Medications, dry mouth and dental caries among older people: a longitudinal study

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Abstract

Much has been written about the role of certain medications as risk factors for both dry mouth and dental caries, and there has been general, uncritical acceptance of the relationship among clinicians for many years. While there have been a number of recent reports on the association between drugs and dry mouth, movement towards a real consensus is slow because of methodological problems and differences among the various studies. In particular, there have been difficulties in the definition and measurement of dry mouth, and in assembling and analysing complex medication data-sets. There is currently no sound information which substantiates the medication-caries causative pathway. Consequently, understanding of the putative medication/dry mouth/caries relationship is not well developed, possibly because researchers in this field face a number of difficult challenges. First, a suitable method must be used for capturing and analysing medication data with sufficient flexibility to enable meaningful analysis. Second, the analysis should be able to take polypharmacy into account: most older people take at least one medication, and the majority of those take more than one. Third, xerostomia (the subjective perception of dry mouth and its consequences) and salivary gland hypofunction (as measured by salivary flow rate) should be measured separately, given the possibility that they may be largely discrete conditions. Fourth, xerostomia should be measured as a continuous variable, so that an estimate of symptom severity can be obtained for each individual, and the possibility of bias due to misclassification is minimised. Fifth, a longitudinal design should be used, so that duration (and the time-ordering) of exposure to the various medications can be examined prospectively. Finally, participants should (ideally) comprise a representative sample so that results can be generalised to the larger population.

The purpose of the current study was to systematically explore the relationship between medications, dry mouth and dental caries in a longitudinal study of older people. The aims were: (1) to develop a flexible, numerically-based system for the capture and epidemiological analysis of medication data; (2) to develop a valid multi-item method of measuring the symptoms of xerostomia which includes the wide range of xerostomia symptoms in a single quantitative measure; (3) to examine the

prevalence of—and concurrence between— reduced salivary flow (SGH) and the symptom of dry mouth (xerostomia); (4) to examine the association between medication exposure and unstimulated whole-salivary flow rate and xerostomia severity while adjusting for multiple medication use; and (5) to examine the association between medication exposure and disease outcomes such as tooth loss and dental caries incidence and increment over five years.

Method

A hierarchical, five-digit numeric system was developed to facilitate the capture and analysis of unit-record-level medication information for both the baseline and five-year data collections. In the longitudinal medication analysis, participants were designated "continuous users" for a given medication category if they had been taking it at baseline and at five years, enabling examination of the association of dry mouth and long-term exposure to medications by comparing their outcomes with those of the remainder of the sample. Confirmation of the general medication prevalence patterns observed in the SADLS study was achieved by comparison with baseline data from the Australian Longitudinal Study of Ageing (ALSA). Dry mouth was not assessed at baseline in SADLS, but was measured at five years using three methods: unstimulated salivary flow was estimated using the "spit" method (and a flow rate of less than 0.1 ml/min was used as the case definition for salivary gland hypofunction,or SGH); a standard single dry-mouth question (*How often does your mouth feel dry?*); and the severity of symptoms was estimated using a new, multi-item approach. The 11-item Xerostomia Inventory was developed and tested at the five-year stage of the SADLS study in order to allow the measurement of the severity of the full range of xerostomia symptoms (both experiential and behavioural) as a continuous scale score. A smaller validation study confirmed the validity and stability of the Xerostomia Inventory (XI) by examining scores over a six-month period in two groups with divergent symptom trajectories. Because of the potential difficulties posed by polypharmacy in examing the association of medications and dry mouth, a two-stage analytical approach was employed: (1) Classification and Regression Tree (CART) analysis was used as an exploratory device in order to elucidate the relationships among the dependent and independent variables; and (2) linear regression analysis was used to verify the observed associations. Dental caries data were collected at baseline and five years

using standard dental epidemiological methods, and estimates of caries incidence and increment were computed by comparing caries status at baseline and at five years for each surface. Tooth-loss incidence and increment were computed using a similar method, but at a tooth-by-tooth level. Although the associations of medication and caries prevalence at baseline were examined as an exploratory study, the principal outcome variables for the investigation were (a) the incidence and increment of tooth loss, and (b) the incidence and adjusted increment of coronal and root surface caries. Multivariate models were then used to identify the medication-exposure sub-groups which had experienced most oral disease over the study period, with particular attention paid to the medication combinations which had been shown to be associated with dry mouth.

Results

Medication data were available for 704 individuals at five years, of whom 528 were dentate and dentally examined. The mean unstimulated salivary flow rate was 0.27 ml/min (sd, 0.22). The prevalence of SGH was 22.1 per cent, and the prevalence of xerostomia was 20.5 per cent but only 5.7 per cent of participants had both conditions. Almost two-thirds of the sample had neither condition, and males and females differed in the degree of concurrence of the two conditions. XI scale scores had a very low correlation with unstimulated flow rate, but a much stronger, positive correlation with the standard dry-mouth question responses. Unstimulated flow rate was: lower among individuals who were female or taking antidepressants at both baseline and five years; and higher among smokers, or people who were taking hypolipidaemic drugs. Xerostomia severity was higher among: (a) individuals taking an anginal without a concomitant β-blocker at five years; (b) individuals taking thyroxine and a diuretic at five years; (c) those taking antiasthma drugs at baseline and at five years; or (d) people who were taking antidepressants at both baseline and at five years. Five-year tooth-loss incidence was 36.2 per cent, with a mean increment of 0.70 (sd, 1.31). Among those who lost one or more teeth, the mean number lost was 1.93 (sd, 1.54). The incidence of tooth loss was higher among individuals who were taking cardiac inotropic drugs at five years; together with those were taking hypoglycaemic drugs at five years, the latter had a higher tooth-loss increment. Coronal caries

incidence was 66.9 per cent, with a mean adjusted five-year increment of 2.65 (sd, 3.14). Coronal caries incidence was higher among individuals who were taking antiasthma drugs at baseline and five years, and also among those who were taking ACEI antihypertensives at five years. The taking of sympatholytic antihypertensives at five years was associated with a lower coronal caries incidence. No medications emerged as predictors of coronal caries increment. Root surface caries incidence was 59.3 per cent, with a mean adjusted five-year increment of 2.21 (sd, 2.23). "Continuous users" of daily aspirin had lower odds of being an incident case of root surface caries, and the root surface caries increment was lower among persons who were taking one or more antihypertensive drugs at five years. The former finding is likely to be due to the more positive, preventively-orientated lifestyles of individuals who are taking daily aspirin.

Conclusions

The outcomes of this study suggest that, in the group studied: (1) xerostomia and SGH were largely discrete conditions, supporting the assertion by other workers that low salivary flow may not be the key factor in the aetiology of xerostomia among older people; (2) that a simple hierarchical medication capture and analysis system can greatly simplify and facilitate the analysis of complex medication-exposure data in epidemiological research; (3) that polypharmacy can be accounted for to a certain extent by using AID analysis in conjunction with more conventional approaches; (4) that the relationship between medications and dry mouth is a complex one, and differs according to which aspect of dry mouth is being examined; (5) there is no strong evidence for particular medications being risk factors for dental caries and its sequelae, other than the association of (a) cardiac drugs and hypoglycaemics with tooth loss, and (b) antiasthma drugs and the incidence of coronal caries.

Declaration

This work contains no material which has been accepted for the award of any other degree or diploma in any university or any other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

I give consent to this copy of my thesis, when deposited in the University Library, being available for loan and photocopying.

Signed

WM Thomson

Date: 30/6/99

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"Ladies and gentlemen, Elvis has left the building"

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1. Review of the literature

This review begins with an overview of saliva and its secretion, followed by descriptions of xerostomia and salivary gland hypofunction (SGH), and then a brief synopsis of the role of saliva in protecting the dentition. Methods of measuring xerostomia and SGH are then described, and the literature on salivary function among older people is examined. The next section reviews the literature on medication prevalence among older populations, and is followed by a review of medications and xerogenicity. An examination follows of current knowledge of dental caries prevalence and incidence among older people. This is followed by a review of published reports of the association between medication and dental caries among older populations. Finally, the proposed model is introduced, and the study hypotheses are specified.

1. 1 Saliva and dry mouth

1.1.1 A brief overview of the physiology of saliva secretion

Saliva is secreted by the parotid, sublingual, submandibular and accessory salivary glands. The term "whole saliva" is used to describe the combined output of these glands. Salivary secretion involves two main steps: (1) an acinar stage which produces a primary saliva which is isotonic with respect to plasma; and (2) the transport and modification of the saliva (by reabsorption of Na^+ and Cl^-, and the secretion of K^+ and HCO_3^-) through the duct system, resulting in a final saliva which is hypotonic (Streckfus *et al*, 1994).

The parotid glands have serous acini which secrete a proteinaceous, watery output, whereas the secretion from the sublingual glands is more mucous, and therefore more viscous. Submandibular glands have a mixed serous and mucous acinar composition which

results in their secretions having a lower protein content and higher viscosity than those from the parotid. Notwithstanding these qualitative differences among specific glandular secretions, approximately 99 per cent of whole saliva is water (FDI, 1992). Table 1.1 lists the constituents that make up the remaining one per cent of saliva.

Table 1.1: Constituents of saliva (FDI, 1992)

Proteins	*Small organic molecules*	*Electrolytes*
Albumin	Creatinine	Ammonia
Amylase	Glucose	Bicarbonate
β-glucuronidase	Lipids	Calcium
Carbohydrases	Nitrogen	Chloride
Cystatins	Sialic acid	Fluoride
Epidermal growth factor	Urea	Iodide
Esterases	Uric acid	Magnesium
Fibronectin		Non-specific buffers
Gustin		Phosphates
Histatins		Potassium
Immunoglobulin A		Sodium
Immunoglobulin G		Sulphates
Immunoglobulin M		Thiocyanate
Kallikrein		
Lactoferrin		
Lipase		
Lactic dehydrogenase		
Lysozyme		
Mucins		
Nerve growth factor		
Parotid aggregins		
Peptidases		
Phosphatases		
Proline-rich proteins		
Ribonucleases		
Salivary peroxidases		
"Secretory component"		
Secretory IgA		
Serum proteins (trace)		
Tyrosine-rich proteins		
Vitamin-binding proteins		

The salivary glands receive their autonomic innervation via two separate anatomic pathways. The sympathetic supply is derived from T1 to T4 via the superior sympathetic ganglion, while parasympathetic innervation comes from the seventh (facial) and ninth (glossopharyngeal) cranial nerves. There is no hormonal control of salivary secretion; it is wholly neuronal (Edgar, 1992). Parasympathetic stimulation leads to intra-glandular vasodilation and subsequent secretion of saliva, whereas sympathetic stimulation leads to vasoconstriction and the release of secretory proteins. The parasympathetic impulses arise from the salivatory nuclei, which are located at the juncture of the pons and the medulla. The superior salivatory nucleus supplies the submandibular and sublingual glands, while the inferior salivatory nucleus supplies the parotid gland. These nuclei are stimulated by gustatory and/or mechanical stimuli from the oral cavity, and can also be stimulated or inhibited by impulses from higher up on the central nervous system (Whelton, 1996).

Normal whole saliva flow rates are defined as being between 0.3 and 0.5 ml per minute for unstimulated flow, and 1.0 and 3.0 ml per minute for stimulated flow. The total daily flow amounts to approximately 500 ml. The unstimulated whole salivary flow volume is provided by the parotid (20 per cent contribution), submandibular (65 per cent), sublingual (7 to 8 per cent) and the minor salivary glands, with 7 to 8 per cent. For stimulated saliva, the relative contributions of the glands alter, with the parotid providing about 50 per cent (Edgar and O'Mullane, 1990).

1.1.2 Dry mouth terminology and definitions

Throughout this thesis, the unqualified term "dry mouth" is used as a catch-all phrase to refer to either xerostomia or salivary gland hypofunction. *Xerostomia* is the subjective feeling of dry mouth, and is assessed by direct enquiry of individuals (Nederfors *et al*, 1997). *Salivary gland hypofunction* (SGH) is an observable reduction of salivary flow, and is diagnosed by using sialometric techniques. Despite these clear distinctions, there is still some confusion about the meaning of the two terms (the reasons for this are discussed further in Sections 1.1.4 and 4.5.1).

The prevalence of xerostomia among older groups has been variously estimated as being between 10 and 38 per cent (Osterberg *et al,* 1984; Osterberg *et al*, 1992; Thomson *et al,* 1993; Gilbert *et al,* 1993; Locker, 1995), depending on (1) how it has been measured, and (2) the source population in whom it was measured. A commonly used criterion for SGH is a stimulated salivary flow of less than 0.5 ml per minute, or an unstimulated salivary flow of less than 0.1 ml per minute, although there are actually no universally accepted standards for any of these parameters (Sreebny and Broich, 1987; Osterberg *et al,* 1984), and estimates of SGH prevalence among older adults are difficult to compare because different approaches and case definitions have been used. Johnson *et al* (1984) reported that 44 per cent of an institutionalised older population had a stimulated parotid flow rate of 0.2 ml/min or less. Osterberg *et al* (1984) reported that 32 per cent of a representative sample of Swedes aged 70 or more had an unstimulated whole-salivary flow rate below 0.1 ml/min; however, those workers measured salivary flow only among 110 of the 973 individuals who answered the xerostomia question, and no description was given of the process which was used to select that subsample. Fure and Zickert (1990) reported a prevalence rate of 22 per cent for unstimulated whole salivary flow rate among a representative sample of 55-, 65- and 75-year-old Swedes. It is apparent from the prevalence estimates for xerostomia and SGH that substantial numbers of older people are affected.

1.1.3 Measuring salivary flow

SGH is assessed by measuring salivary flow. There are two parameters which can be estimated:

- unstimulated salivary flow
- stimulated salivary flow

These can be evaluated by collecting from individual salivary glands (or pairs of glands), or total salivary flow can be evaluated by collecting whole saliva. The latter method is more common, and more closely approximates the *in vivo* situation (Navazesh and Christensen, 1982). This is certainly the case in respect of both saliva's caries-protective function and the fact that dry mouth is usually a multi-glandular condition (Sreebny and Broich, 1987). Typical mean flow rates which are reported are 0.3 ml/min for unstimulated whole saliva, and 1.7 ml/min for stimulated saliva (Dawes, 1996).

Sialometry for whole saliva can be accomplished using any of the "drain", "spit", "suction" or "swab" methods (Navazesh and Christensen, 1982). The "drain method" requires the individuals to allow saliva to passively drain (over a specified time, usually 3 minutes) into a receptacle prior to weight or volume determination. Weight determination has been shown to be a more reliable method of estimating saliva volume (Navazesh and Christensen, 1982). The "spit method" requires the individuals to actively collect saliva in the oral cavity and then void it into a receptacle, again over a specified period. The "suction method" uses a suction tube to collect saliva from the floor of the mouth. The "swab method" uses pre-weighed swabs (for example, dental cotton rolls) which are placed on the floor of the mouth and allowed to collect saliva for a specified time, after which they are weighed and the salivary flow computed. Irrespective of the method used, the mouth is rinsed with water for one minute prior to collection to rid it of any extraneous substances which may act as salivary stimulants. The drain method has been suggested as the most suitable one for large-scale collection of whole saliva in a study such as the present one, where unstimulated whole saliva is more relevant to the study hypotheses, since it confers oral protection for the majority of daytime and nighttime hours (Dr Jonathan Ship, University of Michigan - personal communication, August 1995). Galan and Lynch (1993) have also suggested that unstimulated salivary flow rate may be a more appropriate measurement to make when investigating caries rates in older people. When approximately 700 individuals are to be examined, the ease of saliva collection must be taken into account when selecting the sialometry method.

Stimulated salivary flow for collection purposes can be induced by using either gustatory or masticatory stimuli. Citric acid (in, for example, a 2 per cent solution which is either dropped directly or applied on blotting paper to the dorsum of the tongue) can be used as a gustatory stimulus, while paraffin wax or pre-softened polyvinyl acetate gum is chewed as a masticatory stimulus. Both of the latter agents have a neutral taste.

Minor salivary gland flow provides less than 10 per cent of total salivary flow (but over one-third of the secretory IgA in whole saliva), and has been demonstrated to be unaffected by gustatory stimulation (Shern *et al,* 1990). Such stability of output reflects their specifically protective, lubricatory function. Minor salivary gland flow can be evaluated by using one of three methods, all of which require the mucosa to be wiped with dry gauze prior to collection:

- pipetting, in which secretions are collected directly from single glands over several minutes;
- blotting, in which secretions from a number of glands are collected in a pre-weighed segment of blotting paper which is re-weighed after several minutes; or
- the method described by Shern *et al* (1990), in which a standard strip of high-purity chromatography paper (Whatman 3MM, Whatman International Ltd, Maidstone, England) is applied to the mucosa (labial, buccal or palatal) for 30 seconds, and then its moisture level determined using a Periotron machine (Model 304-6000, Harco Electronics Ltd, Winnipeg, Canada).

The pipetting and blotting methods have the disadvantage of requiring a collection time of between 4 and 15 minutes which, because of the concomitant isolation and drying of the surrounding mucosa, may affect the secretory volume. Both the blotting and Shern methods have the disadvantage that it is not known how many glands are covered by the strip in each location. This means that the data obtained by such methods are only useful for comparing rates for a given surface area among different risk groups or anatomical

locations; the absolute measurements are of little use. It is probable that the role of minor salivary gland secretions in protecting dental hard tissues is negligible, and it was felt that the utility of collecting such data in an epidemiological investigation such as the current study would be questionable.

1.1.4 Measuring xerostomia and salivary gland hypofunction

Essential to an understanding of the intricacies and challenges of measuring dry mouth is the realisation that the relationship between xerostomia and SGH is not straightforward: low salivary flow is not a necessary pre-condition for xerostomia (Atkinson, 1992). Figure 1.1 shows four possible combinations of the two conditions (leaving aside the possibility that SGH may be observed in either the unstimulated or stimulated flows, or in both).

		Xerostomia	
		Present	Absent
SGH	Present	***a***	***b***
	Absent	***c***	***d***

Figure 1.1: Contingency table of the possible relationships between xerostomia and SGH

Individuals in group ***a*** both perceive oral dryness and have observably reduced salivary flow. Those in group ***b*** have no symptoms of oral dryness, yet their salivary flow rate falls below a predetermined criterion. Individuals in group ***c*** have no observable reduction in salivary flow, but report symptoms of dry mouth, while those in group ***d*** have neither reduced salivary flow nor symptoms of dry mouth. The distribution of these combinations across populations of older adults is currently unknown. In fact, the exact nature of the relationship between the two has, to date, remained unresolved (Nederfors *et al*, 1997):

we do not know for a given population if those individuals who have xerostomia are the same ones who have a clinically reduced salivary flow.

Two circumstances have contributed to this lack of understanding. First, most studies have used either convenience samples of xerostomia clinic patients (Fox *et al*, 1987), compliant elders (Billings *et al*, 1996), or dental students (Dawes, 1987), and the population-based approach has only been used in a small number of studies (Nederfors *et al*, 1997; Locker, 1993; Gilbert *et al*, 1993; Osterberg *et al*, 1984), none of which has measured both conditions. It is axiomatic that a comprehensive understanding of the epidemiology and public health significance of a condition requires not only accurate and detailed epidemiological and clinical study, but also unbiased estimates of its occurrence. Second, the method of measuring xerostomia has differed, particularly among the population-based studies which have been conducted. Because it is a symptom, xerostomia must be assessed by directly questioning individuals. Two approaches have been used to date: (1) the single "global" question, and (2) a mix of questions covering various experiential and behavioural aspects of dry mouth. The former has been more common and is easier to interpret, while the latter approach has been faced with the problem of analysing the responses to the different questions separately and finding that each gives a different prevalence estimate.

Each of the population-based studies has used the single global question approach. Osterberg *et al* (1984) used the question "Does your mouth feel distinctly dry?" (binary response option 'yes', 'no'), and conducted measurements of salivary flow on only a small subsample of their study participants. Locker (1993) used the single question "During the last four weeks have you had any of the following - dryness of mouth?" (binary response option 'yes', 'no') but did not measure salivary flow. Nederfors *et al* (1997) used the question "Does your mouth usually feel dry?" (binary response option 'yes', 'no'), and did not measure salivary flow either. None of those studies provided evidence for the validity of the questions used. Gilbert *et al* (1993) reported from a study of a stratified random sample of community-dwelling older Florida residents, which used a number of questions

on mouth dryness, but did not measure salivary flow (9). Their main outcome measure was the question "Is your mouth sometimes dry?", to which 39 per cent of respondents answered affirmatively. The latter question can be criticised on the grounds that it is probably too inclusive for use as a tool for categorising individuals as "xerostomic"; certainly, the obtained prevalence estimate is unusually high in comparison to those from the other studies, and indicates that perhaps the word "often" should have been substituted for "sometimes" in the question that was used.

Handelman *et al* (1989) reported that xerostomia was not associated with reduction in the stimulated salivary flow rate, but was more closely associated with a reduced unstimulated flow rate. Such an association has been reported elsewhere (Sreebny and Valdini, 1988; Ben-Aryeh *et al*, 1985), but it is not as strong as might be expected, for a number of reasons. First, because the "normal" flow rate is not well understood, there is no accepted criterion for defining a "hyposalivatory" flow rate (although less than 0.1 ml/minute and less than 1.0 ml/minute have been used most often as case definitions for unstimulated and stimulated hyposalivatory flows respectively). Second, there is some uncertainty as to which of the unstimulated or stimulated flow rates is more appropriate in defining SGH. The unstimulated flow rate has been reported to be of more importance in the protection of the dentition (Edgar and O'Mullane, 1996; Dr Jonathan Ship, University of Michigan - personal communication, August 1995), yet most sialometric studies assess the stimulated flow rate—presumably because it is easier to measure—but the stimulated flow rate has been described as offering little more than an indication of the glands' secretory capacity (Dawes, 1987). Third, the perception of oral dryness may be induced in an individual through changes in mucosa or oral sensory perception, or by changes in saliva quality, without an apparent reduction in salivary flow. In such a situation, xerostomia is perceived, but SGH not observed when flow rate is assessed (group *"c"* in the 2-by-2 table, Figure 1.1).

Many studies which have used the single-question approach in xerostomia symptomatology have not specified the item which was used. Those which have done so

are listed in Table 1.2, together with those which have explored other aspects of xerostomia.

Table 1.2: Previous approaches to investigating xerostomia

Items used specified in report	*Studies*
Does your mouth feel distinctly dry?	Osterberg *et al,* 1984[a]
Do you sip liquids to aid in swallowing dry foods?	Fox *et al,* 1987
Does your mouth feel dry when eating a meal?	Fox *et al,* 1987
Do you have difficulties swallowing any foods?	Fox *et al,* 1987
Does the amount of saliva in your mouth seem to be too little, too much, or you don't notice it?	Fox *et al,* 1987
Do you feel dryness in the mouth at any time?	Fure and Zickert, 1990
Do you have mouth dryness?	Osterberg *et al,* 1992
Is your mouth sometimes dry?	Gilbert *et al,* 1993[a]
How often does your mouth feel dry?	Thomson *et al,* 1993
During the last four weeks, have you had any of the following… - dryness of mouth?	Locker, 1993[a]
Does your mouth feel dry?	Narhi, 1994
Does your mouth usually feel dry?	Nederfors *et al*, 1997[a]
Exact wording of items used not specified in report but indication given of approach which was used	
Difficulty in eating dry foods	Narhi, 1994
Difficulty in speaking	
Difficulty in swallowing	
Taste impairment	
Dry lips	
Burning sensation in oral mucosa	
Burning sensation in tongue	" "
Itching sensation in oral mucosa	
Itching sensation in tongue	
Mouth breathing	
Dry throat	
Dry nose	
Dry skin	
Dry eyes	

[a]Population-based study

Both items used by Osterberg *et al* (1984 and 1992) appear to relate to respondents' perceptions of dry mouth at the time of interview. If that was not the intention, it is likely that it would have been the way in which many respondents interpreted the question. It could be argued that the reporting of such symptoms at the time of interview might lead to over-estimation of the prevalence of xerostomia, given the data collection situation, where many participants in such a study would find the data collection to be at least mildly stressful in itself, and would be more likely to report dry mouth. Moreover, if sialometry was used at the same time, the conditions required for saliva collection—no drinking of anything other than water during the one hour prior to measurement, so that the sialogenic effects of extraneous substances are minimised—would also tend to cause over-reporting of xerostomic symptoms. The questions used by Gilbert *et al* (1993) and Thomson *et al* (1993) pertain more to everyday symptoms, and would be interpreted as such by study participants. That used by the former (*Is your mouth sometimes dry*?) has the disadvantages of (1) implying a pre-determined level of severity which must be interpreted by the respondent and (2) a dichotomous response variable. As discussed above, it also has a serious flaw in its wording. The question used by Thomson *et al* (1993) (*How often does your mouth feel dry*?) at least offers the possibility of a number of options ("never", "sometimes", "frequently", "always"). It was used to determine the prevalence of xerostomia in a representative sample of older institutionalised New Zealanders, among whom 20 per cent reported dry mouth "frequently" or "always".

The much-cited study by Fox *et al* (1987) investigated the suitability of nine questions by comparing the responses of a convenience sample of 100 consecutive xerostomia clinic attenders with their objectively measured unstimulated and stimulated salivary flow rates. Four questions were found to be more accurate in identifying individuals who manifested *both* xerostomia and SGH (those who would be in group ***a*** in Figure 1.1 above), and are listed in Table 1.2. The usefulness of those findings for studying the *epidemiology* of dry mouth remains unclear because: first, there is a very wide range of flow rates and individuals can only be categorised as having xerostomia on the basis of their subjective symptoms; and second, the sensation of oral dryness is probably related more to the

unstimulated salivary flow (Dawes, 1987). Moreover, which of the questions is more important than the others, and should take precedence in defining the condition and then estimating its prevalence?

The sensation of oral dryness is not the only aspect of xerostomia which can be investigated. Narhi (1994) employed a series of questionnaire items which ranged from the experience of a continuously dry mouth to difficulty in speaking and in swallowing. Less frequently-explored symptoms such as oral burning or itching sensations were also investigated, and were found to be more prevalent in people with dry mouth. More of those individuals reported taste impairment, and difficulties in eating dry foods. Gilbert *et al* (1993) also used a number of different items, although they identified one particular question (discussed above) as their most important one for defining xerostomia. It is therefore feasible to include these more indirect items in any instrument which is intended to measure xerostomia.

There appears to be a need for an instrument which clearly and specifically identifies individuals with xerostomic symptoms. To date, most studies have taken a single-item inventory approach to identifying them. In effect, each was a single-item inventory, with the principal disadvantage that there is no way of knowing what dimension was actually being measured (Neverlien, 1994). There is also a greater theoretical risk of misclassification error because respondents are classified on their response to a single item rather than to a number of their responses to several items; the latter case (in theory at least) allows more discrimination among respondents. The item used by Thomson *et al* (1993), combined with the wide-ranging oral and non-oral complaints explored by Narhi (1994) and the four questions which emerged from the analysis by Fox *et al* (1987), would perhaps (in combination) comprise a satisfactory aggregation of items for investigating the prevalence and severity of xerostomia; it would, in effect, be a multi-item inventory. An essential precondition would be demonstrating (with factor analysis, for example) that the items which were used belonged to a single common "xerostomia dimension", and that the responses to those items had sufficient internal consistency. Such

an instrument—say, a "Xerostomia Inventory"—would be useful if a Likert scale approach was used to capture the xerostomia experience and represent it in an ordinal index as a continuous variable. Comparisons of xerostomia severity would then be possible across groups, and linear regression modelling used to examine its determinants. Thresholds could perhaps be established for the resultant continuous variable by comparison of scores on the inventory with responses to a standard single question embedded elsewhere in the questionnaire. The resultant thresholds (or "cut-off points") could also be validated by use of the inventory in a variety of field situations as part of the validation process.

This approach would surmount the problem of how to use the responses to the individual xerostomia questions used by Fox *et al* (1987), who reported on the efficacy of each individual question in identifying people who manifested both xerostomia and SGH, but did not suggest how they might be used together in data analysis. It would also circumvent the problem encountered by Gilbert *et al* (1993) who, as well as their single main question, used a number of other items to explore other aspects of xerostomia, and found that each resulted in different prevalence estimates. Which takes precedence? Certainly, the authors of those particular frequently-cited reports offered no hints as to how other researchers in this field could use their findings.

In order to ensure adequate empirical grounding for the items in the factor scale which would comprise an inventory for measuring xerostomia, semi-structured interviews with sufferers should be used to support each item's inclusion. This would also ensure that important dimensions of the xerostomia experience were not inadvertently omitted from the instrument. The *Methods* section of this thesis give more details of the process which was used to develop such an instrument.

1.2 The role of saliva in protecting the dentition

Saliva plays a pivotal role in protecting against dental caries. This function is mainly served by the unstimulated salivary secretions (FDI, 1992). The most striking illustration of saliva's function in protecting the integrity of the dentition is the observation that individuals who have undergone radiation therapy for neoplastic disease in the head or neck region can manifest catastrophically reduced salivary flow and rapidly advancing dental caries (Dreizen *et al,* 1977; Jansma *et al,* 1992, Cacchillo *et al,* 1993). In such cases, lesions can appear in atypical sites like the lingual surfaces of lower incisors and canines.

It has long been postulated that, at a less spectacular level, individuals with reduced salivary flow—or "subcatastrophic hyposalivation" (Billings, 1993)—may show marginally greater levels of dental caries activity (and therefore higher caries incidence) than those with normal salivation, particularly where root surface caries is concerned (Ettinger, 1981). The main evidence for this comes from prevalence studies such as that of Papas *et al* (1993), who reported higher numbers of decayed and filled surfaces (DFS) among 60 xerostomic individuals compared with 60 control individuals who had been matched for age, gender, number of teeth, smoking habits and alcohol consumption. It was reported that those with "xerostomia" had higher DFS scores. Close examination of the methods used in that study revealed that the xerostomic group corresponded to group **a** in Figure 1.1, in that they were those who not only reported a dry mouth but were "judged by the dental examiner" to have inadequate salivary flow. Sialometry was used in that particular study, but it is unclear from the report whether measured salivary flow was also used in labelling those individuals, or whether the diagnosis of dry mouth was totally reliant on the examiner's subjective assessment.

Aside from this rather unsatisfactory study, there is a real shortage of published data on the relationship between salivary hypofunction and dental caries. The chief methodological concern when considering the outcome of prevalence studies such as these, is that they are unable to define the time since inception of either the carious lesions or the impairment of

salivary flow. Hence, because the temporal relationship between the two variables is not explicit, their apparent relationship may actually be spurious (Drake and Beck, 1992).

One recent study has reported an association of tooth loss and low salivary flow in older people. Caplan and Hunt (1996) reported on a multivariate analysis of stimulated salivary flow and tooth-loss incidence among North Carolina elders in the Piedmont study. They proposed a model whereby people with low flow rate undergo tooth loss through increased coronal caries, root surface caries or periodontal disease, and reported that individuals with low stimulated salivary flow had greater odds of having lost at least one tooth over a 36-month period (odds ratio 1.52, 95 per cent CI 1.02 to 2.24). Those data indicate a weak relationship, but one which is nevertheless significant, and which offers the prospect of a substantive relationship between caries, SGH/xerostomia and medications. Loss of teeth can occur as a result of dental caries or periodontal diseases, with the former likely to contribute more to tooth loss over time in a given population (Chauncey *et al,* 1989). Moreover, tooth loss is so heavily influenced by extrinsic factors—such as dentists' treatment philosophy, practice type, location, and patients' socio-demographic characteristics and care-seeking behaviour—that it could therefore be argued that the emergence from Caplan and Hunt's multivariate analysis of a relatively "crude" indicator such as tooth loss is perhaps more significant than the confidence interval might indicate, allowing, of course, for the caveat that the time ordering of the two variables is unclear. The current study will concentrate on caries increment rather than tooth loss, although the latter will also be examined in different medication groups in the course of the longitudinal analysis.

1.3 Salivary function among older people

Altered salivary function is more common among older people than other age groups. While salivary flow does not decrease with age *per se* (Baum, 1992; Osterberg *et al,* 1992), there is evidence that older people's salivary systems are more susceptible to the reduction of their capacity by exogenous factors which are, in turn, more common among

older people (Baum, 1992). Examples of these include certain medications, some chronic inflammatory conditions, and radiation (such as that received during radiotherapy for cancer of the head and neck region). As a consequence, the prevalence of both xerostomia and SGH is higher among older people than in the general population (Baum, 1989).

Epidemiological studies have suggested a number of other modifiers of the occurrence of dry mouth among older people. Gender is frequently cited, with the most common finding being that xerostomia is more prevalent among females (Osterberg *et al*, 1984; Narhi, 1994; Locker, 1993; Billings *et al*, 1996). The findings on gender and flow rate are less clear, with some studies reporting lower flow rates among older females (Osterberg *et al*, 1984; Osterberg *et al*, 1992; Narhi *et al*, 1992; Watkins, 1992), but a recent study of a convenience sample of older people in the Rochester area of New York State reported no association (Billings *et al*, 1996). Smoking has also been suggested, but the findings to date are equivocal. Billings *et al* (1996) reported that xerostomia was associated with current smoking among males in the above-mentioned study, but did not report on the possible association between salivary flow rate and smoking, despite having measured salivary flow in that study. Norlen *et al* (1991) reported no association between xerostomia and smoking among a sample of older women who were retiring from the workforce. By contrast, Eliasson *et al* (1996) reported an increased secretion (by 27 per cent) from buccal, labial and palatal minor salivary glands among smokers in a sample of Swedes. While it should be borne in mind that this finding pertained to the minor gland secretions only (as major gland output was not measured), it suggests that the local irritant effect of tobacco smoke may actually increase glandular output. Most recently, Axelsson *et al* (1998) reported from a Swedish population-based study of dental status and smoking among 35-, 50-, 65- and 75-year-olds that males who smoked had significantly higher stimulated salivary flow rates than males who did not smoke. Unstimulated flow rate was not estimated in that study, and it is worthy of note that smokers reported more frequent dry mouth.

On the basis of the evidence from these studies, tobacco usage should be considered to be at least a potential modifier of the occurrence of dry mouth in older people, if only on the basis of the widespread observations of smoking's detrimental associations with many other biological and health characteristics. Similarly, alcohol usage should also be considered to be a potential modifier: while no epidemiological association has reported on alcohol use and dry mouth, a report of increased flow rates in laboratory rats which were chronically exposed to ethanol (Berry and Scott, 1990) suggests that a similar phenomenon might be observed among humans.

To date, only one epidemiological study has reported on changes in xerostomia over time in the same individuals. Locker (1995) reported the temporal trends in xerostomia in a population of people aged 50+ in Toronto. The baseline prevalence of xerostomia was 15.5 per cent (estimated using the question presented in Table 1.2), and at five years this had increased to 29.5 per cent. Most of those who reported xerostomia at five years were incident cases (that is, they had not reported the symptom at baseline), and the remainder were chronic cases (defined as those who had reported the symptom at baseline). Locker emphasised that the estimate of incidence did not include those for whom onset and resolution may have occurred between the two observations. The incidence data from that study are reproduced in Table 1.3.

Table 1.3: Xerostomia occurrence over a five-year period (from Locker, 1995)

	Xerostomia reported at		
	Baseline	**Five years**	**Number (%)**
Case classification			
Non-cases	no	no	397 (65.5)
Resolved cases	yes	no	29 (4.8)
Incident cases	no	yes	115 (19.0)
Chronic cases	yes	yes	65 (10.7)
Total			606 (100.0)

The conclusion from that study was that those at greatest risk of developing xerostomia are older and sicker individuals, and that most who develop it become chronic cases. There is further discussion of that particular study in Section 1.5.

1.4 Medication in older populations

Older people take more medications than any other age group, not only for symptomatic relief of various age-associated chronic diseases, but also in order to reduce the likelihood of complications which may arise from those conditions (Stockton and Jones, 1993). The occurrence of side-effects means that medication-induced illness is relatively common (Black and Somers, 1984; Mackay, 1987), and has been described as the public health problem among the older population which is most amenable to change (Beers and Ouslander, 1989).

Determining medication prevalence can not only allow estimation of the potential for iatrogenic effects, it can also indicate the extent of inappropriate use, such as the taking of combinations of drugs which are mutually contraindicated, or the use of several drugs with very similar pharmacological effects (Campbell *et al,* 1983). Medication prevalence studies can also have another use: examination of drug prevalence can give an approximate indication of an older population's distribution of diagnosed chronic conditions which are severe enough to have warranted treatment by a medical practitioner.

Few reports have been published of medication prevalence among community-dwelling older populations. Campbell *et al* (1983) reported on the medications taken by a population-based sample of 559 older residents of Gisborne in New Zealand. Nearly three-quarters (74 per cent) were taking at least one prescription medication, and six per cent were taking six or more concurrently. The median number of medications taken was 2.0. There were no gender differences in the overall level of medication use but, among the therapeutic categories, psychotropic drugs were more common among the females. Non-

prescription drugs which were taken comprised three groups: analgesics, laxatives and dietary supplements. Helling *et al* (1987) reported on the baseline medication characteristics of 3,467 participants in the Iowa 65+ Rural Health Study. Overall medication prevalence was 88 per cent, and the mean number of preparations taken was 2.87, comprising 1.74 prescription drugs and 1.13 non-prescription drugs. Some 60.5 per cent of preparations taken were prescription-only drugs, the number of which increased with age (unlike the non-prescription drugs, which were constant across the age groups examined). Most of the medications which were taken had been used on the previous day. More recently, Gilbert *et al* (1993) reported on the medications taken by 178 participants in the pilot study for the Australian Longitudinal Study of Ageing, in Adelaide. Medication prevalence was 89 per cent, and 44 per cent were taking four or more different preparations. The number taken increased with age, and females were taking more prescription drugs than males. Cardiovascular drugs and analgesics predominated (62 and 43 per cent respectively), and hypertension was the most commonly-stated therapeutic indication. Hershman *et al* (1995) reported from the Bronx Ageing Study on the medication taken by 488 participants aged 75 to 85 years. Medication prevalence was 93 per cent, and the mean number of medications taken was 3.8 (comprising 2.3 prescribed and 1.5 non-prescribed preparations). Females and older individuals took more medications. Cardiovascular and analgesic medications were the most common therapeutic categories taken.

