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Association between bleeding periodontal pockets and eczemas – Results of the Northern Finland Birth Cohort 1966

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L. Tursas prepared the research design and research plan in collaboration with co-authors. M. Ylipalosaari conducted the statistical analyses. L. Tursas and M. Ylipalosaari analyzed the results with co-authors. L. Tursas wrote the first drafts and prepared the final manuscripts with the co-authors. P.Ylöstalo, A-M. Syrjälä and M. Ylipalosaari prepared the research design and research plan in collaboration with the first author, analyzed the results with first author, and prepared the final manuscript with the first author. K.Tasanen, S-P Sinikumpu, and L.Huilaja prepared the research design plan in collaboration with co-authors and analysed the results with co-authors. P.Tegelberg and A. Tiisanoja interpreted the data and revised the article in collaboration with co-authors.

Data availability statement
The data that support the findings of this study are available from Northern Finland Birth Cohort (NFBC) 1966 Center. Restrictions apply to the availability of these data, which were used under licence for this study. Data are available with the permission of the NFBC1966 Center.

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Abstract

Aim

To investigate whether periodontal condition measured by bleeding periodontal pockets is associated with atopic dermatitis, seborrheic dermatitis, and eczema nummulare.

Materials and methods

The study population (*n*=1871) was obtained from the 46-year follow-up study of the Northern Finland Birth Cohort 1966 study (NFBC1966). The periodontal condition was measured by the number of sites with bleeding periodontal pockets that were ≥ 4 mm deep. The whole skin of the participants was clinically examined, and diagnoses of skin diseases were determined according to the International Classification of Diseases (ICD-10). Prevalence rate ratios (PRR) and 95% confidence intervals (95% CI) were estimated using Poisson regression models with robust error variance.

Results

In this cohort, consisting of 46-year-old members of the Northern Finland Birth Cohort 1966, the presence of 1−3 and ≥4 bleeding deepened periodontal pockets (≥4 mm deep) were associated with seborrheic dermatitis (PRR 1.9, 95% CI: 1.3–2.8 and PRR 2.2, 95% CI: 1.4–3.3, respectively), and with eczema nummulare (PRR 1.7, 95% CI: 0.9–3.1 and PRR 1.7, 95% CI: 0.9–3.3, respectively). For non-smokers, the corresponding estimates were 1.7 for seborrheic dermatitis (95% CI: 1.1–2.6) and 1.8 (95% CI:1.1–3.1) and 1.4 for eczema nummulare (95% CI: 0.7–2.9) and 1.2 (95% CI: 0.5–2.9), respectively. No association was found between bleeding deepened periodontal pockets and

atopic dermatitis. Further adjustments for C-reactive protein, diabetes, and inflammatory diseases did not essentially change the risk estimates among either the total population or the non-smokers.

Conclusion

Bleeding periodontal pockets appeared to be associated with the presence of seborrheic dermatitis and eczema nummulare.

Keywords

Cohort study, eczema, periodontal infection, periodontitis

Clinical relevance

Scientific rationale for the study: Low-grade systemic inflammation has been associated with several conditions, including periodontal diseases, cardiovascular diseases, type 2 diabetes, and skin diseases. This study is the first to investigate whether the periodontal condition is associated with eczemas.

Principal findings: Bleeding deepened periodontal pockets were associated with the risk of seborrheic dermatitis and eczema nummulare.

Practical implications: The findings suggest that co-operation between general practitioners and dentists could be beneficial when treating eczema patients.

1. INTRODUCTION

Eczemas are an inflammatory reaction of the skin and are caused by either internal or external factors. Eczemas are classified based on their pathogenesis and/or expression; the most common subtypes are atopic dermatitis, seborrheic dermatitis, and eczema nummulare (Lazzarini *et al*. 2018). Studies show that the prevalence of eczemas varies between 1.3% and 7.3% in the adult population (Augustin *et al*. 2011, Sinikumpu *et al*. 2014). Histologically, eczema is characterized by inflammatory lesions with swelling of the intercellular spaces in the epidermis and dermis and by dilated blood vessels surrounded by lymphocytes and neutrophils.

Periodontitis affects nearly half of the general population (Eke *et al*. 2015). It begins when the bacteria in the gingival pocket trigger a host inflammatory response, which then leads to the destruction of tooth-supporting tissues (Hegde & Awan 2019, Kinane & Marshall 2001) and creates low-grade systemic inflammation. It has been suggested that low-grade systemic inflammation could be associated with different diseases that have an infectious or inflammatory component, such as cancers, respiratory diseases, rheumatoid arthritis, cardiovascular diseases, and type 2 diabetes, for instance (Cardoso *et al*. 2018).

