

# Relationship between oral health and mortality in cardiovascular diseases

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## Abstract

**Background, aims:** The purpose of the study was to investigate the relationship between periodontal health and fatal cardiovascular diseases (CVD).

**Methods:** The investigation was conducted on a sample of 1393 individuals in the County of Stockholm. The subjects were examined in an epidemiological study in 1970 with respect to dental health. At a follow-up in 1997, the mortality rate of the sample during the years 1970–1996 was registered as well as cause of death according to the death certificate. Stepwise logistic regression analysis was performed in order to evaluate the influence of the investigated variables on the incidence of death from CVD.

**Results:** The interactional effect between plaque and oral health score (a sum of scores for number of missing teeth, apical lesions, caries lesions and marginal bone loss), adjusted for age, gender, smoking and CVD at baseline, was significantly correlated to fatal coronary events. For individuals younger than 45 years of age, the age-adjusted incidence odds ratio of death due to CVD was 2.7 ( $p=0.04$ ) if subjects with mean marginal bone loss of  $>10\%$  were compared with subjects with mean marginal bone loss  $\leq 10\%$ . If the stratum of individuals  $<45$  years of age is confined to smokers, the odds ratio was found to be 3.4 ( $p=0.03$ ).

**Conclusion:** Dental health was found to be a risk indicator of death due to CVD, especially in combination with another risk factor, smoking habits.

Key words: cardiovascular disease; follow-up study; mortality; oral health; periodontal status; risk factor

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Marginal periodontitis is a multifactorial disease with a wide range of local (Kornman & Löe 1993) as well as generalized (Genco & Löe 1993) risk factors modifying the host's response to the primary etiological factor bacterial plaque. Factors like smoking, diabetes and socio-economic conditions belong to identified risk factors at the individual level (for review, see Genco & Löe (1993)).

Cardiovascular disease is another multifactorial disease which may be associated with atherosclerotic lesions, which are characterized as inflammatory processes involving the large and medium-sized muscular arteries. The atherosclerotic lesions can lead to coronary thrombosis and myocardial infarction. Cardiovascular disease is one of

the most common causes of death (Breslow 1997).

During the last decade, poor oral health has been found to be significantly correlated to cardiovascular disease (Mattila et al. 1989, 1993, 1995) as well as to cerebral infarction (Syrjanen et al. 1989) in case-control and follow-up studies. In addition, significant associations between periodontal disease and coronary heart disease have been reported (for review, see Beck et al. 1998). In these studies, the degree of marginal periodontitis has been evaluated by measuring variables such as alveolar bone level, periodontal pocket depths and number of lost teeth. The magnitude of the risk indicator periodontal disease, adjusted for confounding factors like age, gender, smoking and chol-

esterol levels, and expressed by calculating the odds ratio, ranges between 1.2 and 1.5 in a majority of the longitudinal studies (DeStefano et al. 1993, Beck et al. 1996, Janshipura et al. 1996).

The purpose of the present study was to investigate the relationship between oral health and fatal cardiovascular diseases (CVD). In addition, the relative contribution of marginal periodontitis to this association will be explored as well as interactional effects with confounding variables.

## Material and Methods

In order to determine the medical, social and odontological situation and need of care in the County of Stock-



Table 3. Means (SD) for the odontological variables and smoking according to age for individuals alive or having died of cardiovascular disease during the years 1970–1996