A largely consistent pattern is apparent from these studies: (1) medication prevalence among older people tends to be high (usually in the order of 90 per cent); (2) females take more medications than males; (3) older individuals are more highly medicated; and (4) polypharmacy is common, with most individuals taking more than one preparation, and a small proportion taking many different ones. Cardiovascular medications predominate, with analgesics the next most common therapeutic category. The use of non-prescription medications is widespread, and these usually come from the analgesic, vitamin supplement or laxative categories. Hypertension is the most common medical condition being treated,

and there are indications from longitudinal studies in the USA that the use of antihypertensive therapy is increasing (Psaty *et al,* 1993; Glynn *et al,* 1995).

1.5 Medication and dry mouth

Every dentist "knows" that certain medications are associated with dry mouth; it is one of the truisms of dental clinical teaching. What is less clear is exactly what medications are involved, and with which aspect of dry mouth they are associated. Unfortunately, much of what has been written on the topic is based on poor science: clinical anecdote, observations of small convenience samples of dental patients, the unsupported pronouncements of experts, inadequate categorisation of medication exposure, and analytical *faux pas* are just a few of the problems with the bulk of the work which has been done in this field. It is therefore worthwhile examining the merits of the different approaches which either have been taken or are possible to take in this field.

Exploring the association of medication exposure with dry mouth in older populations poses some major methodological challenges. These can be listed as: (1) the difficulties of capturing information on medication exposure in such a way as to enable ready, flexible analysis of the data; (2) the analytical approach to be taken; (3) the problem of polypharmacy among older people; and (4) the issue of whether an observed association is due to the effects of the medication or is a side-effect of the underlying medical condition which is being treated. Each is discussed further below.

1.5.1 Capturing and analysing medication data in epidemiological studies

The estimation of medication prevalence is a useful but often problematic feature of epidemiological studies of elderly populations. Its utility lies not only in identifying the medications taken by participants, but also in estimating the potential for side-effects, and in indicating the extent of inappropriate use, such as the taking of combinations of drugs

which are mutually contraindicated, or the use of several drugs with very similar pharmacological effects (Campbell *et al*, 1983).

Epidemiological studies of elderly people have highlighted the possible risks associated with inappropriate or excessive medication regimens. These have included falls (Sobel and McCart, 1983; Grisso *et al*, 1991), oral side-effects (Baker *et al*, 1991; Thomson *et al*, 1995; Loesche *et al*, 1995), neural effects (Ramsay and Millard, 1986), and even mortality (Campbell *et al*, 1985). Medication has long been regarded as a risk factor for xerostomia, salivary gland hypofunction and dental caries in elderly people, but substantiation of that relationship has been slow to emerge. A major factor in this lack of knowledge has been the difficulties of categorising individuals' exposure to the various types of medication, and the difficulties encountered in analysing such data. Any dental epidemiological study which intends to examine disease patterns in older adults should include some type of systematic approach to capturing data on the medications being taken by the sample.

Medications cannot practically be analysed by name alone, and so some form of coding is required in order to facilitate the analysis. The medication coding system should enable subsequent analysis of the data with a minimum of record handling or data transformation. The type of coding system which is to be used depends on the objective of the study in which it is to be employed (Pahor *et al*, 1994): a study which is to examine the side-effects or benefits of medications would necessarily use a different system to one which intends to examine drug costs. The latter would require brand names and dosage data, whereas it would be more important for the former study to identify generic ingredients and combinations of those. A number of desirable features can be identified for a medication coding system to be used in epidemiological studies which aim to estimate the deleterious or beneficial effects of medication, and these are listed below.

1. It should assign a single unique code to each medication, and that code should have a sufficient number of digits to allow the unambiguous categorisation of any

particular medication. Each medication should appear only once in the classification.

2. The assigned code should be numeric, so as to allow aggregation or disaggregation to any level during analysis.

3. It should not be unnecessarily complex to use, so that it can be used by research assistants or data recorders in the field.

4. It should allow the collection of other relevant information (such as route of administration and dosage amount and frequency), and it should be compatible with any concurrent data collection.

5. The collected data should be easy to analyse.

6. It should be primarily based upon generic medications rather than proprietary names, and its composition should reflect the availability of medications in the country where it is to be used.

7. It should be hierarchical in nature, so that analyses can be performed at various levels of aggregation or disaggregation.

Coding systems for medications already exist, but are not without their disadvantages. Perhaps the most useful is the CHSMeds program (Psaty *et al*, 1992), which is a hierarchical system allocating each preparation a 14-digit code which includes not only information by which it can be identified, but also its dosage form and strength. It is currently in use in the longitudinal Cardiovascular Health Study (Fried *et al*, 1991), and has been used to capture medication data from over 5000 elderly participants. Its major drawbacks are the complexity of the codes—even though a computer-based data entry system is used to speed up the process of code allocation—and the need for strength and

dosage information to be included in the drug code fields. Others which are currently in use in a large epidemiologic study are the Drug Products Information Coding System (DPICS) and Iowa Nonprescription Drug Products Information Coding System (INDPICS) systems (for coding physician-prescribed and self-prescribed medications respectively) which are used in the Iowa-based Established Populations for Epidemiologic Studies of the Elderly (EPESE) study (Pahor *et al*, 1994). These assign numeric codes to individual preparations which are then automatically converted prior to analysis to Iowa Drug Information System (IDIS) codes, which comprise a four-level hierarchical numeric coding system. This enables aggregation (or disaggregation) of the medication data to any of the four levels of the hierarchy in subsequent analyses.

The Italian GIFA (*Gruppo Italiano di Farmacovigilanza nell'Anziano*) study was a pharmacosurveillance study of adverse drug reactions among hospital patients in 41 centres throughout Italy in two periods in 1988 (Pahor *et al*, 1994). Direct-entry capture of medication data was achieved using software which automatically coded a medication after the operator typed in the first few letters of its name and then selected the correct name from the list of medications which then appeared (from a database of all drug products which were available in Italy at the time). Individual medications were coded using two systems. The first was an Italian Ministry of Health (MINSAN, or *Ministero della Sanita*) code (developed for commercial purposes) which assigned a unique numeric identifier for each medication, dosage form and manufacturer. The second code assigned to each medication was a World Health Organisation Anatomic Therapeutic Chemical (ATC) code (WHO, 1995) which had been modified by replacing some (but not all) of the alphanumeric elements of the code by numeric elements. The ATC coding system has the attraction of a sound hierarchical structure, but the use of alphanumeric codes means that it is very difficult to analyse at any level beyond that of individual preparations.

Analysis with an alphanumeric system has been achieved elsewhere, however, using a progenitor (Helling and Venulet, 1974) of the ATC system in a geriatric screening program (Hale *et al*, 1982), but it must have been a complex and analytically cumbersome

process. Each of the Iowa and Italian systems requires a second data coding step so that analysis can proceed. In the final analysis, none of these systems is considered to be suitable for use in dental epidemiological studies because of their complexity, lack of versatility, and (for some) the requirement for further coding prior to analysis. There is a pressing need for a systematic, hierarchical, versatile and relatively simple method of recording and analysing the medications taken by elderly participants in epidemiological studies. However, it should be borne in mind that overcoming the practical challenge of capturing medication data does not, in turn, eliminate the broader issue of the actual use of a particular medication among individuals, where differences in compliance and pharmacokinetics mean that pharmaco-epidemiology is, at best, an inexact science.

1.5.2 Having captured the data, what analytical approach should be used to examine the association with dry mouth?

Certain medications are known to be associated with both xerostomia and SGH, and have usually been referred to in this context as "xerostomic" or "hyposalivatory", often with little distinction between the two terms. The term "xerogenic" may be more appropriate (Sreebny and Valdini, 1988), in that drugs so defined may exert their action either by reducing the volume of saliva secreted, or by altering the individual's threshold for dry mouth perception so that xerostomia is experienced.

Three general approaches might be used to study the purported xerogenicity of specific medication categories. First, the researcher can look for associations between xerostomia/SGH and the overall number of medications which are being taken. The second approach involves examining by therapeutic categories of medication (or even by individual preparations), and the third approach is to examine by putative xerogenicity of the medication being taken by the sample. The advantages and disadvantages of each will be discussed.

The first approach is to examine for associations between xerostomia or SGH and the overall number of different medications taken. This poses fewest problems with data recording and analysis, as each medication variable is recorded as a dichotomous variable and the total number taken can then be summed. Locker's 1993 report on xerostomia prevalence among older Canadians is an example of this approach: he found that the number of medications taken was one of the three variables which emerged from a logistic regression as a significant predictor of xerostomia (the other two variables were income and recent experience of a stressful life event). In a subsequent report, Locker (1995) took this non-specific medication-as-risk-factor approach further in examining the development of xerostomia over a five-year period (Table 1.4).

Table 1.4: Risk factors for xerostomia over a five-year period (from Locker, 1995)*

	Xerostomia reported at		
	Baseline	**Five years**	**Odds ratio**
Significant bivariate associations: (with xerostomia at follow-up)	Age 65+	Age 65+*	1.04 (1.01-1.07)
	Edentulism	Edentulism	
	1+ chronic medical conditions	1+ chronic medical conditions*	2.57 (1.38, 4.77)
	1+ limitations in activities of daily living		
	Fair/poor self-rated general health	Fair/poor self-rated general health*	2.80 (1.40, 5.34)
	1+ prescribed medications at baseline	1+ prescribed medications at baseline	
		1+ prescribed medications at 5-year follow-up*	1.40 (1.12, 1.70)

*The shaded areas indicate variables which emerged as risk factors in the multivariate analysis of xerostomia at five-year follow-up.

Risk factors for both baseline and five-year follow-up prevalence of xerostomia were examined. Greater use of medications at baseline was found to increase the risk of xerostomia at follow-up. Multivariate analysis revealed that medication use was a risk factor for xerostomia at follow-up, but that baseline medication use was not. Locker's analysis did not examine different medication categories (or, for that matter, different categories of chronic medical condition), but the findings support the prevailing view that medication is a risk factor for xerostomia, without actually adding to our knowledge of which medications are actually responsible.

In another population-based study of xerostomia, Nederfors *et al* (1997) found that its prevalence was higher among people taking one or more medications than among those who were not (32.1 and 16.9 per cent respectively).

A second approach is to examine by therapeutic category of medication. An example of this potentially more informative approach would be to examine the associations between the taking of (say) anticholinergics and the occurrence of xerostomia/SGH. This allows the very specific testing of associations, and enables more useful and clinically relevant hypothesis generation than does the approach of Locker (1993 and 1995) where the researcher can end up having demonstrated that medication is a risk factor for xerostomia, but still faced with the issue of which types of medication were actually responsible for the observed associations. However, even where individual types of medication have been captured and analysed using a cross-sectional design, there still remains the problem of only having current exposure data, which weakens the scientific impact of any observed associations. Where medication exposure has been recorded on two separate occasions using the cohort study design, there is the opportunity for more sophisticated examination of associations between medication and the various outcomes which are of interest. The work of Psaty *et al* (1995) offers an analytical approach which may be useful for categorising exposure using longitudinal medication-exposure data.

Category	Taken at baseline?	Taken at five years?
Continuous users	Yes	Yes
Starters	No	Yes
Stoppers	Yes	No
Nonusers	No	No

It might be expected that, if a particular drug was a cause of dry mouth, the effect would show a gradient whereby it was strongest among the *Continuous users*, approximately the same among the *Starters* and *Stoppers*, and weakest among the *Nonusers*. While there would be real difficulties in distinguishing between the *Starters* and *Stoppers* in terms of medication exposure, there might be real advantages in modifying the approach to compare the *Continuous users* with the remainder of the sample for each medication (or to compare three groups: *Continuous users, Starters* and the others). An interesting side-issue would be whether more variance in dry mouth was explained by using this longitudinal approach to exposure than by using exposure at the second observation only (that is, by treating the later data as a simple cross-sectional study). It would be more economical for researchers examining the xerogenicity of medications to be able to accomplish the same (or better) research outcomes by using the cross-sectional approach instead of having to conduct expensive, administratively complex and time-consuming longitudinal studies. At present, it is not known whether the history of exposure is important or not.

A third—and more problematic—approach is to examine by putative xerogenicity, whereby medications taken by individuals are first categorised according to a previously-determined classification of xerogenicity. Such classifications appear to have been fashionable in the mid-1980s, with three having been published (Handelman *et al,* 1986; Grad *et al,* 1985; Sreebny and Schwartz, 1986). It is perhaps not surprising that they vary

greatly in both the number and types of medications listed (Table 1.4). The Sreebny and Schwartz classification is particularly broad; moreover, those authors published an update in 1997 (Sreebny and Schwartz, 1997) which still contained over 400 different preparations. The empirical grounds for classification of many medication categories as xerogenic were particularly weak, and their inclusion in such lists appears to owe more to the assertions of the *US Physician's Desk Reference* than to any empirical evidence of their actual xerogenicity. Moreover, the utility of such classifications is limited. First, there is no indication of whether the medications listed are purported to cause either xerostomia or SGH, when it is now realised that distinguishing between the two is becoming increasingly important in studying the natural history of those conditions. Second, the variation manifested across such classifications (and which is apparent in Table 1.5) is itself testimony to their arbitrary nature and lack of scientific evidence.

Table 1.5: Composition of published xerogenic medication classifications (● indicates inclusion)

Medication type	Grad *et al,* 1985	Handelman *et al,* 1986[a]	Sreebny and Schwartz, 1986[b]
Antihypertensives	●	●	●
Antipsychotics	●	●	●
Antidepressants	●	●	●
Antispasmodics*	●	●	●
Antihistamines	●	●	●
Anticholinergics		●	●
Antiparkinsonians	●	●	●
Antiarrhythmics	●		●
Anorectics	●		●
Anticonvulsants	●		●
Anxiolytics	●	●	●
NSAIDs		●	●
Diuretics	●		●
Analgesics			●
Antiarthritics			●
Antidiarrhoeals			●
Antinauseants			●
Antineoplastics			●
Antipruritics			●

[a]Handelman *et al* classified xerogenic medications as having either a "definite" or a "probable" hyposalivatory effect; only the former are included here.
[b]Sreebny and Schwartz also included one drug from each of the following categories: bronchial dilator, antiulcer agent, antihyperlipidaemics, antiacne drugs.

Third, even if such a classification is successfully used in a research project, the question which the researcher will ultimately be obliged to answer is: *which specific medications were associated with the occurrence of dry mouth?* That this is the very same issue which is unresolved in the approach used by Locker (1993 and 1995) underlines the wisdom of seeking a classification and coding system which enables a much more flexible approach to medication analysis to be used.

1.5.3 The challenge of polypharmacy among older people

Polypharmacy is one of the major challenges which must be adequately dealt with in any epidemiological study of medications and their effects among older people. To date, the issue has not been satisfactorily resolved. For example, if an association between antidepressant use and lowered unstimulated whole-salivary flow rate is observed in such a study, one of the first issues which must be addressed is whether the effect was actually due to the effects of concurrent pharmacotherapy. That is, was the observed association actually due to the other medications that most (or all) of those on antidepressants were taking? At the individual (clinical) level, the issue is still a challenge, but it is a relatively simple matter to examine the person's other medications and, in the light of what is currently known about medications and dry mouth, arrive at a considered judgment about the likely aetiology of the individual's condition.

As clinicians, we wish to know which drugs are more likely to be associated with dry mouth so that we can ensure that patients taking those preparations are advised on the appropriate preventive measures which they can take to ensure that any associated carious threat to the dentition is minimised or averted. The knowledge-base upon which we act is built largely from two types of source: (1) case reports and clinical observations; and (2) the findings of epidemiological studies of the occurrence of dry mouth. An epidemiologist would regard the former as generating hypotheses to be "fleshed out" by data from the

latter, whereas the clinician would consider the latter to merely offer confirmation of the former source. Irrespective of the investigator's perspective, polypharmacy poses a severe challenge. The number of potential combinations of drugs being taken is enormous, and considerations of statistical efficiency preclude a satisfactory examination of the associations of each combination; the required sample size would be prohibitively large. Even if a limited number of the most common combinations is examined, there is the issue of multiple testing and an associated likelihood of Type I error (see below).

The fundamental issue is: *which medications should we be wary of, and which can we discount when considering dry mouth among older people?* A prognostic model approach may be useful in this regard. Prognostic models combine two or more items of data on individuals to predict clinical outcomes, and are purported to be potentially useful when clinicians are faced with difficult decisions like ordering invasive tests or selecting which patients are likely to benefit from scarce resources (Wyatt and Altman, 1995). The latter scenario is more apposite to the dilemma facing the dental clinician or the researcher who is investigating the association between drugs and dry mouth: which older, medicated individual is more likely to manifest some aspect of dry mouth and thereby merit more intensive preventive efforts?

Aitchison *et al* (1995) reported on their development of a model for indicating the prognosis for individuals who have had invasive primary cutaneous malignant melanomas removed by excision biopsy. Full survival analysis using a proportional hazards approach was used, based on five-year survival data on 1978 patients. The prognostic accuracy of the model was tested on a further sample of 300 individuals. The outcome of the study was an apparently satisfactory, validated tool which produced prognostic estimates by placing individuals within a two-level classification, which used (1) sex, and (2) presence or absence of ulceration in the lesion. This general approach may be useful in the investigation of dry mouth, particularly when sex appears to be an important factor. Classification and Regression Tree (CART) analysis (Stewart and Stamm, 1991) holds some promise as a useful analytical tool for this purpose, particularly when the task at

hand is predominantly exploratory (such as with dry mouth). Many medications have been implicated in the drugs-dry mouth relationship but, because of the many flaws in the research which has been reported to date, there is still doubt about exactly which drugs are associated with the condition (Atkinson and Wu, 1995), and the use of an exploratory device is highly appropriate. Thus, an inductive approach may be more appropriate than a deductive one, especially when there are so many potential predictor variables (Williams, 1979). In studying medications and dry mouth among older people, the fundamental problem is in finding which of the putative predictors are actually associated with the dependent variable, and in what way they are associated with each other. Polypharmacy presents a formidable analytical challenge; most older people take at least one medication, and a majority take more than one.

A similar technique to CART analysis has actually been used previously in the field of drugs and dry mouth, in a study of the association between salivary flow rate and medication use among institutionalised older people in Sweden (Johnson *et al*, 1984). That study used Automatic Interaction Detection (AID) analysis as an exploratory device, and found that individuals taking antidepressants (and antihistamines) and diuretics had lowered flow rates; however, because the drugs in the analysis had already been categorised according to their hypothesised effect on saliva secretion, it is possible that this *a priori* approach may have missed some important associations. Moreover, the number of participants was relatively low, at 154, and there was no AID analysis presented of the association between medication use and the symptoms of dry mouth. Because AID analysis requires that a continuous dependent variable (such as flow rate) be recoded (that is, aggregated) to an ordinal variable with a maximum of 31 categories, CART analysis is considered to be more appropriate, as it permits the use of an untransformed dependent variable (Stewart and Stamm, 1991).

Aside from the attempt by Johnson *et al* (1984), none of the reported analyses of medications and dry mouth (Table 1) has satisfactorily addressed the issue of the effects of multiple medication use. There are at least two possible reasons for this. First, it is

analytically complex, and the risk of Type I error increases with the increased number of statistical tests which are required when conventional approaches are used. Second, there are very real sample size limitations; for example, if only the most prevalent 20 medication types are examined in an epidemiological study of older people, there are still 2^{19} (or 1,048,576) different possible combinations of medications to examine. For there to be meaningful numbers in each combination subgroup, the number of individuals in the sample would have to be prohibitively large. If an approach such as the Bonferroni correction is used to reduce the chance of Type I error, the required α level for that number of statistical procedures is prohibitively small. Moreover, because so much is unknown about the relationship between medication use and dry mouth, conventional *a priori* approaches carry the very real risk of missing a substantial association, and analyses therefore need to have more of an exploratory approach than would be normally expected in an epidemiological study. Thus, conventional approaches to the drugs-dry mouth issue suffer (at least potentially) from the following problems:

1. the predictors of interest (medications) are not normally distributed; rather, they are categorical variables;
2. there are differences in the type and extent of measurement error in the dependent and independent variables (predictors);
3. the relationships may not be linear;
4. there are various intercorrelations among the predictors (for example, someone taking an anginal is more likely to be taking a beta-blocker than someone who is not);
5. the problem of polypharmacy means that the number of potential combinations is enormous;
6. there may be interaction effects, and these may be extremely difficult to detect using conventional approaches, and require considerable *a priori* knowledge (Williams, 1979).

The CART method was developed as a possible solution to these problems, particularly where large data-sets are to be used. It is a well-established, robust, nonparametric procedure which is used for detecting predictive patterns and interactions among predictors. It has been described as a good alternative or complement to conventional procedures (Stewart and Stamm, 1991). It provides an in-depth examination of the associations of a set of independent variables (say, with each medication type having dichotomous exposure categories: taken, not taken) with a continuous (such as the unstimulated salivary flow rate) or categorical (such as the responses to a dry mouth question with four ordinal response options) dependent variable. In the former case, the Regression tree method is used; for the latter, the Classification tree method applies. The variables in the data-set can be any combination of continuous or categorical variables.

The procedure uses a stepwise algorithm; it begins by dividing the sample (at what is termed the "root node") into two or more non-overlapping subgroups whose split optimises a predetermined goodness-of-split criterion. It then splits those groups into smaller subgroups using an iterative process which pinpoints the best predictor at each level, until for each given node, the stopping criterion is met and the process terminates; that is, when no further predictors are statistically significant, and the subgroups are either too small for further division (the minimum cell size is specified in advance), or the predictive power is not sufficiently improved to justify further subdivision of the data-set. The outcome is a classification tree diagram with estimates of the effect of the categories of each predictor at each level.

It is possible that this essentially empirically-driven analytical strategy may help to circumvent some of the analytical problems posed by polypharmacy because of (1) its hierarchical approach, and (2) its systematic, exploratory nature. Its main utility in this respect may be its use in preliminary analysis (to identify potential independent variables) to the development of a predictive model for the dependent variable using conventional multivariate analysis. The use of CART analysis in the field of medications and dry mouth

has not been reported previously, and its examination in the current study may indicate whether it is useful or not.

1.5.4 The problem of distinguishing the effects of medications on dry mouth from those of the underlying medical conditions

Any research into the association of medications and dry mouth is faced with this thorny issue. For example, if someone who complains of a dry mouth is also taking antiasthma medication, are the symptoms merely due to some pharmacological side-effect of the drugs taken, or are they due to the increased effort required for breathing by that individual, who must often resort to mouth-breathing?

Is it possible to account for certain drugs being associated with xerostomia but not lowered flow rate? Dawes (1987) proposed a physiological model for xerostomia, in which he related the sensation of oral dryness to dehydration of areas of the oral mucosa, or friction between adjacent dehydrated mucosal areas. He hypothesised that it is possible therefore that, because saliva is not evenly spread throughout the oral cavity, it might be possible for such locally dehydrated areas to occur even in the presence of what is to all appearances a clinically adequate whole-salivary flow rate. This might also be exacerbated by: (1) local absorption of water from saliva (which, after all, is hypotonic with respect to interstitial fluid); and (2) water evaporation from the oral cavity, which would be more marked among mouthbreathers.

Interference with neural transmission is thought to be the main means by which certain drugs are able to inhibit salivary flow. For example, the cyclic antidepressant preparations are sympathomimetic; that is, they potentiate the action of noradrenaline by inhibiting its uptake from the synaptic junction. It is therefore thought that the sympathomimetic effect

of these preparations on the salivary system leads to a reduction in secretory activity by the salivary glands.

Some medical conditions may be associated with dry mouth. A recent report from a study by Nederfors *et al* (1997) highlighted being female, increasing age, and taking more medications as risk indicators for xerostomia (using a multivariate approach). Where medications were concerned, the authors emphasised that it was not possible to distinguish between their effects on mouth dryness and those of the underlying medical conditions for which they were being taken. This aspect of the problem is a major challenge for researchers, and a solution is not in sight at present.

Circum- and post-menopausal symptoms are a case in point. These are often treated with hormone replacement therapy (HRT), and dry mouth has been reported to be part of the circum- and post-menopausal set of potential symptoms. A recent Finnish study reported lowered stimulated whole-salivary flow rates among postmenopausal women compared with perimenopausal individuals; the flow rates of both groups had increased three and six months after each group had started HRT (Laine and Leimola-Virtanen, 1996). While xerostomia was investigated in that study, it was not satisfactorily reported. In contrast, Streckfus *et al* (1998) reported no difference in stimulated or unstimulated salivary flow rates between older women who were taking HRT as their only medication and those who were not taking any medication, and Ship *et al* (1991) reported no difference in flow rates between postmenopausal women taking HRT and those who were not. None of these studies examined xerostomia, and it is not clear what the expected effects of HRT on dry mouth symptoms might be.

As discussed above, older individuals who suffer from emphysema or asthma may suffer the symptoms of dry mouth as a result of continual mouth-breathing, and the same issue presents itself. Dry mouth might also be an associated symptom for people with anxiety disorders, and might lead to an apparent association with the use of psychotherapeutic medications (sedatives or hypnotics).

There appears to be no simple answer to these questions. Certainly, there has been little acknowledgment of this difficult issue in the literature on medications and dry mouth.

1.5.5 Reported associations between medications and dry mouth

Much has been written about various medications as putative risk factors for dry mouth, but current knowledge of the effects of medications on dry mouth is inadequate: Loesche *et al* (1995) observed that, although more than 400 medications have been cited in various sources as being xerogenic, "most of the evidence linking a particular medication with xerostomia is anecdotal." Medication types which have been shown in epidemiological or experimental studies to be associated with *xerostomia, SGH* and *both aspects* are shown in Table 1.6.

Table 1.6: Medication types reported to be associated with xerostomia and/or SGH

Medication type	Associated with xerostomia	Associated with SGH
Antihypertensives	Narhi *et al* (1992)	Streckfus *et al* (1994)
Antipsychotics	Osterberg *et al* (1984)	
Antidepressants	Loesche *et al* (1995)	Johnson *et al* (1984) Loesche *et al* (1995)
Antihistamines	Osterberg *et al* (1984)	Johnson *et al* (1984)
Anticholinergics	Osterberg *et al* (1984) Thomson *et al* (1993)	
Anxiolytics	Persson *et al* (1991) Osterberg *et al* (1984)	Loesche *et al* (1995)
Diuretics	Atkinson *et al* (1989)	Johnson *et al* (1984) Persson *et al* (1991) Osterberg *et al* (1984)
Analgesics	Narhi (1994)	
Cardiac agents (including angina medications)	Narhi *et al* (1992) Loesche *et al* (1995)	
Antiasthma drugs	Loesche *et al* (1995) Narhi (1994)	
Antiulcer drugs	Loesche *et al* (1995)	Loesche *et al* (1995)

Eleven medication categories have been observed to be associated with xerostomia, and six with SGH. Each medication category which has been observed to be associated with SGH has also been shown to be associated with xerostomia, although not necessarily in the same study.

It is indeed remarkable that not one study has reported using multivariate analysis to examine the association between medications and dry mouth. After all, the technical demands of such an analysis are not high, and—leaving aside the difficulties to date of adequately measuring xerostomia—salivary flow rate provides a continuous dependent variable with a distribution which is sufficiently normal to satisfy the criteria for linear regression analysis.

It is difficult to account for most of the observed associations in Table 1.6. It could be argued that medications with a purported anticholinergic effect would be more likely to be associated with low salivary flow, and that is certainly borne out by the antidepressants. However, it is extraordinary that no association between anticholinergic drugs and SGH has been reported, despite two studies having found one with xerostomia. The local dehydrating effect of diuretics could account for the associations observed with them, but many of the other associations in Table 1.6 are unable to be explained using current knowledge. Many factors appear to be involved, and a useful summary is reproduced in Table 1.7 from Sreebny and Schwartz (1997).

Table 1.7: Drugs and dry mouth: overview of putative pharmacologic, physiologic and behavioural factors

Pharmacodynamic factors	*Pharmacokinetic factors*	*Physiologic and psychologic factors*	*Behavioural factors*
Class of drug	Dose of drug	Age and sex	Timing of doses, re meals and sleep
Salivary gland size	Drug absorption	Potential for adaptation	Intake of alcohol, tobacco, caffeine
Chemical structure of drug	Route of administration	Organic diseases	Illicit drug use
Bioavailability	Dosage form (eg. extended release)	Nervous system changes	Compliance
Intrinsic drug action	Frequency of intake	Depression/anxiety	OTC drug use
Types and numbers of multiple drugs taken	Duration of drug regimen	Total body water	Diet
Drug interactions	Drug distribution	Alteration in end-organ responsiveness	Oral hygiene and preventive care
• Additive	Lean-to-fat ratio	Body weight	
• Antagonistic	Plasma protein binding	Malnutrition	
• Synergistic	Drug interactions	Baseline flow rates	
Drug metabolism	Drug clearance	Physical and chemical character of saliva	
Drug additives and propellants	Drug metabolism	Salivary gland size	
	Hepatic biotransformation	Iatrogenic factors (eg radiation, surgery)	
	Hepatic metabolising systems and renal perfusion		

In closing this section, it is worth quoting Atkinson and Wu (1994), who wrote: "Although about 400 medications have been associated with xerostomia, the salivary effects of most of these drugs have not been studied in clinical trials *[or in epidemiological studies - WMT]*. Also, many clinical studies are conducted with healthy, young volunteers. At least one study found that the inhibitory effects of medications on salivation appear more pronounced among the elderly. Therefore, the relationship of salivary function and individual medications in the unhealthy elderly is largely untested."

It therefore appears that there is much that we do not know about the relationship between medications and dry mouth among community-dwelling older populations.

1.6 Dental caries in older populations

This section provides an overview of the recent literature on the prevalence and incidence of both coronal and root surface caries among older people.

1.6.1 Dental caries prevalence

A large number of studies have reported on the prevalence of both coronal and root surface caries in older people.

1.6.1.1 Coronal caries prevalence

A summary of the results of recent studies of coronal caries prevalence in various community-dwelling older populations is presented in Table 1.8. Criteria for inclusion in the table were that a report was either: (1) from an Australasian study with relevance to the current study; (2) from one of the major longitudinal studies of older people which are currently being conducted; or (3) considered to have relevance for the current study by virtue of its size, findings or population under study.

Table 1.8: The prevalence of coronal caries in older community-dwelling populations

Authors, site and year published	Number of people	Age range	Mean values			
			Teeth present	DT	FT	DFT
Powell and McEniery, Brisbane, 1988	102	65+	14.3	1.1	6.3	7.4
Slade and Spencer, Adelaide, 1996	853[a]	60+	16.3	0.3	8.3	8.6
Slade and Spencer, Adelaide, 1996	640[a]	65+	15.7	0.2	8.2	8.4
Bergman *et al*, Melbourne 1991	108	60+	ng	1.2	5.4	6.6
Brown *et al*, Dunedin, 1987	66	65+	13.0	0.5	6.0	6.5
Cautley *et al*, Dunedin, 1992	95	70+	14.4	2.3	4.8	7.1
McGuire *et al*, New England, 1993	718	70+	ng	ng	ng	9.7
Hunt *et al*, Piedmont Study, 1992	809	65+	ng	ng[b]	ng	ng
Ambjornsen, Norway, 1986	159	67+	13.9	1.1	8.8	9.9
Locker and Leake, Ontario, 1993	699	50+	18.9	ng[b]	ng	ng

[a]These are from the same survey; the 65+ data are presented to aid comparison with other surveys
[b]Only surface-level data presented

The general picture which emerges from those studies is that the mean number of remaining teeth in the "typical" dentate older population is relatively low, and that the filled component is the major contributor to the accumulated disease experience (represented by the DFT estimate) of its members. There is the suggestion that the mean

number of teeth present is greater in the more recent studies, and in those in which the lower age bound is younger.

Multivariate models of coronal caries prevalence

Drake and Beck (1992) modelled coronal caries prevalence among participants in the Piedmont study, using the presence of any decayed coronal surfaces as the dependent variable in a logistic regression analysis. Their findings underlined the multifaceted nature of caries occurrence, with two socio-behavioural variables and two dental health variables emerging as significant: the former comprised (1) a lack of regular dental care and (2) an interaction term encompassing ethnicity and perception of financial well-being (whereby whites who were well-off had substantially lower odds of having decayed coronal surfaces than blacks or those with financial problems); the two dental health variables were (1) the presence of decayed root surfaces and (2) a lower stimulated salivary flow rate.

Locker and Leake (1993) reported on their use of linear regression analysis to model coronal DFS prevalence among participants (aged 50 or more) in a dental longitudinal study in Ontario. The model explained 42 per cent of the variance in the dependent variable, and showed that coronal DFS was greater among individuals with greater numbers of remaining teeth, a regular dental visiting pattern, higher educational attainment, and who had been born in Canada. The number of remaining teeth was the single most important explanatory variable, and accounted for virtually all (39 out of the 42 per cent) of the variance in coronal DFS explained by the model.

1.6.1.2 Root surface caries prevalence

A summary of the findings from recent studies of the prevalence of root surface caries in non-institutionalised older populations is presented in Table 1.9. Criteria for inclusion were those set out in section 1.6.1.1. It is apparent from those data that the prevalence of root surface caries is high in older people, although arguably not as high as that of coronal

caries. This is at least partly due to the fact that a necessary pre-condition for root surface caries is the exposure of root surfaces as a result of periodontal attachment loss. The relatively late occurrence of most periodontal attachment loss means that, relative to coronal caries, root surface caries is a late-onset condition. Aside from the strikingly high estimate reported by Cautley *et al* (1992)—about which there is undoubtedly a correspondingly large confidence interval, due to the relatively small number of individuals—the Root Caries Index values (RCI; Katz, 1980) are reasonably consistent, ranging from 5.1 per cent to 12.8 per cent of susceptible root surfaces affected.

Table 1.9: The prevalence of root surface caries in older community-dwelling populations

Authors, site and year published	Number of people	Age range	Teeth present	Per cent with 1+ DFS	Mean no. Surfaces affected/person	RCI[a]
Beck *et al,* rural Iowa, 1985	520	65+	18.8	63%	2.3	ng
Wallace *et al,* Alabama 1988	603	60+	23.5[b]	69.7%	3.1	8.1%
Cautley *et al,* Dunedin, 1992	95	70+	14.4	68.4%[c]	2.6[c]	43.8%
Graves *et al,* Piedmont study, 1992	809	65+	15.3 to 20.4[c]	33.9 to 56.6%[d]	1.3 to 2.4[d]	5.1 to 10.9%[c]
Locker and Leake, Ontario, 1993	699	50+	18.9	70.9%	3.6	ng
Slade and Spencer, Adelaide, 1996	853[e]	60+	16.3	72.4%	3.1	11.9%
Slade and Spencer, Adelaide, 1996	640[e]	65+	15.7	75.3%	3.5	12.8%

[a]Root Caries Index - calculated according to Katz (1980)

[b]One of the entry criteria for this study was that individuals had to have 15+ remaining teeth

[c]Decayed surfaces only; does not include filled surfaces

[d]Data were presented separately for different ethnic and gender groups

[e]These are from the same survey; the 65+ data are presented to aid comparison with other surveys

There is a clear pattern among the root caries prevalence studies which are presented in Table 1.9. First, susceptibility is almost universal: virtually all dentate individuals over age 60 have at least one exposed root surface as a result of loss of periodontal attachment, and are therefore at risk of root surface caries. Second, root surface caries prevalence is not randomly distributed among populations: it is more prevalent among sub-groups, for example, the finding by Beck *et al* (1985) that all of the decayed root surfaces were confined to 25 per cent of their sample. It appears therefore that, while periodontal loss of attachment is a necessary pre-condition for root surface caries, its presence alone is not sufficient. Third, root surface caries prevalence differs according to certain socio-demographic indicators. It appears to be greater in older age groups, and among males, and both Wallace *et al* (1988) and Graves *et al* (1992) reported ethnic differences, with greater overall root surface caries prevalence (ie decayed and filled surfaces) among whites, but greater numbers of untreated decayed surfaces among blacks.

Multivariate models of root surface caries prevalence

There are few reports of multivariate modelling of root surface caries prevalence, but those that have appeared suggest that modelling of that condition is generally less successful than coronal caries models in explaining the observed variance in prevalence. Beck *et al* (1987) modelled root surface caries prevalence among 520 dentate people aged 65+ in Iowa, using a conceptual framework in which socio-demographic, physical/medical, environmental, behavioural and oral risk factors interacted to determine oral disease (Figure 1.2). The overall variance explained by the model was 28.2 per cent for females and 34.4 per cent for males. Much of the variance was explained by "non-dental" factors. For example, among females the number of years of education (which were positively associated with root decay), physical/medical conditions (specifically cancer, Parkinson's disease, joint stiffness, liver disease or cataracts), and negative physical life events (that is, chronic diseases diagnosed within the previous year) contributed 70 per cent of the total explanatory power of the model, in that those factors

explained 19.6 per cent of the total variance. Among males, the contribution of such "non-dental" variables to the model's explanatory power was less substantial, at 37 per cent, and the variables in question—physical/medical conditions (specifically arthritis, emphysema/chronic bronchitis, anaemia or fractures since age 50) and negative social life events (such as death of a spouse or change of residence)—differed from those which were significant for females.