Skin diseases, such as atopic dermatitis have recently been reported to be associated with low-grade systemic inflammation (Sinikumpu *et al*. 2018). There is also some evidence that oral infections exacerbate eczemas: Tanaka and co-workers (Tanaka *et al*. 2009) reported that skin symptoms were alleviated after dental treatment in 13 patients suffering both from severe odontogenic infections and treatment-resistant eczema nummulare and Igawa and co-workers showed (Igawa *et al.* 2005) that symptoms of atopic dermatitis were relieved after dental treatment. Based on the above-mentioned findings, we hypothesized that individuals with poor periodontal condition are likely to be more susceptible to eczemas and consequently have more eczemas than periodontally healthy

individuals. Therefore, this paper aims to study whether periodontal condition, as measured by bleeding periodontal pockets ≥ 4 mm deep, is associated with different types of eczemas.

2. MATERIAL AND METHODS

Study population

This study is a part of the Northern Finland Birth Cohort 1966 (NFBC1966) 46-year follow-up survey. The cohort members, who at the time of data collection resided within a 100 km radius of the city centre of Oulu, Finland (*n*=3150), were invited to participate in a comprehensive clinical examination. The final study population comprised 1871 participants (males=862, females=1009). The oral examination was performed at the Institute of Dentistry, Faculty of Medicine, University of Oulu. The skin examinations were done at the premises of the Faculty of Medicine, University of Oulu. All the data were collected between April 2012 and May 2013 (University of Oulu, 1966). The study included all participants who underwent a skin examination and oral clinical examination and who agreed to use their data for research purposes. Participants who denied the use of their data for the research and participants who would have required antibiotic prophylaxis for periodontal examinations were excluded from the study (Fig.1).

Participation in the follow-up survey was completely voluntary and the participants signed their informed consent. All data were handled with complete anonymity and patients were only identified by the study identification codes that were allocated to them at the start of the study. The full cohort study (74/2011) and the present study (227/2012) were conducted according to the Declaration of Helsinki and were approved by the Ethical Committee of the Northern Ostrobothnia Hospital District. The study followed the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.

Skin examination and oral clinical examination

This paper used data obtained from a skin examination, oral clinical examinations, and health questionnaires. The health questionnaires were collected via mail before the clinical examinations, and they included all non-clinical data used in the analyses.

The whole skin of every participant was clinically examined by a specialist in dermatology or experienced residents. Skin diseases and findings such as benign and malignant skin tumours and inflammatory and infectious skin diseases were identified according to the International Classification of Diseases (ICD-10) and were registered in the database. The inter-observer kappa statistic value between examiners varied from good (0.87) to very good (100.0) for eczemas and skin infections (Sinikumpu 2018).

The oral clinical examinations were performed by calibrated dentists using a standardized oral clinical examination protocol in a dental office equipped with modern instruments. The oral clinical examinations included the registration of both periodontal and dental conditions, salivary flow, and oral mucosal lesions. The inter-examiner agreement for probing pocket depth (PD) measurements was 70%, whereas the intra-examiner agreement was 82%. The Cohen's kappa values for probing pocket depth were 0.35 for inter-examiner agreement. Information on oral health behaviour was collected using a postal questionnaire.

Classification of eczemas

Eczemas are classified on the basis of clinical features. In the current analysis, we used atopic dermatitis, seborrheic dermatitis, and eczema nummulare as outcome variables. Cases of eczema infectiosum were included in the 'eczema nummulare' group, because the two types have a shared pathogenesis and expression (Sinikumpu *et al.* 2014).

Periodontal measurement

Periodontal probing depth was measured using an oral mirror and an LM ball-pointed gingival probe with a ballpoint diameter of 0.5 mm and a scaling of 2 mm (LM 8-520B, Lääkintämuovi, Finland). Inexact measurements were rounded down. The probe was inserted parallel to the vertical axis of each tooth. A measuring force of 25 g was calibrated using a letter scale before each examination.