Age (years)		No. remaining teeth	Russell's index	Marginal bone loss index	No. apical lesions	No. surfaces with caries	Relative frequency of smokers	Plaque
18–30	alive	27.5 (4.31)	1.38 (1.09)	1.17 (0.24)	0.64 (1.37)	5.24 (7.21)	0.55 (0.50)	1.29 (0.66)
	dead	28.0 (3.57)	1.70 (1.04)	1.26 (0.29)	0.78 (1.39)	7.78 (8.96)	0.78 (0.44)	1.54 (0.84)
31–40	alive	23.6 (7.79)	2.40 (1.65)	1.62 (0.61)	1.31 (2.00)	5.09 (7.42)	0.48 (0.50)	1.47 (0.69)
	dead	22.1 (9.08)	3.08 (1.67)	1.94 (0.62)	0.91 (1.64)	6.82 (10.4)	0.73 (0.47)	2.00 (0.67)
41–50	alive	21.7 (7.15)	2.97 (1.59)	2.02 (0.77)	1.07 (1.52)	3.76 (4.43)	0.39 (0.49)	1.64 (0.67)
	dead	18.0 (8.22)	3.02 (1.83)	2.12 (0.85)	1.44 (2.16)	5.44 (6.20)	0.56 (0.50)	1.83 (0.65)
51–60	alive	16.4 (9.93)	3.32 (1.64)	2.27 (0.79)	1.58 (2.83)	3.33 (4.12)	0.28 (0.45)	1.74 (0.63)
	dead	11.5 (14.9)	3.76 (1.82)	2.62 (1.13)	1.31 (2.17)	3.98 (5.83)	0.36 (0.48)	1.99 (0.68)
61–66	alive	11.7 (10.5)	2.95 (1.13)	2.14 (0.51)	0.60 (1.04)	2.20 (3.53)	0.20 (0.41)	1.68 (0.54)
	dead	11.1 (9.60)	4.12 (1.73)	3.09 (1.48)	1.09 (1.61)	3.80 (5.27)	0.25 (0.44)	2.01 (0.70)

in 1970 (Table 2). The degree of marginal bone loss, number of tooth surfaces with caries and presence of plaque were significantly increased for smokers compared to non-smokers (Table 2).

Mean values for the investigated variables, stratified according to age and death due to cardiovascular disease, are illustrated in Table 3. The relative frequencies of smokers vary between 0.20 and 0.78 for different strata. The number of remaining teeth in 1970 was found to be lower in all age groups, except in the interval 18–30 years, for individuals who had died of CVD compared to those still alive in 1996. In addition, the marginal bone loss and number of surfaces with caries were increased for this group of individuals irrespective of age. The mean oral health score is higher in all age groups for individuals who have died of CVD compared to those still alive in 1996 (Fig. 1).

The independent variables number of remaining teeth, marginal bone loss, number of apical lesions, number of surfaces with caries, plaque and smoking were all significantly correlated to death due to CVD when adjusted for age and gender ( $p < 0.05$ , Table 4). However, the most significant correlation was found for oral health score (partial correlation = 0.11,  $p < 0.01$ ). For smokers, and with increasing amounts of plaque, these correlations were strengthened for a majority of the investigated variables, illustrated by the significant interactional effects (Table 4).

The results of the stepwise logistic regression, using the occurrence of death due to CVD between the years 1970 and 1996 for dentate individuals as the dependent variable, showed that age, gen-

der, cardiovascular disease in 1970 and the interactional effect between oral health and plaque index were the re-

maining significant independent variables in the final step of the analyses when also adjusted for smoking (Table

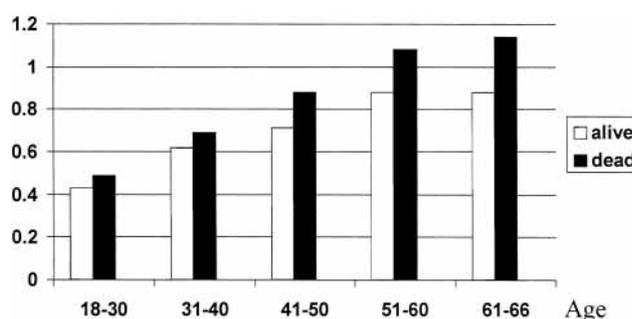


Fig. 1. Mean oral health score according to age and incidence of death due to CVD.

Table 4. Partial correlations between investigated variables and death due to cardiovascular disease in a multiple logistic regression model with age and gender included as independent variables; significant ( $p < 0.05$ ) interactional effects are presented

Variable	Partial correlation	$p$
no. teeth	-0.05	<0.05
Russell's index	0.01	NS
marginal bone loss index	0.05	<0.05
no. apical lesions	0.05	<0.05
no. surfaces with caries	0.09	<0.01
oral health score	0.11	<0.01
plaque	0.06	<0.05
smoking	0.05	<0.05
cardiovascular disease in 1970	0.08	<0.01
<b>Interactional effects:</b>		
no. teeth*; no. surfaces with caries	0.06	<0.05
smoking*; Russell's index	0.08	<0.01
smoking*; marginal bone loss index	0.05	<0.05
smoking*; no. surfaces with caries	0.12	<0.01
smoking*; plaque	0.08	0.01
marginal bone loss index*; plaque	0.08	0.01
plaque*; no. surfaces with caries	0.10	<0.01
oral health score*; plaque	0.12	<0.01
cardiovascular disease in 1970*		
marginal bone loss index	0.09	<0.01

