The Role of Gingivitis in the Loss of Periodontal Attachment and Teeth

Marc Schätzle

MALMÖ UNIVERSITY

Department of Periodontology

Faculty of Odontology
Malmö University, Sweden

UNIVERSITÄT BERN

Department of Periodontology and
Fixed Prosthodontics
School of Dental Medicine
University of Berne, Switzerland

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To Harald and Klaus

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PREFACE

This thesis is based on the following studies, which will be referred to by their roman numerals:

I **Schätzle, M.,** Löe, H., Bürgin, W., Ånerud, Å., Boysen, H. & Lang, N. P.:
The Clinical Course of Chronic Periodontitis: I. The role of gingivitis
Journal of Clinical Periodontology 2003; 30: 887-901.

II Heitz-Mayfield, L. J. A., **Schätzle, M.,** Löe, H., Ånerud, Å., Boysen, H., Bürgin, W. & Lang, N. P.:
The Clinical Course of Chronic Periodontitis: II. Incidence, characteristics and time of occurrence of the initial periodontal lesion
Journal of Clinical Periodontology 2003; 30: 902-908.

III **Schätzle, M.,** Löe, H., Lang, N. P., Heitz-Mayfield, L. J. A., Bürgin, W., Ånerud, Å., & Boysen, H.:
The Clinical Course of Chronic Periodontitis: III. Patterns, Variations and Risks of Attachment Loss
Journal of Clinical Periodontology 2003; 30: 909-918.

IV **Schätzle, M.,** Löe, H., Lang, N. P., Bürgin, W., Ånerud, Å. & Boysen, H.:
The Clinical Course of Chronic Periodontitis: IV. Gingival inflammation as a risk factor for tooth mortality
Journal of Clinical Periodontology 2004; 31: 1122-1127.

V **Schätzle, M.,** Lang, N. P., Ånerud, Å., Boysen, H., Bürgin, W. & Löe, H.:
The influence of margins of restorations on the periodontal tissues during 26 years
Journal of Clinical Periodontology 2001; 28: 57-64.

INTRODUCTION

Knowledge of the transition from health to disease and the progression of the disease through various stages of severity are important to the development of effective strategies of prevention and treatment. It is well established that bacterial irritants from supra- and subgingival plaque are essential for the maintenance of the gingival and periodontal inflammation (Waerhaug 1952, Russel 1957 a,b). Also the understanding of disease initiation and progression is important as it impacts on the ability to classify, diagnose and treat the disease.

During the last 50 years, the prevailing clinical concept of the pathogenesis of the early lesion in chronic periodontitis included (1) the formation and maturation of the supra-gingival plaque and the development of gingivitis (Löe et al. 1965), (2) the extension of the bacterial plaque and the chronic inflammatory process into the subgingival area and the initial destruction of the connective tissue attachment of the teeth (Lindhe et al. 1975), (3) the apical extension of the junctional epithelium and the formation of the periodontal pocket and loss of alveolar bone (Waerhaug 1952, Saxe et al. 1967, Lindhe, et al.1975).

The concepts of the initiation and progression of the disease originated from extensive cross-sectional epidemiological studies performed during the 1950's and 1960's (Russel 1957a,b, Greene 1963, Waerhaug 1967). Based on these surveys periodontal disease was defined as a plaque-dependent disease that begins as gingivitis associated with poor oral hygiene and affecting the majority of the adult population after the age of 35 to 40 years, and gradually becoming worse with increasing age.

In humans and other mammals periodontitis is predominantly associated with gram-negative strictly anaerobic microorganisms (Tanner et al. 1979) residing in the dental plaque. Up to date, it has, however, not been possible to identify a single bacterial organism to be the causative agent in the aetiology of periodontitis. Nether has it been possible to prove a specific bacterial agent in the aetiology of periodontal disease according to the criteria of Koch's postulate (Koch 1882).

Following the original experimental gingivitis studies (Löe et al. 1965), many investigations have used this human model to demonstrate the causal relationship between the formation and maturation of the bacterial plaque and the development of the gingival inflammation (Theilade et al. 1966, Jensen et al. 1968, Lang et al. 1972, 2002, Kelner et al. 1974, Matsson 1978, Brecx et al. 1987a,b, 1988a,b). While the colonization and maturation of bacterial plaque (Theilade et al. 1966, Loesche & Syed 1978, Syed & Loesche 1978), as well as the development and clinical features of gingivitis are reasonably well understood (Löe et al. 1965), the sequence of events, the incidence, pattern and timing of the initial periodontal lesion are less well defined.

Cross-sectional epidemiological studies from many countries have demonstrated that gingivitis is common in the primary and permanent dentitions of children (Kinane & Hodge 2001), and affects most adults (Brown & Löe 1993). National probability surveys in some industrial countries have found that gingivitis occurs in about 60% of teenagers and 40-50% of adults, but that, on average, only 5-6% of the total gingival sites appeared to be inflamed (Brown et al. 1989, 1990, Brown & Löe 1993). Similar data based on probability samples are, however, not available for developing countries, but it has been suggested that gingivitis is highly prevalent, extensive and severe throughout the developing world (Pilot 1998).

Clearly, not all gingivitis lesions progress to periodontitis. However, developing periodontitis seems to be preceded by gingivitis (Löe & Morrison 1986, Page & Kornman 1997). The proportion of gingival lesions converting to periodontitis and the factors causing this conversion are presently not understood (Page & Kornman 1997).

Attachment loss is rarely observed in children and yet, initial loss of attachment appears to start during the late teens (Hugoson & Jordan 1983, Löe et al. 1986, Bhat 1991, Hugoson et al. 1992, Brown & Löe 1993). Most young individuals between the age of 20 to 30 years have one or more sites with attachment loss (Ånerud et al. 1983).

While traditional epidemiological surveys described the distribution of disease and factors influencing this distribution (Lilienfeld 1978), a more recent concept emphasizes that “epidemiology is essentially an inductive science, concerned not merely with

describing the distribution of disease, but equally or more with fitting it into a consistent philosophy" (Frost 1941). Hence, epidemiological studies should extend beyond a mere description of the prevalence, severity and the distribution of the disease in a population (descriptive epidemiology) and include more analytical methods (Papapanou & Lindhe 2002).

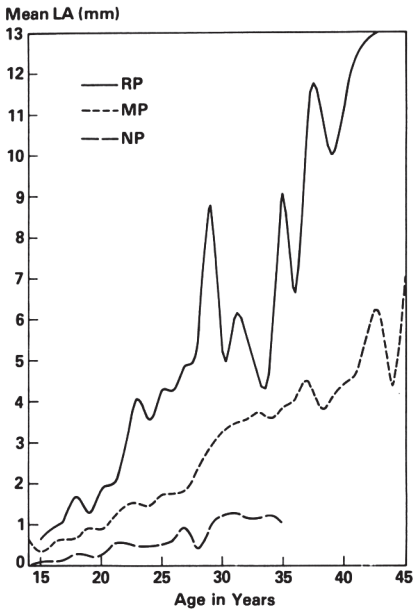
Cross-sectional studies make it difficult to characterize a continuous process of disease such as the transition from gingivitis to periodontitis and the temporal association between the various factors influencing the initiation and progression of this disease. Cross-sectional studies have also failed to provide a rate with which the lesions progress during various age periods of human life, the incidence of disease and the associated risk factors.

The hypothesis that periodontitis was a continuous, slowly progressive destructive disease was challenged (Goodson et al. 1984) based on a study of 12 months duration, in which periods of exacerbation and remission as well as periods of inactivity for an unknown numbers of weeks to months were postulated. Similar conclusions of a dynamic disease process in which periods of exacerbation and remission affect a few individuals in so-called bursts of activity resulting in relatively short time intervals in which attachment loss occurred, were drawn from other short term studies as well (Lindhe et al. 1983, Socransky et al. 1984).

Based on a prospective cohort study on Sri Lankan tea labourers initiated in 1970, a twenty year longitudinal study covering the age span of 15 to 51 years, the natural history of periodontal disease was investigated (Löe et al. 1978a-c). This study population had no caries and did not receive any type of dental treatment before or during the observation period. Nor were there any conscious efforts to prevent or intervene with the development of oral diseases. In the absence of any interventions and over the long term the study demonstrated that the loss of periodontal attachment is continuous and that given time the progressive destruction of the periodontium led to the exfoliation of the teeth (Löe et al. 1986).

Three different subpopulations were identified on basis of average attachment loss and tooth mortality rates: (1) subjects showing a rapidly progressing destruction of the periodontium (RP), leading to the complete loss of teeth around the age of 40 years (8%), (2) subjects with relatively moderately progressing disease (MP) (80%) and (3) subjects with no disease progression (NP) (12%) (Fig. 1). For subjects in RP and MP cohorts loss of periodontal attachment started in the late teens and appeared to continue with different progression rates through adult life. The relatively small cohort with no progressing disease (NP) showed essentially no progress of periodontal disease beyond the gingival lesion (Löe et al. 1986).

Figure 1: Mean loss of attachment – Sri Lanka (mesial root surfaces for all valid observations) (Löe et al. 1986)



Cross-sectional studies can not establish causal or temporal relationships, but may point to factors influencing the pathogenesis, and may be considered “risk indicators”. However, the determination of true risk factors requires longitudinal studies. To evaluate the course of disease and its temporal sequence the study of potential risk factors, represents an important aspect of epidemiological analysis. A true risk factor is a component which, on the basis of epidemiological evidence, is known to be associated

with disease related conditions. Such an attribute may be associated with an increased probability of occurrence of a particular disease without necessarily being a causal factor. A risk factor may also be modified by interventions thereby reducing the likelihood for the development of a particular disease (Beck 1994).

The information presented in this thesis was obtained through parallel longitudinal studies of periodontal disease in man conducted in Norway between 1969 and 1995, and Sri Lanka between 1970 and 1990. The main purpose of these investigations was to study the initiation and progression of periodontal disease in two very different population groups.

The two groups showed geographical, racial, cultural, socioeconomic and educational differences, and they represented extremes as to perceived severity of periodontal disease, general health care delivery systems and to dental care (Löe et al. 1978a). The Sri Lanka population had never been exposed to any program of oral professional or self care. The Norwegian population, on the other hand, was exposed to conventional care throughout life starting at age 3 years. All results presented in this thesis are based only on analyses of the data collected on this Norwegian population.

The Norwegian cohort was established in Oslo in 1969 and consisted of 565 healthy male students, graduate students and young university academics between 16 and 34 years of age. The older age groups were randomly drawn from the census file with the Central Bureau of Statistics, and the younger age groups came from three high schools in Oslo, selected by the City Board of Education. None of these subjects studied or taught in dental or medical schools.

Starting shortly after World War I, the City of Oslo launched a comprehensive oral health care program for the improvement of oral health in it's children. From 1936 (Gythfeldt 1937) all children were entitled to comprehensive oral examinations and treatment on an annual recall schedule, and by 1946, every school child was offered systematic dental care including preventive, restorative, endodontic, orthodontic and surgical therapy. Over time, other programs were added to include both preschool children and university students, so the dental care program covered the age span from 3 to 23

years. All patients participating in this study had been in the City Dental Program of Oslo and subsequently reported to have seen their private dentists at least on a regular annual basis. Children and youths who had chosen not to participate in the school dentistry program (<10 %) continued to see their private family dentists on a regular basis (Hansen 1976, Hansen & Johansen 1976). All participants reported that subsequent to the release from public programs, they continued to see their private dentist on a regular basis.

Indeed, there are very few population groups in the world, who in 1995 and at the age of almost 60 years could document an exposure to systematic dental care similar to that of those participating in this investigation. It is, therefore, fair to state that the chosen population represents a group of individuals that had had a continuous exposure to conventional dental care throughout life. For detailed information on the study design, demography and baseline data see Löe et al. (1978a-c) and Ånerud et al. (1991).

As already mentioned, the initial examination in 1969 included 565 individuals. Subsequent surveys took place in 1971, 1973, 1975, 1981, 1988 and 1995. As in most longitudinal studies of this size and length, a certain number of the sample dropped out and could not be followed up. Others would miss one or more examinations, but showed up at the last survey. Of the 565 subjects who started in the main investigation in 1969, 487 individuals could be reexamined at least once, 223 showed up for the last examination 26 years later and 54 presented at all 7 surveys. Thus, the study covers the age range of 16 to 59 years. The average observation period of a patient was 16.6 years.

The examinations were performed in well-equipped clinical facilities at the Dental Faculty, University of Oslo, Norway. The clinical examinations included assessments of the periodontal tissues and caries and associated factors (Löe et al. 1978a).

At each appointment the participants answered questions regarding personal dental care and oral practices as well as smoking habits. Missing teeth were recorded in all participants at each appointment (Löe et al. 1978c). The clinical examinations of the periodontal tissues and adjacent portions of the dentition included measurements and

scoring of all teeth, except third molars by the same two examiners. From 1981 (Survey 5) onwards, the clinical examinations also included the distal and lingual surfaces.

The following clinical indices or measurements were used:

- Plaque Index (PlI) (Silness & Löe 1964)
- Calculus Index (CI) (Löe 1967)
- Gingival Caries Index (GCI) (Löe 1967)
- Gingival Restoration Index (GRI) (Löe 1967)
- Gingival Index (GI) (Löe & Silness 1963)
- Loss of attachment (LA) (Glavind & Löe 1967) was assessed to the nearest millimeter
- Beginning in 1975, gingival recession was also recorded.
- Furcation Index (Hamp et al. 1975) was assessed from 1975 onwards

(For the details and specific criteria for the various parameters see appendix.)