The periodontal pockets of all teeth, excluding wisdom teeth and residual roots, were probed at four sites in the following order: mesiobuccal, midbuccal, distobuccal and midoral. Mucosal pockets of dental implants were also probed. Approximal probing was done as close to tooth contact points as possible. The probing was done first and bleeding on probing (BOP) was viewed 20−30 seconds after probing each site. The depth of the periodontal pocket, which is the distance between the gingival margin and the base of the pocket, was measured in millimetres (mm). The number of bleeding periodontal pockets 4 mm or deeper was used as an explanatory variable. In the analyses, they were classified as 0, 1−3, 4 or more bleeding deepened periodontal pockets (≥ 4mm).

Other variables

Education was categorized into three categories: basic, intermediate, and higher. Basic education included persons who had graduated from a vocational school or lower. Intermediate education included those who had graduated from a vocational college or university of applied sciences, and higher education included persons who graduated from a university. The categorization complied with the international standard classification of education.

The participants' smoking status was classified as 1) non-smoker 2) former smoker or 3) current smoker. Non-smokers included those cohort members who had never smoked the former smokers category included those who had quit smoking totally; and current smokers included those cohort members who smoke on a regular basis 1–7 days per week or who smoke occasionally.

To measure C-reactive protein (CRP), fasting blood samples taken from the participants were stored at -70 °C. An Immune Nephelometric assay (BN ProSpec, Siemens Healthcare Diagnostics INC., Newark, DE, USA) was used to define the concentration of high-sensitivity CRP (hs-CRP). The values of hs-CRP were classified as normal, elevated and highly elevated, <1 mg/l, 1–3 mg/l, and >3 mg/l, respectively (Pearson *et al.* 2003).

Medical diagnoses (ICD-10 codes) of general diseases such as diabetes mellitus (E10, E11), inflammatory bowel diseases (K50, K51), lung diseases (J41, J42, J43, J44, J45, J46) and rheumatic diseases (M05.0, M05.8, M05.9, M06.0, M06.4, M06.8, M06.9, M08.0, M45) were obtained from the Care Register for Health Care, a database maintained by the Finnish Institute for Health and Welfare.

Statistical methods

Prevalence rate ratios (PRR) and 95% confidence intervals (CI 95%) were estimated using Poisson regression models with robust error variance (Zou 2004). Statistical analyses were done with the SPSS 24.0 software package for Windows (SPSS, Inc.). Confounding factors were selected on the basis of literature. Four models were made, and all models were adjusted for sex, educational level and smoking status. Additional models were adjusted for hs-CRP (model 2), hs-CRP, presence of diabetes, inflammatory bowel diseases, lung diseases and rheumatic diseases (model 3), and absence of diabetes and bowel diseases, lung diseases and rheumatic diseases (model 4). All 4 models were also analysed excluding current smokers.

3. RESULTS

The results showed that of the 46-year-old study participants of the Northern Finland Birth Cohort 1966, 4.8% (*n*=89) had atopic dermatitis, 7.3% (*n*=136) had seborrheic dermatitis and 3.4% (*n*=64) had eczema nummulare. Table 1 presents the general characteristics of the whole study population

and the prevalence of eczemas in the study population, stratified by category of explanatory variable.

In the study population, 2.9% (*n*=13) of those with atopic dermatitis had 1–3 bleeding deepened periodontal pockets (≥4 mm) and 5.0% (*n*=15) had 4 or more bleeding deepened periodontal pockets (≥4 mm). The corresponding numbers were 10.3% (*n*=46) and 12.0 % for seborrheic dermatitis (*n*=36) and 4.7% (*n*=21) and 5.3% (*n*=16) for eczema nummulare (Table 1).

Table 2 shows the unadjusted PRRs with 95% CI while Tables 3 and 4 show the four different adjusted models. The results in the total population showed that after adjustments for sex, educational level and smoking status, the presence of 1−3 and ≥4 bleeding deepened periodontal pockets (≥4 mm) was associated with seborrheic dermatitis (PRR 1.9, CI:1.3–2.8, PRR 2.2, CI:1.4–3.3, respectively), and eczema nummulare, (PRR 1.7, 95% CI: 0.9–3.1, PRR 1.7, 95% CI: 0.9–3.3, respectively) (Table 3). The risk estimates did not essentially change by further adjustments for hs-CRP, diabetes, and inflammatory diseases (Table 3).