Table 5. Results of stepwise logistic regression analysis (adjusted for age, gender, smoking and CVD in 1970) for dentate individuals using the occurrence of death due to cardiovascular disease between the years 1970 and 1996 as the dependent variable ( $n=1001$ , 91.5% of the cases correctly predicted)

Independent variable	Coefficient	Standard error	<i>p</i>
age 1970 (years)	0.11	0.01	<0.001
gender (0=female, 1=male)	0.80	0.26	0.001
cardiovascular disease in 1970	1.1	0.36	0.003
smoking (0=no, 1=yes)	0.28	0.26	0.32
oral health score *plaque index	0.38	0.12	0.002
constant	-8.1	0.66	<0.001

Table 6. Results of stepwise logistic regression analysis (adjusted for age, gender, smoking and CVD in 1970) for dentate individuals. (A)  $\geq 45$  years old in 1970 and (B)  $< 45$  years old in 1970, using the occurrence of death due to CVD between the years 1970 and 1996 as the dependent variable

Independent variable	Coefficient	Standard error	P
<b>A. Age <math>\geq 45</math> years (<math>n=287</math>, 91.8% of the cases correctly predicted)</b>			
age 1970 (years)	0.15	0.03	<0.001
gender (0=female, 1=male)	0.94	0.31	0.002
cardiovascular disease in 1970	1.2	0.40	0.004
smoking (0=no, 1=yes)	0.13	0.33	0.69
oral health score	1.2	0.48	0.01
constant	-11	1.6	<0.001
<b>B. Age <math>&lt; 45</math> years (<math>n=714</math>, 96.8% of the cases correctly predicted)</b>			
age 1970 (years)	0.07	0.03	0.03
gender (0=female, 1=male)	0.73	0.48	0.13
cardiovascular disease in 1970	1.1	1.2	0.35
smoking (0=no, 1=yes)	0.75	0.51	0.14
marginal bone loss index *plaque index	0.17	0.08	0.04
constant	-7.1	1.2	<0.001

5). After stratification according to gender, the significant interactional effect of oral health and plaque on mortality rate was valid for women ( $p=0.047$ ) as well as for men ( $p=0.004$ ). No significant difference in mortality rate was found between dentate and non-dentate individuals when adjusted for age, gender, smoking and CVD at baseline.

If the dentate individuals were divided into two strata according to age, a significant effect of oral health score on mortality due to cardiovascular disease was found for subjects  $\geq 45$  years

in 1970 when controlling for age, gender, smoking and CVD at baseline ( $p=0.01$ , Table 6A). However, for subjects  $< 45$  years old, an interactional effect between marginal bone loss and plaque was the only significant independent variable besides age ( $p=0.04$ , Table 6B). This relationship was also valid for men in the age group  $< 45$  years after stratification according to gender ( $p=0.02$ ), while a significant association was not found for women in the same age interval ( $p=0.35$ ).

The mean oral health score values are

higher in all age groups for individuals who have died of CVD irrespective of smoking habits (Fig. 2) compared to those still alive in 1996. However, for the non-smokers of the population, none of the investigated variables, except age, gender and CVD in 1970, were significantly correlated to the incidence of death due to CVD (Table 7A). In the group of smokers, besides age and gender, a significant interactional effect between oral health score and plaque was found ( $p<0.001$ , Table 7B).

For individuals younger than 45 years of age, the age-adjusted incidence odds ratio of death due to cardiovascular disease was 2.7 ( $p=0.04$ ) if individuals with mean marginal bone loss of  $>10\%$  were compared with those with mean marginal bone loss  $\leq 10\%$ . If the stratum of individuals  $< 45$  years of age is confined to smokers, the corresponding odds ratio was found to be 3.4 ( $p=0.03$ ). Finally, after further restriction of the stratum to male smokers younger than 45 years of age, the marginal bone loss was significantly predictive of death due to CVD, with an age-adjusted odds ratio of 4.2 ( $p=0.04$ ).