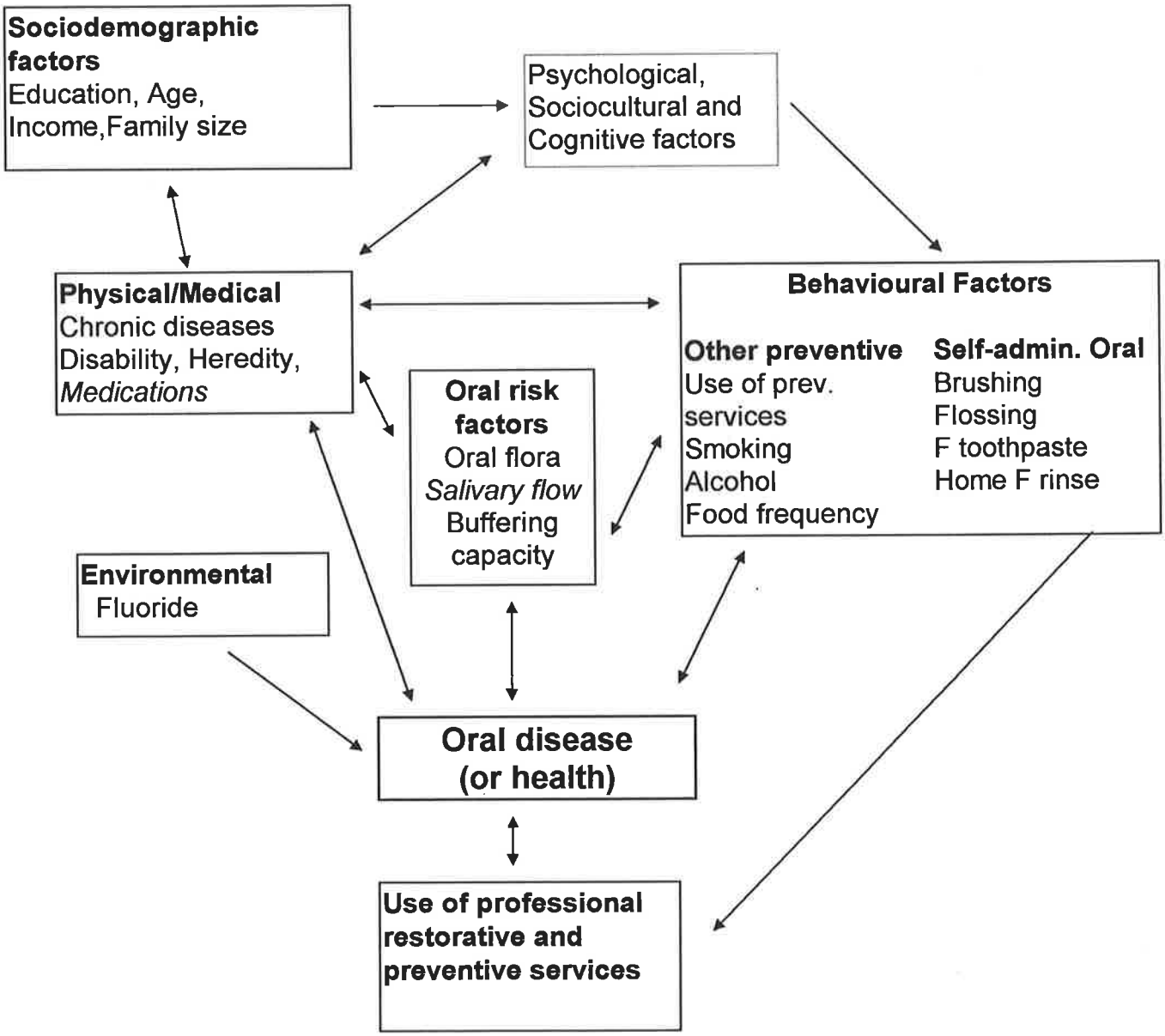


Figure 1.2: Framework for risk factors in oral disease (adapted from Beck *et al*, 1987)

Locker *et al* (1989) reported on their modelling of root surface caries prevalence among a relatively small sample of 183 dentate individuals aged 50+ in Ontario, and concluded that oral health factors were more important than general health, demographic or dental care factors as explanatory variables, as, of the latter, only age stayed in the multivariate model. The conclusion of that pilot study was not substantiated by subsequent investigation: Locker and Leake (1993) used a broadly similar framework to that of Beck *et al* (1987) to model root surface caries prevalence among a larger sample of 699 dentate Ontario residents aged 50 years or more. Analyses for females and males were not presented separately. The model accounted for 35 per cent of the variance in root DFS, and the significant dental variables were: the number of surfaces with recession (positive Beta); the number of coronal DFS (positive Beta); and the number of teeth (negative Beta). The significant "non-dental" variables were age (greater in older individuals), gender (greater in males) and being a current smoker (all of which had a positive Beta). When root DS was used as the dependent variable, it was found to be positively associated with mean periodontal attachment loss and the number of decayed coronal surfaces, and negatively associated with the number of remaining teeth. The model explained 19 per cent of the variance, and the authors emphasised the broad similarity of the models for root DFS and root DS.

The data from these studies generally support the utility of the model proposed by Beck *et al* (1987), and suggest an important role for socio-demographic, medical, social and behavioural factors in the aetiology of root surface caries (Figure 1.2). However, modelling of coronal and root surface caries prevalence among older populations has particular limitations. First, the time order is not determined: the temporal relationships among variables are not clear. Second, defining caries experience without taking missing teeth into account (for example, by either counting the number of decayed and filled coronal surfaces or identifying individuals with one or more decayed coronal surfaces) means that there may be some misclassification of individuals according to their total caries experience. Third, the observed caries prevalence is likely to differ substantially from the incidence because it has most likely accumulated over a prolonged period prior

to the observation (Beck *et al,* 1987), unlike the situation when the incidence and prevalence of a condition are very similar and any observed associations between the disease and designated explanatory characteristics are more likely to represent the situation which actually exists regarding risk factors. Inevitably, these factors affect the utility of any multivariate models which are developed, and mean that the main use of the technique in prevalence studies is to identify risk indicators which may subsequently be tested in incidence studies (Beck, 1994). The following section reviews the recent literature on the incidence of caries among older populations.

1.6.2 Dental caries incidence and increment

To date, only a small number of reports have been published on the incidence of dental caries among older populations, although this is expected to increase substantially in the next few years as the findings of the major dental cohort studies of older people become available. As well as the current study, there are large cohort studies under way in North Carolina, Iowa and Ontario. Early reports from these studies show that the progression of dental caries continues among older individuals, despite a perception among dental professionals and policy-makers that the disease is mostly only active in younger people (Drake and Beck, 1992).

1.6.2.1 Coronal caries incidence

A number of different approaches to describing coronal caries incidence can be used. These are summarised in Table 1.10, together with their advantages and disadvantages.

Table 1.10: Analytical approaches to dental caries incidence and increment

Approach	*Brief description*	*Advantages*[a]	*Disadvantages*
"Conventional" incidence eg. Hawkins *et al*, 1997 (Ontario study)	Case-based definition of incidence. Requires rigid case definition.	Simple to understand, particularly for lay people. Allows use of simple logistic regression modelling.	Allows view of only the broad picture; subtle differences missed, as the individual is the unit of analysis.
Caries increment (CI) Described in Beck *et al*, 1997	Caries severity at baseline simply subtracted from that at follow-up.	Simple to calculate. Useful when the risk of the event occurring is constant, or tooth or participant loss is low	Inaccurate. Does not allow for reversals.
Crude caries increment Described in Beck *et al*, 1997	Caries increment calculated using a surface-by-surface comparison of baseline and follow-up data.	More accurate than the previous approach, as the change in status for each surface is included.	Analytically more difficult. Does not allow for reversals.
Net caries increment (NCI) eg. Hawkins *et al*, 1997 (Ontario study)	As above, but with the number of reversals subtracted from the gross caries increment.	Includes adjustment for reversals. Intuitively sound.	Does not allow for different types of reversal, and assumes that the number of 'examiner reversals' made in each direction is the same.
Adjusted caries increment (ADJCI) eg. Beck *et al*, 1995 Drake *et al*, 1997 (Piedmont study)	Uses a reversal-adjusted caries increment, on the basis that 'examiner' reversals are more common than 'true' reversals. Frequency of examiner reversals proportional to t_0 caries.	In taking reversals into account but adjusting them for t_0 caries prevalence, it is not as drastic as the NCI, and offers a compromise between the NCI and CCI.	Analytically more complex. Shouldn't be used when reversals are < 10% of the carious lesions detected at t_0. Does not distinguish between "true" reversals and examiner error.
Incidence density eg. Lawrence *et al*, 1996 (Piedmont study)	Number of events divided by the total amount of observation time at risk.	Accounts for the time that each surface is at risk, and takes into account the censoring of events.	Computing time at risk involves assumptions which may or may not be valid. Complex. Appropriate when time-series has >2 observations per surface

[a]All but the first approach can produce an annualised rate of caries increment for use in comparisons among groups

A report by Hand *et al* (1988) on the 36-month incidence of coronal caries among older people in Iowa recounted a mean increment of 2.4 surfaces; 64.9 per cent had a coronal caries increment of 1 or more DFS. Drake *et al* (1994) reported eighteen-month coronal caries increments of 0.6 and 1.0 surfaces for blacks and whites respectively among a population of North Carolina older people. The three-year caries incidence findings from that study have recently been published (Drake *et al*, 1997), with a net increment for blacks and whites of 1.6 and 2.1 surfaces respectively. The coronal caries incidence estimates for those two groups were 45 and 59 per cent respectively. The respective annualised caries increment rates for blacks and whites were 0.8 and 1.6 surfaces per 100 surfaces at risk. Drake *et al* (1997) highlighted the difficulties posed by teeth which have been crowned during the time between observations, and suggested that increments be reported both with and without including crowns in the calculations. They observed that a major part of the difference between blacks and whites in their caries increment was the contribution of newly-crowned surfaces to the estimates.

Hawkins *et al* (1997) reported on coronal caries incidence among participants in the Ontario study: 53.2 per cent of participants aged 65+ were incident cases, and the mean net DFS increment was 1.5 surfaces for the three-year period. Coronal caries incidence among those aged 50+ was used as the dependent variable in a logistic regression analysis, and the following characteristics were found to be predictors: not having had a tertiary education; having a partner (common-law or married); having a lower mean periodontal loss of attachment at baseline; and having a greater number of teeth at baseline. The total number of medications was not associated with coronal caries incidence. As discussed above, there was no analysis by individual medication types in this study. A model of coronal caries incidence was also briefly described for participants aged 65 or more: the only two predictors were marital status and education.

It is noteworthy that the caries incidence rates reported above are comparable to those reported from studies of children and adolescents where, for example, a mean 36-month increment of 2.9 surfaces was reported for 11-15-year-old children in rural Michigan who were drinking non-fluoridated water (Burt *et al,* 1988), and a mean 36-month increment of 1.3 surfaces was reported for a population of Swedish 12-year-olds (Mattiasson-Robertson and Twetman, 1993).

Finally, Fure (1997) recently reported on the five-year incidence of coronal caries in Swedes aged 60 (N = 69), 70 (N = 70) or 80 years (N = 28), but the small numbers involved in that study compromise its utility.

1.6.2.2 Root surface caries incidence

Older people may be considered to be even more at risk than children and adolescents because root surface caries can also contribute to their caries increment, whereas it is extremely uncommon among individuals under 20 years of age (Galan and Lynch, 1993). The reported root surface caries increment among older Iowans of 1.1 surfaces over 36 months (Hand *et al,* 1988a) was less than that group's coronal caries increment for the same period, but its clinical significance is indisputable, in that a second, "later-onset" form of dental caries made a substantial contribution to disease incidence in that group. Moreover, their root surface caries attack rate (expressed as a proportion of susceptible surfaces) was actually greater than that for coronal caries. Considering both types of caries together, the annual increment of any caries was calculated to be 1.44 surfaces per individual in the same population (Hand *et al,* 1988b), equivalent to a 36-month caries increment of approximately 4.3 surfaces. Locker (1996) reported on the three-year incidence of root caries from the Ontario study of people aged 50 and over. Some 27.4 per cent of individuals had one or more root DFS increments, with a mean increment of 0.6 DFS per person, equivalent to a mean annual increment of 0.2 surfaces. Locker modelled root caries incidence using logistic regression, and only age emerged as a predictor

(offering support for the notion that the Canadians' considerably lower increment than that reported from the Iowa study may be at least partly accounted for by the difference in age distribution of the two cohorts). When root DS increment was modelled, the significant predictors were age, the use of a partial denture, and an episodic dental visiting pattern. Neither the number of chronic medical conditions nor the number of prescription medications taken emerged as predictors of either root DFS or DS increment.

Lawrence *et al* (1996) recently reported from the Piedmont study on the five-year incidence of root surface caries among older blacks and whites living in North Carolina. Root caries was described using incidence attack rate (the number of new root DFS in the 5-year period divided by the baseline number of surfaces exposed, and expressed as a percentage; this is a longitudinal analogy to the RCI), net root surface caries increment, and incidence density. The latter was calculated as the number of surfaces developing new root surface carious lesions (either DS or FS) during the 5-year period divided by the total number of surface-months at risk for all participants with one or more exposed root surfaces at baseline or at five-year follow-up. This paper is notable for being the first to use the incidence density approach for root surface caries. Approximately one in three participants had a root DFS increment, and there was no difference between blacks and whites. There was no ethnic difference in attack rates either, with 2.42 and 2.23 surfaces affected per 100 at risk for blacks and whites respectively ($P > 0.05$). The incidence density rate—described in terms of new lesions per 60 surface-months at risk—was higher for blacks (0.26, sd 0.03) than for whites (0.19, sd 0.02), although this difference only just reached statistical significance ($P = 0.047$). There was no report on any observed associations (or otherwise) between root surface caries increment and medication exposure.

These data for coronal and root surface caries suggest that older people are indeed a caries-active population, and that, when their potential for caries increments from both types of caries is taken into account, they may be more at risk of caries than children and adolescents.

1.7 Dry mouth and dental caries in older populations

There are few reports of associations between dental caries (or its sequelae) and either xerostomia or SGH. The work of Papas *et al* (1993) has already been described (and criticised) in Section 1.1.3, and can be discounted as shedding very little light on the dry mouth-caries relationship. As described in Section 1.6.1.1, Drake and Beck (1992) modelled coronal caries prevalence among participants in the Piedmont study, using the presence of any decayed coronal surfaces as the dependent variable in a logistic regression analysis. Low stimulated salivary flow rate emerged as a significant variable. Unstimulated salivary flow rate was not recorded in that study. As the authors pointed out, that was the only study (to date) which has observed an association between salivary flow rate and untreated coronal caries. Regarding the sequelae of dental caries, Caplan and Hunt's report (1996) of a significant association between stimulated salivary flow rate and three-year tooth-loss incidence offers weak support for the role of SGH as a risk factor for dental caries. There have been two reports of investigations of the relationship between salivary flow rate and root surface caries. Billings (1989) reported no statistically significant relationship between root caries prevalence and either stimulated or unstimulated salivary flow rates among adults aged 60 and over. Few details of the methods or results of that particular study were given in that abstract, and a more comprehensive report has not been published subsequently. Beighton *et al* (1991) reported that stimulated salivary flow rate did not emerge from a logistic regression analysis of root surface caries prevalence among routine dental attenders aged 55 or more. The utility of that finding is compromised by the limitations of the study design and the sampling frame, in that it was a cross-sectional study, and those attending regularly may have been doing so because of their propensity for developing root surface caries in the first place.

1.8 Medication and dental caries in older populations

Failure to demonstrate an association between certain medications and dental caries in older people to date reflects first, the methodological shortcomings of published studies, and second, that any effect which may exist is not a strong one. Nevertheless, there is *intuitive* support for such a relationship, based upon its having been demonstrated with animal models: rats who underwent long-term dosage with the antihypertensive drug propranolol had increased susceptibility to caries, as well as reductions in salivary protein concentration (O'Connell *et al*, 1993). The stimulated saliva flow rate was not affected. In humans, such an association is most likely to be demonstrated among dentate older people, a highly medicated group who, because of the retention of their teeth, remain at risk from coronal and root surface caries. Further intuitive support comes from the widespread belief among dentists that certain medication types are associated with dental caries. However, there is little evidence at this stage to even support the notion of medication being a risk indicator for dental caries, let alone a risk factor for the disease, and it is possible to argue that dentists' current conception of the alleged relationship are tantamount to folklore. There is therefore a need to carefully examine the relationship in a carefully-conducted longitudinal study. There is also a need to compare the utility of the different approaches which are available for investigating different medications' effect-modification of the caries process.

Medications which have been most commonly implicated in the relationship are antihypertensives, anticholinergics, antidepressants, antipsychotics and antihistamines (Ettinger, 1981; Johnson *et al*, 1984; Sreebny and Schwartz, 1986; Grad *et al,* 1985; Handelman *et al,* 1986). Medications which have also been included, but less consistently, include antiparkinsonian drugs (Ettinger, 1981; Sreebny and Schwartz, 1986; Edgar, 1992), diuretics (Ettinger, 1981; Sreebny and Schwartz, 1986), anorectics (Sreebny and Schwartz, 1986; Edgar, 1992) and psychotherapeutic agents such as sedatives and hypnotics (Sreebny and Schwartz, 1986). A report from a prevalence study that diuretics appeared to increase the xerogenicity of tricyclic antidepressants (Johnson *et al*, 1984)

highlights the possibility that certain medications may exert their effects in combination with more obviously xerogenic drugs.

Another factor to consider with older individuals is the potential for the side-effects of medications to be exaggerated as a result of drug clearance rates reducing with age (Terezhalmy 1989, Persson *et al,* 1991). This means that, for a given dose, a drug and its active metabolites can persist at pharmacologically active levels for longer than normal, and so a drug which may not be particularly xerogenic in a younger person may be so in an older person.

The proposed model for the relationship (Figure 1.3) characterises medication as a modifier rather than a determinant of the occurrence of coronal and root surface caries. That is, it is a primary causal agent which acts to modify the effect of the causal factors which determine each disease. Firstly, it may act to reduce salivary flow to the extent that the normal salivary buffering mechanisms (bicarbonate, phosphate and proteins) are not present in sufficient volume to deal with the acid challenge and maintain the oral cavity's balance towards remineralisation; the end result may be a positive caries increment. Secondly, there may be no detectable change in whole salivary flow, but the medication may act to produce the symptom of xerostomia by changing saliva quality, the perception of salivary flow, or the mucosa itself (for example, by reducing minor salivary gland flow). This in turn may lead the individual to seek symptomatic relief by adopting dentition-threatening practices such as the "dryness-related behaviour" (eg. chewing hard candies or mints) reported by 19 per cent of a sample of older Florida people (Gilbert *et al,* 1993). Such practices tend to promote demineralisation, and therefore an increase in caries incidence would be expected among those individuals. The posited association between xerogenic medication and caries may be mediated by either or both of these two separate pathways.

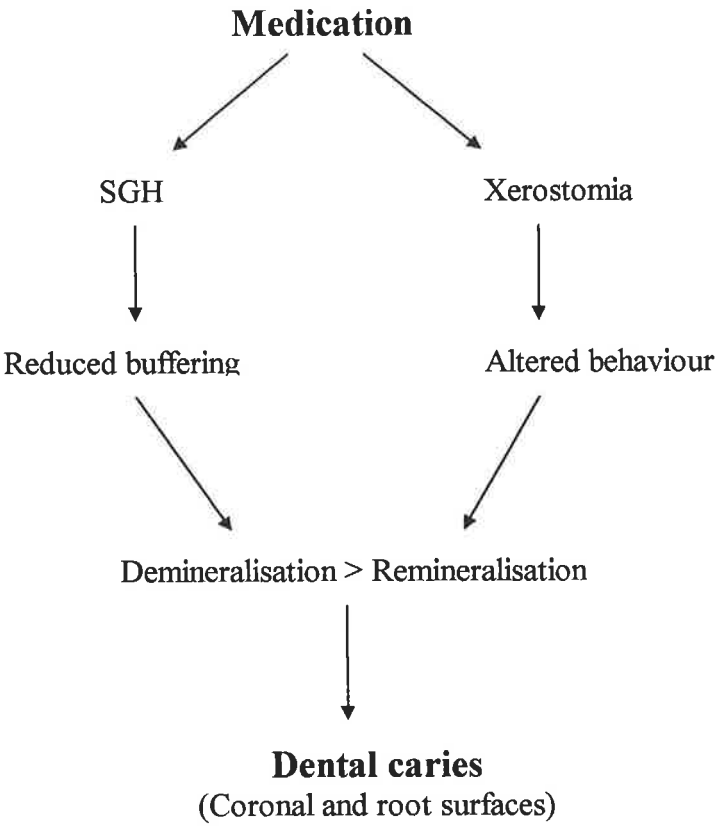


Figure 1.3: Posited relationship between xerogenic medication, SGH, xerostomia and dental caries

1.9 Study hypotheses

The relationship between certain medications and dental caries in older people needs to be carefully explored so as to maximise the chances of uncovering any association which might exist.

The research hypotheses are:

(1) that long-term exposure to certain categories of medication will be associated with an increase in five-year tooth-loss incidence;

(2) that long-term exposure to certain categories of medication will be associated with an increase in five-year coronal caries incidence and increment; and

(3) that long-term exposure to certain categories of medication will be associated with an increase in five-year root surface caries incidence and increment among community-dwelling older South Australians.

The conceptual model (Figure 1.2) of Beck *et al* (1987) will be used as a framework for the testing of these hypotheses. Exposure to xerogenic medications can be categorised in that model as either (i) a "Physical/Medical" factor which acts to directly reduce salivary flow rate (and consequently the buffering of the plaque-acid challenge) or (ii) a "Behavioural factor" which acts to increase the severity of the symptoms of dry mouth and increasing the intake frequency of cariogenic food or drink as a consequence.

2. Method

2.1 The general approach of the investigation

The relationship between certain medications and dental caries in elderly people must be carefully explored so as to maximise the chances of uncovering any association which might exist. It was intended that the current study should: (1) examine more than one data set, with at least one of them derived from a longitudinal study design; (2) examine the occurrence of both xerostomia and hyposalivation; (3) take into account the length of time that individuals have been exposed to particular medications; and (4) use dental examination data which have been collected in such a way that surface-level caries increments are able to be compared among participants in different medication-exposure categories.

Data from three studies were used. The first was the Australian Longitudinal Study of Ageing (ALSA), which is a epidemiological investigation of ageing which is being conducted by the Centre for Ageing Studies, Flinders University of South Australia, and for which baseline data collection commenced in 1993. The second study was the South Australian Dental Longitudinal Study (SADLS), a specifically dental epidemiological study which is being conducted by the Department of Dentistry in the University of Adelaide. SADLS is mainly funded by the National Health and Medical Research Council of Australia. The third study from which data were used was the Xerostomia Inventory Validation Study, a small longitudinal study funded by the Health Research Council of New Zealand. It was conducted in 1997 and 1998.

Three complementary approaches were used in order to test the study hypotheses and maximise the likelihood of detecting a relationship.

(1) Baseline oral health data were analysed from an existing cohort of persons aged 60+ years who were randomly selected in 1991/92 from the non-institutionalised elderly

populations of Adelaide and Mt. Gambier. The baseline data collection was undertaken as the first stage of the South Australian Dental Longitudinal Study (SADLS). Baseline medication data were coded and analysed using a comprehensive system developed by this candidate as part of the current investigation (Thomson, 1997), and associations between medication use and baseline (coronal and root-surface) caries prevalence were examined.

(2) Cross-sectional data from the baseline data collection phase of the ALSA study were examined in order to confirm the medication-use patterns observed in the SADLS data-set, and to provide confirmatory data on the reported duration of use of particular medication subcategories.

(3) Five-year caries incidence and increment data were examined and related to changes in medication prevalence over the five-year duration of the SADLS study. These were collected in late 1996 and early 1997 from the same group, together with updated medication information, in which each medication's dose and frequency of administration was recorded. This enabled examination of the relationship between specific medications and five-year dental caries incidence in the SADLS sample.

2.2 Sampling procedures and data collection

2.2.1 The Australian Longitudinal Study of Ageing (ALSA)

The target population was all persons aged 70+ who were living in the Adelaide Statistical Division. The sampling frame was the State Electoral Database, which listed individuals by name, gender, date of birth, and postal and residential address. With the assistance of the Australian Bureau of Statistics (ABS), a random sample of 3,263 people was selected and stratified by age (into 70-74, 75-79, 80-84, and 85+ age groups) and gender. In addition to the specified person (whose sequence number ended in one), that person's spouse was also included and assigned a sequence number ending in 2, and any other household member aged 70+ was also included, and assigned a sequence number ending in 3. Details of sample numbers are presented in Table 2.1.

Table 2.1: Number of persons selected in the ALSA sample[a]

Age groups (years)	No. in population	No. in sample selected (per cent of population)
70-74 years		
Males	16,601	600 (3.6)
Females	20,968	345 (1.6)
75-79 years		
Males	11,392	585 (5.1)
Females	16,445	345 (2.1)
80-84 years		
Males	6,426	600 (9.3)
Females	11,383	360 (3.2)
85+ years		
Males	3,600	795 (22.1)
Females	8,554	705 (8.2)
Total	95,369	4,335 (4.5)

[a]Source: ALSA manual, Centre for Ageing Studies, 1995.

Baseline data were collected using the BLAISE system for computer-assisted interviewing, and 2087 face-to-face interviews were conducted, with an average interview time of 132 minutes. The 2087 successful interviews represent a response rate of 53.4 per cent (Table 2.2). The data used in the current analyses were obtained from the baseline interviews.

Table 2.2: ALSA sample response to PALs and interview approach[a]

Category	No. of respondents	Per cent "in scope"
Out of scope	279 (3,905 in scope)	(6.7% of sample out of scope)
Unable to contact	198	5.1
Unable to interview	652	16.7
Refused	968	24.8
Interviewed	2,087	53.4
Total	4,184[b]	100.0

[a]Source: ALSA manual, Centre for Ageing Studies, 1995.
[b]Includes selected respondents who received a PAL (Primary Approach Letter) and eligible members of the household - ie those found through the interview approach

Of the 2087 interviews which were conducted: 2,016 (96.6%) participants fully responded themselves; 18 (0.9%) fully responded through an interpreter; 11 (0.5%) were partly interviewed and then refused to proceed; 24 (1.1%) were incomplete; 11 (0.5%) were proxy interviews which were incomplete; and, 7 (0.3%) fully responded in a foreign language.

The age and gender of those who were interviewed are presented in Table 2.3.

Table 2.3: Interviews in ALSA by gender and age group[a]

Age groups (years)	Male	Female	All
65-69[b]	11 (0.5%)	114 (5.5%)	125 (6.0%)
70-74	279 (13.4%)	288 (13.8%)	567 (27.2%)
75-79	280 (13.4%)	241 (11.5%)	521 (25.0%)
80-84	238 (11.4%)	192 (9.2%)	430 (20.6%)
85+	246 (11.8%)	198 (9.5%)	444 (21.3%)
Total	1,054 (50.5%)	1,033 (49.5%)	2,087 (100.0%)

[a]Source: ALSA manual, Centre for Ageing Studies, 1995.
[b]Represents spouses only.

Concerning the respondent type, 1,477 (70.8%) of those interviewed were the specified person, 597 (28.6%) were the spouse of the specified person, and 13 (0.6%) were other household members aged 70+.

Medication recording in ALSA was done at the time of the face-to-face interview. Participants were asked to show all medications (prescribed and self-prescribed) which they had taken in the previous fortnight, and the details of each were entered directly into the electronic database. The interviewer's script was as follows:

> *The next few questions are about medicines. We are interested in any medicines prescribed by a doctor that you have taken or were supposed to take in the last two weeks. We are also interested in any medicines not prescribed by a doctor such as aspirin, headache pills, laxatives, cold medicine, cough medicine, etc. Could you please show me the medicines that you take.*

Interviewers were instructed to check the container labels. The specific information recorded for each medication is presented in Table 2.4. The coding of these was subsequently achieved electronically, using the system developed by the author (Thomson, 1997) and the RECODE procedure in SPSS.

Table 2.4: Variables entered for each medication in ALSA at baseline

Variable	Units entered	Format
Drug name	N/A	Alphanumeric
Drug code	N/A (coded subsequently)	Numeric
Container seen?	1=yes, 2=no	
Strength	As recorded on label	Alphanumeric
Taken in last 2 weeks?	1=yes, 2=no	Numeric
Taken yesterday?	1=yes, 2=no	Numeric
Taken for how many days in last 2 weeks?	Number of days	Numeric
Usual number taken in a day?	Number of units taken	Numeric
What do you take this for?	N/A	Alphanumeric
How long have you been taking it?	1=weeks, 2=months, 3=years	Numeric
Prescribed by a doctor?	1=yes, 2=no	Numeric

2.1.2 The South Australian Dental Longitudinal Study (SADLS)

This study was conducted in two South Australian cities: Adelaide (the State capital) and Mt. Gambier (a rural city in the State's south east).

2.1.2.1 Baseline recruitment of sample

In 1991, a stratified random sample of non-institutionalized persons aged 60+ years was selected from the State Electoral Database, which is a compulsory register for non-

institutionalised Australian citizens (aged 18 or more) which includes their name, age and residential address. The sampling method defined 24 strata; 18 in the Adelaide Statistical Division, and six within the Mt Gambier City and District Council. The former comprised three age groups (60-64, 65-74 and 75+ years), two genders and three locality groups (which were based on their distance from one of 32 public and school dental clinics which were used for dental examinations), while the latter was comprised of the same three age groups and two genders. For each stratum, a different probability of selection was used to draw a simple random sample of participants, and those who were residents in nursing homes or hospitals (but not hostels for the aged) were excluded, so that the sample was a non-institutionalised one. The purpose of the stratification was to select approximately equivalent numbers of people in six groups defined by sex and age. In addition, dentate people (those who had one or more natural teeth) were oversampled, by excluding a percentage of edentulous people which ranged from 100 per cent in Mt Gambier to 50 per cent among the Adelaide residents aged 60-64. Thus, only dentate persons were sampled in Mt Gambier. The sampling scheme was designed to allow sufficient numbers and groups to detect hypothesised group differences in prevalence of 30 per cent and 40 per cent with a type I error of 5 per cent; a type II error of 20 per cent; and non-equivalent group sizes of up to 40 per cent. A further correction factor of 1.1 was used to increase the sample size and account for the increased variance associated with the clustered sampling design (Slade and Spencer, 1994).

The sample size requirements for each stage and each group in the study are discussed in greater detail elsewhere (Slade and Spencer, 1990), but, in brief, calculation of the number of participants to be drawn from the sampling frame involved reconciling the sample requirements with the expected rates of recruitment, participation and retention. These calculations drew on experience from the pilot studies where the same sampling frame yielded 89 per cent of participants who were alive and who could be located. An overall participation rate in the baseline interviews of 74 per cent was predicted (varying by age group), and participation in the examinations was estimated at 64 per cent for dentate individuals, and 56 per cent for those who were edentulous. Attrition rates due to

migration and mortality were based on data from the Australian Bureau of Statistics and compounded annually. Average participation rates of 90 per cent (interviews) and 75 per cent (examinations) were expected at two and five years. The attrition rates closely resembled those obtained in a similar study conducted in Iowa (Hand *et al*, 1988). The expected number of participants at each stage is summarised in Table 2.5.

Table 2.5: Projected participation and retention rates over the duration of SADLS[a]

	Number of participants in each age group			
Stage of study	60-64	65-74	75+	Total
Baseline				
Interviews	539	717	748	2004
Examinations (all)	370	454	421	1245
Examinations (dentate only)	294	327	286	907
Year two				
Interviews	453	579	496	1528
Examinations (all)	268	293	200	761
Examinations (dentate only)	219	219	146	584
Year five				
Interviews	373	440	278	1091
Examinations (all)	190	178	81	449
Examinations (dentate only)	159	138	63	360

[a]Source: Slade and Spencer, 1990

This level of recruitment was intended to ensure a sufficient number (360) of dentate participants at five years to examine the most critical differences, which were in rates of periodontal attachment loss. The expected retention rate was therefore estimated to be sufficient for examining the incidence of dental caries. It should, however, be noted that

the question of examining medication subgroups did not arise at the planning stage of SADLS; consequently, there were problems with insufficient numbers of participants at some levels of the investigation, particularly for important but not highly prevalent medication subcategories such as the antidepressants. This was particularly marked when the analysis identified participants who were taking a particular medication at baseline and at five years (the *Continuous users*).

Sampled people were notified by letter, and a trained interviewer visited each person's address to advise about the study and encourage participation. Those who agreed to participate then took part in a 72-item face-to-face household interview which included questions about use of prescription medications. People were asked "Do you have any prescribed medicines that you have taken or were supposed to take regularly in the last two weeks?". Those who reported in the affirmative were asked to provide the name of each one, and the name of each medication was written in full on the data capture form. Other information (for example, duration, dosage, source of prescription) on each medication was not recorded. When necessary, interviewers asked to see the labels of the medicines to confirm the names, but no additional effort was made to verify the self-reported medication use.

A full dental examination was undertaken at baseline, and the procedures for this are described fully below. Xerostomia and hyposalivation were not measured.

2.1.2.2 The five-year data collection

Over the five years which had elapsed since the baseline data collection, maintenance of the panel had been maximised by using a number of strategies:

1. the collection of contact details on third parties who would be likely to know of a participant's circumstances or new address were he or she to be uncontactable in the usual manner;

2. a birthday card was sent to each participant every year, and this enabled either (1) notification of the study when a panel member had died, moved or decided to discontinue participation, or (2) forwarding of the card where someone had changed address; and,
3. the two-year data collection served to increase awareness of the longitudinal nature of the study, so that the commitment of panel members was heightened.

Participants were contacted by telephone as close as possible to the fifth anniversary of their baseline interview and examination. The five-year interview was conducted by telephone from the AIHW Dental Statistics and Research Unit, and an appointment was made at that time for a subsequent dental examination. Where possible, the dental examination was undertaken in a public dental clinic using a dental light, but a small number of participants had to be examined in their homes because of problems with mobility. In addition, postal questionnaires were sent out for the Oral Health Impact Profile (Slade and Spencer, 1994) and Xerostomia Inventory (Section 2.1.2.2.2), with a request for these to be either returned by post (using a stamped, addressed envelope) or handed to the dental examiner at the time of the dental appointment.

2.1.2.2.1 Medication recording and analysis

Medication recording and analysis were conducted using the MedCap system (Thomson, 1997; Appendix 1). It assigned five-digit codes to individual medications, and these were entered into a data-base. In the subsequent analysis, the COUNT procedure in SPSS was used to arrive at the number of different medication types for each individual. These were then dichotomised as present (code 1) or absent (code 0) in order to facilitate analysis by specific medication categories.

For the initial description of exposure to each major class of medication at five years, individuals were assigned to one of four exposure groups according to the classification

used by Psaty *et al* (1995): *Continuous users*, taken both at baseline and 5-year follow-up; *Starters*, taken at follow-up but not at baseline; *Stoppers*, taken at baseline but not at follow-up; and *Non-users*, taken at neither data collection period. This enabled examination of the temporal patterns in medication use over the five years of the study.

For the SADLS baseline data-set, information on medications which each participant had taken in the two weeks prior to interview had been recorded in longhand on the interview form. Coding of that information was carried out subsequently, and the code for each medication was key-punched by WMT. This was a very laborious way of doing the task, but it was the first use of the system, and it was essential to ensure: (1) accuracy in coding; and (2) that any design flaws in the system be identified and eliminated. This method of coding and data entry also required that the operator had some knowledge of pharmacology and therapeutics in order to decipher some of the medication names which had been recorded in the field by interviewers. The process of "hand-coding" the preparations in this way revealed a number of deficiencies in the original MedCap listings which were then able to be addressed prior to its use in the ALSA study (below) and the SADLS five-year study.

For the ALSA study, coding was less laborious, as the way in which the information had been collected allowed a greater degree of automation. Medication information in that study had been entered in full into an electronic database, and the conversion of the medication names into five-digit codes was accomplished using the RECODE procedure in SPSS. This enabled the bulk of the coding to be done very quickly and efficiently (certainly much more so than with the SADLS baseline data), and any medications which were misspelt (or which were still not on the list at that stage) were subsequently recoded manually.

For the SADLS five-year data collection, the medication details were recorded in full on dedicated forms (Appendix 2), from which the preparations were subsequently coded and entered into an electronic data-base. It had been intended that this phase of the study

would employ direct, electronic data entry at the time of the examination, but the RAM requirement of the dental status data-base was such that it was not possible, and manual recording was used instead. The details entered in the data-base for each individual medication are presented in Table 2.6.