Table 4 shows PRRs when current smokers were excluded. After adjusting for sex, educational level and smoking status, the PRRs for the presence of 1−3 and ≥4 bleeding deepened periodontal pockets (≥4 mm) with seborrheic dermatitis were 1.7 (95% CI: 1.1–2.6) and 1.8 (95% CI: 1.1–3.1), respectively. The corresponding figures for eczema nummulare were 1.4 (95% CI: 0.7–2.9) and 1.2 (95% CI: 0.5–2.9). In the models that excluded current smokers, the risk estimates for seborrheic dermatitis and eczema nummulare were attenuated when compared to the results in Table 3. The number of bleeding periodontal pockets ≥4 mm deep was not associated with atopic dermatitis (Tables 3 and 4).

4. DISCUSSION

This study showed that periodontal condition, as measured by the number of bleeding periodontal pockets (≥4 mm), was associated with the presence of seborrheic dermatitis and eczema nummulare but not with atopic dermatitis. The findings are partly in line with a Japanese study, which reported that skin symptoms were relieved after dental treatment in patients suffering from both severe oral infections and treatment-resistant eczema nummulare (Tanaka *et al*. 2009).

The specificity, i.e., finding, that a periodontal condition was associated specifically with seborrheic dermatitis and eczema nummulare but not with atopic dermatitis supports the view that the association between a periodontal condition and eczemas is not due to confounding, i.e., caused by determinants in common. It is worth noting that the association between bleeding pockets and eczema nummulare was not statistically significant, nor did the association follow an exposure-response pattern. However, this lack of statistical significance and lack of an exposure-dependent pattern can be due to the small number of eczema nummulare patients.

To rule out the effect of other inflammatory conditions, we generated a number of different models. In the model that took into account inflammatory diseases such as inflammatory bowel, lung and rheumatic diseases and diabetes, we observed that the strength of the association did not change much compared to the model that did not adjust for such inflammatory diseases (model 3 versus model 2). We interpret this to mean the association of a periodontal condition with seborrheic dermatitis and eczema nummulare is not a result of the inflammatory condition related to these systemic diseases.

We also examined whether the association between a periodontal condition and seborrheic dermatitis and eczema nummulare is mediated through periodontally-derived low-grade

inflammation. The miniscule difference in PRRs between model 1 and model 2 suggests that neither of the associations are mediated through low-grade inflammation related to periodontitis.

Since smoking is an important risk for periodontal diseases and a potential risk for eczemas, we further analysed the association between bleeding pockets and eczemas by excluding current smokers. When current smokers were excluded from the analysis (Table 4), the risk estimates for eczema nummulare and seborrheic dermatitis, in particular, were somewhat lower. The difference in PRRs between these models and the unadjusted models supports the view that smoking confounds the association between a periodontal condition and eczemas. This is surprising because the role of smoking in the aetiology of eczemas is not clear. An alternative interpretation is that the attenuation of risk estimates is related to associated behavioural factors, such as poor health habits.

Strengths and limitations of the study

One of the main strengths of this study is that it was a well-designed cohort study that analysed medical, dental and laboratory variables. The NFBC 46-year follow-up cohort participants were middle-aged at the time of the data collection, which is the age when both periodontal diseases and eczemas often manifest. Since the NFBC is a Finnish cohort, the study population is genetically fairly homogeneous and as participants were living in the same area, environmental factors are likely to have had an equal effect on the incidence of skin diseases among all study participants. Another strength of the study is that we took into account possible confounding factors in regression models and controlled for the effect of smoking by restricting current smokers in the models (Table 4). On the other hand, it is obvious that there might be unidentified and thus uncontrolled confounding factors. These may relate to behavioural factors, or shared susceptibility to both conditions. The main limitation of this study is that due to its cross-sectional study design it could not provide information about the temporal sequence between a periodontal condition and

skin diseases. Another limitation regarding the periodontal examination is that the attachment level was not registered.

One advantage of this study is that the explanatory variable combined two clinical parameters, namely pocket depth and bleeding, which can be expected to measure periodontal inflammation better than individual parameters. The study protocol included a thorough calibration of the examiners before and during the data collection period. However, in spite of these measures, the reproducibility of periodontal data proved to be no higher than moderate. All participants were clinically examined by a specialist in dermatology or experienced residents, and the diagnosis of skin diseases showed a high reproducibility.

One limitation of the study is its low participation rate (59.4 %) even though three attempts were made to invite non-participating cohort members to participate. It is true that a low response rate can cause bias; non-participants may be different in relation to oral hygiene and dental visiting habits and overall health-related habits such as smoking and diet. In this follow-up study, it was observed that those who participated were more often from a higher social class, were employed, married, and had children compared to those who did not participate (Nordström *et al*. 2022). However, as the focus of this article is on the association of periodontal inflammatory condition with eczemas, we believe that somewhat low participation rate is not major concern.