There were no statistically significant differences in correlations between investigated variables for cases with and without autopsy. Occurrence of diabetes or hypertension as one of the registered contributing causes of death did not have any significant influence on the estimated correlations between the investigated variables.

**Discussion**

In the present study, the mortality rate of a sample from a cross-sectional epidemiological study (Lavstedt 1975) was followed up for 26 years. The causes of death were registered from the death certificates and in 34% of the cases death was followed by autopsy, which

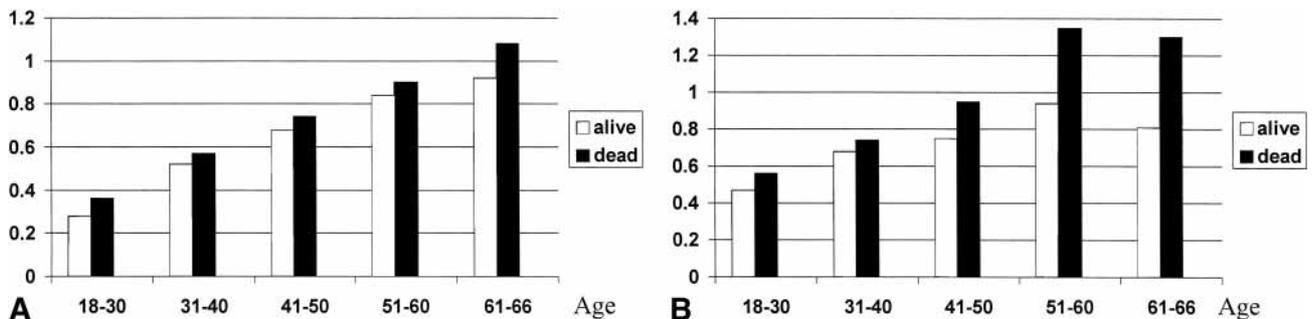


Fig. 2. Mean oral health score according to age and incidence of death due to CVD for non-smokers (A) and smokers (B).

Table 7. Results of stepwise logistic regression analysis for (A) non-smoking dentate individuals and (B). Smoking dentate individuals, using the occurrence of death due to cardiovascular disease between the years 1970 and 1996 as the dependent variable

Independent variable	Coefficient	Standard error	p
<b>A. non-smokers (n=489, 92.4% of the cases correctly predicted)</b>			
age 1970 (years)	0.16	0.02	<0.001
gender (0=female, 1=male)	0.79	0.36	0.03
cardiovascular disease in 1970	1.3	0.47	0.006
oral health score *plaque index	0.18	0.18	0.35
constant	-10.5	1.20	<0.001
<b>B. smokers (n=512, 91.6% of the cases correctly predicted)</b>			
age 1970 (years)	0.08	0.02	<0.001
gender (0=female, 1=male)	0.94	0.39	0.02
cardiovascular disease in 1970	0.76	0.61	0.21
oral health score *plaque index	0.54	0.15	<0.001
constant	-6.8	0.72	<0.001

was not found to significantly influence the associations between the investigated variables. In 1970, a sample of individuals from the County of Stockholm was investigated according to need for medical and social care (Bygren 1974) and an odontological investigation was also performed in 1393 individuals (Lavstedt 1975). However, the purpose of the present study is not to describe the oral health of the investigated population but to study the relationship between odontological variables and mortality from cardiovascular diseases.

The precision and the accuracy of the intraoral radiographic assessments have been evaluated in an earlier study (Lavstedt 1975). Consequently, systematic errors from these registrations are not expected to be present, increasing the probability of a high internal validity. The individuals of the present study constitute a random sample from the County of Stockholm and are expected to be representative of this population. Conclusions about the external validity outside this population requires judgments about the degree to which the results can be extrapolated. The degree of generalizability is dependent on the total knowledge from several studies on different populations studying the association between oral health and presence of cardiovascular disease.