Table 2.6: Variables entered for each medication in SADLS at 5 years

Variable	Units entered	Format
Drug code	N/A	Numeric
Source of information	1=container, 2=memory, 3 = follow-up	Numeric
Prescriber	1=doctor/dentist, 2=self, 8=don't know	Numeric
Type	1=prescription, 2=over-the-counter	Numeric
Name on container	1=participant's name, 2=other name; 8=don't know/other name	Numeric
Date on container	N/A	dd-mm-yy
Strength	milligram equivalents	Numeric
Frequency of dose	daily, bid, tid, qid, weekly, /fortnight, other	Alphanumeric

It was considered that asking participants to estimate the length of time for which they had been taking each of their medications would have been difficult and taken up too much time of what was already a very full clinical appointment. Copying medication details from container labels was laborious enough, but to then ask the panel member about how long he/she had been taking each medication would have been extremely time-consuming, and the validity of the data may have been affected by recall problems. Bearing in mind that the ALSA baseline data-set already had adequate information on duration of exposure for the most prevalent therapeutic categories, it was decided to forego the collection of these data for the SADLS five-year phase. Further justification for this omission came from the intention to classify participants according to their exposure status at baseline and five years according to Psaty *et al*, 1995.

Information on the frequency and size of dose was also collected for each medication, together with whether it had been self-prescribed, or prescribed by a medical/dental practitioner.

Together with the xerostomia questions and sialometry data, the collection of dosage and length-of-medication information was designed to enable very specific exploration of any xerogenic and caries-incidence effects of the different medications.

2.1.2.2.2 Xerostomia and hyposalivation

(i) Measurement of xerostomia

Xerostomia was measured in the five-year SADLS data collection using two methods. First, responses to a standard single xerostomia question ("How often does your mouth feel dry?" Response options: 'Never', 'Occasionally', 'Frequently', 'Always') were collected during the telephone interview stage of the study. The latter item—which has been previously used in an epidemiological study of older people (Thomson *et al*, 1993)—was intended to serve as the 'gold standard' against the second method could be compared for the assessment of its concurrent validity. Second, the Xerostomia Inventory (XI) was developed to measure the severity of xerostomia symptoms.

The development of the XI involved a combination of qualitative and quantitative techniques. A literature search revealed a number of items which had been developed and used by other workers using single-item inventory approaches (Table 1.2), and this enabled a framework to be developed for semi-structured interviews which were undertaken with a convenience sample of four diagnosed long-term sufferers of xerostomia who were patients in the high caries clinic at the Adelaide Dental Hospital. It is not known how representative those individuals were of xerostomia sufferers in general, but they identified as being typical of patients seen in that clinic. Responses were recorded

in longhand, and content analysis was used to identify dominant themes which were then either developed into new XI items—using the interviewees' own words where possible—or used to confirm and/or modify those which had been obtained from the literature. This process resulted in 18 separate items, and ensured: (1) that they were grounded in the experiences of xerostomia sufferers; (2) that those which were used reflected many manifestations of the xerostomia experience; and, (3) that their most appropriate wording was determined.

The initial 18 items were then assembled into an inventory format for testing in the SADLS five-year data collection phase. The items used in the initial Xerostomia Inventory were:

- I sip liquids to aid in swallowing food
- My mouth feels dry when eating a meal
- I get up at night to drink
- I have difficulty in eating dry foods
- My mouth feels dry
- I suck sweets or cough lollies to relieve dry mouth
- I have difficulties swallowing certain foods
- I have a burning sensation in my gums
- I have a burning sensation in my tongue
- My gums itch
- My tongue itches
- The skin of my face feels dry
- My eyes feel dry
- My lips feel dry
- The inside of my nose feels dry

The response options for each item were *Never* (scoring 1), *Hardly ever* (2), *Occasionally* (3), *Fairly often* (4), and *Very often* (5). These were identical to the response options used

in the Oral Health Impact Profile (Slade and Spencer, 1994), which the SADLS participants had already encountered at baseline and two years. A large font was used for ease of reading by the study participants.

(ii) Further testing of the Xerostomia Inventory (XI) - the validation study

In order to examine the concurrent and construct validity and temporal stability of the XI, a smaller study was conducted in New Zealand (and funded by the Health Research Council of New Zealand). Ethical approval for the study was granted by the ethics committees of what were then the Southern, Central, Midland and Northern Regional Health Authorities. Two groups were recruited who would, in theory, have dissimilar dry-mouth symptom trajectories over a six-month period:

1. the *Onset* group comprised individuals aged 40 or more and who were about to commence radiotherapy for head/neck cancer; and
2. the *Normal* group comprised older individuals who would not be expected to undergo substantial change in their perceived dry mouth severity (or lack thereof) over the study period.

It was hypothesised that scores would increase greatly in the *Onset* group and remain the same in the *Normal* group. The *Onset* group was recruited first, and over an 18-month period, by the staff of Auckland, Dunedin, Christchurch, Wellington, Palmerston North and Waikato hospitals. Recruitment of the *Normal* group commenced once two-thirds of the *Onset* group had been recruited; this was so that the sex mix of the two groups would be similar. The former was recruited from the membership list of the Otago Medical Research Foundation Auxiliary, who are volunteers (mostly older people) who take a keen interest in the research work which is conducted in the city. Many are retired academics. Different sampling proportions were used for males and females in order to closely match the sex distribution of the *Onset* group. For males, a one-in-two random sample was

used, and for females, a one-in-three random sample was employed. This ensured a male-female ratio of 2:1, which was similar to that of the *Onset* group.

A mail survey approach was used. Each participant completed the XI form (as well as the standard question) at baseline, two, four and six months. No measurement of saliva flow was undertaken. Data were entered into a Microsoft Access database and analysed using SPSS.

(iii) Measurement of saliva flow in SADLS

Hyposalivation was assessed by using sialometry which took place prior to the oral examination. The spit method (Navazesh and Christensen, 1982) was used, whereby each participant was asked to (i) refrain from food, beverages and smoking for the 60 minutes prior to collection; (ii) rinse his/her mouth thoroughly and then wait for 3 minutes prior to saliva collection; (iii) swallow, and then told to actively spit saliva into a pre-weighed plastic collection tube over a 4-minute period. At the end of that time, the participant was asked to expectorate any remaining saliva into the tube. the tube was then sealed tightly and placed into cool storage until it could be weighed in the Oral Pathology laboratory of the University of Adelaide. The new weight was recorded both on the tube itself and in a notebook from which the electronic data-base was compiled. Unstimulated saliva flow (in ml/min) was calculated as the weight of saliva collected (assuming 1g = 1ml) divided by the collection time. Where the time of collection differed from 4 minutes, this was taken into account in the calculation of salivary flow rate by altering the denominator accordingly.

2.1.2.2.3 The dental examinations

As previously mentioned, the dental examinations were conducted in a fully-equipped public dental clinic wherever possible. At baseline, a two-stage process was used for data entry and recording, whereby the data were initially entered into Optical Mark Reader (OMR) forms and then subsequently scanned to build an ASCII data-set. At five years, data entry was effected directly into an electronic data-base on a portable laptop computer. The data-base had been designed specifically for the study by Mrs Judith Stewart, of the AIHW Dental Statistics and Research Unit at the University of Adelaide. The baseline and five-year examination criteria were identical, except that different codes were used in the data-sets. In the description which follows, the codes given are those which were used at the five-year examination; the baseline code is presented in square brackets (for example '[3]') immediately after the five-year code.

(i) Missing/replacement/present teeth

The examiner first passed through the upper arch (from 18-28) and then the lower arch (from 38-48) marking tooth status as follows:

Missing **M [1]** was coded for teeth which had been extracted, as well as those which may not have erupted. There was no distinction according to presumed reason for extraction.

Replaced with removable denture **Mr [2]** was coded when the space of a missing tooth had been replaced by a removable denture (full or partial) which was worn on a daily basis at least.

Replaced with fixed bridge **Mf [3]** was coded when the space of a missing tooth had been replaced by a fixed bridge.

No Space **NS [4]** was coded when there was a lack of space (that is, less than one half-unit) due to drifting of adjacent teeth which had precluded any prosthodontic replacement of the missing unit.

Where there had been no replacement but sufficient space existed for prosthodontic replacement, the tooth was scored as **Missing [1]**.

Crown coverage **C [6]** was scored when there was full coverage with a cast crown, regardless of the reason for placement.

Root Decayed **RD [7]** was scored when one quarter or less of the crown remained and had been affected by caries.

Root Sound **RS [8]** was scored when one quarter or less of the crown remained, but was sound.

Sound **S [5]** was scored when all coronal surfaces were sound and unrestored. This was entered only after assessing all surfaces of the tooth in question.

Present **P [0]** was scored for a tooth that was present but was not **C**rowned, **RD**, **RS**, or **S**ound.

At five years, for any tooth scored as **M**, **Mr**, **Mf**, or **NS**, the computer would:

(1) skip the rest of the caries assessment for this tooth and go on to the next tooth status; and
(2) automatically mark that tooth as *Missing* **M** for the subsequent periodontal assessment.

Where teeth had been scored as **RD** or **RS**, the crown and root surfaces assessment was skipped, and the examiner moved on to the tooth treatment and occlusal attrition assessment, if applicable.

Where teeth had been scored **C**, the crown surface assessment was omitted, and the root surface & tooth treatment assessments were completed.

Thus, crown surface assessment was only done for those teeth which had been coded as **P**, and not for those marked as **M**, **Mr**, **Mf**, **NS**, **C**, **RD** or **RS**. Similarly, the root surface assessment was only done for those teeth whose status was entered as **P**, **S** or **C**, and not for those scored as **M**, **Mr**, **Mf**, **NS**, **RD** or **RS**)

The sequence was as follows: the examiner passed through the upper arch (from 18-28) and then the lower arch (from 38-48) scoring: (1) crown surfaces; (2) root surfaces; (3) tooth treatment; and (4) occlusal attrition for each required tooth before moving on to the next tooth.

(ii) Assessment of Coronal Surfaces

Data entry used four fields for anterior teeth (13-23; 33-43) and five fields for posterior teeth (14-18, 24-28, 34-38, 44-48). For each tooth, the coding started at the occlusal field (for posterior teeth) and then moved to the mesial (coding started at the mesial for anterior teeth), buccal, distal and lingual fields

Sound **S [5]** was scored when the surface is sound and unrestored.

Filled **F [1]** was scored when the surface contained one or more permanent restorations, regardless of the reason for placement. An exception was made for full crown coverage, which was marked as **C [6]** above. No other coronal surfaces were marked for teeth with

full coverage. Crowns of less than full coverage were scored surface by surface, as for other teeth.

In order to be scored as *Filled*, restorations had to be free of:

(i) recurrent current caries (*Recurrent* **R [4]**); and
(ii) non-carious defects (*Filled unsatisfactory* **Fu [2]**).

The *Filled* (**F [1]**) category included restorations which had the following acceptable deficiencies:

(a) surface which was irregular, rough or discoloured;
(b) abnormal aesthetic appearance but not displeasing;
(c) undercontouring, or faulty occlusal contact;
(d) mal-contouring of embrasures which could be corrected;
(e) marginal discrepancy which could be penetrated by a probe;
(f) overhang which could be corrected; or
(g) joined or repaired restorations.

Filled unsatisfactory (**Fu [2]**) was marked when a filled surface featured one or more of the following unacceptable defects which would not have been able to be corrected:

(a) surface which was flaking or fractured;
(b) surface which was aesthetically unacceptable;
(c) dentine or base exposed;
(d) missing or fractured and mobile restoration;
(e) traumatic occlusion causing pain or damage to tissues;
(f) malcontouring of embrasures;
(g) gross marginal discrepancy with potential for recurrent caries;

(h) overhang causing tissue damage; or

(i) temporary fillings.

Decayed (**D [3]**) coronal surfaces were coded using the following criteria (based on Radike, 1968):

Frank lesions were coded as **D [3]** when cavitation and softening of the cavity floor were present. Cavitation was defined as a discontinuity of the enamel surface caused by the loss of tooth substance. It had to be distinguished from fractures, erosion and abrasion.

Lesions not showing frank cavitation could still be coded as decayed under the following circumstances:

Pits and fissures

Where possible, diagnosis was achieved visually, rather than by tactile means. This minimised the probing of teeth.

1. The area was coded as **D [3]** when the explorer "caught", or resisted removal after insertion, into a pit or fissure with moderate pressure, and when one or more of the following was present:

(a) softness at the base of the area;

(b) opacity indicating adjacent undermining or demineralization; or

(c) softened enamel that could be scraped away with the explorer.

2. The area was coded as **D [3]** if there was loss of the normal translucency of enamel around a pit or fissure, even if the explorer did not “catch” or penetrate the fissure.

Smooth surfaces (buccal and lingual)

1. The area was coded as **D [3]** if the surface was etched or there was a white spot, and if dentine seemed to be involved, as indicated by:

(a) penetration with an explorer; or
(b) scraping away with an explorer.

2. If there was no softness, the area was considered to be sound.

Proximal surfaces

For areas exposed to direct visual or tactile examination, the criteria for buccal and lingual smooth surfaces were used. If this was not possible, three diagnostic techniques were used:

1. *visual examination*: if the marginal ridge showed darkening as evidence of undermined enamel, the proximal surface was considered to be carious;

2. *tactile examination*: any discontinuity of the enamel able to be entered by an explorer was considered to be carious if it also showed other evidence of decay such as softness, shadow by illumination or loss of translucency; and,

3. *transillumination* (for anterior teeth mainly): a loss of translucency producing a characteristic shadow in a calculus-free and stain-free proximal surface was considered to be adequate evidence of caries.

Additional notes:

Stain and pigmentation were not regarded as evidence of caries, since they occur in sound teeth.

Erosion, abrasion, hypoplasia, attrition, fractures, mottled enamel, and enamel opacities on exposed hard surfaces were not classified as carious.

Recurrent (**R [4]**) caries was marked when a surface had caries which was contiguous with a restoration. The criteria above for each of the tooth surfaces were applied when determining the existence of recurrent caries.

(iii) Assessment of root surfaces

Four surfaces were scored, starting at the mesial surface and then moving on to the buccal, distal and lingual surfaces.

Decayed (**D [3]**) surfaces were marked when there was a discrete, well-defined or discoloured cavitation on the root surface and softness into which the explorer entered easily.

Filled (**F [1]**), *Filled Unsatisfactory* (**Fu [2]**) and *Recurrent caries* (**R [4]**) were recorded, if present, using the criteria described above for coronal surfaces.

Sound exposed roots (**S [5]**) were marked where there was gingival recession (that is, the root surface was visible) but the exposed root surface was sound (neither filled nor decayed).

(iv) Additional considerations during the dental examination

All teeth, including wisdom teeth, were assessed. When any part of a crown projected through the gum, the tooth was considered to have erupted. In the case of supernumerary teeth, only the tooth which is regarded as the "legitimate" one was scored.

If less than one quarter of the crown remained, it was coded as a root fragment.

Surfaces which were not visible and which could not be probed were regarded as sound.

The natural, coronal landmarks were used to define surfaces when a tooth was rotated, rather than the "new" orientation which had been adopted.

Calculus was not removed for the purpose of the examination.

The order of examination for surfaces was as follows: occlusal (if present), mesial, buccal, distal and lingual.

Incisal edges were not considered as separate surfaces. If a lesion was confined solely to an incisal edge, the nearest surface was coded.

If both the coronal and root surfaces were affected by caries or a restoration, it was necessary to determine the lesion's origin. If more than half of the lesion was above the CEJ, it was regarded only as a coronal lesion; if more than half of the lesion was below the CEJ, it was regarded only as a root surface lesion.

For scoring multiple surfaces on crowns or roots, the "one third rule" was used for restorations or carious lesions which were continuous over one or more of the mesial, buccal, distal or lingual surfaces. The restoration or lesion had to extend at least one third of the circumferential distance across the surface. If a restoration or lesion extended less

than one third of the circumference around both surfaces, the examiner selected the surface which had the majority of that circumferential distance. For restorations or lesions which extended for more than one-third of a surface beyond the occlusal surface (ie over the marginal ridge), the other surface(s) was always included.

2.1.2.3 Data analysis

For ALSA, the analysis took two general approaches. First, the prevalence of the various medication types at baseline was computed, and then the duration of taking each medication type was calculated, using a syntax file of the form presented in Appendix 3.

The SADLS analysis took two general forms: the first approach examined baseline associations between medications and caries prevalence; and the second examined (1) associations between medications and dry mouth, and (2) associations between medications and five-year caries incidence and increment.

The baseline analysis began with the computation of univariate statistics describing the prevalence of dental caries and medication usage. Bivariate analysis elucidated potential risk indicators by examining associations between caries, background characteristics and medication variables. Finally, multivariate analysis was used to verify the status of key variables as risk indicators for coronal and root surface caries prevalence.

Classification and Regression Tree analysis (CART) was used to explore the associations of medications and the occurrence of dry mouth, using the SPSS program Answer Tree (Answer Tree Version 1.0; SPSS Inc., 1998). The intention of this preliminary analysis was to identify potential independent variables (medications) which were then entered into conventional predictive multivariate models for the dependent variables. Only medications were used as predictors in that procedure, in order to fully elucidate their relationships with the dependent variable.

For the five-year data, the analysis first produced statistics describing the prevalence and severity of caries at five years. Along with the conventional caries descriptive data items, an "attack rate" was computed for coronal caries. This is the equivalent of the Root Caries Index (Katz, 1980), expressed as the percentage of coronal surfaces which were observed to be decayed or filled at five years. In the second stage of the five-year caries analysis, univariate statistics describing incidence rates and attack rates of coronal and root surface caries (next paragraph), after which bivariate analysis focused on incidence ratios (relative risk) for those same conditions among cohort sub-groups. Teeth which had been extracted or crowned since the baseline examination were omitted from the analysis of caries increment, as it was considered that any bias arising from this would be considerably less than that which would arise from assigning them an arbitrary number of surfaces in the increment.

Dental caries incidence and increment were computed using a surface-by-surface approach which compared caries status at baseline and at five years for each surface. That is, pairs of observations were created for each surface, with the first observation being its baseline status, and the second, its status at the five-year follow-up examination. The "DePaola matrix" (DePaola, 1990) which was employed is presented in Table 2.7. It shows the important decisions which were made at the analysis stage.

Table 2.7: Conventions used to define events ("De Paola matrix") for caries increment computations

		Number of events/No. of years at risk				
		Follow-up status of same surface				
		U	S	D	R	M
Baseline status of surface	Unexposed [U][a]	Omitted	Omitted	***Event***	Omitted	Omitted
	Sound [S]	Omitted	Omitted	***Event***	Omitted	Omitted
	Decayed/filled [D]	***Reversal***	***Reversal***	Omitted	Omitted	Omitted
	Root fragment [R]	Omitted	Error	Omitted	Omitted	Omitted
	Missing [M]	Omitted	Omitted	Omitted	Omitted	Omitted

[a]Root surfaces only

Teeth which had been lost in the intervening period were not included in the caries analyses. Newly-crowned surfaces were also not included in the caries increment, on the assumption that crowns are placed for reasons other than the direct consequences of dental caries, and any potential bias from including them was likely to be greater than that from not including them in the increment (Drake *et al*, 1997). Decayed retained roots were also not included in the calculation of the increment, because of the difficulty of allocating an appropriate number of decayed surfaces to them.

Two approaches were used in the calculation of caries increment for both coronal and root surface caries: first, net caries increment (NCI) was computed by subtracting the number of reversals from the gross caries increment; and second, the adjusted caries increment (AdjCI) was used (Beck *et al*, 1995; Lawrence *et al*, 1997).

Risk prediction models (Beck, 1998) were then assessed by dichotomising disease outcomes (*incidence*) and developing multivariate models with logistic regression analysis. Where there was a sufficient distribution of disease *increment* within the sample, least squares regression analyses were undertaken, using that increment as the continuous dependent variable. Because the purpose of the models was to maximize their predictive capacity, previous markers of disease activity as well as medication, behavioural and socio-demographic risk indicators were included as explanatory variables. The models were then used to identify the medication-exposure sub-groups which were most likely to experience future oral disease.

The use of a variety of approaches, together with a rigorous method of medication data collection, was intended to maximise the likelihood of uncovering any relationship which existed between medication use and dental caries incidence among elderly people.

3. Results

This section first describes the baseline findings, and then presents the findings at five years.

3.1 Baseline results

It should be noted that the baseline analysis was essentially a secondary analysis; the data had already been collected, and there had been no opportunity to tailor the baseline data collection to the task of investigating the relationship between medications and dental caries. Thus, the approach was essentially a *post hoc* one.

3.1.1 Participation rate and characteristics of the sample

Of the 4,857 persons who were sampled in SADLS, 2,751 were eligible, and 1,650 of them (60.0 per cent) took part in interviews. At baseline, oral examinations of 1,226 persons (of whom 911 were dentate) were conducted by four calibrated dentists. Satisfactory medication data were collected from 1643 participants (the remaining seven had incomplete medication records), and on medication and caries prevalence from 848 dentate participants. The latter figure differs from the 911 dentate individuals examined because of a procedural error in data recording which was only detected after the first 63 participants had been examined (GD Slade, personal communication, 1995). There were 1158 participants (edentulous and dentate) from Adelaide, and 485 (dentate only) from Mt Gambier. Dental examinations were performed on 343 of the Mt Gambier participants.

Analysis of non-participants indicated minimal effects of non-participation bias on prevalence rates (Slade and Spencer, 1994b): examined individuals were younger (on average) by one year; more examined individuals had made a dental visit during the

previous year (62.4 and 54.6 per cent respectively); and those who were examined were more likely to perceive a need for dental care (33.2 and 25.0 per cent respectively).

The demographic characteristics of the sample are presented in Table 3.1. The age range for the sample was 60 to 99; for Adelaide residents (and females) it was 60 to 99, and for Mt Gambier residents (and for males) it was 60 to 95.

Table 3.1: Mean age of participants by gender and place of residence at baseline

	Number	Mean age (sd)
ALL PARTICIPANTS		
All	1645	71.7 (7.6)
Gender		
Male	867	72.0 (7.7)
Female	778	71.5 (7.5)
Place of residence		
Adelaide	1159	72.3 (7.7)[a]
Mt Gambier	486	70.5 (7.1)
EXAMINED DENTATE PARTICIPANTS ONLY		
All	848	70.8 (7.4)
Gender		
Male	490	71.2 (7.4)
Female	358	70.2 (7.3)
Place of residence		
Adelaide	505	71.2 (7.6)
Mt Gambier	343	70.3 (7.1)
INTERVIEW-ONLY PARTICIPANTS (DENTATE AND EDENTULOUS)		
All	797	72.7 (7.7)
Gender		
Male	377	72.9 (7.8)
Female	420	72.5 (7.5)
Place of residence		
Adelaide	654	73.1 (7.7)[a]
Mt Gambier	143	70.9 (7.0)

[a]P<0.01

3.1.2 Dental caries experience and numbers of missing teeth

Unless otherwise indicated, subsequent results are presented for dentate individuals only.

The overall mean number of missing teeth was 15.70 (sd, 7.38), and the mean coronal DFS was 19.92 (sd, 18.16). The overall mean root surface caries DFS was 3.19 (sd, 3.63). Bivariate associations of dental caries experience and the mean number of missing teeth are presented, by gender in Table 3.2, and by age group in Table 3.3.

Table 3.2: Mean number of missing teeth at baseline, and coronal and root surface caries experience, by gender (sd)

	Male	Female	P value[a]
Number of individuals	490	358	n/a
Missing teeth	15.61 (7.31)	15.82 (7.49)	0.7
Coronal caries			
Decayed surfaces	0.38 (0.93)	0.31 (1.23)	0.3
Filled surfaces	17.68 (16.88)	22.15 (19.62)	<0.01
Decayed and filled surfaces	18.07 (16.86)	22.46 (19.55)	<0.01
Attack rate[b]	22.89 (17.96)	27.62 (18.70)	<0.01
Root surface caries			
Surfaces at risk	29.64 (16.49)	25.28 (14.93)	<0.01
Sound surfaces	26.15 (15.50)	22.50 (13.90)	<0.01
Decayed surfaces	0.67 (1.67)	0.37 (0.87)	<0.01
Filled surfaces	2.81 (3.58)	2.41 (3.19)	0.1
Decayed and filled surfaces	3.48 (3.87)	2.78 (3.24)	<0.01
Root Caries Index[c]	13.05 (14.90)	11.58 (12.78)	0.1

[a]Calculated using ANOVA
[b]Calculated as the number of decayed or filled coronal surfaces multiplied by 100 and divided by the total number present
[c]Calculated according to Katz (1980)

Males and females did not differ in their mean number of missing teeth. Coronal DFS was greater among females, who had substantially higher numbers of filled surfaces than males. There was no gender difference in the number of decayed coronal surfaces. The number of exposed root surfaces was higher among males. Root surface DFS was greater among males, and the main contribution to this difference was the number of decayed surfaces. There was an apparently higher RCI among males, but this was not statistically significant.

Table 3.3: Mean number of missing teeth at baseline, and coronal and root surface caries experience, by age group

	60-64	65-74	75+	P value
Number of participants	212	357	279	n/a
Missing teeth	13.77 (7.51)	15.55 (7.23)	17.35 (7.12)	<0.0001[a]
Coronal caries				
Decayed surfaces	0.39 (1.10)	0.34 (1.20)	0.34 (0.84)	0.8
Filled surfaces	21.85 (18.93)	20.17 (18.44)	17.06 (17.09)	0.01[b]
Decayed and filled surfaces	22.24 (18.78)	20.51 (18.43)	17.40 (17.07)	0.01[b]
Attack rate	25.23 (17.06)	25.28 (18.63)	24.12 (19.16)	0.7
Root surface caries				
Surfaces at risk	25.17 (16.22)	27.59 (15.16)	30.07 (16.57)	0.003[b]
Sound surfaces	22.60 (15.11)	24.32 (13.97)	26.50 (15.82)	0.01[b]
Decayed surfaces	0.57 (1.87)	0.43 (1.03)	0.67 (1.37)	0.08
Filled surfaces	1.99 (2.91)	2.83 (3.43)	2.90 (3.71)	0.006[c]
Decayed and filled surfaces	2.56 (3.43)	3.26 (3.52)	3.57 (3.86)	0.009[c]
Root Caries Index	11.11 (13.69)	12.50 (13.57)	13.33 (14.90)	0.2

[a]One-way ANOVA; Tukey's b test: all age groups differ significantly from one another
[b]One-way ANOVA; Tukey's b test: the 75+ and 60-64 age groups differ significantly
[c]One-way ANOVA; Tukey's b test: the 60-64 age group differs significantly from the 75+ and 65-74 age groups

The mean number of missing teeth increased across the three age groups, while coronal FS and DFS decreased. The number of exposed root surfaces increased across the age

groups, with the oldest and youngest groups being significantly different. Root surface DS did not show the age-group difference which was apparent with root surface FS and root surface DFS. Once the number of surfaces at risk was taken into account, the differences across age groups effectively disappeared.

Table 3.4: Mean number of missing teeth, and coronal and root surface caries experience, at baseline by place of residence

	Mt Gambier	Adelaide	P value
Number of participants	343	505	
Missing teeth	16.30 (7.15)	15.29 (7.51)	0.05
Coronal caries			
Decayed surfaces	0.39 (1.30)	0.32 (0.88)	0.4
Filled surfaces	17.13 (17.20)	21.23 (18.70)	<0.01
Decayed and filled surfaces	17.52 (17.13)	21.55 (18.67)	<0.01
Attack rate	22.10 (17.79)	26.78 (18.62)	<0.01
Root surface caries			
Surfaces at risk	25.29 (14.29)	29.50 (16.85)	<0.01
Sound surfaces	22.39 (13.22)	26.12 (15.85)	<0.01
Decayed surfaces	0.62 (1.61)	0.49 (1.23)	0.2
Filled surfaces	2.29 (3.08)	2.89 (3.62)	0.01
Decayed and filled surfaces	2.90 (3.46)	3.38 (3.73)	0.06
Root Caries Index	12.02 (13.99)	12.70 (14.11)	0.5

The number of filled coronal surfaces (and, hence, coronal DFS) was greater among Adelaide residents, and the direction of the difference between the two populations persisted when the number of surfaces at risk was taken into account (with the "attack rate"). However, there were no differences between Mt Gambier and Adelaide participants when the mean RCI scores were compared, although the Adelaide people had a larger number of exposed root surfaces and higher root surface FS.

3.1.3 Medication prevalence

Data on the frequency of prescription medication usage in the dentate sample are presented in Table 3.5. The number of prescribed medications taken ranged from 0 to 12; 295 people (34.8 per cent) took none, and 365 (43.0 per cent) took two or more. Four or more drugs were taken by 126 (14.9 per cent). The mean number taken was 1.71 (sd, 1.98). Older individuals took more prescribed medications ($P < 0.01$), but the number taken by dentate males and females did not differ significantly.

Table 3.5: Number of participants and prescribed medications at baseline, by age and gender

	Prescribed medications	
	Mean number (sd)	Range
Age group		
60-64 years	1.3 (1.6)	0 to 8
65-74 years	1.7 (2.0)	0 to 12
75+ years	2.0 (2.1)	0 to 12
P-value	<0.01	
Gender		
Female	1.8 (2.0)	0 to 12
Male	1.6 (2.0)	0 to 11
P-value	0.28	

The mean number of medications by place of residence is presented in Table 3.6.

Table 3.6: Numbers of dentate participants and prescribed medications at baseline by age and gender, according to place of residence

	Place of residence			
	Adelaide		**Mt Gambier**	
	Number	Mean number of prescribed medications (sd)	Number	Mean number of prescribed medications (sd)
All participants[a]	505	1.8 (2.1)	485	1.5 (1.8)
Age group[b]				
60-64 years	121	1.3 (1.6)	91	1.3 (1.5)
65-74 years	205	1.8 (2.1)	152	1.5 (2.0)
75+ years	179	2.2 (2.3)	100	1.8 (1.9)
P-value		< 0.01		< 0.05
Gender				
Female	289	1.9 (2.02)	142	1.6 (1.9)
Male	216	1.7 (2.08)	201	1.5 (1.9
P-value		0.28		0.76

[a]ANOVA; $P < 0.05$
[b]Tukey-B test: the 60-64 age group differs significantly from the other two age groups

Dentate participants in Adelaide and Mt. Gambier differed substantially in their medication prevalence (Table 3.6). Differences among the age groups were significant in both areas, but males and females did not differ.

Table 3.7 presents the number of dentate individuals taking various classes of medication, and highlights the predominance of cardiovascular drugs (including diuretics). Analgesics were the only non-cardiovascular class among the four most numerous categories which together accounted for almost three-quarters of the medications taken. Antihypertensive drugs and analgesics accounted for close to 60 per cent of the medications taken by the sample.

Table 3.7: Distribution of medication types at baseline

Medication category	Number taking	% taking
Antihypertensives[a]	310	36.6
Analgesics[b]	153	18.0
Antiangina drugs	107	12.6
Daily aspirin[c]	80	9.4
Psychotherapeutics	47	5.5
Antiasthma drugs/antiasthmatics	45	5.3
Cardiac preparations	36	4.2
Antiulcer drugs	35	4.1
Hypoglycaemics	33	3.9
Antidepressants	31	3.7
Antithrombotics	31	3.7
Hypolipidaemics	30	3.5
Nutrient agents	29	3.4
Non-thyroid hormones	25	2.9
Antibiotics	24	2.8
Uncodables[d]	21	2.5
Thyroid hormones	19	2.2
Anticonvulsants	13	1.5
Potassium preparations	12	1.4
Antipsychotics	11	1.3
Miscellaneous others	11	1.3
Anti-neoplastics	11	1.3
Anticholinergics[e]	10	1.2
Antiinflammatory, steroid	9	1.1
Antihistamines	9	1.1
Laxatives	8	0.9
Antidiarrhoeals	6	0.7
Other CV agents	5	0.6
Topical agents	6	0.7
Antiarthritics	3	0.4
Antinauseants	2	0.2
Antimigraine agents	1	0.1
Anorectics	1	0.1
Peripheral vasodilators	1	0.1

[a]Includes diuretics

[b]Includes antigout drugs

[c]Aspirin was counted separately from the analgesics in order to reflect its current use in the prevention of CVA and MI.

[d]These are medication names which were recorded and which proved unclassifiable.

[e]Includes antiparkinsonian and antispasmodic medications

3.1.4 Bivariate associations between medication, missing teeth and caries prevalence

Summary data on missing teeth, caries prevalence and medication usage are presented in Table 3.8.

Table 3.8: Mean number of missing teeth and mean caries indices (sd) among medication groups at baseline

	Number of prescribed medications taken		
	None	1-2	3+
Number of participants	295	337	216
Missing teeth	14.16 (8.24)	14.97 (7.12)	15.06 (7.29)
Coronal caries			
Decayed surfaces	0.28 (0.80)	0.40 (1.08)	0.39 (1.33)
Filled surfaces	19.63 (18.77)	20.15 (17.46)	18.58 (18.62)
Decayed and filled surfaces	19.91 (18.73)	20.54 (17.39)	18.97 (18.58)
Attack rate[a]	23.83 (18.36)	26.20 (17.98)	24.27 (19.13)
Root surface caries			
Sound surfaces	24.97 (14.83)	25.12 (15.20)	23.32 (14.69)
Decayed surfaces	0.55 (1.37)	0.51 (1.51)	0.58 (1.24)
Filled surfaces	2.53 (3.35)	2.63 (3.43)	2.81 (3.51)
Decayed and filled surfaces	3.08 (3.56)	3.14 (3.59)	3.40 (3.79)
Root Caries Index[b]	12.02 (13.90)	11.50 (12.50)	14.43[c] (16.26)

[a]Calculated as the number of decayed or filled coronal surfaces divided by the total number present
[b]Calculated according to Katz (1980)
[c]ANOVA; Tukey-B test; the 1-2 and 3+ groups differ significantly at the $P < 0.05$ level

There was no significant difference in the mean number of missing teeth according to medication level. Only the Root Caries Index (RCI) differed significantly according to medication level, with participants who were taking three or more prescription medications having a higher RCI than those taking one or two, and those who were taking

none. Although subsequent analyses should, strictly speaking, have been confined to root surface caries because the coronal caries attack rate showed no association with medication level, the associations between coronal caries parameters and the most frequent medication classes have been presented for the sake of completeness.

Coronal DFS data by medication type are presented in Table 3.9.

Table 3.9: Coronal DFS scores among key medication categories at baseline

Medication category	Coronal DFS (sd) Taken	Not taken	P value
Antihypertensives	17.86 (16.65)	21.11 (18.89)	0.01
Analgesics	19.78 (18.90)	19.95 (18.38)	0.91
Antiangina drugs	16.28 (15.17)	20.45 (18.50)	0.03
Cardiac preparations	17.03 (15.93)	20.05 (18.25)	0.33
Psychotherapeutics	17.53 (18.31)	20.06 (18.15)	0.35
Antiasthma drugs	19.42 (18.03)	19.95 (18.18)	0.85
Daily aspirin	20.18 (18.88)	19.89 (18.10)	0.90
Antiulcer drugs	19.57 (17.64)	19.94 (18.19)	0.91
Hypoglycaemics	17.00 (19.39)	20.04 (18.11)	0.35
Antidepressants	21.58 (19.93)	19.86 (18.10)	0.60
Anticoagulants	20.13 (17.78)	19.91 (18.18)	0.95
Hypolipidaemics	22.73 (17.84)	19.82 (18.17)	0.39

Coronal DFS was higher among those who were not taking antihypertensive medication, and among those who were taking anginals, but there were no other significant associations.

Table 3.10 presents data on the coronal caries "attack rate" scores among the 12 most prevalent medication categories.

Table 3.10: Coronal caries "attack rate" scores[a] among key medication categories at baseline

Medication category	Coronal caries "attack rate" (sd) Taken	Not taken	P value
Antihypertensives	23.84 (18.41)	25.49 (18.41)	0.21
Analgesics	25.37 (18.90)	24.78 (18.32)	0.72
Antiangina drugs	21.41 (16.94)	25.39 (18.58)	0.04
Cardiac preparations	22.87 (19.13)	24.98 (18.39)	0.50
Psychotherapeutics	23.88 (18.07)	24.95 (18.45)	0.70
Antiasthma drugs	25.69 (20.89)	24.84 (18.28)	0.76
Daily aspirin	24.63 (17.47)	24.91 (18.53)	0.90
Antiulcer drugs	25.89 (15.05)	24.84 (18.56)	0.74
Hypoglycaemics	22.25 (19.01)	24.99 (18.40)	0.40
Antidepressants	25.38 (15.89)	24.87 (18.52)	0.88
Anticoagulants	25.43 (17.07)	24.87 (18.48)	0.87
Hypolipidaemics	29.55 (16.01)	24.72 (18.49)	0.16

[a]Calculated as the number of decayed and filled coronal surfaces divided by the number of surfaces present

Antiangina drugs comprised the only category which was associated with a significantly different coronal caries attack rate, and in their case, it was lower among people taking that medication type than among those who were not.

Mean root DFS scores among key medication categories are presented in Table 3.11. The overall mean root DFS was 3.18 (sd, 3.63), made up of a mean root DS of 0.54 (1.40) and a mean root FS of 2.64 (3.42).

