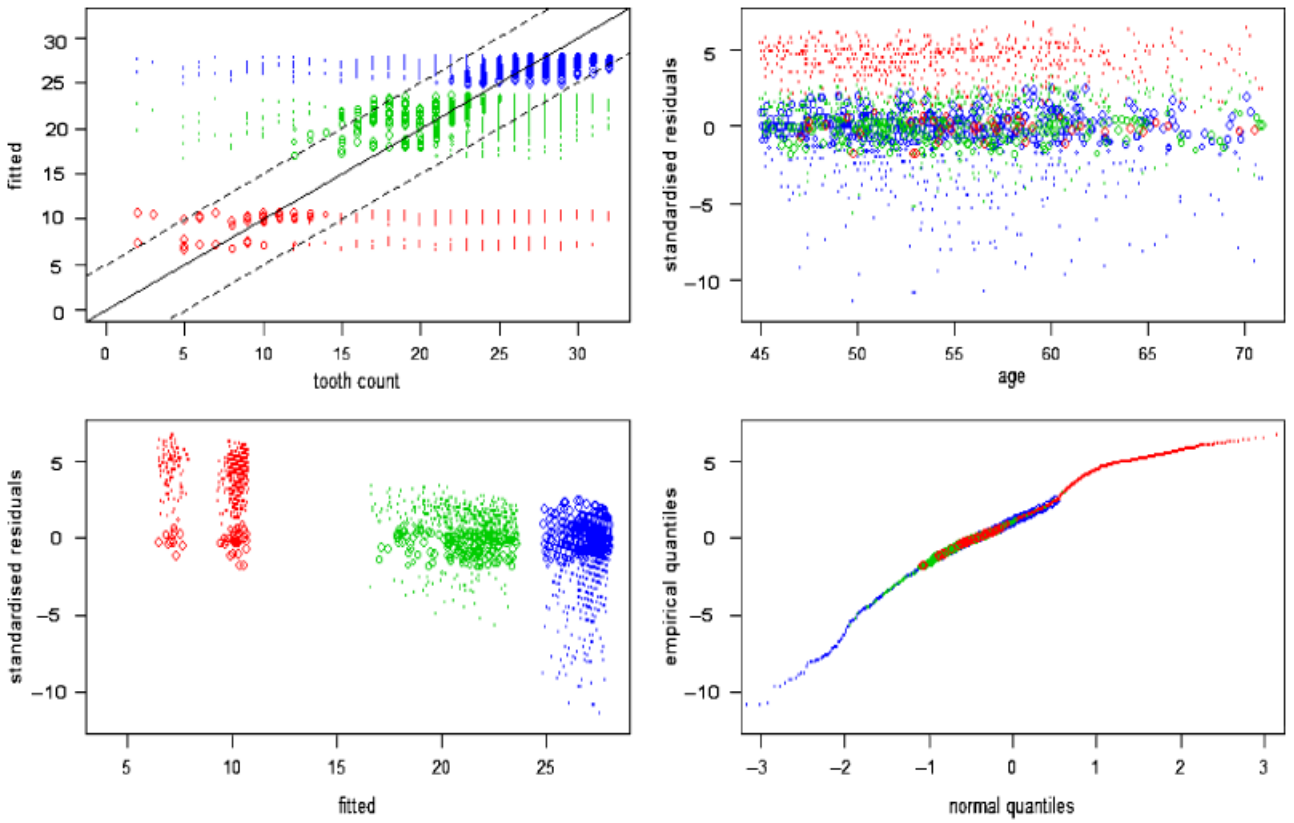

Fig. 4. Fitted values are plotted against observed values of tooth counts, standardized residuals against age and against fitted values, and a normal quantile plot shown for the standardized residuals. The size of the dots represents the posterior probability, and the color denotes the cluster or equation used to calculate the fitted value.

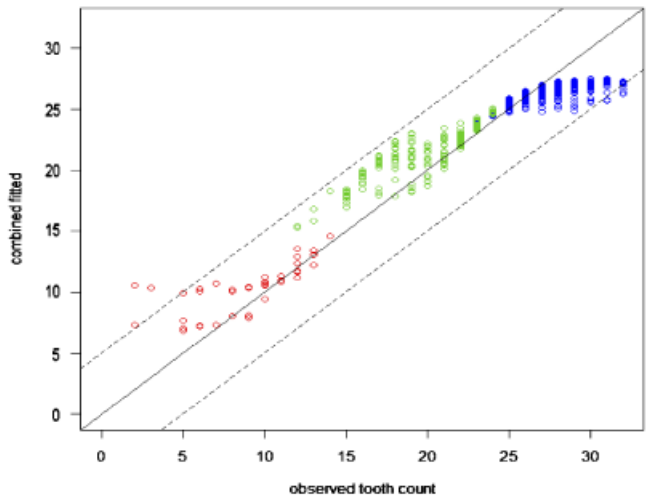

Fig. 5. Combined fitted values against observed data with dotted lines at ± 5 teeth.

lumbar spine and mandibular bone density (Jacobs et al. 1996).