5. CONCLUSION

The findings suggest that periodontal condition measured by bleeding periodontal pockets is associated with the presence of seborrheic dermatitis and eczema nummulare.

References

Augustin, M., Herberger, K., Hintzen, S., Heigel, H., Franzke, N., & Schäfer, I. (2011). Prevalence of skin lesions and need for treatment in a cohort of 90 880 workers. *The British journal of dermatology*, *165*(4), 865–873. https://doi.org/10.1111/j.1365-2133.2011.10436.x

Cardoso, E. M., Reis, C., & Manzanares-Céspedes, M. C. (2018). Chronic periodontitis, inflammatory cytokines, and interrelationship with other chronic diseases. *Postgraduate medicine*, *130*(1), 98–104. https://doi.org/10.1080/00325481.2018.1396876

Eke, P. I., Dye, B. A., Wei, L., Slade, G. D., Thornton-Evans, G. O., Borgnakke, W. S., Taylor, G. W., Page, R. C., Beck, J. D., & Genco, R. J. (2015). Update on Prevalence of Periodontitis in Adults in the United States: NHANES 2009 to 2012. *Journal of periodontology*, *86*(5), 611–622. https://doi.org/10.1902/jop.2015.140520

Hegde, R., & Awan, K. H. (2019). Effects of periodontal disease on systemic health. *Disease-a-month: DM*, *65*(6), 185–192. https://doi.org/10.1016/j.disamonth.2018.09.011

Igawa, K., Nishioka, K., & Yokozeki, H. (2007). Odontogenic focal infection could be partly involved in the pathogenesis of atopic dermatitis as exacerbating factor. *International journal of dermatology*, *46*(4), 376–379. https://doi.org/10.1111/j.1365-4632.2007.03101.x

Kinane, D. F., & Marshall, G. J. (2001). Periodontal manifestations of systemic disease. *Australian dental journal*, *46*(1), 2–12. https://doi.org/10.1111/j.1834-7819.2001.tb00267.x

Lazzarini R., de Figueiredo Silva Hafner M., Rocha V.B., Lorenzini D. (2018) Eczemas. In: Bonamigo R., Dornelles S. (eds) Dermatology in Public Health Environments. Springer, Cham. https://doi.org/10.1007/978-3-319-33919-1_18

Nordström, T., Miettunen, J., Auvinen, J., Ala-Mursula, L., Keinänen-Kiukaanniemi, S., Veijola, J., Järvelin, M. R., Sebert, S., & Männikkö, M. (2022). Cohort Profile: 46 years of follow-up of the Northern Finland Birth Cohort 1966 (NFBC1966). *International journal of epidemiology*, *50*(6), 1786–1787j. https://doi.org/10.1093/ije/dyab109

Pearson, T. A., Mensah, G. A., Alexander, R. W., Anderson, J. L., Cannon, R. O., 3rd, Criqui, M., Fadl, Y. Y., Fortmann, S. P., Hong, Y., Myers, G. L., Rifai, N., Smith, S. C., Jr, Taubert, K., Tracy, R. P., Vinicor, F., Centers for Disease Control and Prevention, & American Heart Association (2003). Markers of inflammation and cardiovascular disease: application to clinical and public health practice: A statement for healthcare professionals from the Centers for Disease Control and Prevention and the American Heart Association. *Circulation*, *107*(3), 499–511. https://doi.org/10.1161/01.cir.0000052939.59093.45

Sinikumpu, S. P., Huilaja, L., Jokelainen, J., Koiranen, M., Auvinen, J., Hägg, P. M., Wikström, E., Timonen, M., & Tasanen, K. (2014). High prevalence of skin diseases and need for treatment in a middle-aged population. A Northern Finland Birth Cohort 1966 study. *PloS one*, *9*(6), e99533. https://doi.org/10.1371/journal.pone.0099533

Sinikumpu, S. P., Huilaja, L., Auvinen, J., Jokelainen, J., Puukka, K., Ruokonen, A., Timonen, M., & Tasanen, K. (2018). The Association Between Low Grade Systemic Inflammation and Skin Diseases: A Cross-sectional Survey in the Northern Finland Birth Cohort 1966. *Acta dermato-venereologica*, *98*(1), 65–69. https://doi.org/10.2340/00015555-2795

Sinikumpu, SP. (2018). Skin diseases and their association with systemic diseases in the Northern Finland Birth Cohort 1966. Acta Universitatis Ouluensis D Medica, 1446. Juvenes print: Tampere 2018.