Table 3.11: Root DFS scores among key medication categories at baseline

Medication category	Root DFS (sd) Taken	Not taken	P value
Antihypertensives	3.23 (3.74)	3.16 (3.57)	0.78
Analgesics	3.24 (3.70)	3.17 (3.62)	0.83
Antiangina drugs	3.78 (3.52)	3.12 (3.63)	0.07
Cardiac preparations	3.58 (4.27)	3.17 (3.60)	0.50
Psychotherapeutics	3.94 (3.80)	3.14 (3.62)	0.15
Antiasthma drugs	3.76 (3.45)	3.15 (3.64)	0.28
Daily aspirin	2.98 (2.81)	3.21 (3.70)	0.58
Antiulcer drugs	4.86 (3.99)	3.11 (3.60)	<0.01
Hypoglycaemics	3.52 (3.36)	3.17 (3.64)	0.60
Antidepressants	4.19 (3.53)	3.15 (3.63)	0.12
Anticoagulants	3.90 (3.91)	3.16 (3.62)	0.26
Hypolipidaemics	2.57 (3.19)	3.21 (3.64)	0.34
Closer examination of specific sub-categories:			
Antiulcer drugs[a]			
H_2-receptor antagonists	4.77 (4.20)	3.13 (3.60)	0.01
Multiple actives/antacids	5.20 (2.77)	3.17 (3.63)	0.21

[a]No individuals were taking prostaglandin antiulcer drugs or proton pump inhibitors, and only 2 were taking cytoprotectants.

The antiulcer medications were associated with higher root DFS scores, and this was particularly significant among those taking the H2-receptor antagonists. Those who were taking the multiple actives/antacids manifested an even greater mean root DFS, but there were only five cases, and so there was a lack of statistical power.

Table 3.12 presents root surface caries index (RCI) scores among individuals who were taking particular medication types. The overall mean RCI score was 12.43 (14.06).

Table 3.12: Root Caries Index[a] scores among key medication categories at baseline

Medication category	Root Caries Index (sd) Taken	Not taken	P value
Antihypertensives	12.97 (15.03)	12.11 (13.46)	0.39
Analgesics	13.01 (14.04)	12.30 (14.07)	0.57
Antiangina drugs	15.66 (16.81)	11.96 (13.56)	0.01
Cardiac preparations	15.83 (18.54)	12.28 (13.82)	0.14
Psychotherapeutics	13.75 (14.28)	12.35 (14.05)	0.51
Antiasthma drugs	15.64 (15.59)	12.25 (13.95)	0.12
Daily aspirin	13.11 (15.55)	12.36 (13.90)	0.65
Antiulcer drugs	19.40 (16.86)	12.13 (13.86)	<0.01
Hypoglycaemics	15.11 (18.53)	12.32 (13.85)	0.26
Antidepressants	17.58 (17.50)	12.23 (13.88)	0.04
Anticoagulants	15.42 (18.30)	12.31 (13.87)	0.23
Hypolipidaemics	11.43 (12.78)	12.46 (14.11)	0.69
Closer examination of specific sub-categories:			
Antiangina drugs			
Organic nitrate vasodilators	15.66 (16.81)	11.96 (13.56)	0.01
Other vasodilators	none taken		
Antiulcer drugs[b]			
H_2-receptor antagonists	19.51 (17.74)	12.16 (13.84)	<0.01
Multiple actives/antacids	17.90 (6.89)	12.39 (14.08)	0.38
Antidepressants			
Cyclic antidepressants	19.83 (19.47)	12.26 (13.88)	0.02
Others[c]	14.02 (13.87)	12.40 (14.07)	0.69

[a]Calculated according to Katz (1980)
[b]No individuals were taking prostaglandin antiulcer drugs or proton pump inhibitors, and only two were taking cytoprotectants.
[c]No individuals were taking MAOIs, and only four were taking other types of antidepressant, so they were combined with the serotonin uptake inhibitors.

Those taking antidepressants, antiangina drugs and antiulcer drugs had significantly higher Root Caries Index values. Closer examination of the antiulcer drugs revealed that the H_2-receptor antagonists (for example ranitidine, nizatidine, famotidine) were the subclass which was associated with greater root surface caries attack rates. Among the

antidepressants, those which were associated with higher root caries attack rates were the cyclic antidepressants (for example amitriptyline, imipramine). Among the antiangina agents, there were none other than the organic nitrates being taken, so comparison of these with quinolone vasodilators or other types was not possible.

3.1.5 Multivariate modelling of baseline caries prevalence

3.1.5.1 Coronal caries

Coronal DFS was modelled using linear regression with the following independent variables (after the model of Beck, 1987): age, gender (female = 1; male = 0), city of residence (Adelaide = 1; Mt Gambier = 0), number of missing teeth, number of medications taken, usual reason for dental visit (check-up = 1; problem = 0), age when left school (<16 = 0; 16+ = 1), toothbrushing frequency (2+ times/day = 1; <2 = 0), flossing frequency (once/week or more = 1; intermittently/never = 0), cigarette smoking status (smoker = 1; non-smoker = 0) and the taking of anginals.

The results of the multivariate analysis are presented in Table 3.13.

Table 3.13: Linear regression model for coronal DFS at baseline[a]

Independent variables	B	Standard error of B	95% CI[a] for B	Significance of T
Female	4.442	1.091	2.30, 6.58	<0.01
Age	-0.071	0.079	-0.23, 0.08	0.37
Smoker	-4.270	1.736	-7.67, -0.87	<0.05
Living in Adelaide	0.396	1.126	-1.81, 2.60	0.73
Left school at age 16+	6.357	1.111	4.18, 8.53	<0.01
Brush 2+ times/day	-1.423	0.078	-3.60, 0.75	<0.01
Floss regularly	0.403	1.135	-1.82, 2.63	0.72
Number of missing teeth	-0.115	1.082	-2.24, 2.01	0.92
Regular dental attender	6.030	1.122	3.83, 8.23	<0.01
Taking an antihypertensive	-1.986	1.133	-4.21, 0.23	0.08
Taking an anginal	-1.856	1.772	-5.33, 1.62	0.30
Constant	41.378	5.591	30.42, 52.34	<0.01

[a] $R^2 = 0.550$

The final model explained 55.0 per cent of the variance in the dependent variable. Neither of the medication categories reached significance. Coronal DFS was greater among females, those with more education and regular dental attenders. It was lower among more frequent tooth-brushers, and smokers.

The "attack rate" for coronal caries was also modelled, using the same independent variables. The outcome of that analysis is presented in Table 3.14.

Table 3.14: Linear regression model for coronal caries "attack rate" at baseline[a]

Independent variables	B	Standard error of B	95% CI[a] for B	Significance of T
Female	3.997	1.393	1.27, 6.73	P<0.01
Age	-0.054	0.100	-0.25, 0.14	0.59
Smoker	-6.352	2.207	-10.68, -2.03	P<0.01
Living in Adelaide	1.488	1.438	-1.33, 4.31	0.30
Left school at age 16+	6.981	1.421	4.20, 9.77	P<0.01
Number of missing teeth	-0.476	0.099	-0.07, 0.28	P<0.01
Brush 2+ times/day	-0.576	1.452	-3.42, 2.27	0.71
Floss regularly	-0.161	1.385	-2.88, 2.55	0.91
Regular dental attender	8.584	1.434	5.77, 11.40	P<0.01
Taking an anginal	-2.961	2.206	-7.29, 1.36	0.18
Constant	28.787	7.150	14.77, 42.80	P<0.01

[a]$R^2 = 0.240$

The model explained 24.0 per cent of the variance in coronal caries "attack rate". The taking of anginals did not reach significance, but the "attack rate" was greater among females, those with more education, and regular dental attenders. It was lower among smokers.

3.1.5.2 Root surface caries

Root surface DFS was modelled using linear regression with the following independent variables (after the model of Beck, 1987): age, gender (female = 1; male = 0), city of residence (Adelaide = 1; Mt Gambier = 0), number of missing teeth, number of medications taken, usual reason for dental visit (check-up = 1; problem = 0), age when left school (<16 = 0; 16+ = 1), toothbrushing frequency (2+ times/day = 1; <2 = 0), flossing frequency (once/week or more = 1; intermittently/never = 0), cigarette smoking status (smoker = 1; non-smoker = 0) and the taking of antiulcer drugs.

The outcome of the linear regression procedure is presented in Table 3.15.

Table 3.15: Linear regression analysis for baseline root DFS[a]

Independent variables	B	Standard error of B	95% CI[a] for B	Significance of T
Female	-0.587	0.292	-1.16, -0.02	P<0.05
Age	0.058	0.021	0.02, 0.10	P<0.01
Smoker	-0.459	0.462	-1.37, 0.45	0.32
Living in Adelaide	0.019	0.297	-0.56, 0.60	0.95
Left school at age 16+	0.175	0.297	-0.41, 0.76	0.56
Number of missing teeth	-0.046	0.021	-0.09, -0.01	P<0.05
Brush 2+ times/day	0.066	0.303	0.01, 0.13	0.83
Floss regularly	-0.335	0.290	-0.91, 0.24	0.25
Regular dental attender	1.383	0.301	0.79, 1.97	P<0.01
Taking an antiulcer drug	2.227	0.752	0.75, 3.70	P<0.01
Constant	-0.643	1.494	-3.57, 2.29	0.67

[a] $R^2 = 0.099$

The model explained 9.9 per cent of the variance in the dependent variable. The taking of antiulcer medication was positively associated with the root DFS.

The Root Caries Index was also modelled, using the following independent variables: age, gender (female = 1; male = 0), city of residence (Adelaide = 1; Mt Gambier = 0), number of missing teeth, number of medications taken, usual reason for dental visit (check-up = 1; problem = 0), age when left school (<16 = 0; 16+ = 1), toothbrushing frequency (2+ times/day = 1; <2 = 0), flossing frequency (once/week or more = 1; intermittently/never = 0), cigarette smoking status (smoker = 1; non-smoker = 0) and the taking of antiulcer drugs, anginals or antidepressants. The outcome of that analysis is presented in Table 3.16.

Table 3.16: Linear regression model for Root Caries Index scores at baseline[a]

Independent variables	B	Standard error of B	95% CI[a] for B	Significance of T
Female	-1.070	1.238	-3.50, 1.36	0.39
Age	0.086	0.089	-0.09, 0.26	0.34
Smoker	-3.240	1.952	-7.07, 0.59	0.10
Living in Adelaide	-0.613	1.264	-3.09, 1.86	0.63
Left school at age 16+	1.730	1.261	-0.74, 4.20	0.17
Number of missing teeth	0.176	0.088	0.01, 0.35	P<0.05
Brush 2+ times/day	-0.448	1.295	-2.99, 2.09	0.73
Floss regularly	-1.229	1.236	-3.65, 1.19	0.32
Regular dental attender	4.729	1.275	2.23, 7.23	P<0.01
Taking an antiulcer drug	6.332	3.195	0.07, 12.59	P<0.05
Taking an anginal	3.967	1.929	0.19, 7.75	P<0.05
Taking an antidepressant	1.431	3.538	-5.50, 8.37	0.69
Constant	2.323	6.351	-10.13, 14.77	0.72

[a]$R^2 = 0.063$

The model explained 6.3 per cent of the variance. The taking of antiulcer drugs or anginals was associated with a higher RCI value. Regular dental attenders and people with more missing teeth also had higher RCI scores.

3.2 Results at five years

The following sections of this document examine in detail the associations at five years between medications, dry mouth and dental caries. Although the dentate individuals are the group upon whom the bulk of attention is focused—being the group in whom the purported link between medications and dental caries will be explored in detail—the entire sample which remained at five years is examined where dental data are not used. This is to ensure that there are sufficient numbers in the various subgroups for meaningful analysis of the relationship between medications and dry mouth, and to maximise the likelihood of uncovering those medication-dry mouth associations which are present. Thus, the earlier analyses in this section include both dentate and edentulous individuals. Where only dentate people are included, it is made explicit in the titles of Tables and in the text which describes them.

3.2.1 Retention of the sample

Of the 939 people (56.9 per cent of the 1650 people interviewed at baseline) who participated in the study at five years, 483 (50.6 per cent) were male and 456 (49.4 per cent) female. The ages of study members ranged from 65 to 100, with a mean age of 75 years (sd, 7 years). Xerostomia questionnaires were mailed to the 708 (75.4 per cent) who had a dental examination appointment. Of these, 201 (31.0 per cent) were from Mt Gambier and 448 (69.0 per cent) were Adelaide residents. The XI questionnaires were completed and returned by 649 (71.0 per cent) of those individuals. Where there were difficulties in getting co-operation from participants, priority was given to the dental examination rather than the saliva collection; consequently, saliva samples were collected from 676 (95.5 per cent) of those examined at five years. Responses to the standard single-item question were available from those who took part in the telephone interview. Overall, XI, flow-rate, medication and interview data were all available for 623 (88.0 per cent) of the dentally-examined individuals (including those who were edentulous).

The baseline characteristics of the dentate people who remained in the study at five years and those who did not are presented in Table 3.17.

Table 3.17: Comparison of baseline characteristics of dentate individuals who remained in the study at five years and those who did not (brackets contain percentages except where otherwise indicated)

	Lost to follow-up	Examined
Number	351 (39.9)	528 (60.1)
Female	141 (40.2)	231 (43.8)
Living in Adelaide	221 (63.0)	310 (58.7)
Mean age (sd)	72.8 (7.9)	69.5 (6.7)[a]
Income of $21,000 or more	73 (21.8)	137 (28.2)[a]
Educated past age 16	115 (32.8)	189 (35.9)
Regular dental visitor	119 (33.9)	236 (46.6)[b]
Brush teeth at least once/day	328 (93.7)	510 (96.8)[a]
Floss teeth at least once/week	152 (43.3)	264 (50.0)
Mean number of medications taken	2.0 (2.2)	1.5 (1.8)[b]

[a]P<0.05
[b]P<0.01

The comparison showed that the group which remained was younger, and comprised proportionately more females and regular users of dental services, and more whose dental self-care habits were favourable. The number of medications taken was also lower.

Data on the characteristics of those who supplied flow-rate, medication or XI data and those for whom they were not available are compared in Table 3.18.

Table 3.18: Comparison of characteristics of individuals for whom flow-rate, medication or XI data were available and those for whom they were not, by dentate status at five years

All participants remaining at five years:

	Adelaide residents (%)	Females (%)	Mean age (sd)	Mean no. of chronic medical conditions (sd)
Flow rate data				
Available	479 (68.6)	316 (45.3)[a]	69 (7)	2.2 (1.4)
Not available	153 (71.5)	134 (62.6)	70 (7)	2.2 (1.5)
Medication data				
Available	485 (68.8)	321 (45.5)[b]	70 (7)	2.3 (1.5)
Not available	147 (71.0)	129 (62.3)	70 (7)	2.1 (1.5)
XI data				
Available	448 (69.0)	300 (46.2)[a]	69 (7)	2.2 (1.4)
Not available	184 (70.0)	150 (57.0)	71 (7)	2.2 (1.5)

Dentate participants remaining at five years:

Flow rate data				
Available	284 (56.9)[a]	217 (43.5)[a]	69 (7)	2.1 (1.4)
Not available	50 (72.5)	41 (59.4)	70 (7)	2.3 (1.7)
Medication data				
Available	288 (57.1)[b]	220 (43.7)[b]	69 (7)	2.2 (1.4)
Not available	46 (71.9)	38 (59.4)	70 (7)	2.2 (1.7)
XI data				
Available	268 (57.4)	206 (44.1)	69 (7)	2.2 (1.4)
Not available	66 (65.3)	52 (51.5)	71 (7)	2.2 (1.6)

[a]P<0.01
[b]P<0.05

Among the entire examined sample remaining at five years, proportionately more of those for whom saliva samples were not taken were female, and a similar relationship was

apparent for the medication data. There were no significant differences with the XI data. Similar relationships were apparent among the examined dentate individuals.

Owing to variation in the participation rates for the various aspects of the study, different numbers of individuals provided data for the dry mouth and medication estimates. The numbers involved in each are presented in Table 3.19, for all individuals and for dentate participants.

Table 3.19: Number (%) of dentally-examined participants providing the medication and dry mouth data at five years

All participants remaining at five years (N = 939)

	XI data	Standard q.	Flow rate	Medications
XI data	649 (69.1)	637 (67.8)	635 (67.6)	636 (67.7)
Standard question		896 (95.4)	684 (72.8)	688 (73.3)
Flow rate			699 (74.4)	697 (74.2)
Medications				704 (75.0)

Dentate participants only remaining at five years: (N = 568)

	XI data	Standard q.	Flow rate	Medications
XI data	467 (82.2)	460 (81.0)	456 (80.3)	459 (80.8)
Standard question		557 (98.1)	490 (86.3)	494 (87.0)
Flow rate			499 (87.9)	498 (87.7)
Medications				504 (88.7)

3.2.2 Medication exposure

This section begins with the presentation of data on the overall prevalence of medication (both prescription and self-prescribed) in the sample at five years. This is followed by data on the source of medication information at five years, after which the prevalence of the 20 most frequent medication types is detailed, along with changes over the five years since baseline.

3.2.2.1 Medications

Medication data were collected from 704 individuals at five years, comprising 42.8 per cent of the 1643 individuals in the baseline sample from whom similar information was obtained. Of the 848 who were dentate at baseline, 504 (59.4 per cent) supplied medication data at five years. The number of prescription drugs taken at five years ranged from none to 17. Data on the number of prescription medications taken at baseline and five years are presented in Table 3.20 (it should be noted that only information on prescription medications was collected at baseline). There were no apparent differences between males and females, but older participants took more medications than those in the younger age groups.

Self-prescribed drugs were taken by 126 individuals (17.9 per cent); the mean number taken was 0.29 (sd, 0.73). The number of self-prescribed drugs taken ranged from none to six. There were no differences by age group, gender or dentate status.

Summing the self-prescribed and doctor-prescribed medications at five years gave the mean total number of medications taken as 3.18 (sd, 2.63).

Table 3.20: Number of participants and prescription medications taken at baseline and five years by age group at five years, gender and dentate status

	Number	Mean number of medications at baseline (sd)	Mean number of medications at five years (sd)	Five-year increment
Age group				
65-69 years	203	1.39 (1.56)	2.29 (2.20)	0.90 (1.70)
70-79 years	302	1.56 (1.86)	2.93 (2.59)	1.37 (1.98)
80+ years	199	1.77 (1.82)	2.91 (2.54)	1.74 (2.11)
P-value		P < 0.01	P < 0.01	P < 0.01
Oneway ANOVA:		Groups 1 & 3 differ	All 3 groups differ	Group 1 differs from 2 & 3
Gender				
Female	320	1.69 (1.87)	3.06 (2.73)	1.37 (2.20)
Male	384	1.47 (1.68)	2.78 (2.36)	1.32 (1.75)
P-value		P = 0.09	P = 0.14	P = 0.72
All combined[b]	704	1.57 (1.77)	2.91 (2.54)	1.34 (1.97)
Dentate participants only:				
Age group				
65-69 years	152	1.34 (1.56)	2.16 (2.25)	0.82 (1.74)
70-79 years	220	1.55 (1.96)	2.92 (2.50)	1.37 (1.83)
80+ years	132	1.74 (1.90)	3.39 (2.57)	1.27 (1.85)
		P = 0.19	P < 0.01	P < 0.01
Oneway ANOVA:			Group 1 differs from 2 & 3	Group 1 differs from 2 & 3
Gender				
Female	220	1.68 (1.94)	2.95 (2.62)	1.27 (1.93)
Male	284	1.43 (1.74)	2.70 (2.38)	1.27 (1.78)
		P = 0.12	P = 0.28	P = 0.99
All combined[c]	504	1.54 (1.83)	2.81 (2.49)	1.27 (1.85)

[a]The total number of medications taken is the sum of doctor-prescribed and self-prescribed preparations
[b]There were 704 participants for whom medicaiton data were available at both baseline and five years
[c]There were 504 participants (1) who were dentate and (2) for whom medication data were available at both baseline and five years

Although 69 individuals (9.8 per cent) were taking fewer medications after five years, most (440, or 62.5 per cent) were taking more, and only 195 (27.7 per cent) were taking the same number of preparations.

3.2.2.2 Source of medication information

Medication data were obtained directly from the drug containers for 417 (71.4 per cent), from the individual's memory (for at least one preparation) for 163 (27.9 per cent), and from a follow-up telephone call soon after the examination for four individuals (0.7 per cent). These rates did not vary much among the major categories of preparation (Table 3.21), although thyroxine had the highest—and analgesics the lowest—presentation rate for containers at the time of the dental examination.

Table 3.21: Source of medication information at five years by major medication category

	Source of information (%)		
	Container	*Memory*	*Follow-up*
Medication type			
Antihypertensives	82.9	16.5	0.6
Cardiac preparations	88.0	12.0	0.0
Anginals	88.7	11.3	0.0
Analgesics	73.9	25.1	1.0
Antiasthma drugs	77.6	20.7	1.7
Hormone Replacement Therapy (HRT)	87.2	12.8	0.0
Antiulcer drugs	80.7	18.3	0.9
Hypoglycaemics	77.1	22.9	0.0
Daily aspirin	74.9	24.6	0.5
Psychotherapeutics	78.8	21.2	0.0
Antidepressants	89.2	10.8	0.0
Thyroxine	93.5	6.5	0.0
Hypolipidaemics	84.5	15.5	0.0
All combined	71.4	27.9	0.7

3.2.2.3 Medication prevalence by therapeutic category

Medication prevalence data are presented for the medication categories which were most prevalent at five years in Table 3.22, using the unmodified classification of Psaty *et al* (1995), described in Section 1.5.2. For the purposes of examining the association of medication exposure and dry mouth over the five years of the study, this classification was modified. Individuals who were taking preparation X at both baseline and five years were assumed to have been continuously exposed during that intervening period; they were categorised as *Continuous users*. The remainder of the sample were not taking preparation X at both data collections, and were aggregated.

Table 3.22: Medication prevalence at five years - distribution of users for the 20 most prevalent medication categories[a], for all (N = 708) and for dentate participants only (N = 504).

Medication category	Number of participants (%)	Number of dentate participants (%)	Prevalence at five years only (%)[b]	
			All	Dentate only
Antihypertensives			372 (52.7)	272 (51.5)
Continuous users	237 (33.6)	170 (32.2)		
Starters	135 (19.1)	102 (19.3)		
Stoppers	18 (2.5)	12 (2.3)		
Nonusers	316 (44.8)	244 (46.2)		
β-blockers			101 (14.3)	69 (13.1)
Continuous users	29 (4.1)	19 (3.6)		
Starters	72 (10.2)	50 (9.5)		
Stoppers	33 (4.7)	22 (4.2)		
Nonusers	572 (81.0)	437 (82.8)		

Diuretics			171 (24.2)	124 (23.5)
Continuous users	88 (12.5)	70 (13.3)		
Starters	83 (11.8)	54 (10.7)		
Stoppers	42 (5.9)	31 (5.9)		
Nonusers	493 (69.8)	373 (70.6)		
ACEIs			127 (17.9)	89 (16.9)
Continuous users	4 (0.6)	3 (0.6)		
Starters	123 (17.4)	86 (16.3)		
Stoppers	0 (0.0)	0 (0.0)		
Nonusers	577 (82.0)	439 (83.1)		
CCBs			142 (20.1)	100 (18.9)
Continuous users	58 (8.2)	41 (7.8)		
Starters	84 (11.9)	60 (11.4)		
Stoppers	71 (10.1)	46 (8.7)		
Nonusers	492 (69.8)	381 (72.2)		
Sympatholytics			29 (4.1)	25 (4.7)
Continuous users	11 (1.6)	11 (2.1)		
Starters	18 (2.5)	14 (2.7)		
Stoppers	11 (1.6)	8 (1.5)		
Nonusers	666 (94.3)	495 (93.8)		
Cardiac drugs			51 (7.2)	37 (7.0)
Continuous users	8 (1.1)	6 (1.1)		
Starters	43 (6.1)	31 (5.9)		
Stoppers	14 (2.0)	10 (1.9)		
Nonusers	641 (90.8)	481 (91.1)		
Anginals			53 (7.5)	37 (7.0)
Continuous users	22 (3.1)	17 (3.2)		
Starters	31 (4.4)	20 (3.8)		
Stoppers	46 (6.5)	36 (6.8)		
Nonusers	607 (86.0)	455 (85.7)		
Analgesics			210 (29.7)	163 (30.9)
Continuous users	86 (12.2)	68 (12.9)		
Starters	124 (17.6)	95 (18.0)		
Stoppers	39 (5.5)	23 (4.4)		
Nonusers	457 (64.7)	323 (64.8)		

Simple analgesics			22 (3.1)	17 (3.2)
Continuous users	1 (0.1)	1 (0.2)		
Starters	21 (3.0)	16 (3.0)		
Stoppers	3 (0.4)	1 (0.2)		
Nonusers	681 (96.5)	510 (96.6)		
NSAIDs			100 (14.2)	79 (15.0)
Continuous users	46 (6.5)	36 (6.8)		
Starters	54 (7.6)	43 (8.1)		
Stoppers	40 (5.7)	26 (4.9)		
Nonusers	566 (80.2)	423 (80.1)		
Antigouts			43 (6.1)	38 (7.2)
Continuous users	23 (3.3)	19 (3.6)		
Starters	20 (2.8)	19 (3.6)		
Stoppers	4 (0.6)	4 (0.8)		
Nonusers	659 (93.3)	486 (92.0)		
Narcotic & combination analgesics			79 (11.2)	57 (10.8)
Continuous users	11 (1.6)	7 (1.3)		
Starters	68 (9.6)	50 (9.5)		
Stoppers	10 (1.4)	5 (0.9)		
Nonusers	617 (87.4)	466 (88.3)		
Antiasthma drugs			57 (8.1)	41 (7.8)
Continuous users	21 (3.0)	14 (2.7)		
Starters	36 (5.1)	27 (5.1)		
Stoppers	8 (1.1)	7 (1.3)		
Nonusers	641 (90.8)	480 (90.9)		
HRT			40 (5.6)	27 (5.1)
Continuous users	15 (2.1)	12 (2.3)		
Starters	25 (3.5)	15 (2.8)		
Stoppers	6 (0.8)	5 (0.9)		
Nonusers	660 (93.5)	496 (93.9)		
Antiulcer drugs			110 (15.6)	83 (15.7)
Continuous users	21 (3.0)	14 (2.7)		
Starters	89 (12.6)	69 (13.1)		
Stoppers	6 (0.8)	3 (0.6)		
Nonusers	590 (83.6)	442 (83.7)		

Hypoglycaemics			48 (6.8)	30 (5.7)
Continuous users	24 (3.4)	14 (2.7)		
Starters	24 (3.4)	16 (3.0)		
Stoppers	4 (0.6)	1 (0.2)		
Nonusers	654 (92.6)	497 (94.1)		
Daily aspirin			217 (30.6)	160 (30.3)
Continuous users	52 (7.4)	40 (7.6)		
Starters	165 (23.4)	120 (22.7)		
Stoppers	13 (1.8)	12 (2.3)		
Nonusers	476 (67.4)	356 (67.4)		
Psychotherapeutics			54 (7.6)	36 (6.8)
Continuous users	21 (3.0)	15 (2.8)		
Starters	33 (4.7)	21 (4.0)		
Stoppers	10 (1.4)	9 (1.7)		
Nonusers	642 (90.9)	483 (91.5)		
Antidepressants			37 (5.2)	23 (4.4)
Continuous users	12 (1.7)	8 (1.5)		
Starters	25 (3.5)	15 (2.8)		
Stoppers	9 (1.3)	6 (1.1)		
Nonusers	642 (93.5)	499 (94.5)		
Thyroxine			31 (4.4)	18 (3.4)
Continuous users	18 (2.5)	15 (2.8)		
Starters	12 (1.7)	3 (0.6)		
Stoppers	2 (0.3)	0 (0.0)		
Nonusers	674 (95.5)	510 (96.6)		
Hypolipidaemics			58 (8.2)	41 (7.8)
Continuous users	23 (3.3)	16 (3.0)		
Starters	35 (5.0)	25 (4.7)		
Stoppers	12 (1.7)	7 (1.3)		
Nonusers	636 (90.1)	480 (90.9)		

[a]Antihypertensives and analgesics have each been presented *in toto*, but have also been disaggregated into subcategories, as these differ substantially

[b]The five-year prevalence can be computed by adding the *Continuous users* and the *Starters*, while the baseline prevalence can be computed by adding the *Stoppers* and the *Continuous users*.

The baseline prevalence of a given drug type can be estimated from Table 3.22 by adding the estimates for the *Continuous users* and the *Stoppers*. Overall, there were broad

similarities in medication prevalence between the entire sample and the dentate individuals. A feature of Table 3.22 is the high prevalence of antihypertensive medications; very few individuals stopped taking them over the five years since baseline, and 19 per cent of the sample commenced antihypertensive therapy. Diuretics and ACE inhibitors were the most common, with the latter showing a large increase in prevalence since baseline, reflecting their increased availability since the early 1990s. Analgesics were also very common, being taken by almost one-third of study members; this represents a near doubling of their prevalence in the time since baseline. Among the analgesics, the NSAIDs were the most prevalent, and the relatively large number of *Starters* and *Stoppers* reflected a comparatively high turnover in their usage. Antiulcer medication showed a relatively high increase in prevalence since baseline, rising from 3.8 per cent to 15.6 per cent in the general sample. Daily aspirin showed a very large increase in prevalence since baseline, to the extent that it was second in prevalence only to the antihypertensive drugs. Similarly, the hypolipidaemic drugs more than doubled in prevalence over the same period.

3.2.3 Exposure to cigarette smoking and alcohol at five years

3.2.3.1 Smoking

Some 404 (44.3 per cent) of the sample at five years reported ever having smoked cigarettes, 491 had not, and 17 (1.9 per cent) did not respond to this item. Of the 404 who had ever smoked, 56 (13.9 per cent, or 6.1 per cent of the entire sample) reported currently smoking. Of those individuals: 20 (35.7 per cent) smoked fewer than 10 cigarettes per day; 18 (32.1 per cent) smoked 10 to 19 per day; 16 (28.6 per cent) smoked 20 to 30 per day; and 2 (3.6 per cent) smoked more than 30 per day.

3.2.3.2 Alcohol

Some 625 individuals (68.5 per cent) reported having drunk alcohol in the previous year, while 270 (29.6 per cent) did not, and data were missing for 17 (1.9 per cent). Drinking alcohol in the previous month was reported by 517 (82.7 per cent) of those who reported drinking in the previous year. Among those individuals, the number of standard drinking occasions in the previous month ranged from one to 90, with a mean of 9.9 (sd, 13.4). The number of drinks taken each time ranged from one to 15, with a mean of 1.1 (sd, 1.4).

Monthly alcohol exposure (expressed as the number of standard drinks per month) was computed by multiplying the number of drinks each time by the estimated number of drinking occasions in the previous month. Among the drinkers of alcohol, the monthly alcohol exposure ranged from one to 450 standard drinks, with a mean of 20.0 (sd, 37.5).

3.2.4 Salivary flow rate

This section describes the findings on unstimulated whole-salivary flow rate. Stimulated whole-salivary flow rate or individual glandular flows were not examined. Participants in the study were usually diffident at first when asked to spit into a container for four minutes, but almost all found it to be a novel experience. A sense of humour certainly helped, both for the individual concerned and for the dental examiner who had to cajole him/her into spitting.

3.2.4.1 Details of saliva collection

The preweighed containers used for the saliva collection had a mean initial weight of 8.6300g (sd, 0.0900g), including the label which was used to identify each individual, and the container lid. After saliva collection and storage, containers were weighed unopened. The time of saliva collection ranged from 45 to 300 seconds, with a mean collection time of 219 seconds (sd, 33 sec). Mean flow rates by collection time are presented in Table 3.23.

Table 3.23: Mean flow rates by collection time

Collection time (sec)	Number (%)	Flow rate (sd) (ml/min)
45	1 (0.1)	0.21 (—)
120	25 (3.6)	0.32 (0.21)
160	2 (0.3)	0.35 (0.23)
180	178 (25.4)	0.26 (023)
190	2 (0.3)	0.13 (0.08)
200	2 (0.3)	0.51 (0.44)
210	6 (0.9)	0.39 (0.28)
220	5 (0.7)	0.21 (0.09)
230	6 (0.9)	0.35 (0.39)
240	470 (67.1)	0.27 (0.22)
250	2 (0.3)	0.34 (0.11)
300	1 (0.1)	0.09 (—)
All combined	700 (100.0)	0.27 (0.22)

The correlation between flow rate and collection time was negative, low and not significant ($r = -0.034$; $P = 0.37$).

3.2.4.1.1 Flow rates and sociodemographic characteristics

Unstimulated flow rate data were available for 700 individuals. The flow rate ranged from 0.00 ml/min to 1.84 ml/min, and the mean was 0.27 ml/min (sd, 0.22). The distribution of flow rates is presented in Table 3.24.

Table 3.24: Distribution of unstimulated flow rates

Percentile	Flow rate (ml/min)
10	0.06
20	0.09
30	0.13
40	0.17
50	0.21
60	0.27
70	0.34
80	0.42
90	0.53
100	1.84

The distribution of flow rates was a moderately skewed one (Figure 3.1).

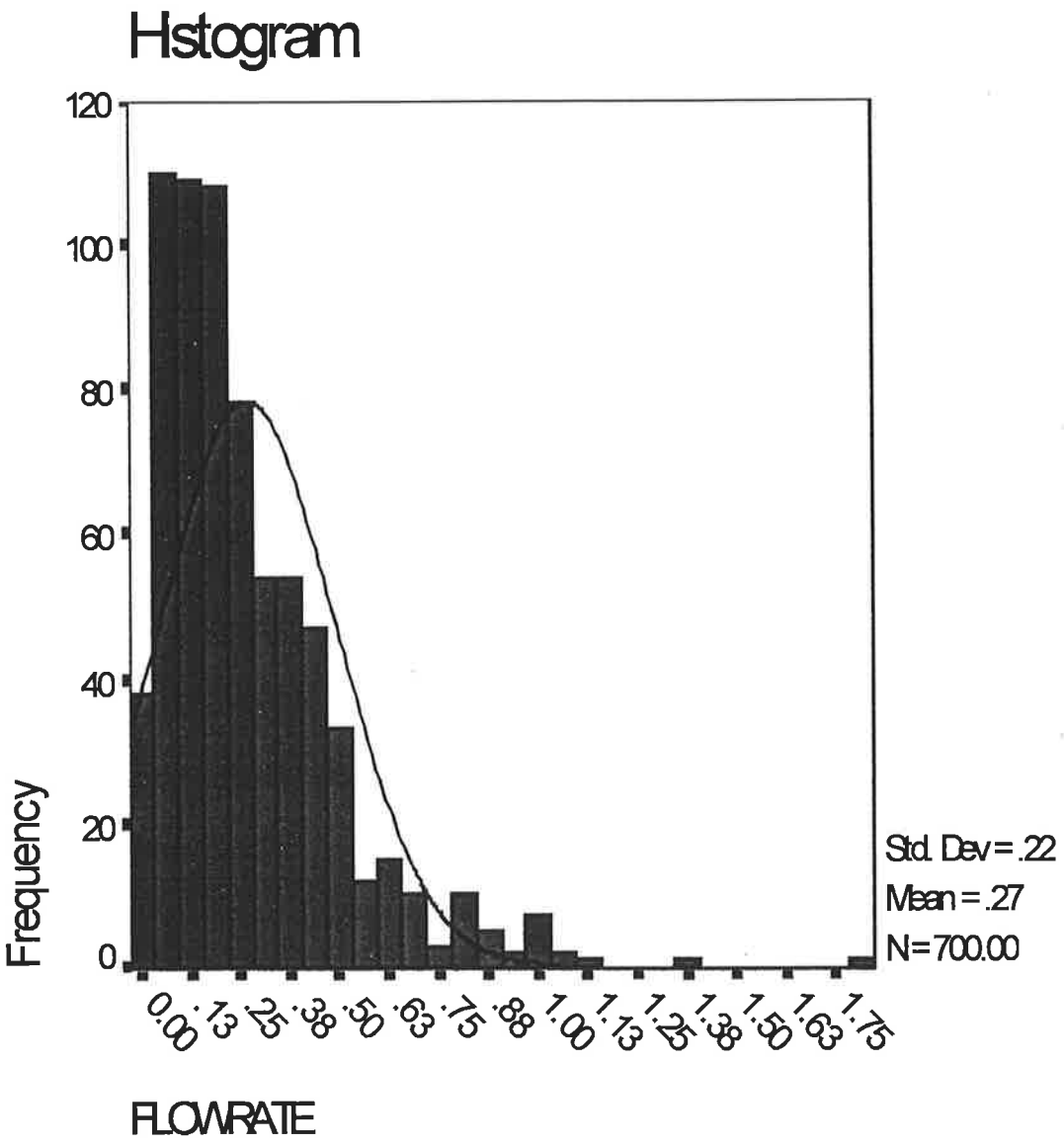


Figure 3.1: Distribution of unstimulated flow rates with normal curve superimposed.

Mean flow rates and the prevalence of salivary gland hypofunction (SGH; defined by a unstimulated flow rate of less than 0.1 ml/min) by sociodemographic characteristics and dentate status are presented in Table 3.25, for both the whole sample and for dentate individuals only.

Table 3.25: Mean unstimulated flow rates and SGH prevalence by age group, gender and dentate status

	Mean flow rate (sd)	SGH prevalence (%)
All participants		
Age group		
65-69 years	0.29 (0.25)	41 (22.0)
70-79 years	0.27 (0.22)	63 (20.0)
80+ years	0.25 (0.20)	54 (27.1)
Gender		
Female	0.23 (0.19)[a]	85 (26.4)[b]
Male	0.30 (0.24)	73 (19.3)
Dentate status		
Dentate	0.27 (0.23)	111 (22.2)
Edentulous	0.26 (0.21)	47 (23.5)
All combined	0.27 (0.22)	158 (22.6)
Dentate participants only:		
Age group		
65-69 years	0.29 (0.25)	32 (23.4)
70-79 years	0.28 (0.22)	44 (19.0)
80+ years	0.25 (0.21)	35 (26.5)
Gender		
Female	0.30 (0.25)[a]	56 (25.9)
Male	0.23 (0.19)	55 (19.4)

[a]P<0.01
[b]P<0.05

Females had lower mean flow rates and a higher prevalence of SGH than males. There were no significant differences across the three age groups or by dentate status.