Table 1: Overview of all parameters recorded in Norway (1969 – 1995):

Parameters	1969	1971	1973	1975	1981	1988	1995
Personal Data	•	•	•	•	•	•	•
Age	•	•	•	•	•	•	•
Nr. of Teeth	•	•	•	•	•	•	•
Smoking habits	•	•	•	•	•	•	•
Plaque Index	•	•	•	•	•	•	•
Plaque Samples						•	•
Calculus Index	•	•	•	•	•	•	•
Gingival Caries Index	•	•	•	•	•	•	•
Gingival Restoration Index	•	•	•	•	•	•	•
DMF(S)					•		
Gingival Index	•	•	•	•	•	•	•
Loss of Attachment	•	•	•	•	•	•	•
Furcation Index				•	•	•	•
Gingival Recession			•	•	•	•	•
Mesial-Buccal	•	•	•	•	•	•	•
Distal-Lingual					•	•	•

The overall aim of this thesis was to analyze the initiation, progression and pattern of periodontal attachment loss in a population maintaining regular professional and personal oral care.

AIMS

All analyses are based on data from the 26 year longitudinal investigation of the initiation and progression of periodontal disease in a randomized group of middle class Norwegian men aged between 16 and 59 years. Specific aims included:

1. to determine the influence of various levels of gingival inflammation on the pathogenesis of chronic periodontitis,

2. to examine the initiation and progression of periodontal disease during adult life, in order to evaluate the time of occurrence and the incidence of the early periodontal lesion,

3. to describe the pattern and rates of attachment loss, the variations in the starts and stops, and risks for converting healthy periodontal sites to chronic periodontitis,

4. to asses the influence of various severity levels of gingival inflammation on the of tooth loss, and

5. to elucidate the effects of subgingival margins of dental restorations on plaque, gingivitis and loss of periodontal attachment.

MATERIAL & METHODS

Sample Size

For the evaluation of *Study I, III, IV and V*, the subjects were divided into 9 age cohorts (<20, 20-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59 years of age) (Table 2). For the evaluation of *Study II*, the subjects were initially divided into 8 age cohorts (16-17, 18-19, 20-21, 22-23, 24-25, 26-27, 28-29 and 30-34 years of age). The entire population was followed for 26 years (Fig. 2).

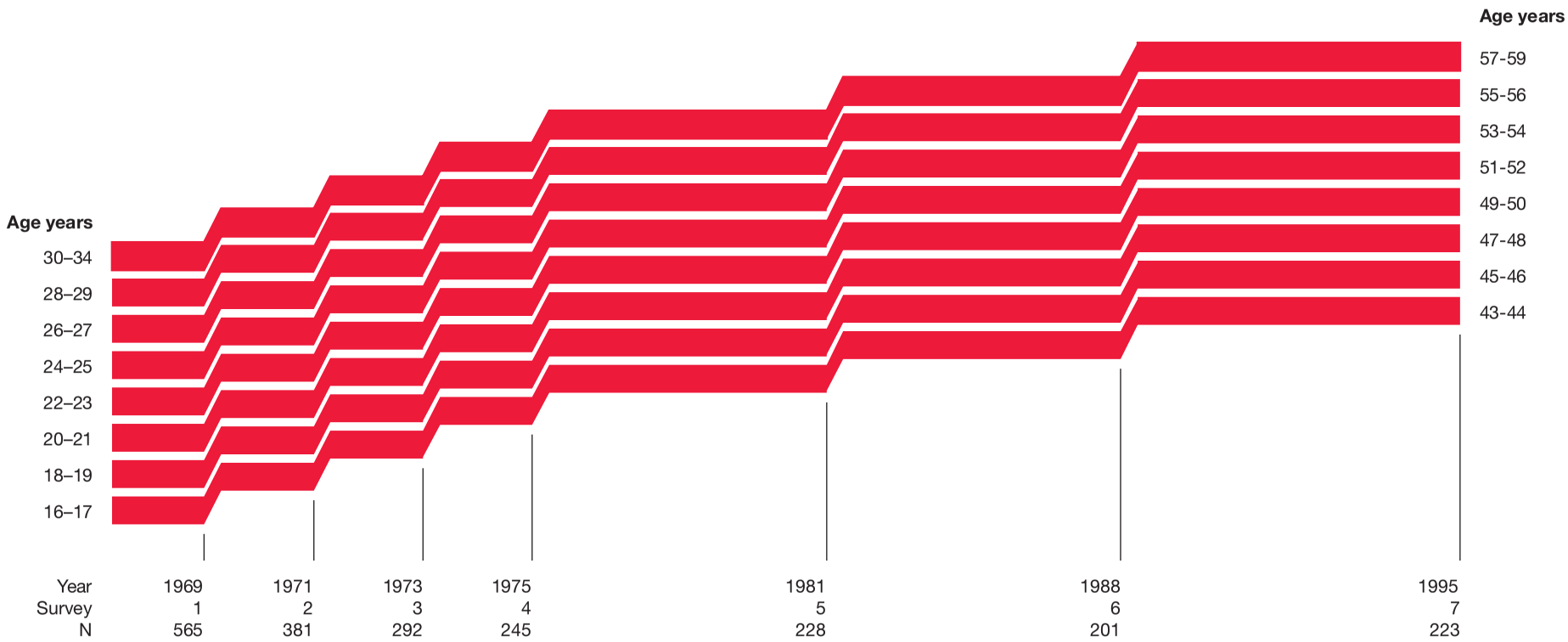
Table 2: Number of patients examined at each survey during 26 years

Age Group	Survey 1	Survey 2	Survey 3	Survey 4	Survey 5	Survey 6	Survey 7	Patients per Age Group
< 20	143	65						208
20-24	224	149	117	51				541
25-29	161	116	102	88	45			512
30-34	36	45	65	89	92			327
35-39	1	6	8	16	74	77		182
40-44				1	17	82	30	130
45-49						41	104	145
50-54						0	66	66
55-59						1	23	24
Patients per Survey	565	381	292	245	228	201	223	

Mean observation period: 16.6 years

Patients in 2 or more surveys: 487

Figure 2: Norwegian age cohorts at baseline & subsequent re-examinations



Study I: Role of Gingivitis

For site specific calculations, three Gingival Index levels corresponding to their history of gingival inflammation over the 26 years were established (Table 3):

1. Sites which always scored GI = 0 (healthy sites)
2. Sites always scoring GI = 1 (slightly inflamed)
3. Sites which always scored GI = 2 (inflamed with bleeding on probing)

All other sites with various scores for inflammation during the observation period were not considered for further evaluation.

Table 3: Frequency distribution of number of sites for different Ginigival Index levels by age groups

Age-Group	N Sites	GI = 0		GI = 1		GI = 2	
		n	%	N	%	N	%
< 20	8694	3054	35.13%	4644	53.42%	996	11.46%
20 – 24	20522	5683	27.69%	11677	56.90%	3162	15.41%
25 – 29	18900	3928	20.78%	11671	61.75%	3301	17.47%
30 – 34	11500	2250	19.57%	6959	60.51%	2291	19.92%
35 – 39	6560	1658	25.27%	3843	58.58%	1059	16.14%
40 – 44	5059	1480	29.25%	2891	57.15%	688	13.60%
45 – 49	5398	1321	24.47%	3107	57.56%	970	17.97%
50 – 54	2623	497	18.95%	1621	61.80%	505	19.25%
55 – 59	827	148	17.90%	544	65.78%	135	16.32%

Study II: Initial Loss of Attachment

In the data analysis, 3 subsets of individuals were considered.

Subset 1: Individuals included in the study that were available for examination at one or more surveys, referred to as All Valid Observation (AVO), N = 565

Subset 2: Individuals present both at the First and Last surveys, referred to as First and Last (F&L), N = 223

Subset 3: Individuals present at all examination, referred to as In All Surveys (IAS), N = 54

Loss of attachment was measured using a blunt probe with a point diameter of 0.6 mm and graded at 1, 2, 3, 4, 5, 7, 9, 11 mm. The same probes were used at all examinations. Loss of attachment is the distance from the CEJ to the bottom of the clinical pocket. In cases where the marginal gingiva has been subject to recession and the CEJ is exposed, the loss of attachment equals the sum of pocket depth and the distance from gingival margin to the CEJ: a + b = LA (Löe et al. 1978b).

Initial loss of attachment (ILA) was defined as the first attachment loss of 2 mm or more as measured from the cemento-enamel junction.

The age of individuals having ILA at 1 or more sites and at ≥10%, ≥ 20%, ≥ 50% of sites, was analyzed within each subset of subjects. The frequency distribution of ILA at different surfaces was evaluated over time.

Study III: Incidence and Risks of Attachment Loss

As indicated for *Study II* loss of attachment was measured with the probe specified and according to the methods already described. The mean individual rate of attachment loss was calculated as the difference between the individual mean attachment loss of all sites of a subject between 2 examinations divided by the years between the two examinations.

The level for **"sites with periodontal attachment loss"** was set at 2 mm or more. Periodontal attachment loss was presented as only pocket formation (Pocket Depth ≥2 mm), as only recession (Recession >0 mm, Pocket Depth <2 mm) or as combinations of the two. This analysis consisted of sites with *initial loss of attachment* (first occurrence of 2 mm or more of periodontal attachment loss) as well as sites in which loss of attachment had been recorded in a previous examination.

"Reversed sites" were defined as sites that already had a recorded loss of attachment at a previous survey and yet, had less than 2 mm of attachment loss at one of the following survey(s).

"Healthy sites" were defined as sites that never passed the threshold of 2 mm attachment loss.

Based on the results of Glavind & Löe (1967) reporting a measurement error of less than 0.5 mm for individual sites in assessing pocket depth and loss of attachment, a threshold of 1 mm was set as the criterion for a site to lose further periodontal attachment over time after initial attachment loss had been recorded. Sites with attachment loss at baseline were not considered for this part of evaluation. For these calculations, the last measured value and the time of initial loss of attachment were compared:

- Initial loss of attachment = LoA value assessed at the latest examination, **Non-progressing (stable) sites**
- Initial loss of attachment < LoA value assessed at the latest examination, **Progressed sites**
- Initial loss of attachment > LoA value assessed at the latest examination, **Reversed sites**

Sites with loss of attachment of 2 mm or more at baseline or with initial loss of attachment at Survey 7 (1995) were not considered for this part of the analysis.

Study IV: Gingivitis and Tooth Mortality

For tooth-specific calculations, three groups reflecting the history of inflammation of the surrounding gingivae (GI-scores) over 26 years were established. For that reason, the minimal and maximal GI value of all sites were determined and used to define three GI severity groups:

– GI Severity Group I: Teeth with surrounding gingival units scoring a minimum of one site with GI = 0 and a maximum of three sites out of four with GI = 1 over the observation period (mean tooth GI between 0-0.75).

– GI Severity Group II: Teeth with surrounding gingival units scoring a minimum of one site with GI = 1 and a maximum of three sites out of four with GI = 2 over the observation period (mean tooth GI between 1-1.75).

– GI Severity Group III: Teeth with surrounding gingival units always scoring a minimum of GI = 2 (bleeding on probing) at all sites over the observation period (mean tooth GI ≥ 2)

All other teeth not fulfilling these criteria (e.g.: teeth with one site scoring GI=2 and three sites scoring GI=0 at any time) were not considered for further evaluation (Tables 4a,b).

Table 4a: Number of retained and lost teeth by Gingival Index severity levels (only selected teeth)

GI Severity Group I GI_Min = 0 and GI_Max < 1				GI Severity Group II GI_Min = 1 and GI_Max < 2				GI Severity Group III GI_Min ≥ 2			
Teeth retained		Teeth lost		Teeth retained		Teeth lost		Teeth retained		Teeth lost	
N	%	N	%	N	%	N	%	N	%	N	%
5793	99.72	16	0.28	3348	97.72	78	2.28	103	88.79	13	11.21

3934 teeth (29,8%) did not fulfill the selection criteria, 19 (0.48 %) were lost during the 26 years of observation.

Table 4b: Cumulative number of lost teeth by Gingival Index severity levels and age groups (only selected teeth)

Age Group	GI Severity Group I (0 ≤ GI < 1) Teeth lost		GI Severity Group II (1 ≤ GI < 2) Teeth lost		GI Severity Group III (GI ≥ 2) Teeth lost	
	N	%	N	%	N	%
< 20	1	6.25 %	1	1.28 %	1	7.69 %
20 – 24	6	37.50 %	12	15.38 %	0	0.00 %
25 – 29	2	12.50 %	20	25.64 %	3	23.08 %
30 – 34	4	25.00 %	13	16.67 %	5	38.46 %
35 – 39	0	0.00 %	12	15.38 %	1	7.69 %
40 – 44	1	6.25 %	9	11.54 %	0	0.00 %
45 – 49	2	12.50 %	7	8.97 %	3	23.08 %
50 – 54	0	0.00 %	4	5.13 %	0	0.00 %
55 – 59	0	0.00 %	0	0.00 %	0	0.00 %
Total	16	14.95 %	78	72.90 %	13	12.15 %

For tooth loss survival analysis, the time points of permanent tooth eruption were considered for each tooth type. This was based on data published for Danish males by Helm and Seidler (1974) (Table 5) that are in agreement with the timing of incisor tooth eruptions for Norwegian males (Alstad 1973). Hence, the tooth age was calculated as the time period between the mean age for tooth eruption and the midpoint of the two latest surveys, when the tooth was still present and the survey during which the tooth was lost.

Table 5: Age of permanent tooth eruption in Danish boys (Helm & Seidler 1974):

Maxilla:

Tooth	Mean age of emergence in years	Standard error	Standard Deviation
I1	7.18	0.024	0.74
I2	8.21	0.030	0.87
C	11.45	0.036	1.21
P1	10.59	0.038	1.46
P2	11.43	0.041	1.47
M1	6.25	0.028	0.71
M2	12.39	0.041	1.26

Mandible:

Tooth	Mean age of emergence in years	Standard error	Standard Deviation
I1	6.19	0.027	0.66
I2	7.38	0.029	0.90
C	10.54	0.032	1.13
P1	10.68	0.040	1.48
P2	11.53	0.041	1.44
M1	6.21	0.028	0.68
M2	11.90	0.041	1.30

Study V: Margins of Restorations and Attachment Loss

For this analysis, 160 of all 565 subjects who were examined in 1969 were selected on the basis of the Gingival Restoration Index (Löe 1967): (1) having no fillings, or no filling margins extending closer than 1 millimeter from the gingival margin on the mesial surfaces of all available premolars and molars, and (2) being present at the examinations in Surveys 2 (1971) and 3 (1973).