Tanaka, T., Satoh, T., & Yokozeki, H. (2009). Dental infection associated with nummular eczema as an overlooked focal infection. *The Journal of dermatology*, *36*(8), 462–465. https://doi.org/10.1111/j.1346-8138.2009.00677.x

University of Oulu: Northern Finland Birth Cohort 1966. University of Oulu. http://urn.fi/urn:nbn:fi:att:bc1e5408-980e-4a62-b899-43bec3755243

Zou G. (2004). A modified poisson regression approach to prospective studies with binary data. *American journal of epidemiology*, *159*(7), 702–706. https://doi.org/10.1093/aje/kwh090

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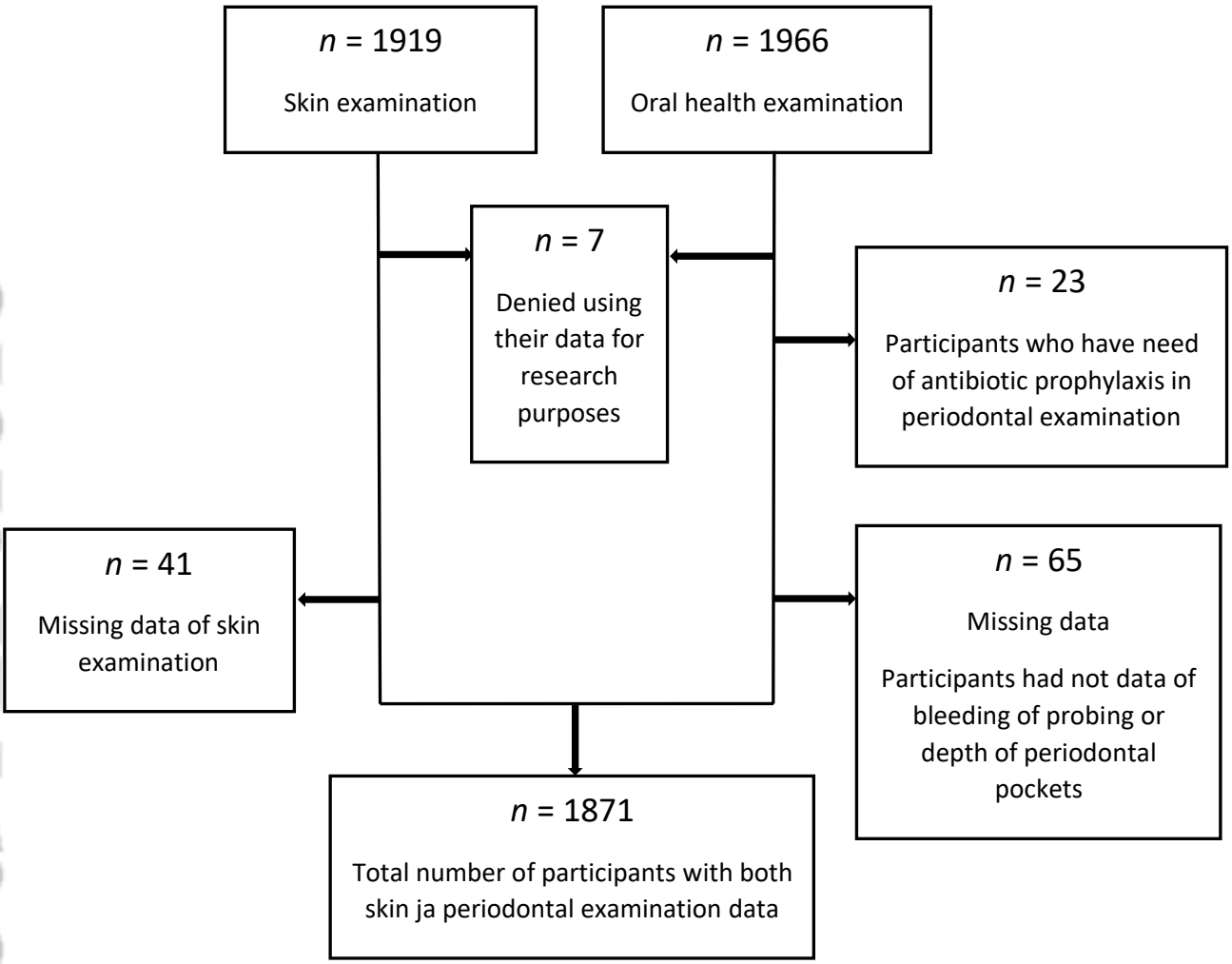

Table 1. Characteristics of the total study population stratified by the number of bleeding deepened periodontal pockets (≥4 mm).