3.2.4.2 Flow rates and medication exposure

The bivariate findings which follow are from two separate analyses of flow rate and medication exposure: the first is a "conventional" bivariate comparison of the mean flow rate of individuals exposed to a particular medication type compared with those who were not taking it; and the second is the outcome of the AID analysis of medication exposure and flow rate.

3.2.4.2.1 Bivariate analysis - conventional approach

The mean flow rates among individuals taking the most prevalent medication types at five years are presented in Table 3.26.

Table 3.26: Mean flow rates among individuals taking particular medications (a) at five years, and (b) at baseline and five years (N = 700)

	Taken at five years only		Taken at baseline and five years	
Medication category	Number (%)	Mean flowrate (sd)	Number (%)	Mean flowrate (sd)
Antihypertensives				
Not taken	335 (47.9)	0.27 (0.23)	468 (66.9)	0.27 (0.22)
Taken	365 (52.1)	0.27 (0.22)	232 (33.1)	0.27 (0.22)
		P = 0.63		P = 0.93
β-blockers				
Not taken	602 (86.0)	0.27 (0.25)	673 (96.1)	0.27 (0.22)
Taken	98 (14.0)	0.25 (0.21)	27 (3.9)	0.29 (0.28)
		P = 0.46		P = 0.61
Diuretics				
Not taken	534 (76.3)	0.28 (0.23)	615 (87.9)	0.27 (0.22)
Taken	166 (23.7)	0.24 (0.20)	85 (12.1)	0.26 (0.23)
		P = 0.05		P = 0.65
ACEIs				
Not taken	574 (82.0)	0.27 (0.23)	696 (99.4)	0.27 (0.22)
Taken	126 (18.0)	0.28 (0.21)	4 (0.6)	0.57 (0.46)
		P = 0.62		P = 0.007
CCBs				
Not taken	559 (79.9)	0.27 (0.22)	642 (91.7)	0.27 (0.22)
Taken	141 (20.1)	0.27 (0.23)	58 (8.3)	0.28 (0.22)
		P = 0.78		P = 0.68
Sympatholytics				
Not taken	671 (95.9)	0.27 (0.22)	689 (98.4)	0.27 (0.22)
Taken	29 (4.1)	0.27 (0.22)	11 (1.6)	0.31 (0.29)
		P = 0.96		P = 0.58
Cardiac drugs				
Not taken	650 (92.9)	0.27 (0.22)	692 (98.9)	0.27 (0.22)
Taken	50 (7.1)	0.25 (0.22)	8 (1.1)	0.17 (0.09)
		P = 0.49		P = 0.22
Anginals				
Not taken	647 (92.4)	0.27 (0.23)	678 (96.9)	0.27 (0.22)
Taken	53 (7.6)	0.25 (0.19)	22 (3.1)	0.23 (0.22)
		P = 0.57		P = 0.35
Analgesics				
Not taken	492 (70.3)	0.27 (0.23)	616 (88.0)	0.27 (0.23)
Taken	208 (29.7)	0.26 (0.21)	84 (12.0)	0.26 (0.20)
		P = 0.35		P = 0.81
Simple				
Not taken	678 (96.9)	0.27 (0.22)	699 (99.9)	0.27 (0.24)
Taken	22 (3.1)	0.26 (0.19)	1 (0.1)	0.27 (—)
		P = 0.83		P = 0.99

NSAIDs				
Not taken	599 (85.7)	0.27 (0.22)	654 (93.4)	0.27 (0.22)
Taken	100 (14.3)	0.27 (0.23)	46 (6.6)	0.28 (0.20)
		P = 0.97		P = 0.67
Antigouts				
Not taken	658 94.0)	0.27 (0.22)	677 (96.7)	0.27 (0.22)
Taken	42 (6.0)	0.25 (0.18)	23 (3.3)	0.23 (0.17)
		P = 0.59		P = 0.37
Narcotic & comb. preps				
Not taken	622 (88.9)	0.27 (0.22)	690 (98.6)	0.27 (0.22)
Taken	78 (11.1)	0.24 (0.21)	10 (1.4)	0.19 (0.18)
		P = 0.23		P = 0.24
Antiasthma drugs				
Not taken	644 (92.0)	0.27 (0.22)	680 (97.1)	0.27 (0.22)
Taken	56 (8.0)	0.29 (0.23)	20 (2.9)	0.28 (0.24)
		P = 0.59		P = 0.87
HRT				
Not taken	661 (94.4)	0.27 (0.23)	688 (98.3)	0.27 (0.22)
Taken	39 (5.6)	0.21 (0.13)	12 (1.7)	0.21 (0.13)
		P = 0.07		P = 0.35
Antiulcer drugs				
Not taken	593 (84.7)	0.27 (0.23)	679 (97.0)	0.27 (0.22)
Taken	107 (15.3)	0.27 (0.19)	21 (3.0)	0.21 (0.16)
		P = 0.89		P = 0.21
Hypoglycaemics				
Not taken	654 (93.4)	0.27 (0.22)	676 (96.6)	0.27 (0.22)
Taken	46 (6.6)	0.29 (0.23)	24 (3.4)	0.27 (0.20)
		P = 0.46		P = 0.99
Daily aspirin				
Not taken	486 (69.4)	0.28 (0.23)	648 (92.6)	0.27 (0.22)
Taken	214 (30.6)	0.25 (0.21)	52 (7.4)	0.26 (0.19)
		P = 0.12		P = 0.82
Psychotherapeutics				
Not taken	648 (92.6)	0.27 (0.22)	679 (97.0)	0.27 (0.22)
Taken	52 (7.4)	0.25 (0.21)	21 (3.0)	0.26 (0.24)
		P = 0.44		P = 0.80
Antidepressants				
Not taken	664 (94.9)	0.27 (0.23)	688 (98.3)	0.27 (0.22)
Taken	36 (5.1)	0.18 (0.14)	12 (1.7)	0.12 (0.08)
		P = 0.01		P = 0.02
Thyroxine				
Not taken	670 (95.7)	0.27 (0.22)	682 (97.4)	0.27 (0.22)
Taken	30 (4.3)	0.28 (0.20)	18 (2.6)	0.30 (0.17)
		P = 0.85		P = 0.56
Hypolipidaemics				
Not taken	642 (91.7)	0.27 (0.22)	677 (96.7)	0.27 (0.22)
Taken	58 (8.3)	0.32 (0.24)	23 (3.3)	0.24 (0.20)
		P = 0.06		P = 0.57

Mean flow rate was markedly higher among the four individuals who were taking ACEIs at both baseline and five years, but there was higher variance among those four, indicating that their range of flow rates was wide; in fact, the flow rates recorded for those individuals were 0.02, 0.35, 0.91 and 1.00, and the person with the lowest of those was taking three different antihypertensive drugs. There was no difference in mean flow rate between those who were taking ACEIs at five years and people who were not. Flow rate also appeared to be higher among those who were taking hypolipidaemic medication at five years, but this was not significant, and there was no effect apparent among the continuous users. Exposure to antidepressant medication was associated with lowered flow rates, both among those taking them at baseline and five years, and those taking them at five years only. The variance was greater among the latter, but it was still substantially less than that observed among the remainder of the sample.

3.2.4.2.2 Bivariate analysis - Classification and Regression Tree (CART) approach

Two exploratory CART analyses were conducted; one for medication exposure at five years only, and the other for "continuous use" of medications. The analyses were conducted separately because the number-driven algorithm would have meant that the effects of the five-year-only exposure variables would have obscured those of the "continuous use" exposure variables anyway (and this was what was found during a preliminary analysis).

The outcome of the first CART analysis is presented in Figure 3.2. Mean flow rates were lower among those who were taking antidepressants; among the remainder, they were lower among individuals taking diuretics, but not among those who were taking a diuretic and an ACE inhibitor concurrently. Individuals who were taking hypolipidaemic drugs (without a concurrent antidepressant or diuretic) had higher mean flow rates.

The outcome of the second CART analysis is presented in Figure 3.3. A lower unstimulated flow rate was associated with the taking of antidepressants at baseline and five years. Flow rates were also lower among those: who were not taking antidepressants; people who were taking antiulcer drugs at both stages; and those were not taking antiulcer drugs but were taking a cardiac inotropic at baseline and five years. It is noteworthy that the mean flow rate for people taking antidepressants at baseline and five years was lower than those for people were taking them at five years only.

3.2.4.2.3 Multivariate model

The significant predictors from each CART analysis were entered into a single linear regression analysis using mean unstimulated flow rate as the dependent variable, and the following first-order potential explanatory variables: sex, age, alcohol use (defined as reported use of alcohol in the previous month), and current smoking status. The outcome of the multivariate analysis is presented in Table 3.27. Because both "continuous antidepressant use' and "antidepressant use at five years only" emerged from the CART analyses as possible predictors, both were entered into the model, but with the latter variable as the "Starters" (Table 3.22) in order to distinguish them from the continuous users. When those two antidepressant exposure variables ("continuous use" and "starters") were entered into the model, the latter was not a significant predictor; it was omitted and the model repeated.

Figure 3.2: CART tree pattern for unstimulated flow-rate using medication exposure at five years only

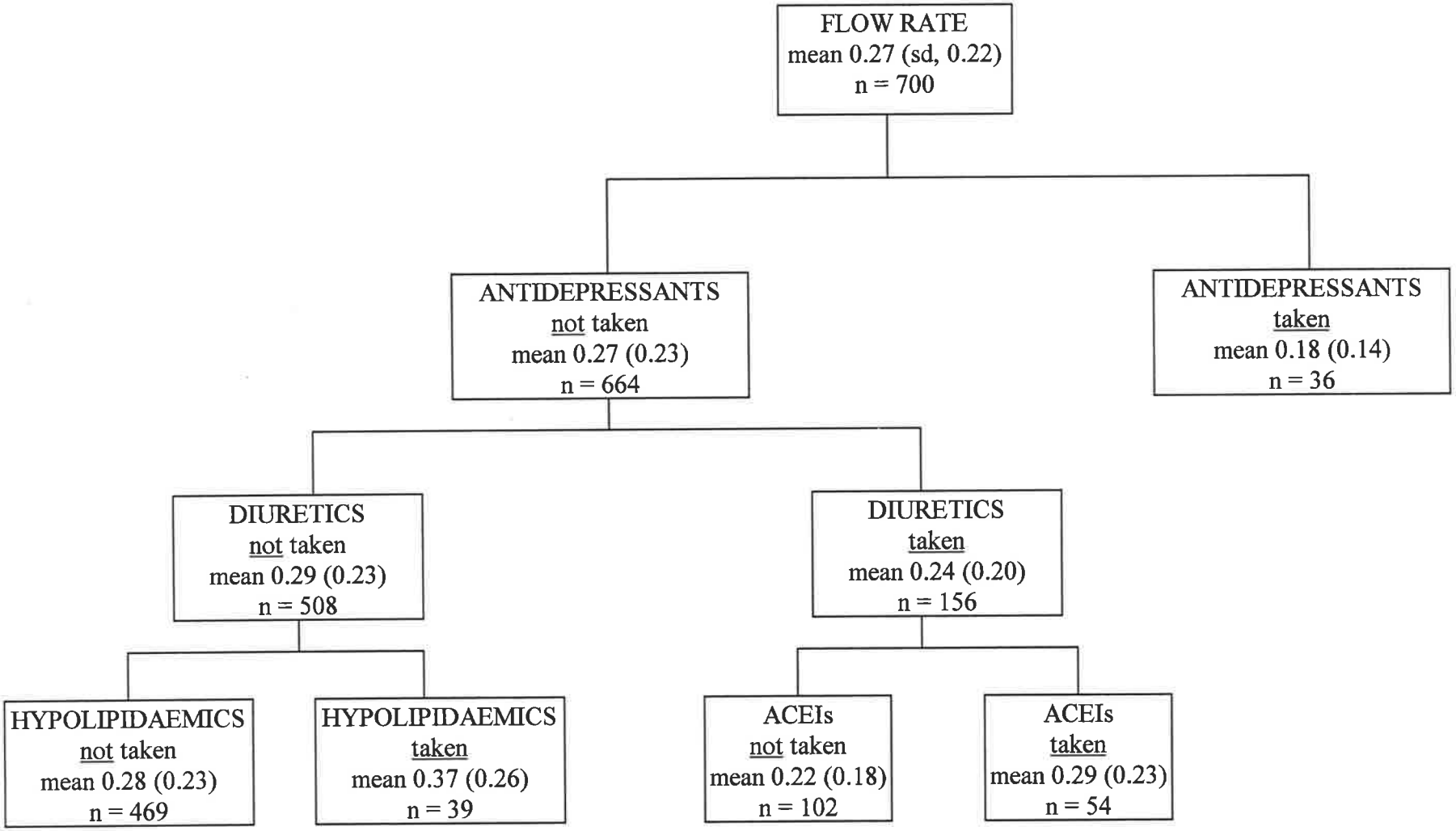


Figure 3.3: CART tree pattern for unstimulated flow-rate using medication exposure at baseline and five years ("continuous users")

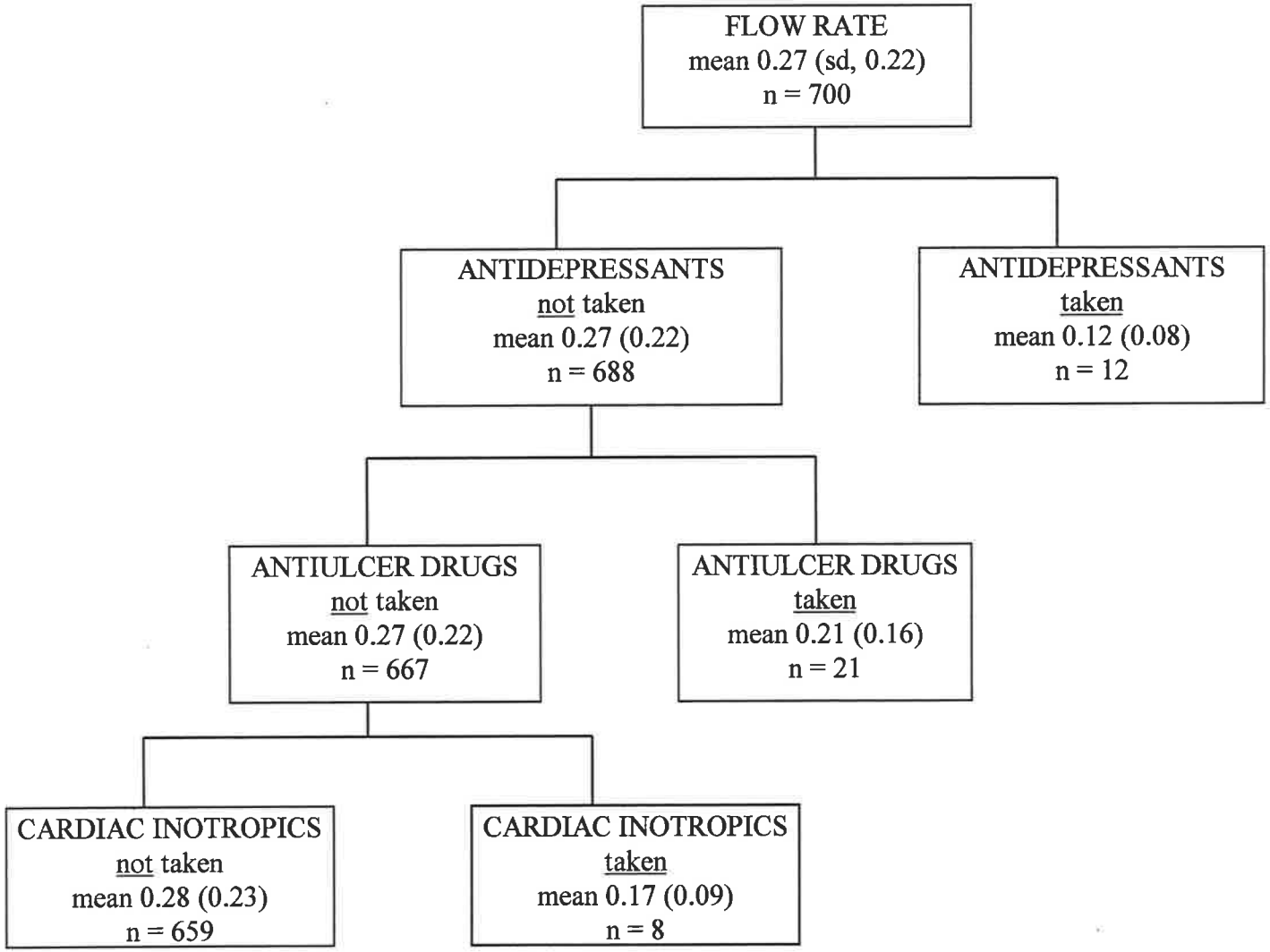


Table 3.27: Linear regression model for unstimulated flow-rate

	B	Standard error of B	95% CI[a] for B	Significance of T
Antidepressants at baseline and at 5 years	-0.161	0.064	-0.286, -0.036	<0.05
Hypolipidaemics at 5 years*	0.101	0.035	0.032, 0.170	<0.01
Cardiac inotropic at baseline and at 5 years	-0.117	0.078	-0.270, 0.036	0.13
Antiulcer drug at baseline and at 5 years	-0.065	0.048	-0.159, 0.029	0.18
Diuretic at 5 years without ACEI	-0.042	0.024	-0.089, 0.005	0.08
ACEI at 5 years without diuretic	0.001	0.027	-0.052, 0.054	0.98
Diuretic with ACEI at 5 years	0.072	0.037	-0.001, 0.145	0.05
Female	-0.067	0.017	-0.100, -0.034	<0.0001
Age 70+	-0.022	0.019	-0.059, 0.015	0.25
Cigarette smoker	0.108	0.035	0.039, 0.177	<0.01
Current drinker	0.019	0.017	-0.014, 0.052	0.26
Constant	0.370	0.034	0.303, 0.437	<0.0001

$R^2 = 0.074$

[a]Confidence interval
[b]Exposure to hypolipidaemics at five years in the absence of antidepressants and diuretics

The model accounted for only 7.4 per cent of the variance in unstimulated whole-salivary flow rate. Taking long-term antidepressants was associated with a lowering of unstimulated flow rate, whereas taking hypolipidaemic drugs was associated with a higher flow, as was being a current cigarette smoker. Being female predicted a lower flow rate.

3.2.5 Xerostomia

This section is divided into two parts: first, the development and testing of the Xerostomia Inventory is described; and second, the occurrence of xerostomia is described, including the bivariate and multivariate associations with medication exposure.

3.2.5.1 The Xerostomia Inventory

Xerostomia questionnaires (Appendix 3) were mailed to the 708 people (75.4 per cent) who had a dental examination appointment. The questionnaires were completed and returned by 649 (91.7 per cent) of those individuals, of whom 201 (31.0 per cent) were from Mt Gambier and 448 (69.0 per cent) were Adelaide residents. Where there were difficulties in getting co-operation from participants, priority was given to the dental examination rather than the saliva collection; consequently, saliva samples were collected from 676 (95.5 per cent) of those examined.

Both xerostomia inventory questionnaire and salivary flow-rate data were available for 636 individuals (89.8 per cent), and 662 (93.5 per cent) supplied saliva samples and answered the standard question.

Responses to individual items are shown in Table 3.28. For all items, "Never" was the most frequent response.

Table 3.28 Responses to individual XI items (N = 649)

	Never	Hardly ever	Occasionally	Fairly often	Very often	Missing
I sip liquids to aid in swallowing food	437	96	83	22	9	2
My mouth feels dry when eating a meal	450	116	63	12	5	3
I get up at night to drink	306	115	152	42	32	2
I have difficulty in eating dry foods	404	119	86	23	12	5
My mouth feels dry	214	154	207	51	18	5
I suck sweets or cough lollies to relieve dry mouth	404	103	106	24	10	2
I have difficulties swallowing certain foods	435	118	67	18	11	0
I have a burning sensation in my gums	574	39	28	2	2	4
I have a burning sensation in my tongue	584	28	15	12	6	4
My gums itch	592	35	14	3	2	3
My tongue itches	583	37	19	5	1	4
The skin of my face feels dry	334	90	150	43	29	3
My eyes feel dry	339	89	149	42	20	10
My lips feel dry	242	150	186	49	18	4
The inside of my nose feels dry	328	106	154	38	16	7

The initial factor analysis revealed three eigen values greater than one (5.06, 1.85 and 1.26 respectively), and solutions with one, two and three factors were considered. Inspection of the loadings after varimax rotation—as well as examination of the scree plot test—suggested that two factors provided the best solution. The first factor explained 29.7 per cent of the variance, while the second explained 8.9 per cent. The factor loadings which show how each item correlated with the underlying latent variable are shown in Table 3.29.

Two scales were constructed by summing the responses to the items which loaded on each factor. The correlations between the unweighted factor scales and those constructed with optimal weighting were 0.93 for the first scale and 0.95 for the second, indicating that the unweighted summated scales represented the underlying factors well. Coefficient α was 0.84 for the first scale, and 0.80 for the second scale. The Factor 1 scale was designated the Xerostomia Inventory (XI) score, while the Factor 2 scale was named the Burning Mouth Syndrome (BMS) score. The correlation between the two scales was positive and significant ($r = 0.40$; $P < 0.01$).

Table 3.29: Outcome of the XI factor analysis[a]

	Factor 1 *"Xerostomia"*	Factor 2 *"Burning mouth syndrome" (BMS)*
I sip liquids to aid in swallowing food (SIPLIQ)	0.69	
My mouth feels dry when eating a meal (MOUTHDRY)	0.74	
I get up at night to drink (NITDRINK)	0.45	
My mouth feels dry (DRYMOUTH)	0.54	
I have difficulty in eating dry foods (DRYFOOD)	0.74	
I suck sweets or cough lollies to relieve dry mouth (SUCK)	0.46	
I have difficulties swallowing certain foods (DIFFSWAL)	0.69	
The skin of my face feels dry (DRYSKIN)	0.39	
My eyes feel dry (EYESDRY)	0.42	
My lips feel dry (LIPSDRY)	0.42	
The inside of my nose feels dry (NOSEDRY)	0.42	
I have a burning sensation in my gums (BURNGUMS)		0.61
I have a burning sensation in my tongue (BURNTONG)		0.72
My gums itch (GUMITCH)		0.65
My tongue itches (TONGITCH)		0.77
Eigen value	5.06	1.85

[a]Order of items in questionnaire: SIPLIQ, MOUTHDRY, LIPSDRY, DIFFSWAL, DRYMOUTH, NITDRINK, GUMITCH, BURNGUMS, TONGITCH, BURNTONG, EYESDRY, DRYFOOD, NOSEDRY, SUCK, DRYSKIN.

Responses to the standard question *"How often does your mouth feel dry?"* from participants who returned XI questionnaires are presented in Table 3.30, along with mean XI and BMS scale scores for each level of the standard question.

Table 3.30: Responses to the standard question and comparison with mean factor scale scores

How often does your mouth feel dry?	Number (%)[a]	Mean XI score (sd)[b]	Mean BMS scale score (sd)[c]
Never	196 (31.4)	16.97 (5.54)	4.37 (1.51)
Occasionally	299 (47.8)	19.49 (3.43)	4.51 (1.27)
Frequently	108 (17.3)	24.54 (7.47)	4.85 (2.20)
Always	22 (3.5)	31.29 (9.71)	6.67 (3.10)
	625 (100.0)	19.95 (7.03)	4.60 (1.67)

[a]Number of participants who responded to the standard question and who also returned XI questionnaires

[b]Oneway ANOVA (Scheffe; $P < 0.0001$): the scores for all four groups differ

[c]Oneway ANOVA (Scheffe; $P < 0.0001$): the score for the *Always* group differs from the other three

The correlation between responses to the standard question and XI scores was 0.42 ($P < 0.01$). There was no difference between males and females in their responses to the standard question, but XI scores differed significantly between males (19.34; sd, 6.85) and females (20.67; sd, 7.19; ANOVA, $P < 0.05$). The correlation between BMS scores and the standard question was 0.16 ($P < 0.01$), but there were no significant gender differences in BMS scores. Across the sample, XI scores were not correlated with age ($r = 0.03$; $P = 0.41$), and BMS scores were also not correlated with age ($r = 0.005$; $P = 0.68$).

Of the individual items, only "My mouth feels dry" showed a significant correlation with unstimulated whole salivary flow rate, although this was very weak ($\rho = -0.09$; $P < 0.05$). Correlation coefficients for the others ranged from -0.08 to 0.07, but none was statistically significant. There was no correlation between XI scores and unstimulated whole salivary flow rates ($r = -0.05$; $P = 0.39$). The correlation between

responses to the standard question and unstimulated whole salivary flow rates was also very weak, but it reached statistical significance (Spearman's $\rho = -0.10$; $P = 0.01$). Thus, both the standard question and the XI scale scores were negatively correlated with the unstimulated salivary flow rate. The correlation between BMS scores and salivary flow rate was positive, but not significant ($r = 0.009$; $P = 0.68$).

Associations between medication exposures and XI scores are presented in Section 3.2.5.3.1.

3.2.5.2 Further testing of the Xerostomia Inventory: the validation study

The outcome of the XI validation study is presented here. Initially, there were 57 in the *Normal* group and 78 in the *Onset* group. The characteristics of each group are presented in Table 3.31.

Table 3.31: Characteristics of the *Onset* and *Normal* groups

	Onset group	*Normal* group
Mean age (SD)	63 (13)	75 (7)
Age range	29 to 87	52 to 90
Number of females (%)	16 (28.1)	18 (32.7)
Number initially recruited	78	58[a]
Number remaining at end of study (%)	57 (72.2)	55 (96.6)
Mean baseline XI score (sd)	23.81 (8.99)	20.04 (7.27)
Per cent responding 'Frequently' or 'Always' to the standard question at baseline	21.1	14.5

[a]Questionnaires initially sent out to 71 individuals who were sampled, but only 58 responded to the baseline mail-out. It is not known how many of those who did not respond had moved from the address on the Foundation's records, or were otherwise unavailable.

The age and sex characteristics of the 21 individuals who were lost to follow-up from the *Onset* group did not differ from those who remained in the study.

The mean XI scores and the proportion responding 'Frequently' or 'Always' to the standard question over the study period are presented in Table 3.32.

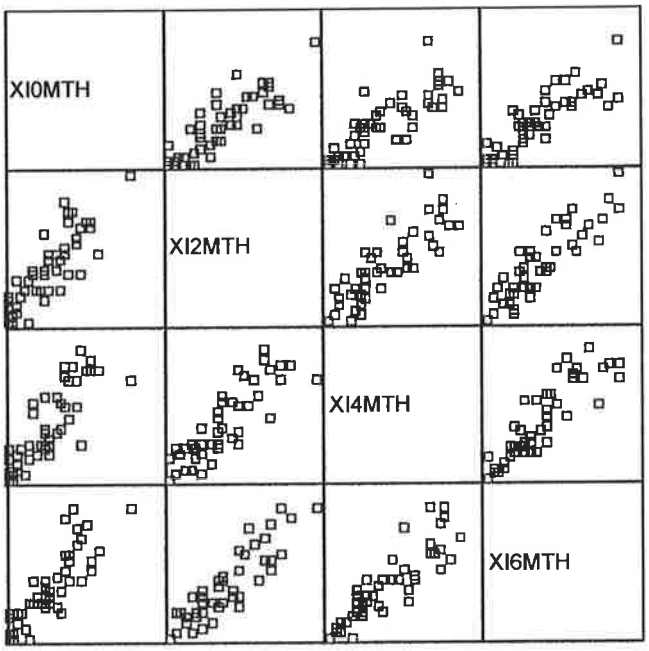
Table 3.32: XI scores and proportion responding 'Frequently' or 'Always' to the standard question over the duration of the validation study

	Mean XI score (sd)			
	Onset group		*Normal* group	
Stage of study				
Baseline	23.81 (8.99)[a]	(1 missing)	20.04 (7.27)	
2 months	31.43 (9.88)	(1 missing)	20.07 (7.04)	(1 missing)
4 months	31.00 (9.64)	(2 missing)	20.81 (7.39)	(3 missing)
6 months	31.12 (9.43)		19.82 (6.88)	
	Dry mouth 'Frequently' or 'Always' (%)			
	Onset group		*Normal* group	
Stage of study				
Baseline	12 (21.1)[b]		8 (14.5)	
2 months	38 (67.9)	(1 missing)	9 (16.3)	(3 missing)
4 months	33 (60.0)	(2 missing)	11 (21.6)	(4 missing)
6 months	33 (58.9)	(1 missing)	12 (21.9)	(5 missing)

[a]Paired t-tests: the mean baseline score differs from those at 2, 4 and 6 months; the latter three scores did not differ from one another.
[b] χ^2 tests: the proportion responding 'Frequently' or 'Always' differs from that at 2, 4 and 6 months; the latter three did not differ from one another.

Baseline XI scores were higher in the *Onset* group. In the *Onset* group, the XI scores and the proportion responding 'Frequently' or 'Always' to the standard question increased substantially between baseline and two months, whereas there was no significant change in the *Normal* group. Scatterplot matrices of the scores in each group at each stage are presented in Figure 3.4. They depict: (1) the relative stability of the scores among the *Normal* group across the study period (indicated by the close clustering of the data-points about the diagonal); and (2) the substantial change among the *Onset* group between baseline and two months (indicated by the relative scattering of the data-points about the diagonal for the XI0MTH and XI2MTH overlap) .

Scatterplot matrix - Normal group



Scatterplot matrix - Onset group

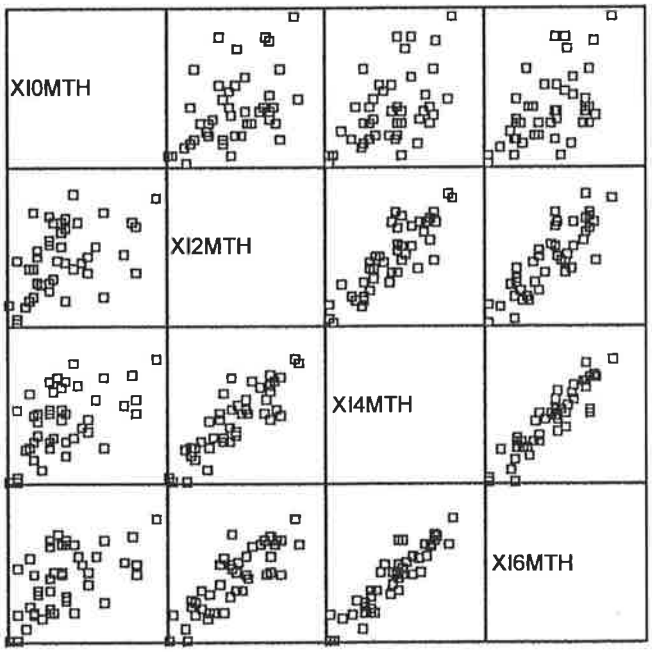


Figure 3.4: Scatterplot matrices for the Normal and Onset groups

The XI score at six months was modelled using linear regression (Table 3.33). The independent variables used were the baseline XI score, age, sex, and group membership.

Table 3.33: Linear regression model of six-month XI scores in the validation study[a]

	B	Standard error of B	95% CI[a] for B	Significance of T
Age	0.025	0.059	-0.091, 0.141	0.68
Female	-0.718	1.377	-3.417, 1.981	0.60
Baseline XI score	0.640	0.077	0.489, 0.791	<0.001
Membership of *Onset* group	9.172	1.496	6.240, 12.104	<0.001
Constant	5.378	4.716	-3.865, 14.621	0.26

[a] $R^2 = 0.594$

The model explained 59.4 per cent of the variance in mean XI scores at six months. The baseline score was a significant predictor. Membership of the *Onset* group was associated with, on average, an increase in XI score by 9 points by six months.

3.2.5.3 The occurrence of xerostomia (prevalence and severity)

The sections which follow describe the prevalence and severity of xerostomia among the sample, including its degree of concurrence with SGH, and its bivariate associations with medication exposure.

3.2.5.3.1 The prevalence of xerostomia

The standard xerostomia question ("How often does your mouth feel dry?") was used to define xerostomia prevalence. Responses to that question were as follows: "Never", 219 responses (32.1 per cent); "Occasionally", 324 responses (47.4 per cent); "Frequently", 116 responses (17.0 per cent); and "Always", 24 responses (3.5 per cent). There was a very weak correlation between unstimulated whole salivary flow rate and responses to the standard question (Spearman's $\rho = -0.10$; $P = 0.01$). The "Frequently" and "Always" responses were collapsed into a single category to identify cases of xerostomia.

The prevalence of xerostomia was 20.7 per cent (N = 143), and that of SGH was 22.6 per cent (N = 158).

3.2.5.3.2 The concurrence of SGH and xerostomia

Data on the occurrence of SGH and xerostomia are presented in Table 3.34 for those sample members for whom data on both aspects were available. Their prevalence of SGH was 22.1 per cent, and their prevalence of xerostomia was 20.5 per cent. Only 39 participants (5.7 per cent) had both conditions, and they comprised 15.5 per cent of the 251 who had either condition. Almost two-thirds of the sample had neither condition.

Table 3.34. Association between xerostomia and salivary gland hypofunction (SGH)[a] by gender

Sexes combined:

		Salivary gland hypofunction		
		Yes	No	Total
Xerostomia	Yes	39 (5.7%)	101 (14.8%)	140 (20.5%)
	No	112 (16.4%)	432 (63.2%)	544 (79.5%)
	Total	151 (22.1%)	533 (77.9%)	684 (100.0%)

Females only:

		Salivary gland hypofunction		
		Yes	No	Total
Xerostomia	Yes	26 (8.1%)	51 (15.9%)	77 (24.1%)
	No	59 (18.4%)	184 (57.5%)	243 (75.9%)
	Total	85 (26.6%)	235 (73.4%)	320 (100.0%)

Males only:

		Salivary gland hypofunction		
		Yes	No	Total
Xerostomia	Yes	13 (3.6%)	50 (13.7%)	63 (17.3%)
	No	53 (14.6%)	248 (68.1%)	301 (82.7%)
	Total	66 (18.1%)	298 (81.9%)	364 (100.0%)

[a]Case definitions: standard question response "Frequently" or "Always"; SGH unstimulated flow rate <0.1 ml/min

Data on the associations between socio-demographic attributes and xerostomia prevalence (using the standard-question approach for case definition) are presented in Table 3.35.

Table 3.35: Xerostomia (standard-question definition) by age group, gender and dentate status

All participants (N = 689)	**"Non-xerostomic"[a]**	**"Xerostomic"[b]**
Age group		
65-69 years	148 (80.0%)	37 (20.0%)
70-79 years	247 (79.9%)	62 (20.1%)
80+ years	151 (77.4%)	44 (22.6%)
		P = 0.76
Gender		
Female	301 (82.5%)	64 (17.5%)
Male	245 (75.6%)	79 (24.4%)
P-value		P = 0.03
All combined	546 (79.2%)	143 (20.8%)
Dentate participants only (N = 495):		
Age group		
65-69 years	111 (80.4%)	27 (19.6%)
70-79 years	183 (79.9%)	46 (20.1%)
80+ years	98 (76.6%)	30 (23.4%)
		P = 0.69
Gender		
Male	226 (81.6%)	51 (18.4%)
Female	166 (76.1%)	52 (23.9%)
		P = 0.14
All combined	392 (79.2%)	103 (20.8%)

[a]19 missing responses to the standard question among this group
[b]Individuals who answered "Never" or "Occasionally" to the standard question.
[c]Individuals who answered "Frequently" or "Always" to the standard question.
[d]10 missing responses to the standard question among this group

3.2.5.3.3 Medication exposure and xerostomia prevalence

The bivariate findings which follow are from two separate analyses of xerostomia prevalence and medication exposure: as with the flow rate findings, the first is a "conventional" bivariate comparison of the proportion with xerostomia among individuals exposed to a particular medication type compared with those who were not

taking it; and the second is the outcome of the AID analysis of medication exposure and xerostomia prevalence.

Bivariate analysis - conventional approach

The outcome of the bivariate analysis of medication exposure at five years and xerostomia prevalence is presented in Table 3.36.