We have shown in this study that osteoporosis at either the hip or spine is a risk factor for tooth loss. The overall effect of osteoporosis was one or two teeth lost depending on whether age was taken into account. Severe osteoporosis may be a co-factor in alveolar bone loss (Phillips & Ashley 1973, Ward & Manson 1973). Study populations that have used young, perimenopausal women (aged 46–55 years), where osteoporosis is less prevalent, are more likely to fail to find any association (Elders et al. 1992). Another study of an older population of women (aged 65–76 years) was unable to find a significant association between self-reported tooth loss and BMD at the hip and spine, but there may have been errors in the accuracy of self-reporting (May et al. 1995).

Some studies have reported an association between osteoporosis and tooth loss, for example, a significant association between risk of hip fracture and tooth counts (Astrom et al. 1990) or that the lumbar spine BMD was significantly lower among patients who acquired dentures at age 40 or earlier (Krall et al. 1994). Osteoporosis may influence the rate of bone loss in chronic periodontitis (Taguchi et al. 1995) which may explain the greater percentage of edentulous subjects found in some studies (Kribbs 1990, Mohammad et al. 2003). Yoshihara et al. (2004) found a weak relationship between BMD and periodontal disease progression, although it was statistically significant, and in a later study found a correlation between BMD of the os calcis and the number of remaining teeth (Yoshihara et al. 2005). Osteoporotic women have a higher risk of tooth loss, and may undergo greater bone resorption after tooth loss, compared with healthy women of the same age range (Bodic et al. 2005).

In our large study population, a statistically significant relationship was

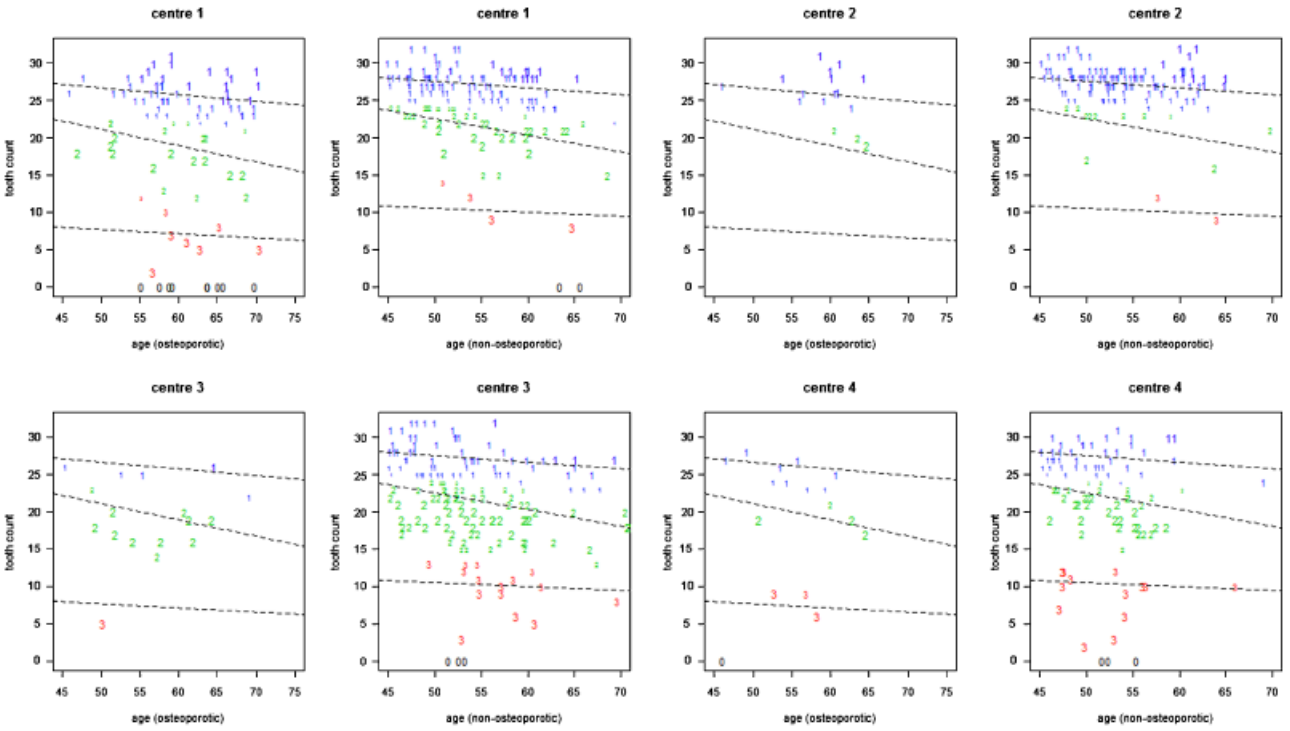

Fig. 6. The model was based on data from all four centres and although it did not include the recruitment centre as a variable it fitted data from each individual centre very well.