The test group of 98 sites was established in 1971 and comprised all mesial surfaces, which had had fillings placed between Surveys 1 and 2 extending more than 1 millimeter below the gingival margin. The control group consisted of 615 sites, that were sound at all 7 surveys, or that yielded filling margins no closer than 1 millimeter from the gingival margin.

Table 6 lists the number of subjects, teeth and surfaces in the test and control groups at each survey.

Table 6: Survey and number of sites examined at each survey during 26 years

	Number of Patients	Patients of the control cohort	Patients of the test cohort	Number of Teeth	Total Control Teeth		Total Test Teeth	
Survey 1	160	159	69	713	615	86.3 %	98	13.7 %
Survey 2	160	159	69	713	615	86.3 %	98	13.7 %
Survey 3	160	159	69	713	615	86.3 %	98	13.7 %
Survey 4	128	127	57	544	465	85.5 %	79	14.5 %
Survey 5	84	83	37	361	313	86.7 %	48	13.3 %
Survey 6	69	68	33	307	264	86.0 %	43	14.0 %
Survey 7	54	53	28	272	237	87.1 %	35	12.9 %

	Total Sites	Total Control Sites		Distribution of the Control Sites			
				Premolars		Molars	
Survey 1	713	615	86.3 %	504	82.0 %	111	18.0 %
Survey 2	713	615	86.3 %	504	82.0 %	111	18.0 %
Survey 3	713	615	86.3 %	504	82.0 %	111	18.0 %
Survey 4	544	465	85.5 %	395	85.0 %	70	15.0 %
Survey 5	361	313	86.7 %	262	83.7 %	51	16.3 %
Survey 6	307	264	86.0 %	220	83.3 %	44	16.7 %
Survey 7	272	237	87.1 %	171	84.6 %	31	15.4 %

	Total Sites	Total Test Sites		Distribution of the Test Sites			
				Premolars		Molars	
Survey 1	713	98	13.7 %	50	51.0 %	48	49.0 %
Survey 2	713	98	13.7 %	50	51.0 %	48	49.0 %
Survey 3	713	98	13.7 %	50	51.0 %	48	49.0 %
Survey 4	544	79	14.5 %	42	53.2 %	37	46.8 %
Survey 5	361	48	13.3 %	23	47.9 %	25	52.1 %
Survey 6	307	43	14.0 %	22	51.2 %	21	48.8 %
Survey 7	272	35	12.9 %	16	45.7 %	19	54.3 %

Data analysis

The Statistical Analysis System Package (SAS Institute Inc., Cary, N.C., USA) was used in order to calculate frequency distributions, means, standard deviations and standard errors.

Study I: Role of Gingivitis

For the calculations of the odds ratios logistic regression models (PROC LOGISTIC, SAS/STAT® Software, Copyright © 2000 by SAS Institute Inc., Cary, NC, USA. All rights reserved) were used to model loss of attachment as a function of the degree of gingival inflammation.

Study II: Incidence of Attachment Loss

In order to gain true longitudinal information, the subset 3, i.e. in all surveys (IAS), was analyzed. Mesial and buccal sites were consistently scored throughout the study. Therefore these sites were chosen for evaluation.

Study III: Progression of Attachment Loss

For comparison of significant changes in the rates of attachment loss between two age groups longitudinally, the Wilcoxon Mann-Whitney U test (Proc NPAR1Way, SAS/STAT® Software, Copyright © 2000 by SAS Institute Inc., Cary, NC, USA. All rights reserved) was used.

Study IV: Gingival Inflammation and Tooth Mortality

For the calculations of the odds ratios, logistic regression models (PROC LOGISTIC, SAS/STAT® Software, Copyright © 2000 by SAS Institute Inc., Cary, NC, USA. All rights reserved) were used to model the binary tooth loss variable as a function of gingival inflammation severity class.

For the calculations of the survival analysis (Kaplan-Meier-Analysis) the PROC LIFETEST, (SAS/STAT® Software, Copyright © 2000 by SAS Institute Inc., Cary, NC, USA. All rights

reserved), was used to model the tooth loss variable as a function of gingival inflammation severity class and tooth age.

Study V: Restoration Margins and Loss of Attachment

Defined test sites with subgingivally located filling margins, placed between Surveys 1 and 2, were compared to defined control sites by using the students t-test for independent samples.

For the comparison of significant changes in the variables between two surveys longitudinally, the Wilcoxon Rank test was used.

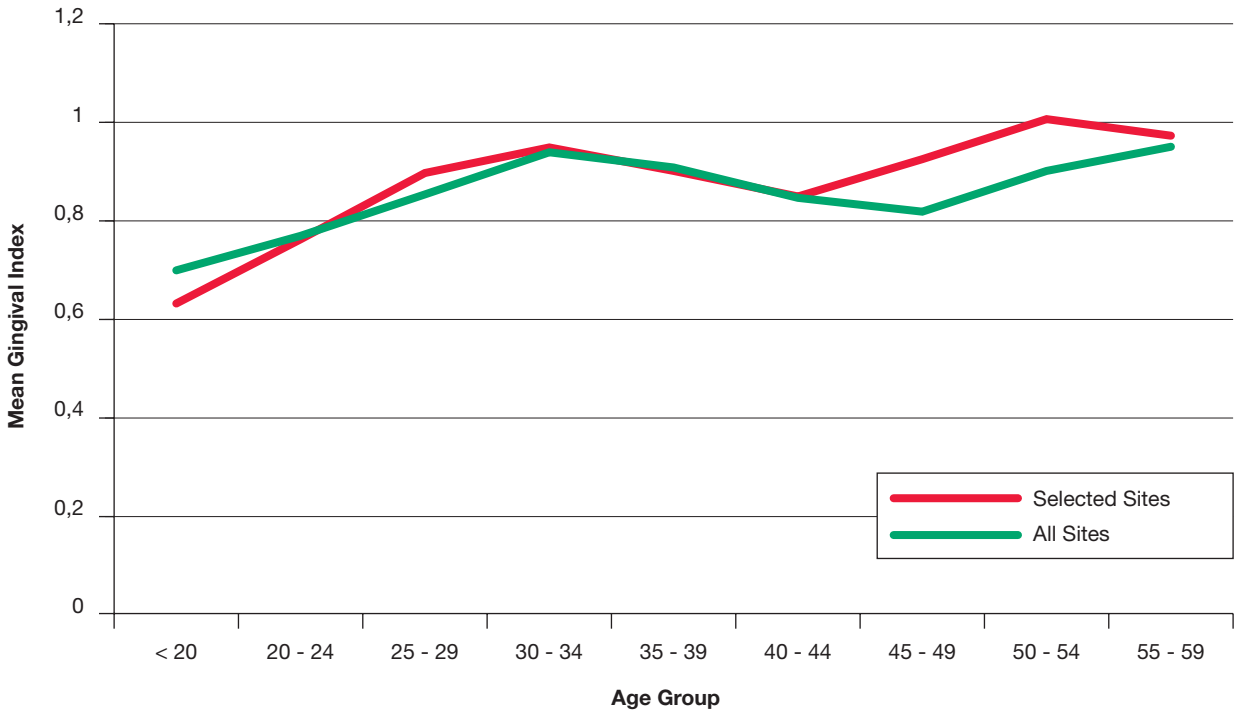
The level of significance was set at $\alpha = 0.05$ for all five studies.

RESULTS

Role of Gingivitis

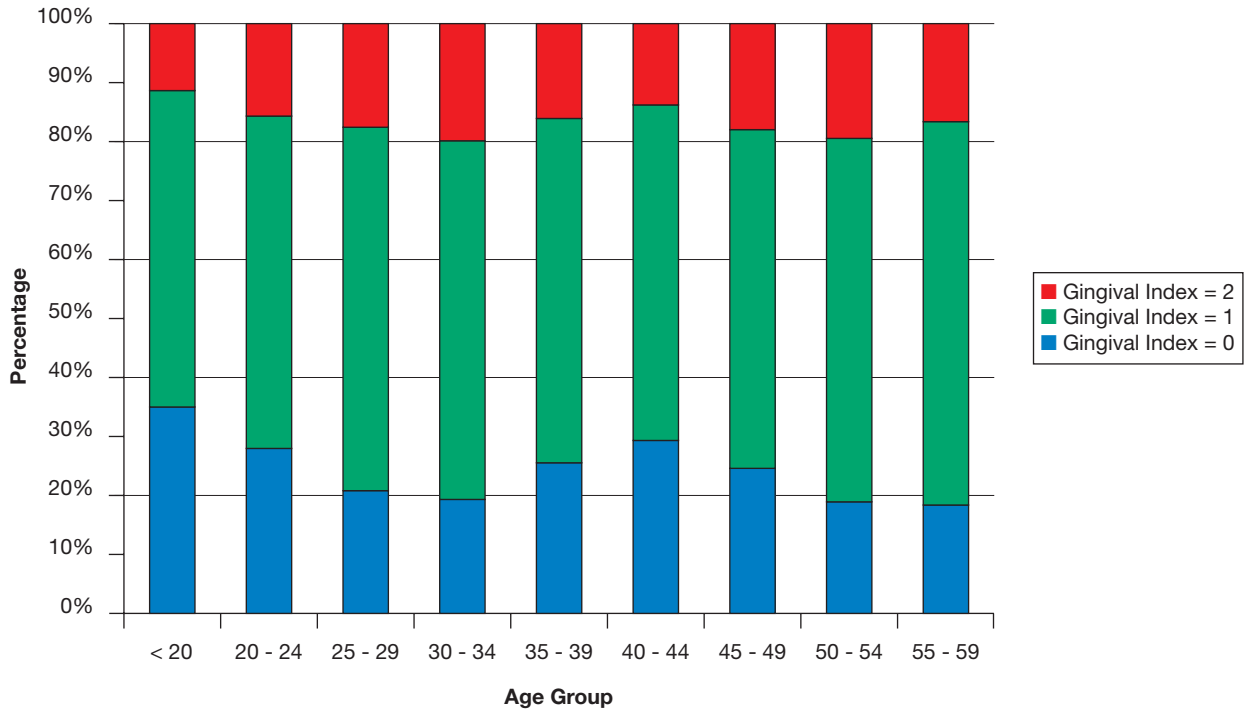
In *Study I*, the mean Gingival Index for the selected tooth sites over the 26-year period, represented good to excellent gingival health and did not differ significantly from the mean Gingival Index scores for all sites (Fig. 3).

Figure 3: Mean Gingival Index by age groups



The relative proportions of the three Gingival Index groups showed that approximately 20-30% were GI=0 sites, 55–65% were GI=1 and 10–20 % were sites GI=2 that bled on probing at all observation periods (Fig. 4).

Figure 4: Frequency distribution of Gingival Index scores by age groups



Loss of Attachment:

In the youngest cohort (<20 years), the mean loss of attachment of the three GI groups varied between 0.08 and 0.16 mm (Fig. 5) *(Study I)*. As the participants approached 60 years of age, the cumulative attachment loss was less than 2 mm (1.94 mm) for the GI=0 group, 2.42 mm for the GI=1 group and 3.32 mm for the GI=2 group. The loss of attachment in the GI=0-group was significantly lower than that of the two other groups during the entire observation period, except in the youngest patient cohort, where all groups started at very low levels. The GI=2-group differed significantly from the GI=1-group in all age cohorts, except the cohort of 40–44 years. In the GI=2 group, the mean attachment loss was always higher than in the two other groups.

Figure 5: Mean loss of attachment values by age groups for different Gingival Index levels