Variable	Total study population	Subjects without bleeding deepened pockets (≥4 mm)	Subjects with 1–3 bleeding deepened pockets (≥4 mm)	Subjects with ≥4 bleeding deepened pockets (≥4 mm)
N	1871	1124	447	300
Sex %				
Female	53.9	58.9	49.7	41.7
Male	46.1	41.1	50.3	58.3
Smoking % (n=1808)				
Non-smoker	44.2	49.3	43.1	26.8
Former smoker	33.2	33.1	35.3	30.6
Current smoker	22.5	17.6	21.7	42.6
Education % (n=1765)				
Basic	6.0	5.5	5.5	8.6
Secondary	66.7	63.4	69.9	74.2
Tertiary	27.3	31	24.6	17.2
Number of teeth mean (SD)	2.1	1.9	2.0	2.7
Eczemas % (n=1870)				
Atopic	4.8	5.4	2.9	5.0
Seborrheic	7.3	4.8	10.3	12
Nummulare	3.4	2.4	4.7	5.3
Hand	9.0	9.8	7.6	8.3
Contact	1.0	1.0	1.3	0.7
Staticum	0.7	0.6	0.7	1.3
Neurodermatitis	1.8	1.6	2.2	2.0
Hs-CRP % (n=1861)				
< 1 mg/l	61.6	64.6	62.1	49.8
1–3 mg/l	27.8	25.8	28.5	34.4

> 3 mg/l	10.5	9.6	9.4	15.7
Diabetes % (n=1807)	2.1	1.7	2.6	2.8
Inflammatory diseases* % (n=1863)	7.9	8.4	8.7	4.7

* Inflammatory diseases: inflammatory bowel diseases, lung diseases and/or rheumatic diseases.

Table 2. Crude associations of periodontal variables and covariates with the presence of eczemas (n=1870).

	Atopic dermatitis Unadjusted PRR (95 % CI)	Seborrheic dermatitis Unadjusted PRR (95 % CI)	Eczema nummulare Unadjusted PRR (95 % CI)
Number of bleeding deepened periodontal pockets (≥4mm) (ref. 0 bleeding deepened pockets)			
1–3	0.5 (0.3–1.0)	2.1 (1.4–3.2)	2.0 (1.1–3.4)
≥ 4	0.9 (0.5–1.6)	2.5 (1.6– 3.8)	2.2 (1.2– 4.1)
Continuous	1.00 (0.96–1.04)	1.04 (1.02–1.05)	1.02 (1.00–1.05)
Sex (ref. male)	1.4 (0.9–2.1)	0.3 (0.2–0.4)	0.4 (0.2–0.6)
Smoking (ref. never smoker) (n=1807)			
Former smoker	1.0 (0.7–1.6)	1.2 (0.8–1.7)	2.2 (1.2–4.0)
Current smoker	0.6 (0.3–1.1)	1.1 (0.7–1.7)	2.2 (1.2–4.2)
Education (ref. basic) (n= 1764)			
Secondary	1.3 (0.5–3.5)	1.0 (0.5–2.0)	0.7 (0.3–1.6)
Tertiary	1.3 (0.5–3.6)	0.9 (0.5–2.0)	0.4 (0.1–1.0)
Number of teeth	1.0 (0.9–1.1)	0.9 (0.9–1.0)	1.0 (0.9–1.0)
Hs-CRP (ref. < 1 mg/l) (n= 1860)			
1–3 mg/l	1.0 (0.6–1.7)	1.2 (0.9–1.8)	1.3 (0.7–2.2)
>3 mg/l	1.9 (1.1–3.3)	1.2 (0.7–2.0)	1.5 (0.7–3.1)
Continuous	1.01 (0.97–1.06)	0.97 (0.91–1.03)	1.04 (0.99–1.10)
Inflammatory diseases* (ref. no inflammatory diseases) (n=1862)	1.2 (0.6–2.3)	0.6 (0.3–1.3)	1.0 (0.4–2.4)
Diabetes (ref. no diabetes) (n=1806)	#	1.1 (0.4–3.3)	2.5 (0.8–7.5)

* Inflammatory diseases: inflammatory bowel diseases, lung diseases and/or rheumatic diseases.