Table 3.36: Prevalence of xerostomia by medication exposure at five years, and at baseline and 5 years (N = 689)

	Taken at five years only		Taken at baseline and five years ("Continuous users")	
Medication category	Number (%)	Dry mouth "Always" or "Frequently"	Number	Dry mouth "Always" or "Frequently"
Antihypertensives				
Not taken	331 (48.0)	48 (14.5)	459 (67.2)	80 (17.4)
Taken	358 (52.0)	95 (26.5)	224 (32.8)	60 (26.8)
		P < 0.0001		P = 0.004
β-blockers				
Not taken	589 (85.5)	121 (20.5)	656 (96.0)	136 (20.7)
Taken	100 (14.5)	22 (22.0)	27 (4.0)	4 (14.8)
		P = 0.74		P = 0.46
Diuretics				
Not taken	523 (75.9)	93 (17.8)	600 (87.8)	118 (19.7)
Taken	166 (24.1)	50 (30.1)	83 (12.2)	22 (26.5)
		P = 0.001		P = 0.15
ACEIs				
Not taken	568 (82.4)	118 (20.8)	679 (99.4)	138 (20.3)
Taken	121 (17.6)	25 (20.7)	4 (0.6)	2 (50.0)
		P = 0.98		P = 0.14
CCBs				
Not taken	551 (80.0)	108 (19.6)	627 (91.8)	126 (20.1)
Taken	138 (20.0)	35 (25.4)	56 (8.2)	14 (25.0)
		P = 0.14		P = 0.38
Sympatholytics				
Not taken	663 (96.2)	133 (20.1)	673 (98.5)	136 (20.2)
Taken	26 (3.8)	10 (38.5)	10 (1.5)	4 (40.0)
		P = 0.023		P = 0.12
Cardiac drugs				
Not taken	638 (92.6)	128 (20.1)	675 (98.8)	137 (20.3)
Taken	51 (7.4)	15 (29.4)	8 (1.2)	3 (37.5)
		P = 0.11		P = 0.23
Anginals				
Not taken	637 (82.7)	123 (19.3)	661 (96.8)	131 (19.8)
Taken	52 (17.3)	20 (38.5)	22 (3.2)	9 (40.9)
		P = 0.001		P = 0.02
Analgesics				
Not taken	483 (70.1)	81 (16.8)	601 (88.0)	113 (18.8)
Taken	206 (29.9)	62 (30.1)	82 (12.0)	27 (32.9)
		P < 0.0001		P = 0.003

Simple				
Not taken	667 (96.8)	136 (20.4)	682 (99.9)	140 (20.5)
Taken	22 (3.2)	7 (31.8)	1 (0.1)	0 (0.0)
		P = 0.19		P = 0.61
NSAIDs				
Not taken	590 (85.6)	116 (19.7)	637 (93.3)	124 (19.5)
Taken	99 (14.4)	27 (27.3)	46 (6.7)	16 (34.8)
		P = 0.08		P = 0.01
Antigouts				
Not taken	646 (93.8)	133 (20.6)	660 (96.6)	135 (20.5)
Taken	43 (6.2)	10 (23.3)	23 (3.4)	5 (21.7)
		P = 0.68		P = 0.88
Narcotics & comb. preps				
Not taken	613 (89.0)	114 (18.6)	675 (98.8)	137 (20.3)
Taken	76 (11.0)	29 (38.2)	8 (1.2)	3 (37.5)
		P < 0.0001		P = 0.23
Antiasthma drugs				
Not taken	633 (91.9)	131 (20.7)	664 (97.2)	138 (20.8)
Taken	56 (8.1)	12 (21.4)	19 (2.8)	2 (10.5)
		P = 0.90		P = 0.28
HRT				
Not taken	649 (94.2)	132 (20.3)	671 (98.2)	136 (20.3)
Taken	34 (5.8)	11 (27.5)	12 91.8)	4 (33.3)
		P = 0.19		P = 0.27
Antiulcer drugs				
Not taken	582 (84.5)	106 (18.2)	662 (96.9)	129 (19.5)
Taken	107 (15.5)	37 (34.6)	21 (3.1)	11 (52.4)
		P = 0.0001		P < 0.0001
Hypoglycaemics				
Not taken	645 (93.6)	135 (20.9)	660 (96.6)	137 (20.8)
Taken	44 (6.4)	8 (18.2)	23 (5.4)	3 (13.0)
		P = 0.66		P = 0.37
Daily aspirin				
Not taken	481 (69.8)	106 (22.0)	633 (92.7)	133 (21.0)
Taken	204 (30.2)	37 (17.8)	50 (7.3)	7 (14.0)
		P = 0.21		P = 0.24
Psychotherapeutics				
Not taken	638 (92.6)	127 (19.9)	663 (97.1)	135 (20.4)
Taken	51 (7.4)	16 (31.4)	20 (2.9)	5 (25.0)
		P = 0.05		P = 0.61
Antidepressants				
Not taken	654 (94.9)	134 (20.5)	672 (98.4)	135 (20.1)
Taken	35 (5.1)	9 (25.7)	11 (1.6)	5 (45.5)
		P = 0.46		P = 0.04
Thyroxine				
Not taken	658 (95.5)	132 (20.1)	665 (97.4)	133 (20.0)
Taken	31 (4.5)	11 (35.5)	18 (2.6)	7 (38.9)
		P = 0.04		P = 0.05
Hypolipidaemics				
Not taken	631 (91.6)	133 (21.1)	660 (96.6)	134 (20.3)
Taken	58 (8.4)	10 (17.2)	23 (3.4)	6 (26.1)
		P = 0.49		P = 0.50

The taking of anginals, antiulcer drugs, antidepressants at both baseline and five years was associated with a higher prevalence of xerostomia. For exposure at five years, a higher prevalence of the condition was associated with taking a diuretic, a sympatholytic antihypertensive, an anginal, a narcotic analgesic, an antiulcer drug or thyroxine.

Bivariate analysis - Classification and Regression Tree (CART) approach

As with flow rate, two exploratory CART analyses were conducted in order to explore the effects of polypharmacy on the dependent variable; one for medication exposure at five years only, and the other for "continuous use" of medications. The outcomes of the two CART analyses are presented in Figures 3.5 and 3.6.

In the analysis of medication exposure at five years only, the prevalence of xerostomia was higher among individuals who were taking narcotic analgesics. Among those who were not taking that category of medication, people taking diuretics had a higher prevalence of xerostomia, as did those who were not taking diuretics but were taking psychotherapeutic drugs. Individuals taking antiulcer drugs had a higher prevalence of xerostomia, as did those who were taking sympatholytic antihypertensive preparations, particularly in conjunction with NSAIDs. Only one medication type emerged from the CART analysis of the "continuous users": those taking antiulcer drugs at baseline and five years had a higher prevalence of xerostomia.

Multivariate model

The medications which were identified as significant predictors from those analyses were entered into a single logistic regression analysis using xerostomia prevalence as the dependent variable, and the following first-order potential explanatory variables:

Figure 3.5: CART tree pattern for xerostomia prevalence using medication exposure at five years only

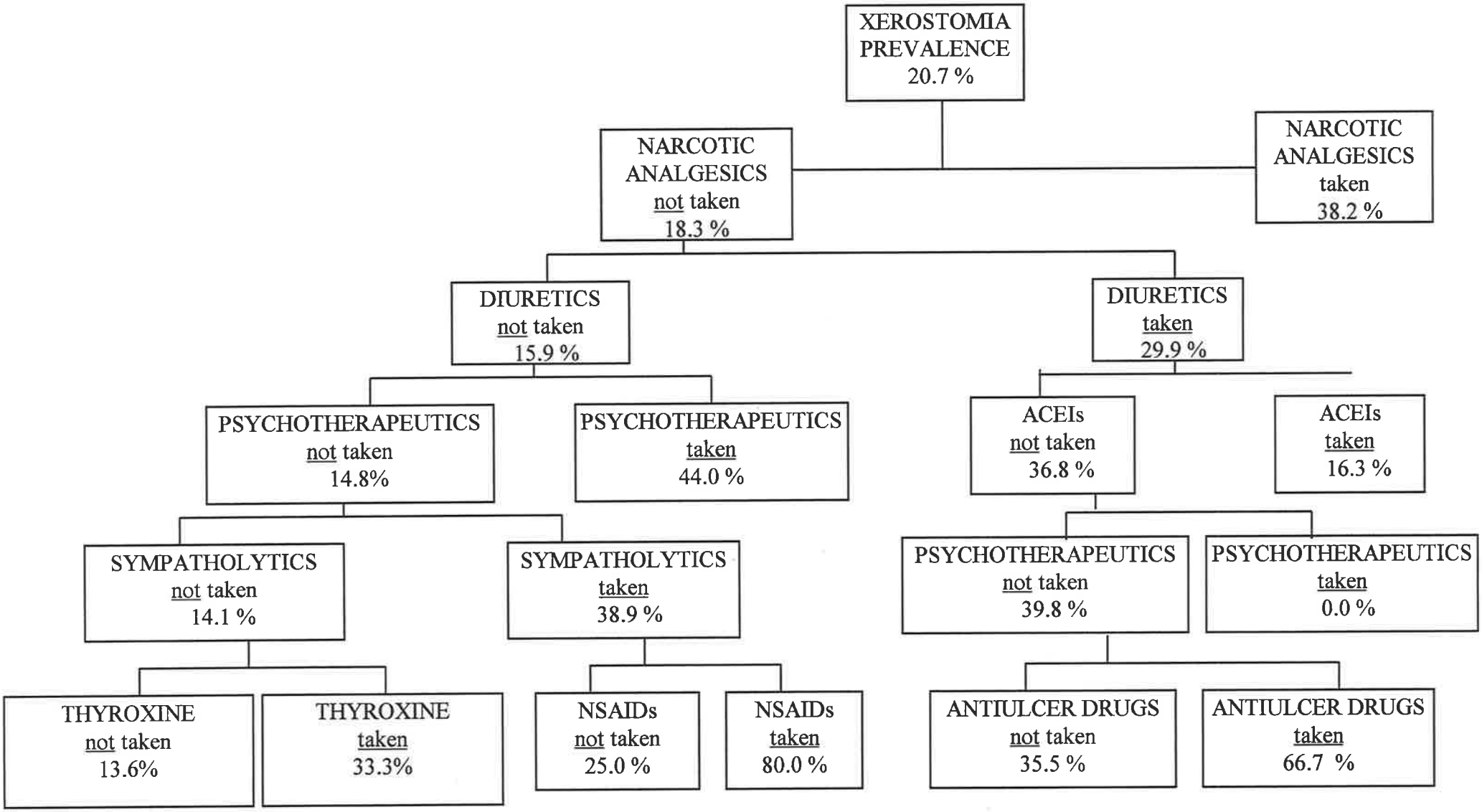
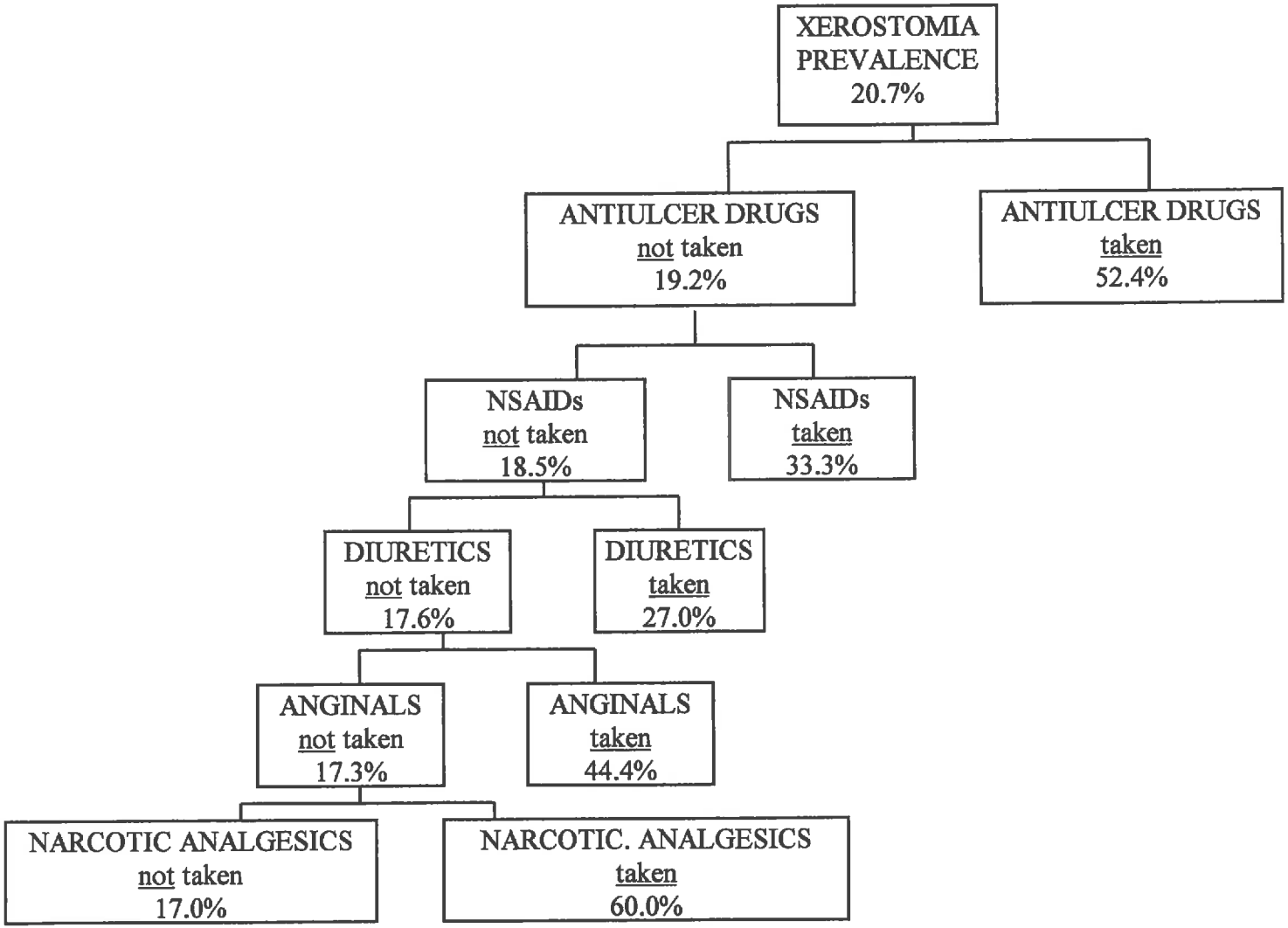


Figure 3.6: CART tree pattern for xerostomia prevalence using medication exposure at baseline and five years



sex, age, alcohol use (defined as reported use of alcohol in the previous month), and current smoking status. The outcome is presented in Table 3.37.

Table 3.37: Logistic regression model for xerostomia defined by the standard question (dry mouth "Always" or "Frequently")

	B	SE	Odds ratio (95% CI)
Female	0.176	0.184	1.19 (0.83, 1.71)
Age at baseline	0.006	0.013	1.01 (0.98, 1.03)
Current smoker	-0.043	0.368	0.96 (0.47, 1.97)
Alcohol drunk in the last month	0.068	0.183	1.07 (0.75, 1.53)
Narcotic & comb. analgesics at 5 years	0.798	0.275	2.22 (1.30, 3.81)
Diuretics at 5 years	0.615	0.216	1.85 (1.21, 2.83)
Psychotherapeutics at 5 years	0.309	0.342	1.36 (0.70, 2.66)
ACE inhibitor antihypertensives at 5 years	-0.294	0.266	0.75 (0.44, 1.26)
Antiulcer drugs at baseline and 5 years	1.512	0.466	4.56 (1.83, 11.36)
Sympatholytic antihypertensives at 5 years	0.942	0.427	2.57 (1.11, 5.92)
NSAIDs at 5 years	0.207	0.260	1.23 (0.74, 2.05)
Thyroxine at 5 years	0.686	0.406	1.99 (0.90, 4.40)

[a]Model $\chi^2 = 44.73$; 12 df; 80.20% correctly predicted

Xerostomia prevalence at five years was associated with taking narcotic-containing analgesics at five years, or sympatholytic antihypertensives at five years, or by taking antiulcer drugs at both baseline and five years. Individuals taking the latter had over four times the odds of being a "case" of xerostomia.

3.2.5.3.1 The severity of xerostomia

Among the 438 dentate individuals for whom XI scores were able to be computed, the mean XI score was 19.57 (sd, 6.75) and the median score was 18.00. The mean XI scores of dentate and edentulous (20.91; sd, 7.78) participants were significantly different (ANOVA; P=0.04). The distribution of XI scores among dentate and edentulous individuals is presented in Table 3.38.

Table 3.38: Distribution of XI scores by dentate status

XI score	All participants (%)	Dentate only (%)
11	47 (7.7)	33 (7.5)
12	21 (3.5)	16 (3.7)
13	41 (6.8)	33 (7.5)
14	36 (5.9)	30 (6.8)
15	48 (7.9)	37 (8.4)
16	26 (4.3)	18 (4.1)
17	40 (6.6)	26 (5.9)
18	43 (7.1)	31 (7.1)
19	41 (6.8)	33 (7.5)
20	33 (5.4)	24 (5.5)
21	28 (4.6)	17 (3.9)
22	26 (4.3)	19 (4.3)
23	22 (3.6)	14 (3.2)
24	22 (3.6)	16 (3.7)
25	17 (2.8)	13 (3.0)
26	18 (3.0)	12 (2.7)
27	14 (2.3)	12 (2.7)
28	11 (1.8)	9 (2.1)
29	11 (1.8)	8 (1.8)
30	9 (1.5)	7 (1.6)
31	12 (2.0)	7 (1.6)
32	3 (0.5)	2 (0.5)
33	4 (0.7)	2 (0.5)
34	4 (0.7)	1 (0.2)
35	5 (0.8)	3 (0.7)
36	4 (0.7)	1 (0.2)
37	6 (1.0)	4 (0.9)
38	2 (0.3)	1 (0.2)
39	5 (0.8)	4 (0.9)
40	1 (0.2)	1 (0.2)
41	1 (0.2)	1 (0.2)
42	1 (0.2)	1 (0.2)
43	1 (0.2)	1 (0.2)
44	1 (0.2)	
45	1 (0.2)	1 (0.2)
46	1 (0.2)	
48	2 (0.3)	1 (0.2)
49	1 (0.2)	
Total	607 (100.0)	438 (100.0)
Mean (sd)	19.95 (7.03)	19.57 (6.75)

Bivariate analysis - "conventional" approach

Data from the bivariate analysis of XI scores and exposure to the most prevalent medication categories at five years are presented in Table 3.39.

Table 3.39: Mean XI scores by medications taken at five years, and at baseline and five years

	Taken at five years only (N = 619)		Taken at baseline and five years ("Continuous users") (N = 605)	
Medication category	Number (%)	Mean XI (sd)	Number (%)	Mean XI (sd)
Antihypertensives				
Not taken	300 (48.5)	19.09 (6.49)	407 (67.3)	19.55 (6.77)
Taken	319 (51.5)	20.75 (7.43)	198 (32.7)	20.61 (7.44)
		P = 0.003		P = 0.08
β-blockers				
Not taken	530 (85.6)	20.16 (7.10)	579 (95.7)	19.93 (7.01)
Taken	89 (14.4)	18.69 (6.50)	26 (4.3)	19.27 (6.98)
		P = 0.07		P = 0.64
Diuretics				
Not taken	470 (75.9)	19.51 (6.83)	532 (87.9)	19.82 (7.00)
Taken	149 (24.1)	21.34 (7.47)	73 (12.1)	20.48 (7.06)
		P = 0.006		P = 0.45
ACEIs				
Not taken	511 (82.6)	19.89 (7.16)	602 (99.5)	19.88 (7.02)
Taken	108 (17.4)	20.20 (6.41)	3 (0.5)	23.67 (3.51)
		P = 0.68		P = 0.35
CCBs				
Not taken	498 (80.5)	19.49 (6.55)	555 (91.7)	19.68 (6.79)
Taken	121 (19.5)	21.84 (8.50)	50 (8.3)	22.28 (8.84)
		P = 0.001		P = 0.01
Sympatholytics				
Not taken	593 (95.8)	19.92 (7.08)	594 (98.2)	19.90 (7.03)
Taken	26 (4.2)	20.62 (5.85)	11 (19.9)	19.91 (5.86)
		P = 0.62		P = 0.99
Cardiac drugs				
Not taken	575 (92.9)	19.83 (6.94)	597 (98.7)	19.87 (6.96)
Taken	44 (7.1)	21.41 (8.11)	8 (1.3)	21.88 (10.12)
		P = 0.15		P = 0.42
Anginals				
Not taken	570 (92.1)	19.57 (6.68)	585 (96.7)	19.69 (6.77)
Taken	49 (7.9)	24.37 (9.26)	20 (3.3)	26.05 (10.52)
		P < 0.0001		P < 0.0001
Analgesics				
Not taken	433 (70.0)	19.36 (6.77)	532 (87.9)	19.66 (6.80)
Taken	186 (30.0)	21.31 (7.45)	73 (12.1)	21.62 (8.18)
		P = 0.002		P = 0.03
Simple				
Not taken	599 (96.8)	19.97 (7.08)	604 (99.9)	19.91 (7.01)
Taken	20 (3.2)	19.35 (5.48)	1 (0.1)	13.00 (—)
		P = 0.70		P = 0.33

NSAIDs				
Not taken	529 (85.5)	19.80 (7.06)	565 (93.4)	19.77 (6.91)
Taken	90 (14.5)	20.82 (6.83)	40 (6.6)	21.75 (8.14)
		P = 0.20		P = 0.08
Antigouts				
Not taken	583 (94.2)	19.83 (6.96)	585 (96.7)	19.79 (6.89)
Taken	36 (5.8)	21.83 (8.02)	20 (3.3)	22.90 (9.56)
		P = 0.10		P = 0.05
Narcotics and combination preps				
Not taken	550 (88.9)	19.63 (6.79)	595 (98.3)	19.87 (6.99)
Taken	69 (11.1)	22.43 (8.34)	10 (1.7)	21.60 (8.13)
		P = 0.002		P = 0.44
Antiasthma drugs				
Not taken	573 (92.6)	19.83 (6.92)	587 (97.0)	19.81 (7.03)
Taken	46 (7.4)	21.46 (8.27)	18 (3.0)	22.89 (5.54)
		P = 0.13		P = 0.07
HRT				
Not taken	573 (92.6)	19.76 (6.96)	594 (98.2)	19.84 (6.96)
Taken	32 (7.4)	22.34 (7.57)	11 (1.8)	23.09 (9.10)
		P = 0.04		P = 0.13
Antiulcer drugs				
Not taken	528 (85.3)	19.68 (6.85)	589 (97.4)	19.81 (6.95)
Taken	91 (14.7)	21.49 (7.85)	16 (2.6)	23.19 (8.55)
		P = 0.02		P = 0.06
Hypoglycaemics				
Not taken	582 (94.0)	19.90 (7.01)	587 (97.0)	19.90 (7.00)
Taken	37 (6.0)	20.68 (7.36)	18 (3.0)	19.94 (7.30)
		P = 0.52		P = 0.98
Daily aspirin				
Not taken	425 (68.7)	19.68 (6.67)	555 (91.7)	19.89 (6.93)
Taken	194 (31.3)	20.53 (7.74)	50 (8.3)	19.94 (7.86)
		P = 0.16		P = 0.96
Psychotherapeutics				
Not taken	575 (92.9)	19.88 (7.01)	586 (96.9)	19.88 (6.97)
Taken	44 (7.1)	20.84 (7.30)	19 (3.1)	20.47 (8.17)
		P = 0.38		P = 0.72
Antidepressants				
Not taken	592 (95.6)	19.87 (7.00)	594 (98.2)	19.82 (6.95)
Taken	27 (4.4)	21.63 (7.72)	11 (7.8)	24.18 (8.81)
		P = 0.20		P = 0.04
Thyroxine				
Not taken	591 (95.5)	19.81 (6.92)	588 (97.2)	19.83 (6.99)
Taken	28 (4.5)	22.89 (8.74)	17 (2.8)	22.18 (7.51)
		P = 0.02		P = 0.17
Hypolipidaemics				
Not taken	567 (91.6)	19.91 (7.00)	583 (96.4)	19.88 (7.00)
Taken	52 (8.4)	20.38 (7.39)	22 (3.6)	20.27 (7.31)
		P = 0.63		P = 0.80

XI scores were higher among individuals who were "continuous users" of CCB antihypertensives, anginals, and antidepressants, and among those who were taking diuretics, CCB antihypertensives, anginals, narcotic analgesics, hormone replacement therapy, antiulcer drugs or thyroxine at five years.

Bivariate analysis - Classification and Regression Tree (CART) approach

The outcome of the CART analysis of XI scores and medications taken at five years only is presented in Figure 3.7. Individuals who were taking anginals had more severe dry mouth symptoms, but those who were taking a concurrent β-blocker did not. Among those not taking anginals, those who were taking thyroxine had more severe dry mouth, and this was more severe if they were taking a concurrent diuretic. Taking HRT (hormone replacement therapy) was associated with more severe xerostomia among those taking neither thyroxine nor anginals.

The outcome of the CART analysis of XI scores and "continuous" medication use is presented in Figure 3.8. The use of anginals was associated with more severe xerostomia. Among those who were not taking anginals at baseline and five years, those taking antidepressants had higher XI scores. The "continuous" use of antiasthma drugs was also associated with higher XI scores among those who were not taking an anginal or an antidepressant at both stages.

Figure 3.7: CART tree pattern for Xerostomia Inventory scores using medication exposure at 5 years only

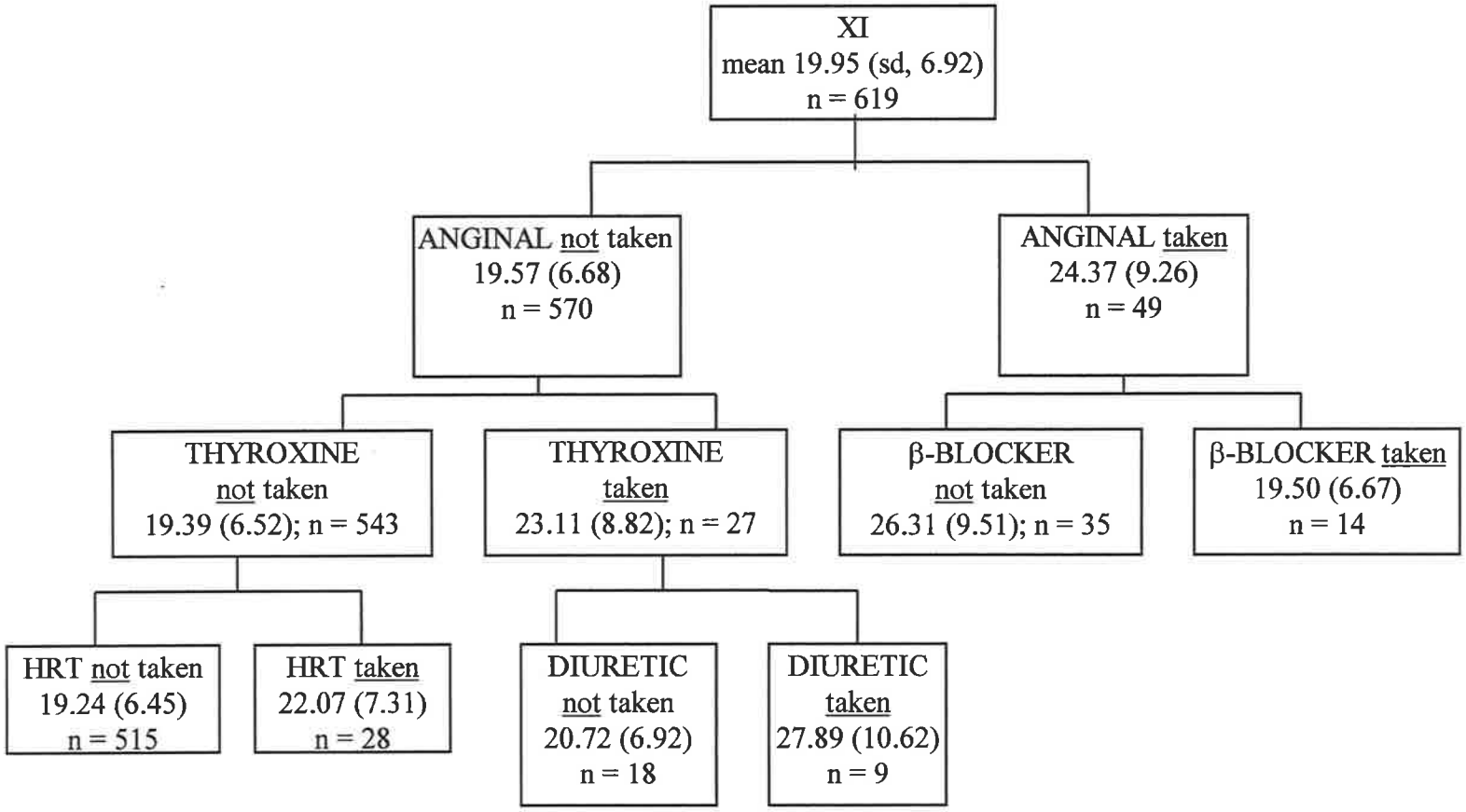
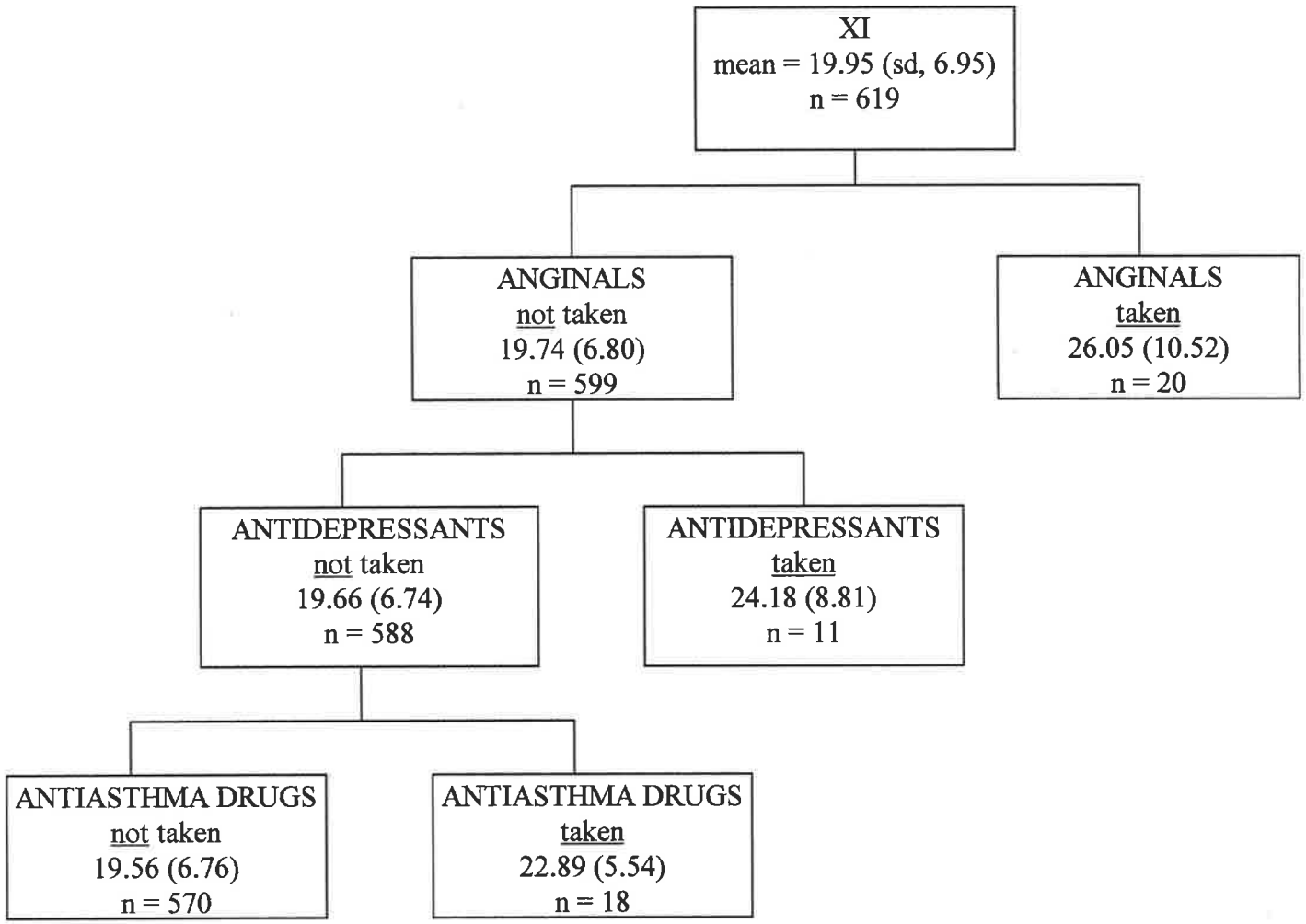


Figure 3.8: CART tree pattern for Xerostomia Inventory scores using medication exposure at baseline and five years ("continuous users")



Multivariate model

The significant predictors from each CART analysis were entered into a single linear regression analysis using the Xerostomia Inventory score as the dependent variable, and the following first-order potential explanatory variables: sex, age, alcohol use (defined as reported use of alcohol in the previous month), and current smoking status. The outcome is presented in Table 3.40. Because anginal use featured in both of the CART analyses for XI scores, another variable was created to identify those who had not taken them at baseline but were taking them at five years. The three anginal groups in the model are mutually exclusive.

Table 3.40: Linear regression model of Xerostomia Inventory scores obtained with the two approaches to medication exposure classification

	B	Standard error of B	95% CI[a] for B	Significance of T
Anginals at baseline & 5 yrs	3.442	1.812	-0.110, 6.994	0.06
β-blocker at 5 yrs	-1.381	0.838	-3.024, 0.261	0.10
Anginal at 5 yrs only without β-blocker	5.184	1.414	2.413, 7.955	<0.01
Anginal at 5 yrs only with β-blocker	0.758	2.509	-4.160, 5.676	0.76
Diuretic at 5 yrs	0.663	0.689	-0.687, 2.013	0.34
Thyroxine & diuretic at 5 yrs	7.808	2.351	3.200, 12.416	<0.01
Thyroxine without diuretic at 5 yrs	1.045	1.651	-2.191, 4.281	0.53
HRT at 5 yrs	2.625	1.356	-0.033, 5.283	0.05
Antiasthma drug at baseline & 5 yrs	3.313	1.631	0.116, 6.510	0.04
Antidepressants at baseline & 5 yrs	4.578	2.069	0.523, 8.633	0.03
Female	0.723	0.598	-0.449, 1.895	0.23
Age group	0.293	0.620	-0.922, 1.508	0.64
Cigarette smoking	1.233	1.137	-0.996, 3.462	0.28
Alcohol drunk in the last month	-0.210	0.575	-1.337, 0.917	0.72
Constant	17.912	1.160	15.638, 20.186	<0.01

($R^2 = 0.103$)

[a]Confidence Interval

The model explained 10.3 per cent of the variance about the mean XI score. XI scores were higher for: people taking anginals at five years without a concurrent β-blocker; those who were taking thyroxine and a diuretic at five years; or those who were using antidepressants at both data collections. HRT at five years almost reached significance. The lack of a significant association between XI scores and β-blockers, thyroxine or diuretics indicated that the anginal-β-blocker and thyroxine-diuretic interactions were independent.

The explanatory power of the model did not improve when age was entered as an untransformed variable instead of the three-category age-group variable.

3.2.6 Dental caries experience at five years

The sections which follow describe dental caries experience among the sample (1) at five years (*prevalence*), and (2) between baseline and the five-year data collection (*incidence* and *increment*). The retention of the sample is described first, followed by description of the distribution of coronal and root-surface caries *incidence* and *increment* among the sample. Increment is described in two ways: (a) the net caries increment (NCI), being the gross caries increment minus the reversals (thus assuming that all reversals were "true" reversals); and (b) the adjusted caries increment, which corrects the gross caries increment using a prevalence-based adjustment.

3.2.6.1 *Retention of the dentate sample*

At baseline, 848 individuals contributed data to the caries examination; at the five-year follow-up, 528 (62.3 per cent) remained, and 316 (37.7 per cent) had been lost. A comparison is presented in Table 3.41 of the baseline characteristics of those who remained and those who were lost to follow-up.

3.2.6.2 Dental caries severity and prevalence at five years

Dental caries data at five years were available for 528 individuals, among whom the mean number of missing teeth was 14.45 (sd, 7.91; range 0 to 31) The prevalence of at least one tooth having been lost was 99.4 per cent; that is, only 3 individuals had not lost any teeth (including third molars).

3.2.6.2.1 Coronal caries

Data on the prevalence and severity of coronal caries at five years by the socio-demographic characteristics of the sample are presented in Table 3.42.

Table 3.42: Coronal caries severity and number of missing teeth at five years, by socio-demographic characteristics

	DS[a] (sd)	FS (sd)	DFS (sd)	Number of missing teeth (sd)
All combined	0.22 (0.73)	17.75 (14.69)	17.97 (14.65)	14.45 (7.91)
Gender				
Male	0.30 (0.88)[b]	16.10 (14.24)[b]	16.40 (14.20)[b]	14.66 (7.91)
Female	0.12 (0.43)	20.00 (15.01)	20.12 (15.00)	14.17 (7.91)
Age group				
65-69	0.20 (0.55)	21.26 (15.64)[b]	21.46 (15.63)[b]	12.67 (8.02)[b]
70-79	0.20 (0.66)	17.44 (14.34)	17.64 (14.34)	14.74 (7.92)
80+	0.27 (0.96)	14.80 (13.69)	15.07 (13.57)	15.80 (7.46)
Domicile				
Adelaide	0.15 (0.59)[c]	17.89 (14.25)	18.05 (14.26)	14.25 (8.03)
Mt Gambier	0.31 (0.88)	17.67 (15.39)	17.98 (15.29)	14.76 (7.74)
Educated past age 16?[d]				
Yes	0.17 (0.50)	22.61 (16.35)[b]	22.78 (16.34)[b]	13.28 (8.02)[c]
No	0.25 (0.83)	15.11 (13.02)	15.36 (12.98)	15.10 (7.79)

[a]Decayed retained roots not included
[b]P<0.01
[c]P<0.05
[d]Data missing for one individual

3.2.6.2.2 Root surface caries

Data on the severity and prevalence of root surface caries at five years by the sociodemographic characteristics of the sample are presented in Table 3.43.