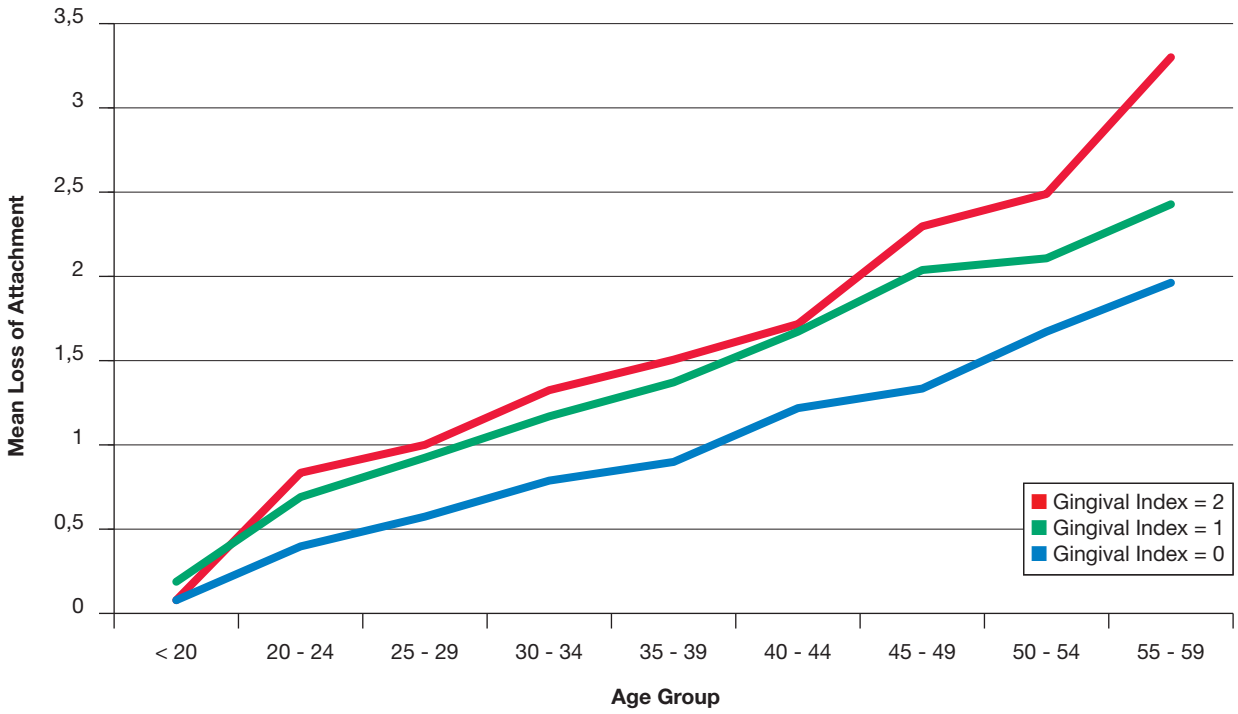
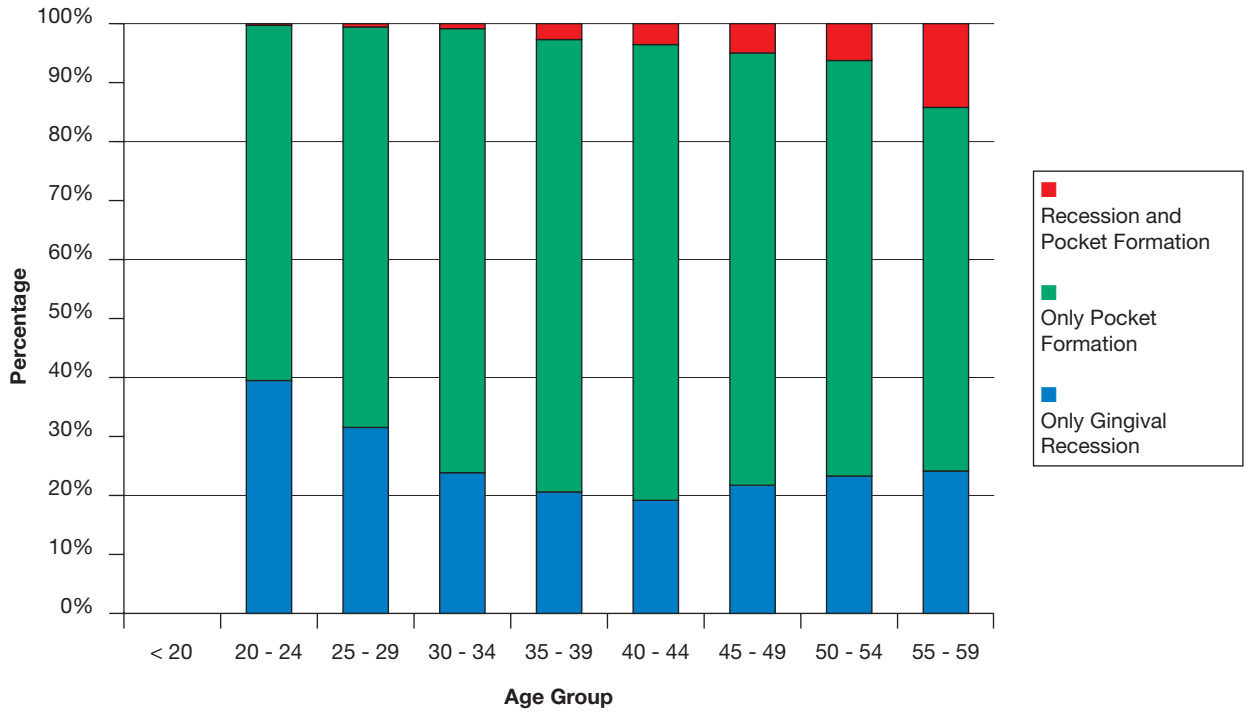


Figure 6 illustrates the frequency of sites with at least 2 mm attachment loss with pocket formation, gingival recession or combinations of the two *(Study I)*. In the youngest cohort (20-24 years), 60% of the sites with periodontal attachment loss presented with pocket formation with or without gingival recession. With increasing age, attachment loss in terms of pocket formation only and in combination of pocket formation and gingival recession increased to 75% of the sites of the 55-59 year old subjects. After the age of 30 years, the total proportion of sites with gingival recession only remained stable in 20-25% of the sites. At the same time, however, there was a slight decrease in proportions of pocket formation (from 76% to 61%) and a modest increase in the proportion of pocket-recession combinations (from 0% to 15%).

Figure 6: Frequency of occurrence of gingival recession, pocket formation and the combination thereof contributing to loss of attachment in various age groups



Overall, the severity of gingival inflammation was the most prominent factor in losing attachment. All the risk factors for attachment loss are depicted in Table 7 *(Study I)*. For sites always scoring GI=1, the odds ratio for attachment loss was 2.29 (Confidence Interval: 2.21–2.39), and for sites always bleeding on probing (GI=2) the odds ratio was 3.22 (C.I.: 3.03–3.42) as compared to non-inflamed sites (GI=0) at any observation time. The odds ratio for loss of periodontal attachment for tooth sites scoring consistently GI=2 was 1.40 (C.I.: 1.33–1.48) compared to tooth sites with only slight gingival inflammation (GI=1).

Adjusting all the risk indicators to these three Gingival Index groups, subgingival calculus (CI=2) presented the highest risk for loss of periodontal attachment in GI=2-group (OR 4.22 (C.I.: 1.61-11.07)).

Table 7: Risk indicators for Further Loss of Attachment for Different Groups Always Scoring GI=0, GI=1 and GI=2, respectively

Risk Factor	GI = 0		GI = 1		GI = 2	
	Odds Ratio	Confidence Interval 95 %	Odds Ratio	Confidence Interval 95 %	Odds Ratio	Confidence Interval 95 %
Plaque Index =1 vs. PII=0	n. s.	,	0.61	0.39 – 0.94	n. a.	,
Plaque Index = 2 vs. PII=0	0.659	0.44 – 0.98	0.44	0.28 – 0.68	n. a.	,
Calculus Index = 1 vs. CII=0	n. s.	,	n. s.	,	n. s	,
Calculus Index = 2 vs. CII=0	n. s.	,	n. s.	,	4.22	1.61 – 11.07
Gingival Caries Index = 1 vs. GCI=0	n. s.	,	n. s.	,	n. a.	,
Gingival Caries Index = 2 vs. GCI=0	n. a.	,	n. a.	,	n. a.	,
Gingival Restoration Index = 1 vs. GRI=0	n. s.	,	0.63	0.45 – 0.89	n. s.	,
Gingival Restoration Index = 2 vs. GRI=0	n. s.	,	0.54	0.39 – 0.74	0.15	0.06 – 0.42
Smokers Vs. Non-Smokers	2.015	1.27 – 3.2	1.41	1.02 – 1.95	1.01 (n. s.)	0.21 – 4.89

In smokers, sites always bleeding on probing (GI=2) had an odds ratio for loss of attachment that did not reach the level of statistical significance and, therefore, did not represent a risk factor.

For the GI=1-group, the odds ratio for smokers was 1.41 (C.I.: 1.02-1.95), and for the GI=0-cohort the odds ratio was 2.02 (C.I.: 1.27-3.2), both of which representing a significant risk factor for attachment loss.

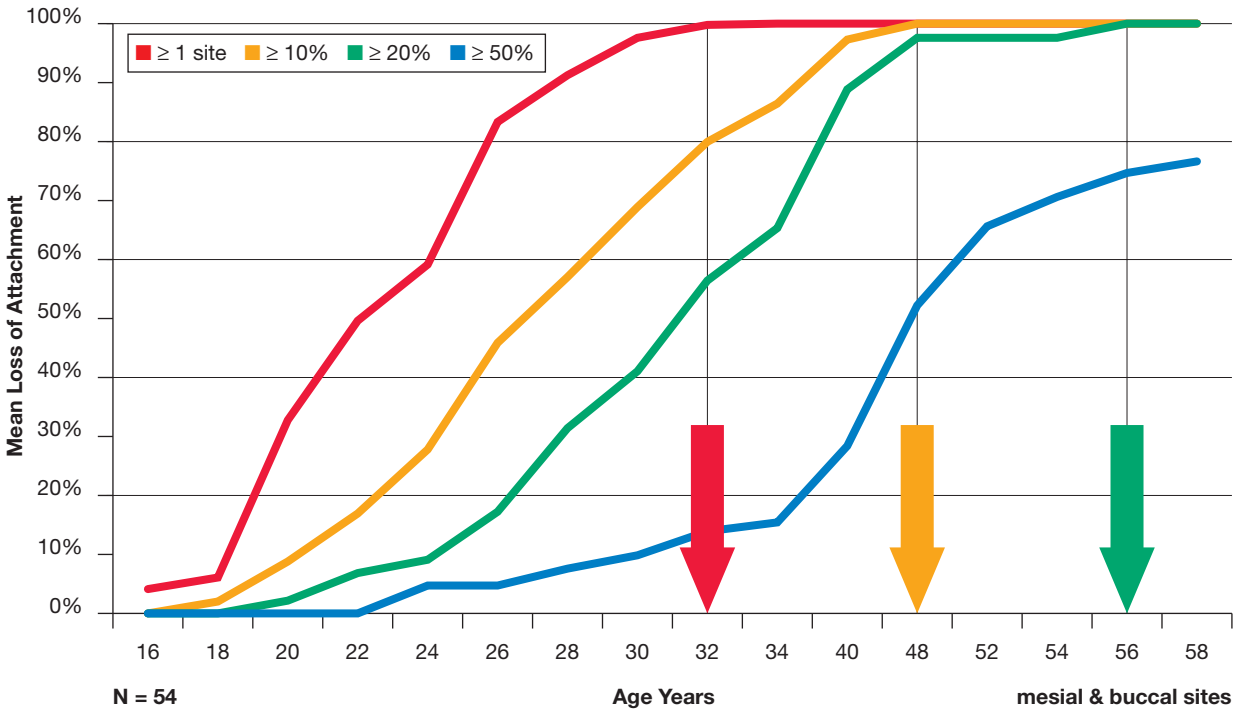
All other possible risk factors (PII, GCI, GRI) examined did not reach the level of statistical significance (Table 7).

Incidence of Initial Loss of Attachment (ILA)

In *Study II*, the analysis of the time of occurrence, lesion characteristics and frequency distribution of the initial periodontal lesions disclosed no significant differences between subjects that were available for examination at one or more surveys (all valid observations (AVO)), individuals present in the first and last surveys (F&L) or individuals who appeared in all surveys (IAS), indicating that the loss to follow-up had no significant impact on the data analyzed.

Five percent of the subjects had initial loss of attachment (ILA) of 2 mm or more at one or more sites at the age of 16 years. The incidence of ILA increased during the twenties, and by the age of 32 years, all men had ILA at one or more sites (Fig. 7). At the age of 48 years, all individuals had ILA at least at 10% of all available sites, and at age 56 years, more than 20% of the sites were affected.

Figure 7: Age at which initial attachment loss occurred at ≥1 site, ≥10%, ≥20%, ≥50% of sites in the subset IAS.



Types of Lesions of Sites with Initial Loss of Attachment

At 20 years of age, almost all ILA lesions presented as gingival recession *(Study II)*. Actually, out of 107 sites with ILA ≥2 mm, only 2 sites showed pocket formation (Fig. 8a). Similarly, at age 30 years, the vast majority of sites was characterized by gingival recession (Fig. 8b). At 40 years of age, still less than 10% of the sites had pockets measuring 3 mm or more (Fig. 8c). At 55 years of age, however, in approximately one third of the sites with ILA, the attachment lost was due to pocket formation (Fig. 8d). With increasing age, increasing proportions of sites with ILA were attributed to pocket formation or combinations of pocketing and gingival recession. As the men approached 60 years of age, almost all buccal surfaces and the majority of interproximal areas had ILA in the form of gingival recession, pocket formation or combinations thereof.