A great majority of the independent variables were found to be significantly correlated to one another. Thus, a collinear relationship between age, gender, smoking and the odontological variables emphasizes the need for multivariable analytical technique to control for confounding effects. However, the multi-collinear associations complicate the interpretation of the results. The

highest correlation (0.70) was found between Russell's index and marginal bone loss. Both variables describe periodontal health but marginal bone loss was slightly more strongly correlated to mortality from cardiovascular disease. Consequently, marginal bone loss was selected as the measure of periodontal health in the oral health score variable. Number of lost teeth, number of surfaces with caries, number of teeth with apical lesions and marginal bone loss were found to be significantly correlated to mortality from CVD when adjusted for age and gender. This fact and the multi-collinear relationship between these odontological variables are the reasons for the selection of a summary variable (oral health score) to express the degree of oral health. A similar score variable of oral health, called Total Dental Index, has been described earlier (Mattila et al. 1989, Mattila et al. 1995), being a sum of scores for the variables number of carious lesions, missing teeth and periapical lesions as well as probing pocket depths and presence of pericoronitis.

In the present study, the number of missing teeth was found to be one of the investigated odontological variables which was significantly correlated to death due to CVD when adjusted for age and gender. A significant correlation between number of missing teeth and ischemic heart disease has also been demonstrated in earlier studies (Paunio et al. 1993, Joshipura et al. 1996). The association between caries disease and cardiovascular diseases has so far not been studied in detail. In fact, no attempts have been made to evaluate the different oral specific conditions except periodontal disease. In this investigation, a significant correlation between

caries and death due to CVD when adjusted for age and gender was demonstrated, indicating that this possible etiological pathway should be further investigated in the future. The number of caries lesions has so far been used as part of the oral health score variable and in the Total Dental Index (Mattila et al. 1989, 1995).

The significant association between oral health and death due to CVD was stronger with increasing amounts of plaque. This interactional effect was also demonstrated between marginal bone loss and plaque. The supragingival bacterial species can penetrate the epithelial barrier of the periodontal tissues and reach the peripheral circulation (Loesche & Lopatin 1998). Another study has reported that individuals with high plaque score values have significantly higher levels of white blood cells than controls (Kweider et al. 1993). Increased white blood cell levels may promote atherosclerotic lesions, which can cause coronary heart disease (Seymour & Steele 1998).

If the subjects were stratified according to age, marginal bone loss in combination with high plaque index values was the most significant independent variable for those younger than 45 years of age if adjusted for age, gender, smoking and presence of cardiovascular disease in 1970. This indicates a greater influence of periodontal disease on mortality in the younger ages, while presence of caries appears to have more impact in the age group  $\geq 45$  years at baseline. The importance of marginal bone loss as an explanatory variable was further increased for men younger than 45 years of age. This result is in accordance with an earlier study (DeStefano et al. 1993), where a relative risk of 1.72 for coronary heart disease incidence was found for men younger than 50 years of age in the presence of periodontal disease. In addition, another study has reported significant associations between dental infection and cerebral infarction in males under 50 years of age (Syrjanen et al. 1989).

Smoking is regarded as a well-established risk factor for periodontal disease (Bergström & Preber 1994, Grossi et al. 1995). The results of the present study indicate a strengthened association between mortality from cardiovascular disease and oral health or marginal bone loss for the individuals who were smokers in 1970. It has been suggested as a hypothesis that vasocon-

striction of the gingival vessels caused by smoking promotes invasion of the periodontal tissues by microorganisms (Loesche & Lopatin 1998). For non-smokers, a non-significant correlation between mortality from cardiovascular disease and oral health was found. However, the odontological variables were more strongly correlated to mortality from CVD than smoking, which was found to be a non-significant independent variable in the final step of the logistic regression analyses.

In order to evaluate whether evidence from observational studies is likely to be causal, guidelines with criteria to determine the nature of a relationship have been proposed (Hill 1965). An essential factor is the temporal relationship, implying that the cause must precede the effect. In the present study, cardiovascular disease was diagnosed at the clinical examination in 1970 in 18% of the fatal cases. Consequently, in a majority of the fatal cases the degree of oral health was registered before the incidence of diagnosed cardiovascular disease.

Several theories have been suggested as possible biological mechanisms in order to explain the significant correlations in clinical studies between dental infection and incidence of atherosclerosis/cardiovascular disease. Initially, case-control studies were published but later several longitudinal studies have been presented (Beck et al. 1998), showing similar results. The multi-collinear relationships between the odontological variables emphasize that, so far, the specificity of the associations of the different oral manifestations may be regarded as low. In a recently published experimental study (Ebersole et al. 1999), systemic manifestations of marginal periodontitis in non-human primates have been demonstrated. However, the results of the clinical studies should be interpreted with caution since dental diseases and coronary heart diseases have several well-known risk factors in common (Seymour & Steele 1998). Thus, further research is needed to elucidate the influence of potential confounding variables before poor dental health can be regarded as an established risk factor for cardiovascular disease.