found between the total number of teeth and osteoporotic status. It must be emphasized that the effect of osteoporosis may be of minor importance in determining tooth loss, with other clinical and socioeconomic factors playing a more influential role. These factors affect the prevalence of periodontal disease; therefore, they may have influenced our tooth loss results. The important roles of patient age and periodontal status have been previously demonstrated (Mohammad et al. 1997) because when these factors were included, tooth loss was not significantly different between subjects with low and high spinal bone density. They concluded that total tooth loss was not directly associated with systemic bone density. Age and smoking have been shown in regression analysis to have a strong influence on tooth number in an elderly population, whereas a history of osteoporotic fracture was not significant (Bollen et al. 2004). Regular maintenance treatment in a cross-section of highly motivated subjects with chronic periodontitis seemed to be successful in preventing progressive periodontal tissue destruction in current smokers (Fisher et al. 2008). The sample in our study was a highly motivated group. In our study, one alternative explanation of the lack of effect of smoking on tooth loss may be due to the selection of subjects and how the smoking variable was defined. In our analysis, we did not distinguish whether subjects were current smokers or had ceased to smoke decades previously. This may have given rise to a misclassification bias. A previous publication (Karayianni et al. 2007) described the BMD and clinical data from our sample in more detail. The Osteoporosis Index of Risk Assessment (OSIRIS) was used which combines information about a patient's age, weight, their hormone replacement therapy and any history of low trauma fracture as clinical risk factors in detecting osteoporosis.

Low serum oestrogen has been shown to increase skeletal (Devlin et al. 1990) and alveolar bone resorption (Binte Anwar et al. 2007) in ovariectomized animals, with destruction of the trabeculae. Further research is required to distinguish this phenomenon from plaque-induced periodontal disease; some clinical human studies have shown no significant association between periodontal disease and systemic BMD (Weyant et al. 1999, Famili et al. 2005). The aetiology of the osteoporosis-induced atrophy of alveolar bone is poorly understood, but fewer teeth have been found in those with low systemic skeletal bone density (Inagaki et al. 2005).

In the present study, whether the patients smoked, their age and osteoporotic status were chosen as explanatory variables because these can be measured reliably and accurately. Inclusion of additional factors in the regression analysis such as body mass index, calcium intake and menopausal status that might affect tooth number is complicated by the collinearity that this inevitably introduces. Collinearity occurs when explanatory variables are significantly correlated with one another, causing an unreliable model that is difficult to interpret.

There are quite possibly various important differences across the nationalities/cultures in the four countries that may affect either/both tooth loss and osteoporosis. Such factors may include differences in nutritional intakes of caffeine, calcium-rich foods and alcohol, all factors found to be associated with osteoporosis risk as well as tooth loss risk. In addition, there may be important geographic variations in solar exposure patterns, which is the principal source of variation in vitamin D levels in many cultures. As can be seen from Fig. 6, the number of osteoporotic cases was small for centres 2, 3 and 4, and the numbers belonging to cluster 3 are 0, 1 and 3 in these centres, respectively. This means that models with an additional variable for centre could not be reliably fitted to the data.

We could not improve the fit by adjusting the regression lines using a centre variable because there are so few data points around some of the regression lines.

In conclusion, we have shown that after adjusting for smoking status and age, those with osteoporosis had fewer teeth than subjects with a normal/osteopenic BMD. Further separate longitudinal studies are planned to determine a causative basis for this finding, which is not possible from data in the present cross-sectional study.

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Clinical Relevance

Scientific rationale for the study: Previous research has shown an inconsistent effect of osteoporosis on tooth loss. We used a large European dataset of 665 subjects, taking into account a confounding factor such as age. Statistical analysis used mixture regression models.
Principal findings: The overall effect of osteoporosis was found to be a reduction of about 1.8 teeth before and after adjusting for smoking, and 1.2 fewer teeth after adjusting for age. The effect of smoking on tooth loss was not significant in addition to osteoporosis status.
Practical implications: Osteoporosis was associated with a significantly fewer number of teeth in this sample of females.