Figure 8a – Age 20 Years

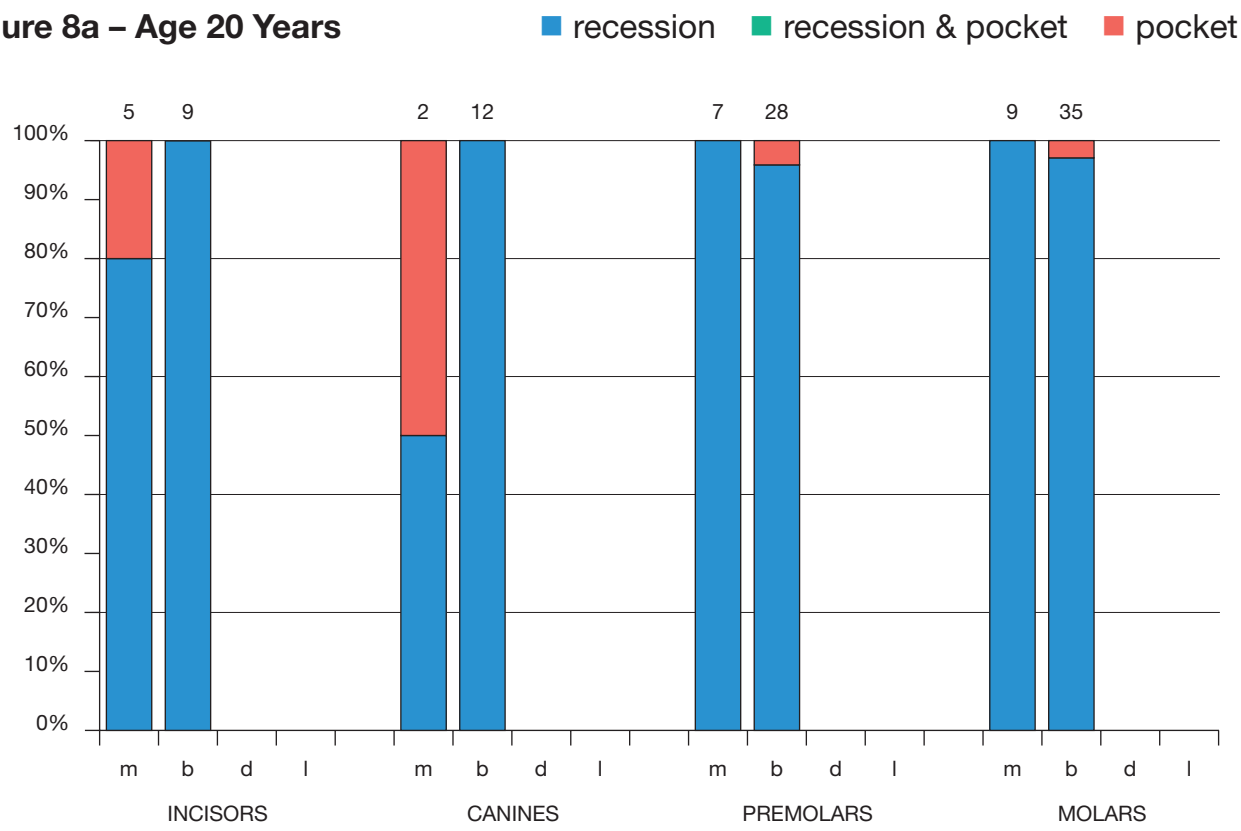


Figure 8b – Age 30 Years

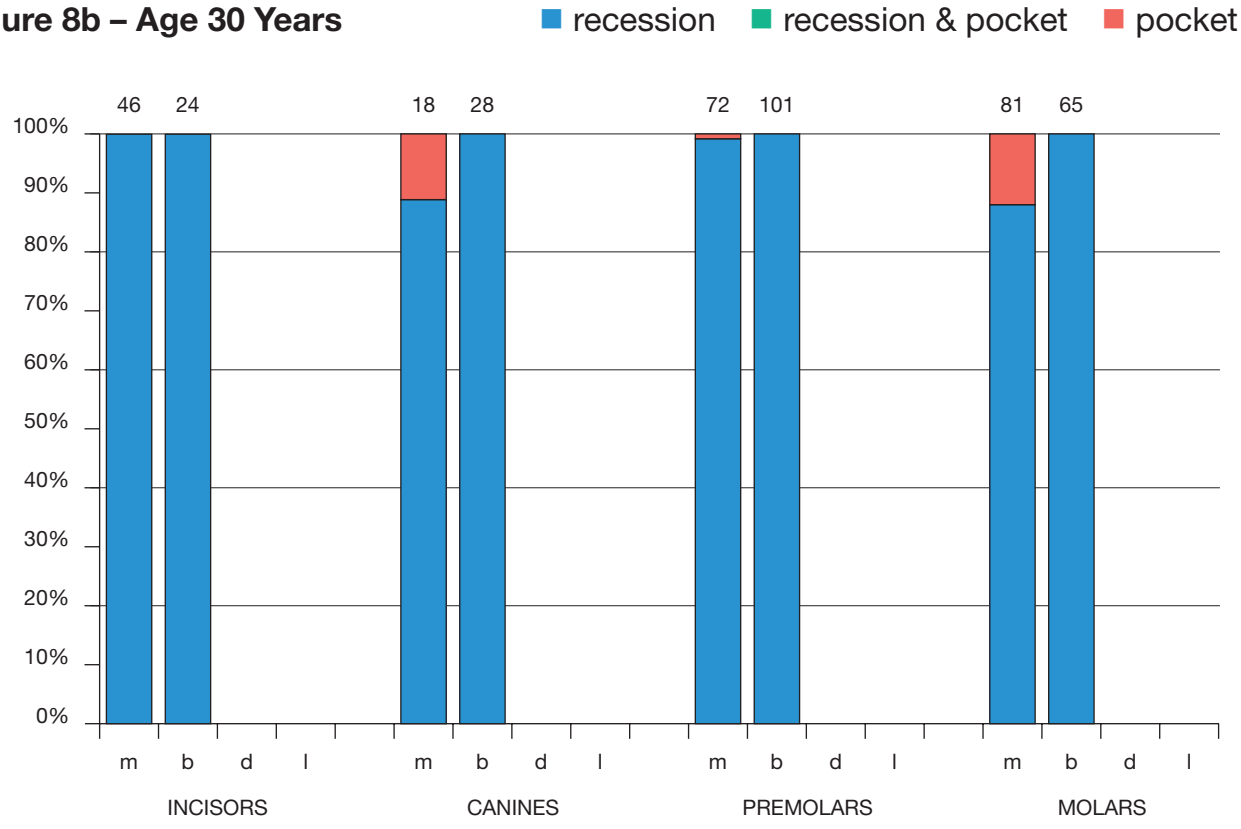


Figure 8c – Age 40 Years

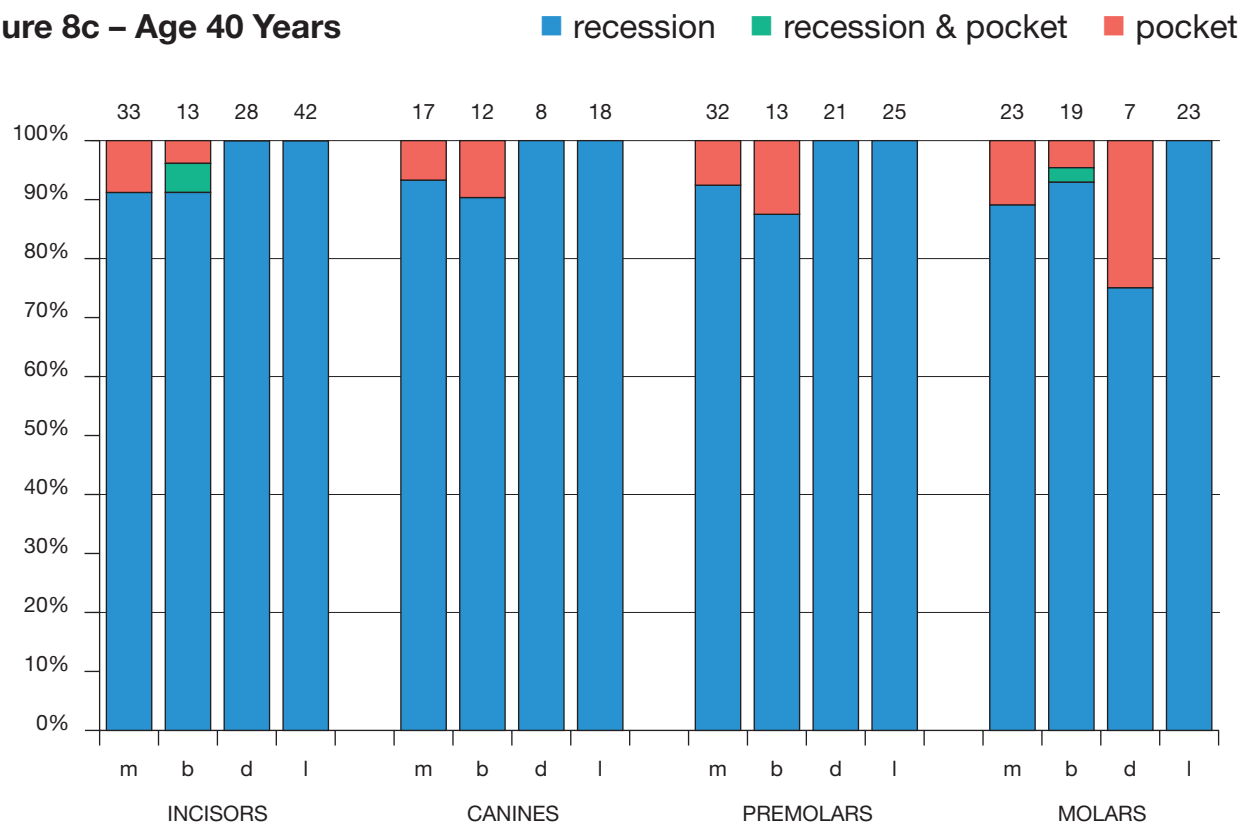
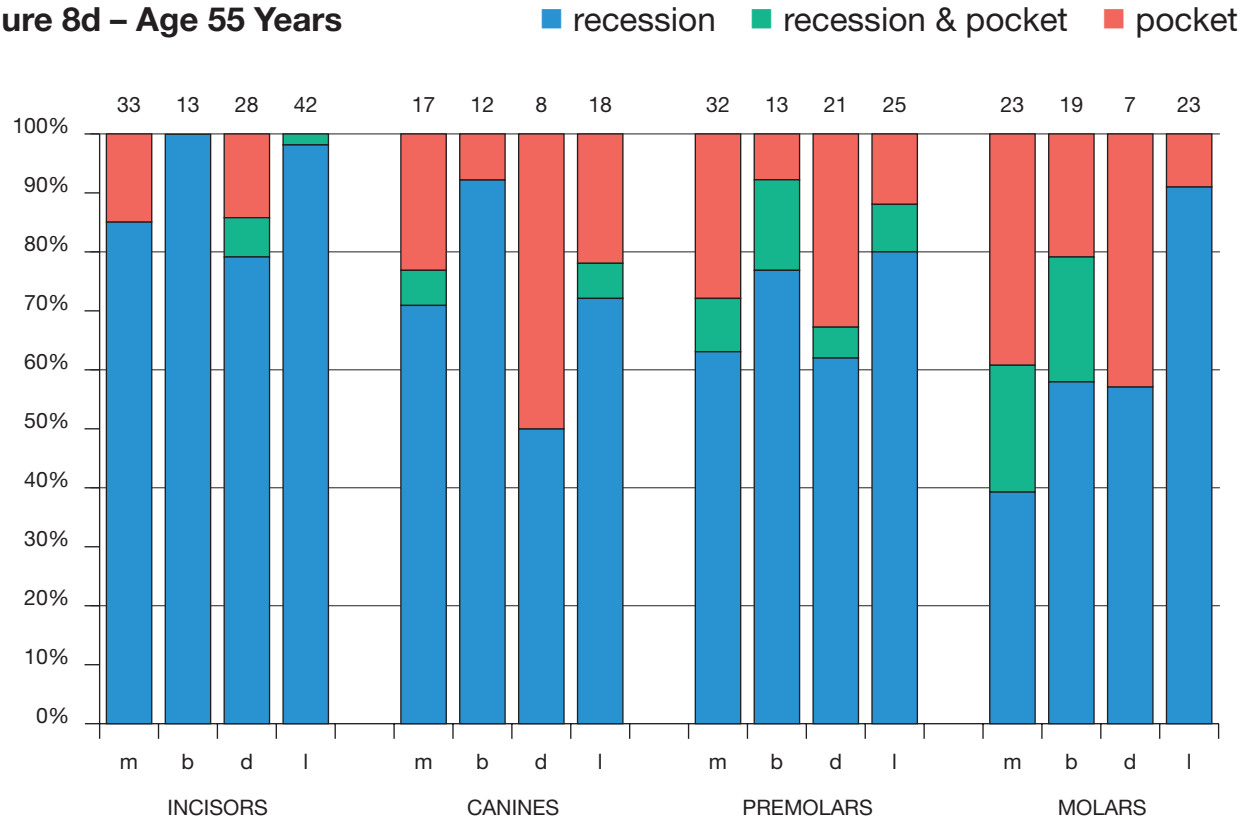


Figure 8d – Age 55 Years



Progression of Initial Loss of Attachment

In 1969, out of 30766 sites examined, 2997 sites had already lost attachment of 2 mm or more. These were, therefore, not considered for further analysis. Also at the last survey, 6135 (25.4%) out of available 24168 sites in 1995, exhibited initial loss of attachment. Since, no statement about their future progression could be made; these sites were not subject to the analysis either.

13390 sites out of a total of 22522 sites with recorded attachment loss were considered for the analysis of the progression of initial attachment loss *(Study III)*.

Table 8 shows the frequency distribution of sites with initial loss of attachment with different recorded characteristics: stable sites, reversed sites and progressed sites. Less than 25% of all sites progressed to lose further periodontal attachment; about 50% of all sites expressing initial loss of attachment within the first 6 surveys remained stable. As individuals approached 60 years of age, 30% of the tooth sites did not exhibit any loss of attachment.

Table 8: Frequency distribution of sites with loss of attachment: Stable sites, progressed sites, reversed sites

	N	Percentage
Stable Sites	6462	48.26 %
Reversed Sites	3991	29.81 %
Progressed Sites	2937	21.93 %
Total	13390	100.00 %

Sites not considered for this evaluation:
2997 sites with initial loss of attachment at baseline (1969)
6135 sites with initial loss of attachment at Survey 7 (1995)

Table 9 shows the frequency distribution of the 22% of sites that showed further attachment loss after initial loss of attachment was recorded. Almost 90% of these sites lost only minor further attachment (≤2 mm). About 10% of the progressed sites lost 3-4 mm in the period from diagnosis to the time point at which the subjects were no longer

followed. Only very few sites (50 of 13390; 0.02%) that had expressed initial loss of attachment showed substantial progression (>4 mm).

Table 9: Frequency Distribution of Further Attachment Loss of Progressed Sites after Initial Loss of Attachment was recorded

Loss of attachment	N	Percentage
1 – 2 mm	2603	88.63 %
3 – 4 mm	284	9.67 %
5 – 6 mm	33	0.01 %
≥ 7 mm	17	0.01 %
Total	2937	100.00 %

Rates of Progression of Attachment Loss

The mean individual cumulative attachment loss ranged from 0.14 mm at 16-19 years of age to 2.44 mm in the 55-59 year old subjects *(Study III)*. The mean rate of annualized loss of attachment before 20 years of age was 0.09 mm/year. As the subjects approached 30 years of age, the rate fluctuated between 0.07 and 0.10 mm/year, after which a statistically significant decrease to 0.05 mm/year was observed. This annual rate of loss of attachment remained stable for the following 20 years of life. During the 6th decade of life, a trend towards an increased annualized rate of loss of attachment was seen. However, this was not statistically significant (Fig. 9).

Frequency analyses showed (Table 10) that before 20 years of age, 14% of the subjects experienced a mean annual rate of attachment loss below 0.02 mm, 29% had an annual rate between 0.02 and 0.06 mm and in 57% of the subjects, loss of attachment progressed at a mean annual rate of more than 0.06 mm. During the forth and fifth decades of life, this annual rate of progression was lower and comprised between 26% and 36% of the subjects, respectively. As they approached 60 years of age, 50% of the men, again, exhibited an annual progression rate of more than 0.06 mm.