In conclusion, in the present study, oral diseases were found to be a risk indicator of death due to cardiovascular disease, especially in combination with an established risk factor, smoking

habits. Marginal bone loss was found to be the only significant odontological risk indicator for younger men.

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### Zusammenfassung

*Beziehung zwischen oraler Gesundheit und Sterberate bei kardiovaskulären Erkrankungen*

Der Zweck dieser Studie war die Untersuchung der Beziehung zwischen parodontaler Gesundheit und fatalen kardiovaskulären Erkrankungen (CDV). Die Untersuchung wurde an einer Population von 1393 Personen aus dem Verwaltungsbereich von Stockholm durchgeführt. Die Personen wurden in einer epidemiologischen Studie im Jahre 1970 bezüglich der dentalen Gesundheit untersucht. In einer Folgestudie im Jahre 1997 wurde die Sterberate der Gruppe während der Jahre 1970 bis 1996 registriert und die Ursache des Todes anhand der Sterbeurkunde erfaßt. Eine schrittweise logistische Regressionsanalyse wurde durchgeführt, um den Einfluß der untersuchten Variablen auf die Incidenz des Todes von CVD zu erfassen. Die interaktionale Effekte zwischen Plaque und oralem Gesundheitswert (eine Summe von Scorewerten für die Anzahl der fehlenden Zähne, der apikalen Läsionen, der Kariesläsionen und des marginalen Knochenverlustes), adjustiert für das Alter, das Geschlecht, das Rauchen und CVD zur Basisuntersuchung, war signifikant korreliert mit fatalen Herzattacken. Für jüngere Personen unter 45 Jahren war die altersadjustierte Incidenz Odds-ratio für den Tod infolge von CVD 2.7 ( $p=0.04$ ), wenn die Personen mit einem mittleren marginalen Knochenverlust  $>10\%$  mit Personen mit einem mittleren marginalen Knochenverlust  $\leq 10\%$  verglichen wurden. Wenn die Schicht der Personen  $<45$  Jahre auf die Raucher beschränkt wurde, war die Odds-ratio 3.4 ( $p=0.03$ ). Zusammenfassend wurde gefunden, daß die Zahngesundheit ein Risikoindikator für den Tod infolge von CVD ist, besonders in Kombination mit dem anderen Risikofaktor Rauchen.

### Résumé

*Relation entre la santé orale et la mortalité par maladies cardiovasculaires*

Le propos de cette étude était de rechercher la relation entre la santé parodontale et les maladies cardiovasculaires fatales (CVD). La recherche a été conduite sur un échantillon de 1393 individus dans le comté de

Stockholm. Les sujets avaient été examinés lors d'une étude épidémiologique en 1970 pour ce qui était de leur santé dentaire. En 1997, le taux de mortalité de l'échantillon pendant les années 1970-1996 fut répertorié ainsi que les causes de décès à partir des certificats de décès. Une analyse de régression logistique stepwise a été réalisée pour évaluer l'influence des variables étudiés sur l'incidence des décès par CVD. Les effets interactifs entre la plaque et la note de santé orale (la somme des notes pour le nombres de dents manquantes, les lésions apicales, les lésions carieuses, et la perte osseuse marginale), ajustés pour l'âge, le sexe, le tabagisme et une maladie cardiovasculaire présente à la consultation initiale, étaient significativement corrélés avec un événement coronaire fatal. Pour les individus de moins de 45 ans, l'incidence de l'odds ratio ajusté à l'âge, pour une mort par CVD était de 2.7 ( $p=0.04$ ) si l'on comparait les sujets avec une perte osseuse marginale moyenne de plus de 10% et ceux avec une perte osseuse marginale moyenne de moins (ou égale à) de 10%. Si la catégorie d'individus de moins de 45 ans était réduite aux fumeurs, l'odds ratio trouvé était de 3.4 ( $p=0.03$ ). En conclusion, il est montré que la santé dentaire est un indicateur de risque de décès par CVD, particulièrement en combinaison avec un autre facteur de risque, le tabagisme.

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