Not able to calculate risk estimates.

PRR, prevalence rate ratio.

Table 3. Association of the number of bleeding deepened periodontal pockets (≥4 mm) with eczemas. The results of multivariate regression models.

Variable	Atopic dermatitis Adjusted PRR (95 % CI)	Seborrheic dermatitis Adjusted PRR (95 % CI)	Eczema nummulare Adjusted PRR (95 % CI)
Model 1	n=1753	n=1753	n=1754
0	1	1	1
1–3	0.6 (0.3–1.1)	1.9 (1.3–2.8)	1.7 (0.9–3.1)
≥ 4	1.2 (0.7–2.2)	2.2 (1.4–3.3)	1.7 (0.9–3.3)
Model 2	n=1743	n=1743	n=1744
0	1	1	1
1–3	0.6 (0.4–1.1)	1.9 (1.3–2.8)	1.7 (0.9–3.0)
≥ 4	1.2 (0.7–2.1)	2.1 (1.4–3.2)	1.7 (0.9–3.1)
Model 3	n=1684	n=1684	n=1685
0	1	1	1
1–3	0.6 (0.4–1.2)	1.9 (1.3–2.8)	1.6 (0.8–2.9)
≥ 4	1.2 (0.7–2.2)	2.0 (1.3–3.1)	1.6 (0.8–3.1)
Model 4	n=1521	n=1521	n=1522
0	1	1	1
1–3	0.6 (0.3–1.1)	1.8 (1.2–2.7)	1.8 (0.9–3.5)
≥ 4	1.4 (0.8–2.4)	2.1 (1.4–3.3)	1.6 (0.8–3.3)

Data are presented as adjusted prevalence rate ratios (PRR) with 95% confidence interval (CI 95 %).

Model 1 was adjusted for sex, education, and smoking.

Model 2 was adjusted for sex, education, smoking and hs-CRP.

Model 3 was adjusted for sex, education, smoking, hs-CRP, diabetes and inflammatory bowel diseases and lung diseases and rheumatic diseases.
Model 4 was adjusted for sex, education, and smoking. Diabetes and inflammatory bowel diseases and lung diseases and rheumatic diseases were excluded.

Table 4. Association of number of bleeding deepened periodontal pockets (≥4 mm) with eczemas. Current smokers have been excluded. The results of multivariate regression models.

Variable	Atopic dermatitis Adjusted PRR (95 % CI)	Seborrheic dermatitis Adjusted PRR (95 % CI)	Eczema nummulare Adjusted PRR (95 % CI)
Model 1	n=1356	n=1356	n=1357
0	1	1	1
1–3	0.6 (0.3–1.1)	1.7 (1.1–2.6)	1.4 (0.7–2.9)
≥ 4	1.3 (0.7–2.4)	1.8 (1.1–3.1)	1.2 (0.5–2.9)
Model 2	n=1349	n=1349	n=1350
0	1	1	1
1–3	0.5 (0.3–1.1)	1.7 (1.1–2.6)	1.4 (0.7–2.8)
≥ 4	1.2 (0.6–2.2)	1.8 (1.1–3.0)	1.2 (0.5–2.8)
Model 3	n=1308	n=1308	n=1309
0	1	1	1
1–3	0.6 (0.3–1.1)	1.7 (1.1–2.6)	1.3 (0.6–2.8)
≥ 4	1.3 (0.7–2.4)	1.8 (1.0–3.0)	1.1 (0.4–2.8)
Model 4	n=1185	n=1185	n=1186
0	1	1	1
1–3	0.4 (0.2–1.0)	1.5 (0.9–2.4)	1.4 (0.6–3.0)
≥ 4	1.5 (0.8–2.8)	1.9 (1.1–3.2)	1.0 (0.3–2.6)

Data are presented as adjusted prevalence rate ratios (PRR) with 95% confidence interval (CI 95%). Model 1 was adjusted for sex, education, and smoking.

Model 2 was adjusted for sex, education, smoking and hs-CRP.

Model 3 was adjusted for sex, education, smoking, hs-CRP, diabetes and inflammatory bowel diseases and lung diseases and rheumatic diseases

Model 4 was adjusted for sex, education, and smoking. Diabetes and inflammatory bowel diseases and lung diseases and rheumatic diseases were excluded.