Figure 9: Mean Annualized Rate of Loss of Attachment by Age Groups

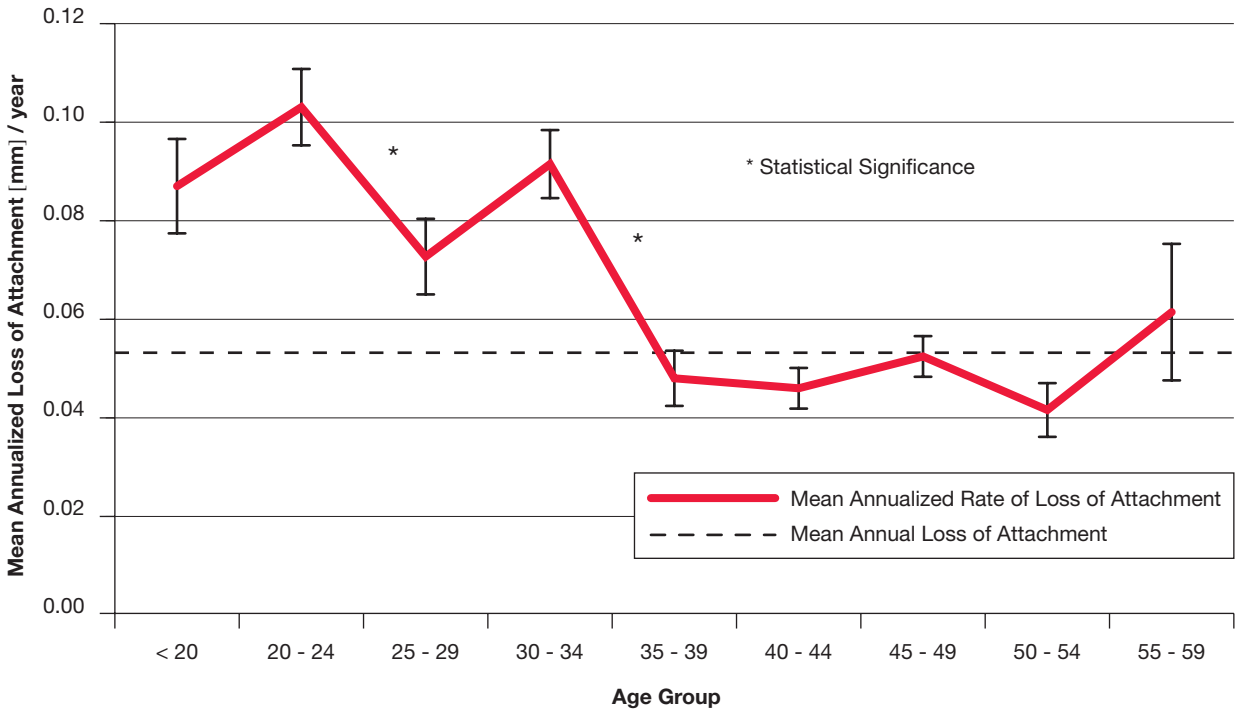


Table 10: Frequency of annualized loss of attachment rates by age groups

Age Group	LoA ≤ 0.02 mm / year		0.02 < LoA ≤ 0.06 mm / year		0.06 < LoA ≤ 0.12 mm / year		0.12 mm/year < LoA	
	N	%	N	%	N	%	N	%
< 20	9	13.85 %	19	29.23 %	22	33.85 %	15	23.08 %
20-24	87	27.44 %	31	9.78 %	62	19.56 %	137	43.22 %
25-29	124	35.33 %	38	10.83 %	68	19.37 %	121	34.47 %
30-34	77	26.46 %	54	18.56 %	60	20.62 %	100	34.36 %
35-39	61	33.70 %	54	29.83 %	50	27.62 %	16	8.84 %
40-44	33	25.78 %	50	39.06 %	38	29.69 %	7	5.47 %
45-49	33	23.57 %	56	40.00 %	38	27.14 %	13	9.29 %
50-54	17	27.87 %	28	45.90 %	15	24.59 %	2	3.28 %
55-59	5	21.74 %	7	30.43 %	8	34.78 %	3	13.04 %

Gingival Inflammation and Tooth Mortality

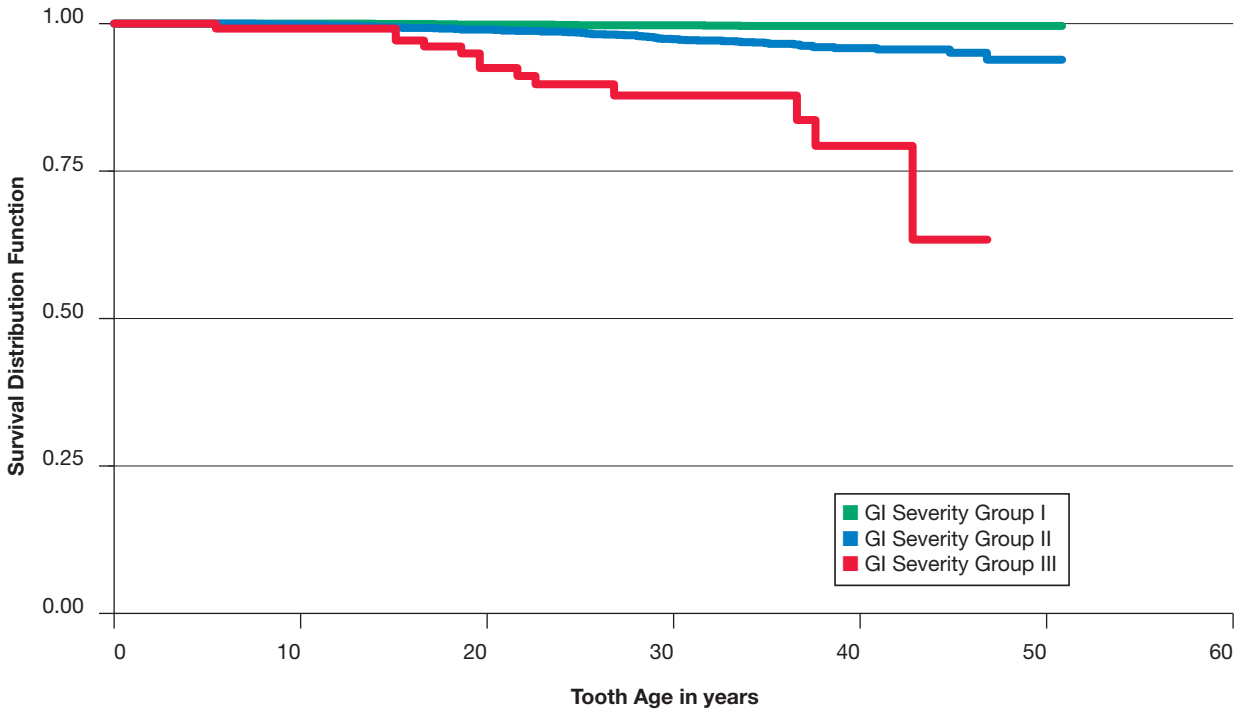
Based on the history of gingival inflammation, in *Study IV*, only 16 out of 5809 (0.28%) teeth with a mean GI <1 (GI Severity Group I), were lost. In the group of teeth scoring a mean GI ≥1 and <2 (GI Severity Group II), 78 (2.28%) out of 3426 teeth were lost. Finally, 13 (11.21%) of 116 teeth scoring a mean GI ≥2 (GI Severity Group III) were lost (Table 4a).

The odds ratio for tooth loss was 8.5 (Confidence Interval: 4.94–14.60) for GI Severity Group II and 45.8 (C.I.: 21.29–97.77) for GI Severity Group III (bleeding on probing) compared to GI Severity Group I. The odds ratio for tooth loss in GI Severity Group III was 5.4 (C.I.: 2.90–10.06) compared to teeth in the GI Severity Group II.

Figure 10 depicts a Kaplan-Meier cumulative survival distribution for the three defined GI Severity Groups. Before a tooth age of approximately 15 years, tooth loss was extremely rare. After a tooth age of 20 years, it is evident that GI Severity Group III yielded a significantly increased cumulative tooth loss when compared to both GI Severity Groups I & II. On the basis of tooth age, the mean tooth survival time for the GI-Severity Group I was 33.6 years (s.e.: 0.013). For the GI-Severity Group II, it was 45.9 years (s.e.: 0.10) and for the GI-Severity Group III, it was 39.4 years (s.e.: 0.94), respectively.

In GI Severity Group I, 99.5% of the teeth were retained after a tooth age of 51 years. In GI-Severity Group II, 93.8% of the teeth were retained after a tooth age of 50 years. However, in GI-Severity Group III, 63.4% of the teeth were retained for a tooth age of 47 years.

Figure 10: Survival Distribution Function for Different Gingival Inflammation Severity Groups



The average number of teeth per subject is depicted in Table 11. Overall, the average number was fairly constant and yielded values between 26.8 and 27.3 teeth per subject.

Table 11: Average Number of Teeth per Subject and Age Group

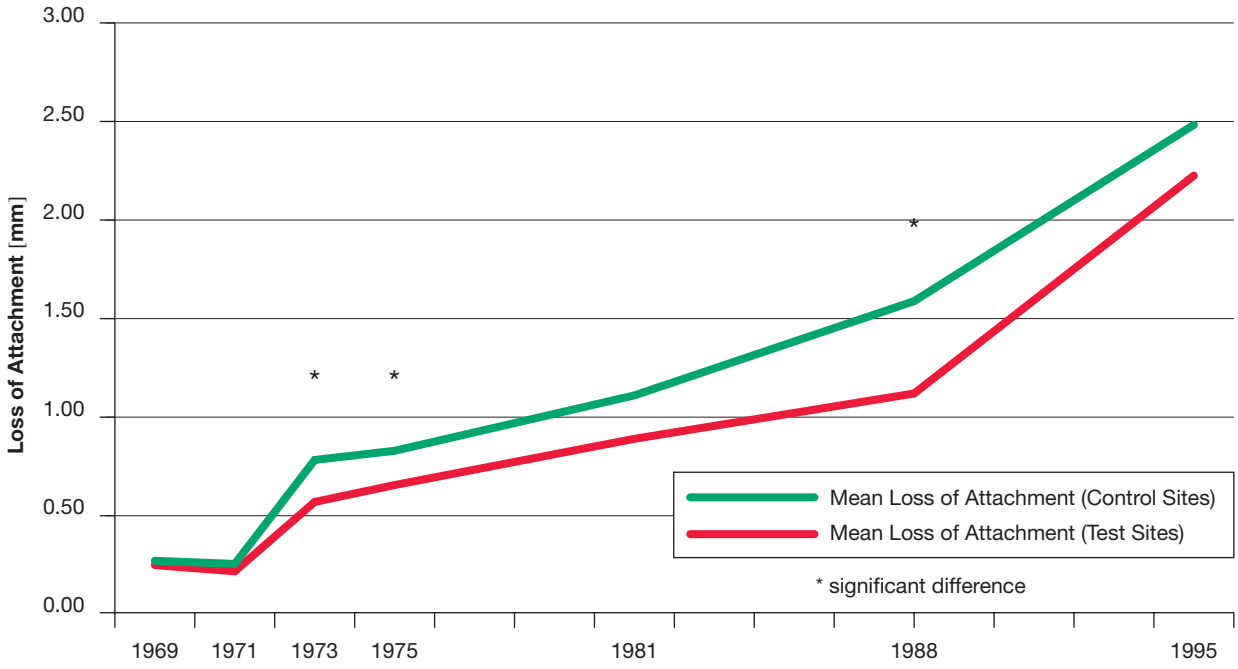
Age Group	Average Number of Teeth per Subject
< 20	27.25
20 – 24	27.30
25 – 29	27.25
30 – 34	27.07
35 – 39	27.10
40 – 44	27.30
45 – 49	27.07
50 – 54	26.77
55 – 59	27.13
Total	27.24

Restorations Margins and Attachment Loss

For this analysis, the cumulative loss of attachment during the entire study period is shown in Figure 11 *(Study V)*. At baseline, the mean loss of attachment of the test and control sites varied between 0.24 and 0.27 mm, respectively. At Survey 3, i.e. 4 years after baseline, a significant difference in the mean loss of attachment was seen between test and control sites, with test sites reaching mean values of 0.78 mm and control sites 0.57 mm, respectively. After 19 years, the cumulative mean loss of attachment was 1.58 mm for the test versus 1.12 mm for the control groups, respectively. At Survey 7, however, the difference between test and control sites was no longer statistically significant.

The greatest increase in mean annual loss of attachment was seen between Surveys 2 and 3, i.e. between 2 and 4 years after baseline and between 19 and 26 years after baseline (Fig. 10).

Figure 11: Mean loss of attachment (mm) for the control and test sites for 26 years



DISCUSSION

In 1969 the main goal of this longitudinal investigation was to study the initiation and progression of chronic periodontitis during major portions of adult life in a randomized population of healthy, well-educated men of the middle class, who had a lifelong exposure to state-of-the-art professional and personal oral health care.

It was expected that in such a group, the clinical course of periodontal disease would transpire in a subtle mode, that the choice of the age cohorts would allow for the recording of the earliest onset of periodontitis, and that, furthermore, the clinical methods chosen would allow for an accurate and reproducible assessment of the earliest signs of the transition from periodontal health to periodontal desease. Both have been born out by previous publications (Löe et al. 1978b, Ånerud et al. 1979, Ånerud et al. 1983) and this thesis.

Role of Gingivitis

On the basis of repeated examinations, *Study I* describes the influence of gingival inflammation on the initiation and progression of chronic periodontitis from adolescence to approximately 60 years of age. Throughout the age range, the mean Gingival Index and the frequency distribution of the different severity levels were maintained, demonstrating no general increase in the prevalence or severity of gingival inflammation from the late teens to approximately 60 years of age. In that respect, the overall gingival health was characterized as “good to excellent”.

Various Gingival Inflammation Levels and Loss of Attachment

The results of *Study I* also demonstrated that over the span of adult life (16-60 years), gingival sites that never scored above GI=0 experienced a mean cumulative loss of attachment of 1.86 mm with a range varying from 0.08 mm to 1.94 mm. For sites exhibiting slight inflammation at all examinations (GI=1), the corresponding loss of attachment was 2.25 mm (range 0.17 mm to 2.42 mm). However, sites presenting at all examinations

with bleedin on probing (GI=2), the mean loss of attachment was 3.23 mm, ranging from 0.09 mm-3.32 mm. This corresponded to an annualized rate of loss of periodontal attachment yielded 0.04 mm for sites with GI=0, 0.05 mm for GI=1 and 0.07 mm for sites with GI=2, respectively. In other words, sites in which the gingiva consistently bled on probing lost approximately 40–75% more attachment per year than healthy or slightly inflamed sites.

According to the working hypothesis of *Study I* it was expected that sites displaying healthy gingivae throughout the adult life would exhibit no or only minute loss of attachment; and then, mainly in the form of gingival recession. This was certainly true for buccal and lingual surfaces. In interproximal sites, where cleansing was less effective and the influence of trauma from tooth brushing would be minimal, gingival recession as a mode of losing attachment was inconspicuous. Less than 20% of the interproximal sites showing clinically healthy gingivae showed loss of attachment, and mainly in conjunction with pocket formation.

The fact that interproximal sites with healthy gingiva occasionally showed pocket formation of 2 mm or more may be explained by intermittent iatrogenic local factors, such as the presence of gingival primary or secondary caries, subgingival restorations placed between examinations *(Study V)*, and various periodontal maintenance procedures impinging on the gingiva (Lindhe et al. 1984, Ramfjord 1993). Intraexaminer variability in scoring gingival health and disease and assessing attachment loss were recognized as being very small (Löe et al. 1978a, Kingman et al. 1991).

It should be remembered, however, that the recording of the various clinical indices expresses the situation at the time of examination only. Obviously, during long intersurvey periods (2 to 7 years), gingival health may have varied, and processes leading to pocket formation may have been triggered.

In a study of periodontal maintenance patients with professional services rendered at intervals of 3 to 5 months (Lang et al. 1986), only 1.5% of the sites that never bled on probing at the maintenance visits lost attachment, while 30% of the sites always bleeding

on probing lost at least 2 mm of attachment. Non-bleeding sites may still express the presence of slight inflammation upon microscopic inspection (Brecx et al. 1987b). Such subclincal inflammation may be enough to elicit a host response responsible for the loss of connective tissue and the formation of a gingival pocket.

Risk for Attachment Loss

The site specific analysis of *Study I* revealed gingival inflammation as the most prominent risk factor for periodontal attachment loss. In addition, in the group of sites always bleeding on probing (GI=2), subgingival calculus represented the only other risk factor reaching statistical significance. The loss of attachment in sites of smokers varied with the level of gingival inflammation. In non-inflamed gingiva smoking appeared as a significant risk factor for attachment loss. However, in inflamed gingiva, smoking did not reach statistical significance as a risk factor. The mean GI and the frequencies for GI=2 were higher in smokers than in non-smokers and yet, continuous smoking over a 20 year period did not appear to be a significant risk factor for loss of attachment in sites with inflamed gingiva. Subsequent analysis of the data set regarding the smoking status of the subjects will further elucidate the influence of smoking on the pathogenesis of periodontal disease (Schätzle et al. submitted).

Incidence of Initial Attachment Loss (ILA)

In *Study II*, a difference of 2 mm or more from the zero level of no loss of periodontal attachment was chosen to represent initial loss of attachment (ILA). Although rarely seen, initial attachment loss of this magnitude did occasionally occur during adolescence. It was detected more frequently among young adults in their twenties. At 32 years of age, all individuals had developed at least one site with initial loss of attachment.

So far, no other longitudinal studies have registered the incidence of ILA over the entire life span and hence, it is difficult to compare the incidence rates of ILA with other patient cohorts. The prevalence of attachment loss in adolescence, however, was described and initial loss of attachment reported to occur in 3-5% of 16 year old European

Caucasians (Van der Velden et al. 1989, Källestål & Mattson 1990, Clerehugh et al. 1990). While these subject prevalence rates coincided well before 20 years of age, the site prevalence of attachment loss was much higher in the USA (Miller et al. 1987) and in England (Clerehugh et al. 1990) than in the presently analyzed Norwegian group, indicating a positive effect of a systematic preventive approach of dental care during childhood and early adolescence.

Study II also showed that the number of affected sites continued to increase with age and that between 40 and 50 years, 10% of all available sites had initial loss of attachment. As the men approached 60 years of age, more than 20% of all sites were affected. Indeed, in approximately 75% of these men, 50% of the sites corresponding to 60-65 sites per individual, had initial loss of attachment. This indicates that in this middle class population with a history of life-long oral health care, the incidence of initial attachment loss continues throughout life. The fastest increase in the incidence of new initial periodontal lesions occurred in the 6th decade of life.

The incidence of initial periodontal attachment loss during adult life has not been studied prior to the present analysis. The findings of an escalating incidence rate in individuals approaching 60 years of age, could lend evidence to the notion that aging per se may be a factor in losing periodontal attachment (Avlund et al. 2001). It should be noted, however, that at present no further information exists relative to incidence rates of initial attachment loss beyond 60 years of age. It has to be realized, also, that the subjets of the present study approaching 60 years of age still displayed at least 50% of the tooth sites in healthy conditions and without attachment loss, reflecting the fact that these subjects had received regular dental care throughout life and were well maintained.

Types of Lesions in Sites with Initial Loss of Attachment

Below the age of 30 years, the vast majority of sites with initial attachment loss was characterized by gingival recession *(Study II)*. Pocket formation of 3 mm or more, was rarely observed and scattered before 40 years of age. Around the age of 50 years,

however, pocket formation increased significantly and coincided with increased incidence of interdental lesions.

Progression of Loss of Attachment

During adult life, a cumulative mean loss of attachment of 2.30 mm (range 0.14-2.44 mm) was observed *(Study III*). This corresponded to an annualized decrease of periodontal support of 0.05 mm. Such a rate of loss is comparable to the results reported for North-Americans of Tecumseh, Michigan (Ismail et al. 1990), but represents a considerably smaller rate than that reported for the adult tea plantation workers in Sri Lanka (Löe et al. 1978b, 1986), for a group of adults in Sweden (Axelsson & Lindhe 1978) and in the People's Republic of China (Baelum et al. 1997). The annual rate of loss encountered in the present population also compares reasonably well with another Scandinavian cohort (Lindhe et al.1989) (Table 12).

Table 12: Mean annual rate of periodontal attachment loss in different populations

Publications	Mean annual Rate
Löe et al. 1978b (Sri Lankan cohort)	0.18 - 0.29 mm / year
Axelsson & Lindhe 1978	0.17 – 0.3 mm / year
Löe et al. 1986 (Sri Lankan cohort)	0.05 – ~1.00 mm / year
Lindhe et al. 1989	0.07 – 0.14 mm / year
Ismail et al. 1990	0.04 mm / year
Baelum et al. 1997	0.15 – 0.19 mm / year
Study III (Norwegian Cohort)	0.04 – 0.10 mm / year

The present analysis of the Norwegian cohort displayed differences in individual rates over the life span. Approximately 25% of the participants never exceeded an annual loss rate of 0.02 mm and essentially went through adult life with a completely healthy periodontium. Approximately 30% of the cohort, exhibited variations in the annual attachment loss rate ranging between 0.02 and 0.06 mm. The remaining 45% of the cohort showed annualized variations beyond 0.06 mm. Before 35 years of age, the

majority of this age group had an annual loss of attachment of more than 0.06 mm. During the forties and fifties of life, however, both the mean annual loss (Fig. 8) and the frequency of occurrence decreased (Table 10). The slight increase in the attachment loss rate observed as individuals approached 60 years of age was not statistically significant.

In Sri Lankan tea laborer cohort (Löe et al. 1986), 3 different subpopulations were identified on the basis of annual rates of attachment loss: (1) 8% of the cohort yielding rapidly progressing destruction of the periodontium with a mean annual loss of 0.13-1.04 mm/year, (2) 80% of the cohort exhibiting moderate progression with a mean annual rate 0.05-0.52 mm/year and (3) 12% of the cohort essentially remaining stable with a low annual rate of attachment loss of 0.04-0.09 mm/year.

The results of the latter group with a low progression rate of periodontal destruction corresponded to the mean annual rate of attachment loss of the Norwegian cohort described in *Study III*. This shows that even in a population with no professional dental care and no personal oral care, a minority of approximately of one eighth of the cohort did not lose more attachment than the subjects of a highly industrialized dentally-minded population maintained on regular preventive dental care.

In the Norwegian cohort described in the present analysis initial attachment loss occurred occasionally in early adult life and were mostly seen in combinations with gingival recession in buccal surfaces. These lesion may have been caused by trauma from tooth brushing (Hirschfeld 1931, Gorman 1967, O'Leary et al. 1968, Sangnes 1976, Löe et al. 1992, Khocht et al. 1993). While initial attachment loss appeared to be related to gingival recession before age 35 years, pocket formation predominately in interproximal areas was associated with initial attachment loss after the age of 35 years.

It was interesting to note that in this patient cohort, a very small proportion of the sites (<1%) with initial attachment loss of ≥2 mm progressed substantially (>4 mm) during the 26 year observation period.

Gingival Inflammation and Tooth Mortality

To evaluate the influence of gingival inflammation of tooth mortality three different severity groups of teeth according to their frequency of occurrence of gingival inflammation were established. GI Severity Group I, in which no bleeding on probing was ever scored at any examination, yielded a cumulative tooth survival of 99.5% at a tooth age of 51 years. This suggests that clinically healthy gingiva is a significant prognostic indicator for tooth longevity. Absence of bleeding on probing of the gingiva has previously been identified as a indicator for periodontal stability (Lang et al. 1990, Joss et al. 1994). The present analysis, however, shows that gingival bleeding on probing to be a prognostic indicator for the loss of teeth.

In contrast to the GI Severity Group I (with absence of bleeding on probing), the GI Severity Group III demonstrated a cumulative tooth survival rate of only 63% after 47 years of tooth age. This, in turn means, that more than one third of the teeth that always bled on probing were lost after a tooth age of 40 years, corresponding to a patient age of at least 50 years. At a patient age of 40 years, corresponding to a tooth age of 30 years, the cumulative tooth survival rate was 88%. Hence, during the 10-year period between the age of 50 and 60 years, tooth survival dropped from 88% to 63%. The fact that the GI Severity Group II demonstrated a cumulative tooth survival rate of 94% after 51 years of tooth age supports the concept that occasional gingival bleeding on probing provides a much smaller risk for tooth loss than sites which regularly bled on probing. Again, this may confirm the predictive role of bleeding on probing for attachment loss studied retrospectively (Lang et al. 1986) and prospectively (Lang et al. 1990, Joss et al. 1994) in periodontal maintenance patients, and emphasizes the role of gingival inflammation as a genuine risk factor for tooth loss.

The risk to lose a tooth showed a wide range of odds ratios. Teeth always surrounded by healthy or occasionally slightly inflamed gingivae (GI Severity Group I) had an 8 times lower likelihood to be lost when compared with teeth consistently surrounded by slightly inflamed and occasionally bleeding gingivae (GI Severity Group II). However, teeth with gingival tissues that always bled on probing (GI Severity Group III) had a 46 times higher

likelihood to be lost than teeth always surrounded with healthy gingivae (GI Severity Group I). Finally, teeth of the GI Severity Group II showed only a 5 times lower likelihood for tooth loss than teeth of the GI Severity Group III. Again, these odds ratios clearly position regularly bleeding gingivae into the category of a risk factor for tooth loss. Similar suggestions were made by Burt et al. (1990) who identified gingival inflammation as the most prominent risk indicator for partial tooth loss.

The fact that teeth with healthy, gingiva were essentially maintained for half a century, i.e. a tooth age of 51 years, clearly shows that the natural tooth is a predictably stable and fully functional chewing element. In recent years, reconstructions supported by endosseous implants have yielded high predictability, and are documented to function successfully with high survival rates of over 90 % after 5 to 10 years (for review see Berglundh et al. 2002). Nevertheless, Karoussis and coworkers (2003) have identified a three fold increased risk for implant loss in patients who previously were treated for advanced periodontitis and who had lost teeth due to periodontitis when compared to patients without a history of periodontitis. Although this 10-year prospective cohort study yielded survival rates for implants after ten years of 90.5% and 96.5% respectively, for the patients with or without a history of periodontitis, it has to be realized that the tooth survival rates revealed in *Study IV* surpass by far those for oral implants. It follows, that the preservation of the natural dentition in a healthy condition with uninflamed gingiva still constitutes a primary and attainable goal for the maintenance of a functional dentition throughout the lifetime.

Restoration Margins and Loss of Attachment

Study V has confirmed and extended the long held concept that restorations placed below the gingival margin are detrimental to gingival and periodontal health (Waerhaug 1960). Following the placement of dental restorations in the test group an increase of loss of attachment was noticed also in the present cohort. Subsequently the level of attachment stabilized over the next 8 years. Then, another significant increase in loss of attachment occurred at the test sites which may be linked to the appearance of

secondary caries. It is conceivable that the latter necessitated the replacement of the fillings at these sites, and which resulted in a new bacterial challenge to the gingiva.

It appeared that subgingival placement of margins of dental restorations resulted in a significant loss of attachment that may be clinically evident 1-3 years after the restorative procedures were completed.

Such an association between the placement of subgingival restorations and the development of gingival inflammation, gingival recession, increasing probing depth and loss of attachment has also been documented in longitudinal studies by Valderhaug and Birkeland (1976), Valderhaug (1980) and Valderhaug et al. (1993). Also, clinical experimental studies (Renggli & Regolati, 1972) have demonstrated that the mere presence of clinically well adapted restorations in the subgingival area may lead to gingival inflammation. Furthermore, the placement of slightly overhanging filling margins was shown to result in a change of the subgingival microbiota adjacent to the subgingival restoration, favoring the colonization of gram-negative, strictly anaerobic rods (Lang et al. 1983). It was suggested that the shift of the composition of the subgingival mircobiota towards an increased proportion of periodontopathic microorganisms eventually lead to loss of periodontal support. However, this pathogenic process may develop slowly, since 1 to 3 years appeared to be needed in order to detect the loss of attachment clinically. Reported studies denying the association between restoration margins and the periodontal conditions (Than et al. 1982, Fisher et al. 1984, Markitziu et al. 1987) must be interpreted with care, since the material analyzed constituted of extracted teeth, or some of the variables had not been controlled (bite-wing radiographs, time interval). While most of the published studies presented only associations between overhanging dental restorations and periodontal conditions (Gilmore & Sheiham 1971, Rodriguez-Ferrer et al. 1980, Lang et al. 1988) or the development of secondary caries (Hammer & Hotz 1979), the present study has documented a temporal association between the placement of subgingival restorations and the loss of periodontal support.

MAIN FINDINGS

The longitudinal studies in Oslo, Norway, have shown that in well-educated middle class men who have had regular professional dental care and performed daily personal home care during childhood, adolescence and adult life, the dentition is maintained in health and function during adult life.

Gingivitis was present in one or more sites in all individuals at age 16 years and was found at all age levels including those approaching 60 years of age. The mean Gingival Index throughout adult life varied little (range 0.7-0.9), and the frequency of GI=2 (bleeding on probing) occurred fairly consistently in 10-20% of the sites of all individuals.

Initial loss of attachment occurred in a few sites already at 16 years of age and mainly as gingival recession on buccal surfaces. Deepened pockets were found occasionally in young adults, but rarely exceeded 3-4 mm. The mean individual loss of attachment and the frequency of sites increased steadily during the 30ies and 40ies and reached its maximum (2.44 mm) as the men approached 60 years of age. Less than 0.5% of the sites exhibited loss of attachment over 4 mm.

The 17 year old men had 27.4 teeth, and no main loss of teeth occurred during the twenties and thirties. At 40 years of age, the mean number of teeth (excl. wisdom teeth) was 27.1, and the mean tooth mortality rate was 0.01 teeth per year. As the men approached 60 years of age, they still had 27.1 teeth present and the mortality rate remained unchanged.

Role of Gingivitis

To analyze the role of gingivitis in the initiation of periodontal attachment loss three Gingival Index severity groups were established for all age levels according to their degree of clinical inflammation over the 26 year observation period:

The results of the analysis demonstrated that throughout adult life (16 to 60 years), gingival sites that never scored above GI=0 experienced a mean cumulative loss of attachment of 1.86 mm (range 0.08-1.94 mm). For sites with slight inflammation (GI=1) the corresponding loss of attachment was 2.25 mm (range 0.17-2.42 mm) and in sites that consistently bled on probing (GI=2) over 26 years, the mean loss of attachment was 3.23 mm (range 0.09-3.32 mm). This corresponded to an annualized loss of periodontal attachment of 0.04 mm for sites with GI=0, 0.05 mm for sites with GI=1, and 0.07 mm for sites with GI=2. In other words, sites that throughout a 26-year observation period bled on probing lost about 40–75% more attachment per year than healthy and slightly inflamed sites.

Gingival sites that bled on probing (GI=2), yielded an odds ratio of 3.22 to lose attachment as compared to healthy sites over the 26 year observation period.

Odds ratio analyses showed that of six major risk indicators selected, gingival inflammation represented the highest risk for loss of attachment.

Incidence of Initial Loss of attachment (ILA)

Definition: Initial loss of attachment (ILA) was defined as the first attachment loss of 2 mm or more as measured from the cemento-enamel junction.

The incidence of ILA was established for all age levels, all teeth and tooth groups, and the type of clinical expression (e.g. recession, pocketing or combinations thereof) was recorded. Initial loss of attachment occurred in a few sites and individuals before the age of 20 years in this population, and then essentially on buccal surfaces.

By 30 years of age, the incidence of new lesions continued to increase in the buccal surfaces of premolars and molars. Very few anterior teeth were affected. The incidence of initial loss of attachment (ILA) in the interdental areas increased slightly between 30 and 40 years of age, but a relatively large increment in the incidence of new interdental

lesions occurred before and after 50 years, when most posterior teeth and half of the anterior teeth exhibited interdental loss of attachment.

This investigation has clearly shown that in a well-maintained population who practices oral home care and sees the dentist for regularly check-ups, gingival recession is the dominating type of incipient lesions during the first 40-50 years of life. Pocket formation started in earnest around the age of 50 years, and increased in incidence towards 60 years of age.

Progression of Attachment Loss

As this population approached 60 years of age, 25% of the men went through adult life with healthy and stable periodontal conditions. The remaining 75% developed slight to moderate loss of attachment with progression rates varying between 0.02 and 0.06 mm/year and a cumulative mean loss of attachment of 2.44 mm as they approached 60 years of age.

Only 20% of the initial lesions of attachment loss (ILA) recorded throughout the 26-year observation period continued to lose further attachment during the remainder of the observation period, and only 0.02% of these sites showed additional loss of attachment (>4 mm).

Gingival Inflammation and Tooth Mortality

Following the baseline examination in 1969 throughout the 26 year observation period until 1995, 15% of the subjects accounted for the loss of 126 teeth out of 13285 teeth (0.96%). This corresponded to an annualized tooth loss of 0.016 teeth per year and individual, an extremely low tooth mortality rate throughout 60 years of life. Most of the teeth lost were molars and premolars; loss of anterior teeth was exceedingly rare.

When teeth lost were analyzed relative to the long term status of their surrounding gingiva, it appeared that 0.28% of teeth surrounded by healthy gingiva at all examination periods, were lost; 2.28% of teeth surrounded by slightly inflamed gingiva were lost,

and 11.21% of teeth with continuous inflammation and bleeding on probing, were lost.

Teeth surrounded by inflammation-free gingiva were maintained for a tooth age of 51 years, while teeth consistently surrounded by inflamed gingiva had a 46 times higher risk of being lost.

This suggested that clinically healthy gingiva might be a prognostic factor for tooth longevity. Conversely, continuous gingivitis represented a risk factor for tooth loss.

Restoration Margins and Attachment Loss

To further analyze the role of iatrogenic factors such as subgingival fillings two tooth groups were established over all surveys representing 1) teeth with sound mesial surfaces and 2) teeth with mesial surfaces with no fillings in the first survey in 1969, but subgingival fillings placed before the second examination in 1971.

Following the placement of dental restorations an increase in the loss of attachment was noticed during the subsequent three years. The level of attachment remained stable thereafter. Another significant increase in loss of attachment occurred at these sites due the occurrence of secondary caries and/or replacement of the restorations.

It appeared that subgingival placement of dental restorations resulted in a significant loss of attachment. This pathogenic process may develop slowly during the first 1-3 years after the completion of the restorative procedures. In other words, a time sequence has been described of the effect of placing subgingival restorations and their impact on the periodontium.

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APPENDIX I: CRITERIA FOR THE VARIOUS CLINCAL PARAMETERS

Smoking habits

Non-smokers	Individuals who at each examination reported that they had never smoked.
Irregular-smokers	Some of the men reported smoking at some examinations, but not at others
smokers	Subjects, who, at every survey in which they participated, reported smoking of 2 or more cigarettes per day

Plaque Index (PI) (Silness & Löe 1964)

PI = 0	No plaque in the gingival area
PI = 1	A film of plaque adhering to the free gingival margin and adjacent area of the tooth. The plaque may only be recognized by running a probe across the tooth surface
PI = 2	Moderate accumulation of soft deposits within the gingival pocket, on the gingival margin and/or adjacent tooth surface, which can be seen by the naked eye
PI = 3	Abundance oft soft matter within the gingival pocket and/or on the gingival margin and adjacent tooth surface

Calculus Index (CI) based on the Retention Index system (Löe 1967)

CI = 0	No calculus
C = 1	Supragingival calculus
CI = 2	Subgingival calculus
CI = 3	Abundance of calculus

Gingival Caries Index (GCI) based on the Retention Index system (Löe 1967)

GCI = 0	No Caries
GCI = 1	Supragingival cavitation
GCI = 2	Subgingival cavitation
GCI = 3	Large cavitation

Gingival Restoration Index (GRI) based on the Retention Index system (Löe 1967)

GRI = 0	No dental restoration in the gingival area or no margin of dental restoration closer than 1mm to the gingival margins
GRI = 1	Supragingival margin of dental restoration extending less than 1 mm below the gingival margin
GRI = 2	Subgingival margin of dental restoration extending more than 1 mm below the gingival margin
GRI = 3	Grossly insufficient marginal fit of dental restoration in a supra- and / or subgingival location

Gingival Index (GI) (Löe & Silness 1963)

GI = 0	Normal gingiva
GI = 1	Mild inflammation – slight change in color, slight oedema. No bleeding on Probing
GI = 2	Moderate inflammation – redness, oedema and glazing. Bleeding on Probing
GI = 3	Severe inflammation – marked redness and oedema. Ulceration. Tendency to spontaneous bleeding.

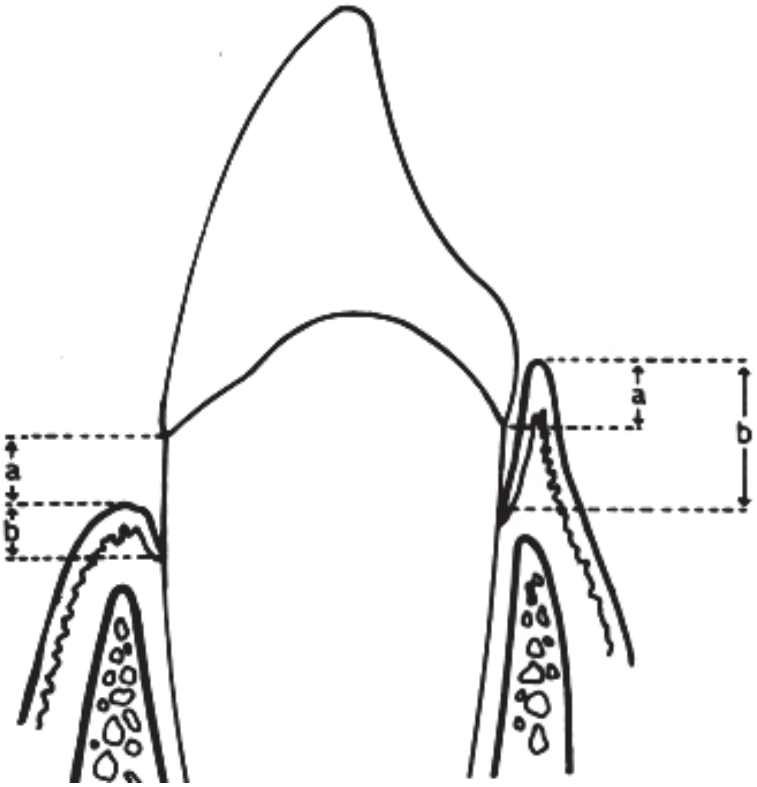
Furcation Index (Hamp et al. 1975)

Degree I	Horizontal loss of periodontal tissue support less than 3mm
Degree II	Horizontal loss of support exceeding 3mm, but not encompassing the total width of the furcation area
Degree III	Horizontal “through-and-through” destruction of the periodontal tissue in the furcation

Loss of attachment (LoA) (Glavind & Löe 1967)

Clinically and quantitatively, loss of attachment is the distance from the cemento-enamel-junction (CEJ) to the bottom of the clinical pocket. When the CEJ is located apical to the gingival margin (right) loss of attachment (LoA) is calculated as the difference between the depth of the pocket (a) and the distance (b) from the gingival margin to the CEJ: a-b = LoA.

In cases where the marginal gingiva has been subject to recession (left) and the CEJ is exposed, the loss of attachment equals the sum of pocket depth and the distance from the gingival margin to the CEJ: a+b = LoA



APPENDIX II: ORIGINAL STUDIES I TO V

This thesis is based on the following studies, which will be referred to by their roman numerals:

I **Schätzle, M.,** Löe, H., Bürgin, W., Ånerud, Å., Boysen, H. & Lang, N. P.:
The Clinical Course of Chronic Periodontitis: I. The role of gingivitis
Journal of Clinical Periodontology 2003; 30: 887-901.

II Heitz-Mayfield, L. J. A., **Schätzle, M.,** Löe, H., Ånerud, Å., Boysen, H., Bürgin, W. & Lang, N. P.:
The Clinical Course of Chronic Periodontitis: II. Incidence, characteristics and time of occurrence of the initial periodontal lesion
Journal of Clinical Periodontology 2003; 30: 902-908.

III **Schätzle, M.,** Löe, H., Lang, N. P., Heitz-Mayfield, L. J. A., Bürgin, W., Ånerud, Å., & Boysen, H.:
The Clinical Course of Chronic Periodontitis: III. Patterns, Variations and Risks of Attachment Loss
Journal of Clinical Periodontology 2003; 30: 909-918.

IV **Schätzle, M.,** Löe, H., Lang, N. P., Bürgin, W., Ånerud, Å. & Boysen, H.:
The Clinical Course of Chronic Periodontitis: IV. Gingival inflammation as a risk factor for tooth mortality
Journal of Clinical Periodontology 2004; 31: 1122-1127.

V **Schätzle, M.,** Lang, N. P., Ånerud, Å., Boysen, H., Bürgin, W. & Löe, H.:
The influence of margins of restorations on the periodontal tissues during 26 years
Journal of Clinical Periodontology 2001; 28: 57-64.

ERRATUM

The Clinical Course of Chronic Periodontitis: I. The role of gingivitis.

Journal of Clinical Periodontology 2003; 30: 887-901

p. 897: second last paragraph of the discussion erroneously states that with increased gingival inflammation levels, the effect of smoking is significant.

The correct statement should read: With increased gingival inflammation levels, the effect of smoking was not significant.