Table 3.43: Root surface caries severity and Root Caries Index at five years, by socio-demographic characteristics

	DS (sd)	FS (sd)	DFS (sd)	RCI[a]
All combined	1.00 (1.83)	3.63 (3.71)	4.63 (4.29)	13.29 (12.15)
Gender				
Male	1.15 (1.98)[b]	3.64 (3.68)	4.80 (4.32)	13.31 (12.34)
Female	0.80 (1.58)	3.61 (3.75)	4.40 (4.25)	13.27 (11.93)
Age group				
65-69	1.16 (2.22)	2.99 (3.54)[c]	4.15 (4.72)	11.05 (11.84)[c]
70-79	0.99 (1.80)	3.81 (3.84)	4.80 (4.30)	13.69 (11.54)
80+	0.87 (1.40)	4.00 (3.61)	4.87 (3.78)	14.91 (13.19)
Domicile				
Adelaide	0.87 (1.59)[c]	3.83 (3.85)	4.70 (4.23)	13.34 (11.93)
Mt Gambier	1.21 (2.11)	3.37 (3.50)	4.58 (4.40)	13.40 (12.51)
Educated past age 16?[d]				
Yes	0.87 (1.81)	3.85 (3.67)	4.72 (4.38)	13.45 (12.51)
No	1.09 (1.85)	3.53 (3.75)	4.61 (4.26)	13.32 (12.01)

[a]After Katz (1980)
[b]P<0.05
[c]P<0.01
[d]Data missing for one individual

The mean number of decayed surfaces was higher among Mt Gambier participants than among those living in Adelaide, and it was higher among males than females. Both the RCI and the number of filled surfaces increased across the three age groups.

3.2.6.3 Associations between five-year dental caries severity and the taking of medications

Data on coronal caries severity among the medication categories at five years are presented in Table 3.44. The "attack rate" is the equivalent of the Root Caries Index (Katz, 1980).

Table 3.44: Coronal caries severity at five years among the various medication categories, by five-year medication prevalence

Medication category	DS (sd)	FS (sd)	DFS (sd)	"Attack rate" (%)
Antihypertensives				
Not taken	0.21 (0.76)	18.89 (15.12)	19.10 (15.04)	26.16 (15.85)
Taken	0.22 (0.67)	16.73 (14.26)	16.96 (14.27)	23.40 (16.24)
	P = 0.88	P = 0.09	P = 0.09	P = 0.05
β-blockers				
Not taken	0.21 (0.73)	17.71 (14.58)	17.92 (14.55)	24.62 (16.01)
Taken	0.29 (0.73)	18.20 (15.63)	18.49 (15.55)	25.56 (16.73)
	P = 0.39	P = 0.80	P = 0.76	P = 0.65
Diuretics				
Not taken	0.19 (0.66)	18.26 (14.96)	18.44 (14.91)	25.24 (16.53)
Taken	0.33 (0.91)	16.22 (13.80)	16.55 (13.84)	23.12 (14.54)
	P = 0.05	P = 0.18	P = 0.21	P = 0.20
ACEIs				
Not taken	0.22 (0.77)	18.07 (14.95)	18.29 (14.91)	25.04 (16.15)
Taken	0.20 (0.48)	16.34 (13.45)	16.54 (13.41)	23.27 (15.82)
	P = 0.80	P = 0.31	P = 0.31	P = 0.34
CCBs				
Not taken	0.23 (0.77)	17.97 (14.61)	18.20 (14.55)	25.00 (15.48)
Taken	0.18 (0.46)	16.94 (15.19)	17.12 (15.22)	23.62 (18.55)
	P = 0.55	P = 0.53	P = 0.51	P = 0.44
Sympatholytics				
Not taken	0.22 (0.74)	17.74 (14.78)	17.97 (14.74)	24.86 (16.16)
Taken	0.16 (0.37)	18.44 (13.56)	18.60 (13.61)	22.41 (14.80)
	P = 0.67	P = 0.82	P = 0.83	P = 0.49
Cardiac drugs				
Not taken	0.20 (0.68)	17.91 (14.76)	18.11 (14.71)	24.78 (16.15)
Taken	0.43 (1.21)	16.03 (14.16)	16.46 (14.33)	24.17 (15.54)
	P = 0.07	P = 0.45	P = 0.51	P = 0.82
Anginals				
Not taken	0.21 (0.68)	17.99 (14.81)	18.21 (14.76)	25.03 (16.16)
Taken	0.32 (1.20)	14.84 (13.13)	15.16 (13.41)	20.86 (14.85)
	P = 0.36	P = 0.21	P = 0.22	P = 0.13
Analgesics				
Not taken	0.18 (0.68)	18.63 (15.12)	18.81 (15.09)	25.05 (16.52)
Taken	0.31 (0.82)	15.86 (13.59)	16.17 (13.57)	24.03 (15.13)
	P = 0.07	P = 0.05	P = 0.06	P = 0.50
Simple analgesics				
Not taken	0.21 (0.72)	17.76 (14.68)	17.98 (14.65)	24.67 (16.10)
Taken	0.65 (0.93)	17.82 (16.14)	18.47 (15.91)	26.91 (16.41)
	P = 0.01	P = 0.99	P = 0.89	P = 0.57
NSAIDs				
Not taken	0.23 (0.77)	18.04 (14.87)	18.27 (14.83)	25.04 (16.35)
Taken	0.18 (0.38)	16.29 (13.74)	16.47 (13.74)	22.99 (14.54)
	P = 0.57	P = 0.33	P = 0.32	P = 0.30

Antigouts				
Not taken	0.19 (0.64)	18.20 (14.91)	18.40 (14.87)	24.84 (16.21)
Taken	0.55 (1.39)	12.29 (10.53)	12.84 (10.73)	23.40 (14.72)
	P = 0.003	P = 0.02	P = 0.02	P = 0.59
Narcotic & combination analgesics				
Not taken	0.23 (0.76)	18.24 (14.81)	18.47 (14.77)	25.02 (16.17)
Taken	0.12 (0.38)	13.96 (13.36)	14.09 (13.34)	22.42 (15.44)
	P = 0.29	P = 0.04	P = 0.03	P = 0.25
Antiasthma drugs				
Not taken	0.20 (0.71)	17.95 (14.67)	18.15 (14.64)	21.82 (16.23)
Taken	0.46 (0.92)	15.68 (15.18)	16.15 (15.10)	23.84 (14.58)
	P = 0.03	P = 0.34	P = 0.40	P = 0.71
HRT				
Not taken	0.23 (0.74)	17.30 (14.61)	17.53 (14.57)	24.25 (15.91)
Taken	0.04 (0.19)	26.25 (14.22)	26.29 (14.24)	33.39 (17.14)
	P = 0.17	P = 0.002	P = 0.002	P = 0.003
Antiulcer drugs				
Not taken	0.24 (0.79)	18.45 (15.01)	18.69 (14.97)	25.00 (15.97)
Taken	0.13 (0.41)	14.16 (12.45)	14.29 (12.390	23.32 (16.80)
	P = 0.23	P = 0.01	P = 0.01	P = 0.39
Hypoglycaemics				
Not taken	0.22 (0.74)	17.97 (14.79)	18.19 (14.74)	24.96 (16.10)
Taken	0.23 (0.50)	14.53 (13.13)	14.77 (13.26)	21.10 (15.87)
	P = 0.92	P = 0.21	P = 0.22	P = 0.20
Prophylactic aspirin				
Not taken	0.22 (0.72)	18.17 (15.04)	18.39 (14.97)	24.79 (15.89)
Taken	0.22 (0.74)	16.86 (13.93)	17.08 (13.97)	24.63 (16.62)
	P = 0.98	P = 0.35	P = 0.35	P = 0.92
Psychotherapeutics				
Not taken	0.22 (0.74)	18.10 (14.72)	18.32 (14.69)	25.03 (16.16)
Taken	0.17 (0.45)	13.36 (13.98)	13.53 (13.92)	20.72 (14.81)
	P = 0.65	P = 0.06	P = 0.06	P = 0.12
Antidepressants				
Not taken	0.23 (0.74)	17.96 (14.72)	18.18 (14.69)	25.04 (16.16)
Taken	0.09 (0.20)	13.78 (14.17)	13.87 (14.09)	18.11 (13.23)
	P = 0.37	P = 0.18	P = 0.17	P = 0.04
Thyroxine				
Not taken	0.23 (0.74)	17.60 (14.64)	17.82 (14.61)	24.67 (16.08)
Taken	0.06 (0.24)	22.89 (16.07)	22.94 (16.16)	26.83 (16.83)
	P = 0.33	P = 0.13	P = 0.15	P = 0.58
Hypolipidaemics				
Not taken	0.21 (0.68)	17.43 (14.61)	17.64 (14.56)	24.39 (16.18)
Taken	0.29 (0.12)	21.88 (15.13)	22.17 (15.52)	29.01 (14.60)
	P = 0.50	P = 0.06	P = 0.06	P = 0.08

A greater number of decayed surfaces was observed among individuals who at five years were taking simple analgesics, antigout preparations or antiasthma drugs. A lower number of filled surfaces (and lower DFS) was observed among those who were taking antigout preparations, narcotic and combination analgesics or antiulcer drugs. By contrast, a higher number of filled surfaces (and greater DFS) was observed among those who were taking hormone replacement therapy (HRT).

Data on coronal caries severity among "continuous users" of the various medication categories are presented in Table 3.45.

Table 3.45: Coronal caries severity at five years among the various medication categories, continuous users compared with the remainder

Medication category	DS (sd)	FS (sd)	DFS (sd)	"Attack rate" (sd)
Antihypertensives				
Others	0.20 (0.70)	18.44 (15.00)	18.64 (14.92)	25.50 (15.71)
Continuous users	0.26 (0.78)	16.38 (14.03)	16.65 (14.09)	23.15 (16.80)
	P = 0.33	P = 0.13	P = 0.15	P = 0.12
β-blockers				
Others	0.22 (0.74)	17.77 (14.65)	17.99 (14.61)	24.76 (15.98)
Continuous users	0.21 (0.42)	18.05 (16.72)	18.26 (16.68)	24.32 (19.34)
	P = 0.96	P = 0.93	P = 0.94	P = 0.91
Diuretics				
Others	0.20 (0.68)	18.50 (15.19)	18.70 (15.14)	25.33 (16.15)
Continuous users	0.20 (0.55)	15.68 (12.52)	15.88 (12.45)	23.66 (16.51)
	P = 0.98	P = 0.11	P = 0.11	P = 0.39
ACEIs				
Others	0.22 (0.73)	17.75 (14.69)	17.97 (14.65)	24.75 (16.09)
Continuous users	0.00 (0.00)	23.00 (20.95)	23.00 (20.95)	23.77 (21.08)
	P = 0.60	P = 0.54	P = 0.55	P = 0.92
CCBs				
Others	0.23 (0.75)	17.90 (14.73)	18.13 (14.69)	24.86 (15.60)
Continuous users	0.12 (0.33)	16.29 (14.53)	16.41 (14.53)	23.32 (21.32)
	P = 0.37	P = 0.50	P = 0.47	P = 0.56
Sympatholytics				
Others	0.22 (0.73)	17.71 (14.72)	17.93 (14.68)	24.77 (16.12)
Continuous users	0.18 (0.40)	20.73 (14.59)	20.91 (14.65)	23.43 (15.65)
	P = 0.86	P = 0.50	P = 0.51	P = 0.79
Cardiac drugs				
Others	0.22 (0.73)	17.89 (14.74)	18.11 (14.71)	24.87 (16.13)
Continuous users	0.00 (0.00)	8.33 (6.92)	8.33 (6.92)	13.47 (6.48)
	P = 0.46	P = 0.11	P = 0.10	P = 0.08
Anginals				
Others	0.21 (0.67)	17.93 (14.79)	18.15 (14.73)	24.95 (16.16)
Continuous users	0.47 (1.70)	13.00 (11.53)	13.47 (12.40)	18.40 (12.90)
	P = 0.15	P = 0.17	P = 0.20	P = 0.10
Analgesics				
Others	0.21 (0.69)	17.96 (14.82)	18.17 (14.77)	24.80 (16.23)
Continuous users	0.29 (0.96)	16.56 (14.00)	16.85 (14.09)	24.32 (15.25)
	P = 0.37	P = 0.47	P = 0.49	P = 0.82
Simple analgesics				
Others	0.22 (0.73)	17.76 (14.72)	17.98 (14.69)	24.72 (16.10)
Continuous users	1.00 (—)	24.00 (—)	25.00 (—)	36.23 (—)
	P = 0.28	P = 0.67	P = 0.63	P = 0.48

NSAIDs				
Others	0.22 (0.75)	17.93 (14.75)	18.16 (14.71)	24.92 (16.14)
Continuous users	0.17 (0.38)	15.64 (14.24)	15.81 (14.27)	22.31 (15.52)
	P = 0.65	P = 0.37	P = 0.35	P = 0.35
Antigouts				
Others	0.20 (0.66)	17.89 (14.78)	18.09 (14.74)	24.64 (16.11)
Continuous users	0.63 (1.71)	14.79 (12.53)	15.42 (12.95)	27.39 (15.89)
	P = 0.01	P = 0.37	P = 0.44	P = 0.47
Narcotic & comb. analgesics				
Others	0.22 (0.73)	17.85 (14.76)	18.07 (14.72)	24.83 (16.11)
Continuous users	0.14 (0.38)	12.14 (9.96)	12.29 (9.76)	18.32 (14.42)
	P = 0.78	P = 0.31	P = 0.30	P = 0.29
Antiasthma drugs				
Others	0.22 (0.73)	17.59 (14.60)	17.81 (14.57)	24.59 (16.14)
Continuous users	0.14 (0.36)	24.79 (17.37)	24.93 (17.39)	30.37 (13.66)
	P = 0.69	P = 0.07	P = 0.07	P = 0.18
HRT				
Others	0.22 (0.73)	17.41 (14.61)	17.64 (14.57)	24.51 (16.14)
Continuous users	0.08 (0.28)	32.15 (11.56)	32.23 (11.58)	34.02 (11.39)
	P = 0.47	P = 0.0003	P = 0.0004	P = 0.04
Antiulcer drugs				
Others	0.24 (0.77)	18.45 (15.03)	18.69 (15.00)	25.01 (16.01)
Continuous users	0.15 (0.43)	13.42 (11.77)	13.57 (11.71)	23.62 (17.52)
	P = 0.38	P = 0.007	P = 0.006	P = 0.50
Hypoglycaemics				
Others	0.22 (0.73)	17.78 (14.72)	18.00 (14.68)	24.71 (16.04)
Continuous users	0.36 (0.63)	17.43 (14.87)	17.79 (15.04)	25.91 (18.74)
	P = 0.47	P = 0.93	P = 0.96	P = 0.78
Prophylactic aspirin				
Others	0.22 (0.74)	17.94 (14.67)	18.16 (14.64)	24.86 (16.11)
Continuous users	0.23 (0.58)	15.73 (15.20)	15.95 (15.11)	23.31 (16.06)
	P = 0.96	P = 0.36	P = 0.36	P = 0.56
Psychotherapeutics				
Others	0.22 (0.74)	18.07 (14.74)	18.29 (14.70)	25.02 (16.09)
Continuous users	0.13 (0.35)	7.73 (9.60)	7.87 (9.49)	15.15 (13.42)
	P = 0.64	P = 0.007	P = 0.007	P = 0.02
Antidepressants				
Others	0.22 (0.73)	17.78 (14.72)	18.01 (14.68)	24.77 (16.16)
Continuous users	0.00 (0.00)	17.25 (14.95)	17.25 (14.95)	22.58 (11.97)
	P = 0.39	P = 0.92	P = 0.88	P = 0.70
Thyroid hormones				
Others	0.22 (0.74)	17.64 (14.66)	17.86 (14.62)	24.68 (16.06)
Continuous users	0.07 (0.26)	22.53 (16.19)	22.60 (16.30)	26.70 (17.87)
	P = 0.41	P = 0.20	P = 0.22	P = 0.63
Hypolipidaemics				
Others	0.22 (0.73)	17.63 (14.69)	17.85 (14.66)	24.52 (16.12)
Continuous users	0.13 (0.50)	22.44 (15.06)	22.56 (15.02)	31.68 (13.89)
	P = 0.60	P = 0.20	P = 0.21	P = 0.08

A greater number of decayed surfaces was observed among "continuous users" of antigout preparations. A lower number of filled surfaces (and lower DFS) was observed among those who were "continuous users" of antiulcer drugs or psychotherapeutic preparations (and the latter had a lower "attack rate"). By contrast, a higher number of filled surfaces (and greater DFS) was observed among those who were "continuous users" of hormone replacement therapy (HRT).

Data on root surface caries severity among the various medication categories at five years are presented in Table 3.46.

Root DFS was lower overall among people taking antihypertensives at five years, but did not differ by antihypertensive subclass. The RCI was lower among "continuous users" of the sympatholytic subclass of antihypertensives, and higher among "continuous users" of simple analgesics.

Table 3.46: Root surface caries severity at five years among the various medication categories, by five-year medication prevalence

Medication category	Root DS (sd)	Root FS (sd)	Root DFS (sd)	RCI
Antihypertensives				
Not taken	1.17 (2.12)	3.89 (3.87)	5.05 (4.58)	14.05 (12.40)
Taken	0.85 (1.50)	3.40 (3.55)	4.25 (3.98)	12.67 (11.90)
	P = 0.05	P = 0.13	P = 0.03	P = 0.19
β-blockers				
Not taken	1.02 (1.84)	3.70 (3.70)	4.71 (4.29)	13.35 (11.89)
Taken	0.93 (1.76)	3.23 (3.77)	4.16 (4.28)	13.26 (13.92)
	P = 0.70	P = 0.33	P = 0.32	P = 0.95
Diuretics				
Not taken	1.07 (1.94)	3.75 (3.79)	4.82 (4.43)	13.58 (12.45)
Taken	0.81 (1.42)	3.26 (3.44)	4.06 (3.78)	12.56 (11.15)
	P = 0.17	P = 0.20	P = 0.09	P = 0.42
ACEIs				
Not taken	0.99 (1.84)	3.61 (3.71)	4.60 (4.26)	13.19 (11.95)
Taken	1.08 (1.79)	3.75 (3.75)	4.83 (4.48)	14.06 (13.16)
	P = 0.68	P = 0.75	P = 0.65	P = 0.54
CCBs				
Not taken	1.07 (1.90)	3.55 (3.72)	4.62 (4.37)	13.31 (12.34)
Taken	0.74 (1.45)	4.01 (3.69)	4.75 (3.96)	13.46 (11.41)
	P = 0.11	P = 0.26	P = 0.78	P = 0.92
Sympatholytics				
Not taken	1.02 (1.86)	3.69 (3.74)	4.72 (4.33)	13.62 (12.27)
Taken	0.68 (1.11)	2.48 (3.04)	3.16 (3.22)	7.71 (7.78)
	P = 0.36	P = 0.11	P = 0.08	P = 0.02
Cardiac drugs				
Not taken	1.00 (1.82)	3.67 (3.74)	4.66 (4.32)	13.49 (12.28)
Taken	1.11 (2.02)	3.24 (3.39)	4.35 (3.92)	11.36 (10.36)
	P = 0.72	P = 0.51	P = 0.67	P = 0.30
Anginals				
Not taken	1.02 (1.85)	3.59 (3.70)	4.62 (4.29)	13.23 (12.02)
Taken	0.78 (1.51)	4.19 (3.89)	4.97 (4.32)	14.78 (13.95)
	P = 0.45	P = 0.35	P = 0.63	P = 0.46
Analgesics				
Not taken	0.98 (1.87)	3.75 (3.79)	4.73 (4.38)	13.11 (11.84)
Taken	1.06 (1.75)	3.37 (3.52)	4.34 (4.10)	13.85 (12.85)
	P = 0.64	P = 0.28	P = 0.46	P = 0.52
Simple analgesics				
Not taken	0.97 (1.78)	3.64 (3.74)	4.61 (4.27)	13.05 (11.78)
Taken	2.12 (2.76)	3.53 (2.98)	5.65 (4.87)	21.85 (19.12)
	P = 0.64	P = 0.90	P = 0.33	P = 0.003
NSAIDs				
Not taken	1.01 (1.89)	3.71 (3.75)	4.72 (4.39)	13.41 (12.48)
Taken	0.99 (1.49)	3.22 (3.51)	4.20 (3.71)	12.90 (10.12)
	P = 0.92	P = 0.28	P = 0.32	P = 0.73

Antigouts				
Not taken	1.01 (1.83)	3.66 (3.74)	4.68 (4.29)	13.36 (11.93)
Taken	0.89 (1.84)	3.32 (3.40)	4.21 (4.32)	13.03 (14.97)
	P = 0.70	P = 0.58	P = 0.52	P = 0.87
Narcotics & comb.				
Not taken	1.00 (1.86)	3.67 (3.74)	4.67 (4.33)	13.15 (11.98)
Taken	1.04 (1.58)	3.39 (3.52)	4.42 (3.98)	14.88 (13.55)
	P = 0.90	P = 0.59	P = 0.68	P = 0.31
Antiasthma drugs				
Not taken	1.02 (1.86)	3.66 (3.74)	4.68 (4.36)	13.15 (11.89)
Taken	0.88 (1.49)	3.32 (3.35)	4.20 (3.36)	15.53 (14.98)
	P = 0.64	P = 0.57	P = 0.49	P = 0.23
HRT				
Not taken	1.01 (1.84)	3.63 (3.71)	4.64 (4.25)	13.31 (12.11)
Taken	0.93 (1.77)	3.74 (4.09)	4.67 (5.11)	14.37 (13.99)
	P = 0.81	P = 0.88	P = 0.97	P = 0.66
Antiulcer drugs				
Not taken	0.97 (1.67)	3.61 (3.75)	4.58 (4.24)	13.01 (11.85)
Taken	1.20 (2.47)	3.76 (3.54)	4.96 (4.58)	15.12 (13.64)
	P = 0.28	P = 0.74	P = 0.46	P = 0.15
Hypoglycaemics				
Not taken	0.97 (1.79)	3.63 (3.74)	4.60 (4.29)	13.15 (12.12)
Taken	1.57 (2.40)	3.70 (3.21)	5.27 (4.35)	16.43 (12.52)
	P = 0.08	P = 0.92	P = 0.41	P = 0.15
Prophylactic aspirin				
Not taken	1.07 (1.94)	3.58 (3.75)	4.65 (4.34)	13.35 (12.46)
Taken	0.86 (1.55)	3.76 (3.64)	4.61 (4.20)	13.30 (11.46)
	P = 0.22	P = 0.62	P = 0.92	P = 0.97
Psychotherapeutics				
Not taken	1.02 (1.86)	3.63 (3.74)	4.65 (4.32)	13.10 (11.83)
Taken	0.81 (1.45)	3.72 (3.32)	4.53 (4.00)	16.56 (15.76)
	P = 0.50	P = 0.89	P = 0.87	P = 0.10
Antidepressants				
Not taken	1.02 (1.86)	3.64 (3.73)	4.66 (4.34)	13.36 (12.25)
Taken	0.78 (1.04)	3.52 (3.30)	4.30 (3.08)	12.87 (10.06)
	P = 0.55	P = 0.88	P = 0.70	P = 0.85
Thyroxine				
Not taken	1.02 (1.84)	3.64 (3.74)	4.65 (4.31)	13.36 (12.13)
Taken	0.72 (1.49)	3.61 (2.950	4.33 (3.87)	12.75 (13.27)
	P = 0.50	P = 0.98	P = 0.76	P = 0.84
Hypolipidaemics				
Not taken	1.01 (1.83)	3.73 (3.76)	4.74 (4.34)	13.75 (12.27)
Taken	0.93 (1.85)	2.56 (2.95)	3.49 93.56)	10.51 (10.34)
	P = 0.77	P = 0.05	P = 0.07	P = 0.13

Data on root surface caries severity among "continuous users" of the various medication categories are presented in Table 3.47.

Table 3.47: Root surface caries severity at five years among the various medication categories, continuous users compared with the remainder

Medication category	Root DS (sd)	Root FS (sd)	Root DFS (sd)	RCI (sd)
Antihypertensives				
Others	1.07 (1.97)	3.78 (3.89)	4.85 (4.55)	13.62 (12.27)
Continuous users	0.88 (1.48)	3.34 (3.31)	4.21 (3.66)	12.74 (11.92)
	P = 0.26	P = 0.20	P = 0.11	P = 0.44
β-blockers				
Others	0.98 (1.80)	3.64 (3.72)	4.62 (4.27)	13.23 (11.84)
Continuous users	1.74 (2.47)	3.53 (3.66)	5.26 (5.02)	16.29 (18.90)
	P = 0.08	P = 0.90	P = 0.52	P = 0.28
Diuretics				
Others	1.07 (1.95)	3.71 (3.79)	4.79 (4.45)	13.49)12.54)
Continuous users	0.82 (1.54)	3.85 (4.03)	4.67 (4.35)	13.17 (12.11)
	P = 0.27	P = 0.77	P = 0.83	P = 0.83
ACEIs				
Others	1.01 (1.83)	3.65 (3.72)	4.66 (4.30)	13.39 (12.17)
Continuous users	0.33 (0.58)	0.67 (0.58)	1.00 (—)	4.91 (3.03)
	P = 0.52	P = 0.16	P = 0.14	P = 0.23
CCBs				
Others	1.05 (1.87)	3.66 (3.75)	4.71 (4.37)	13.48 (12.39)
Continuous users	0.51 (1.12)	3.34 (3.23)	3.85 (3.23)	11.71 (8.83)
	P = 0.07	P = 0.60	P = 0.22	P = 0.37
Sympatholytics				
Others	1.01 (1.84)	3.66 (3.71)	4.67 (4.31)	13.46 (12.20)
Continuous users	0.82 (1.08)	2.64 (3.61)	3.45 (3.62)	7.63 (8.38)
	P = 0.73	P = 0.37	P = 0.35	P = 0.12
Cardiac drugs				
Others	1.01 (1.84)	3.61 (3.69)	4.62 (4.28)	13.26 (12.12)
Continuous users	0.50 (0.84)	6.33 (5.24)	6.83 (5.31)	20.21 (14.59)
	P = 0.50	P = 0.07	P = 0.21	P = 0.16
Anginals				
Others	1.01 (1.83)	3.64 (3.73)	4.65 (4.30)	13.30 (12.21)
Continuous users	0.94 (1.89)	3.41 (3.06)	4.35 (4.24)	14.49 (10.78)
	P = 0.88	P = 0.80	P = 0.78	P = 0.69
Analgesics				
Others	1.02 (1.86)	3.64 (3.75)	4.66 (4.33)	13.35 (12.16)
Continuous users	0.93 (1.63)	3.59 (3.48)	4.51 (4.06)	13.25 (12.21)
	P = 0.15	P = 0.91	P = 0.79	P = 0.95
Simple analgesics				
Others	1.01 (1.830	3.63 (3.72)	4.64 (4.30)	13.31 (12.15)
Continuous users	0.00 (—)	5.00 (—)	5.00 (—)	27.78 (—)
	P = 0.30	P = 0.71	P = 0.93	P = 0.23
NSAIDs				
Others	1.03 (1.87)	3.65 (3.73)	4.68 (4.33)	13.43 (12.33)
Continuous users	0.72 (1.11)	3.42 (3.51)	4.14 (3.70)	12.10 (9.51)
	P = 0.34	P = 0.71	P = 0.47	P = 0.53

Antigouts				
Others	0.99 (1.80)	3.61 (3.72)	4.60 (4.27)	13.19 (11.92)
Continuous users	1.47 (2.44)	4.32 (3.54)	5.79 (4.93)	17.30 (17.19)
	P = 0.26	P = 0.42	P = 0.24	P = 0.15
Narcotic & combination analgesics				
Others	1.01 (1.84)	3.64 (3.72)	4.65 (4.30)	13.36 (12.19)
Continuous users	0.71 (0.95)	3.14 (3.63)	3.86 (4.26)	11.90 (9.67)
	P = 0.67	P = 0.72	P = 0.63	P = 0.75
Antiasthma drugs				
Others	1.02 (1.84)	3.61 (3.72)	4.63 (4.32)	13.26 (12.16)
Continuous users	0.64 (1.34)	4.43 (3.46)	5.07 (3.50)	16.31 (12.05)
	P = 0.45	P = 0.42	P = 0.70	P = 0.35
HRT				
Others	1.01 (1.83)	3.62 (3.71)	4.62 (4.28)	13.30 (12.17)
Continuous users	1.00 (1.73)	4.46 (3.91)	5.46 (4.79)	14.69 (11.77)
	P = 0.99	P = 0.42	P = 0.49	P = 0.69
Antiulcer drugs				
Others	0.97 (1.69)	3.58 (3.71)	4.55 (4.20)	12.96 (11.83)
Continuous users	1.11 (2.46)	3.81 (3.84)	4.92 (4.77)	15.20 (14.08)
	P = 0.53	P = 0.64	P = 0.50	P = 0.15
Hypoglycaemics				
Others	0.98 (1.80)	3.62 (3.73)	4.60 (4.28)	13.21 (12.11)
Continuous users	2.00 (2.63)	4.14 (3.28)	6.14 (4.70)	18.18 (13.33)
	P = 0.04	P = 0.61	P = 0.19	P = 0.13
Prophylactic aspirin				
Others	1.04 (1.86)	3.72 (3.76)	4.76 (4.33)	13.58 (12.27)
Continuous users	0.63 (1.31)	2.63 (2.98)	3.25 (3.56)	10.34 (10.31)
	P = 0.17	P = 0.07	P = 0.03	P = 0.10
Psychotherapeutics				
Others	1.03 (1.85)	3.62 (3.71)	4.65 (4.31)	13.21 (11.91)
Continuous users	0.20 (0.41)	4.13 (3.98)	4.33 (3.94)	17.80 (18.79)
	P = 0.08	P = 0.60	P = 0.78	P = 0.15
Antidepressants				
Others	1.02 (1.84)	3.61 (3.70)	4.62 94.30)	13.28 (12.14)
Continuous users	0.38 (0.52)	5.50 (4.07)	5.88 (3.98)	16.83 (13.76)
	P = 0.33	P = 0.15	P = 0.41	P = 0.41
Thyroxine				
Others	1.01 (1.84)	3.63 (3.73)	4.64 (4.300	13.34 (12.11)
Continuous users	0.73 (1.58)	3.87 (3.04)	4.60 (4.08)	13.23 (14.15)
	P = 0.56	P = 0.81	P = 0.97	P = 0.97
Hypolipidaemics				
Others	1.02 (1.85)	3.66 (3.73)	4.69 (4.32)	13.38 (12.12)
Continuous users	0.44 (0.81)	2.75 (3.09)	3.19 (2.95)	12.07 (13.48)
	P = 0.21	P = 0.33	P = 0.17	P = 0.67

Root surface DS was higher among people who were "continuous users" of hypoglycaemic drugs, and root DFS was lower among those who were taking prophylactic aspirin at baseline and five years. There were no other significant differences.

3.2.6.4 Changes in disease experience between baseline and five years

This section describes tooth-loss incidence and severity, and coronal and root surface caries incidence and increment.

3.2.6.4.1 Tooth loss

The five-year incidence of tooth loss among the 528 dentate individuals who were re-examined at five years was 36.2 per cent; that is, 191 participants lost at least one tooth. The number of teeth lost ranged from 1 to 9, and the mean number lost was 0.70 (sd, 1.31). Among those who lost one or more teeth, the mean number lost was 1.93 (sd, 1.54). Only one tooth was lost by 117 (61.3 per cent) of those who had lost a tooth; the remaining 74 had lost two or more teeth.

The correlation between unstimulated flow rate at five years and the number of teeth lost over the preceding five-year period was very low ($r = 0.046$; $P = 0.29$); that between XI scores and tooth loss was also very low ($r = 0.082$; $P = 0.08$).

The bivariate associations of tooth-loss incidence with the sociodemographic, smoking and alcohol-use characteristics of the sample are presented in Table 3.48.

Table 3.48: Five-year tooth-loss incidence and increment, baseline socio-demographic characteristics, and smoking and alcohol-use characteristics of the sample

	Tooth-loss incidence (%)	Mean number of teeth lost (sd)
Sex		
Male	122 (40.1)[a]	0.86 (1.40)[b]
Female	69 (30.8)	0.48 (1.04)
Age group at baseline		
60-64	43 (29.7)[a]	0.61 (1.32)
65-74	89 (36.9)	0.74 (1.36)
75+	59 (41.5)	0.72 (1.20)
City		
Mt Gambier	76 (34.9)	0.59 (1.13)
Adelaide	115 (37.1)	0.77 (1.42)
Current smoker		
Yes	10 (37.0)	0.70 (1.27)
No	181 (36.1)	0.70 (1.31)
Current drinker		
Yes	118 (36.4)	0.70 (1.27)
No	73 (35.8)	0.70 (1.38)

[a]P<0.05
[b]P<0.01

3.2.6.4.2 Coronal caries

Among the 528 individuals for whom tooth-status data were available, the five-year incidence of coronal caries was 66.9 per cent; that is, 353 individuals had at least one coronal surface which changed from 'sound' to 'decayed', 'sound' to 'filled', or 'filled' to 'filled and decayed'.

Summary data on the occurrence of coronal caries over the five-year period of the study are presented in Table 3.49. The mean net coronal caries increment was 2.23 (sd, 3.32) DF surfaces overall. Among the incident cases, the mean net increment was 3.52

(sd, 3.34) and the mean AdjCI was 3.80 (sd, 3.25). The number of surfaces involved per individual ranged from 0 to 28. The "De Paola grids" are presented in Appendix 4.

Concerning reversals, a net negative increment was observed in 46 individuals, with the following distribution: five surfaces (one individual), three (one), two (six), and one (23). People with a negative net increment were allocated an increment of 0 in the caries incidence calculation, but they were included when the associations of mean net caries increment were examined.

The correlation between unstimulated flow rate at five years and the adjusted coronal caries increment over the preceding five-year period was very low ($r = 0.01$; $P = 0.82$); that between XI scores and the adjusted coronal caries increment was also very low ($r = 0.003$; $P = 0.96$).

3.2.6.3.3 Root surface caries

Among the 528 individuals for whom longitudinal tooth-status data were available, the five-year incidence of root surface caries was 59.3 per cent; that is, 313 individuals had at least one root surface which changed from 'sound' (or 'unexposed') to 'decayed', 'sound' (or 'unexposed') to 'filled', or 'filled' to 'filled and decayed'.

Summary data on the occurrence of root surface caries over the five-year period of the study are presented in Table 3.49. The mean NCI was 1.90 (sd, 3.23) and the mean AdjCI was 2.21 (sd, 2.83). Among the incident cases, the mean NCI was 3.08 (sd, 7.50) and the mean AdjCI was 3.57 (sd, 2.96).

Concerning reversals, a net negative increment was apparent in 65 individuals, with the following distribution: seven surfaces (one individual), six (two), five (four), four (three), three (seven), two (16) and one (32). As with coronal caries, people with a negative net increment were allocated an increment of 0 in the root caries incidence calculation, but they were included when the associations of mean net root caries increment were examined.

The correlation between unstimulated flow rate at five years and the adjusted root surface caries increment over the preceding five-year period was very low and only just reached statistical significance (r = 0.087; P = 0.05); that between XI scores and the adjusted root surface caries increment was also very low (r = -0.015; P = 0.74).

Table 3.49: Summary data on five-year coronal and root surface caries increment (DFS)

	Number	Mean (sd)	Range
Coronal caries			
Gross Caries Increment (GCI)	528	2.81 (3.31)	0, 33
Net Caries Increment (NCI)	528	2.23 (3.32)	-5, 32
Adjusted Caries Increment (AdjCI)	528	2.65 (3.14)	0, 28
Root surface caries			
Gross Caries Increment (GCI)	528	2.60 (2.99)	0, 18
Net Caries Increment (NCI)	528	1.91 (3.21)	-7, 17
Adjusted Caries Increment (AdjCI)	528	2.21 (2.83)	0, 18

The bivariate associations of coronal and root surface caries incidence and increment with the socio-demographic, smoking and alcohol-use characteristics of the sample are presented in Table 3.50, and with the dental service-use and self-care characteristics of the sample in Table 3.51.

Five-year root surface caries increment was higher among alcohol drinkers. There was no difference in the incidence or increment of either type of caries between residents of fluoridated Adelaide and nonfluoridated Mt Gambier.

Table 3.50: Coronal and root surface caries incidence and adjusted increment, baseline sociodemographic characteristics, and smoking and alcohol-use characteristics of the sample

	Coronal caries		*Root surface caries*	
	Incidence (%)	AdjCI (sd)	Incidence (%)	AdjCI (sd)
Sex				
Male	203 (66.8)	2.80 (3.50)	178 (58.6)	2.27 (2.99)
Female	150 (67.0)	2.45 (2.58)	135 (60.3)	2.13 (2.61)
Age group at baseline				
60-64	104 (71.7)	2.64 (2.45)	81 (55.9)	2.20 (3.27)
65-74	155 (64.3)	2.64 (3.41)	146 (60.6)	2.31 (2.86)
75+	94 (66.2)	2.62 (3.31)	86 (60.6)	2.07 (2.26)
City				
Mt Gambier	149 (67.3)	2.51 (3.21)	138 (63.3)	2.24 (3.00)
Adelaide	204 (65.8)	2.75 (3.10)	175 (56.5)	2.19 (2.72)
Current smoker at 5 years				
Yes	16 (59.3)	1.69 (1.74)	18 (66.7)	1.76 (1.80)
No	337 (67.3)	2.70 (3.19)	295 (58.9)	2.24 (2.86)
Current drinker at 5 years				
Yes	222 (68.5)	2.44 (2.99)	197 (60.8)	2.41 (2.98)[a]
No	131 (64.2)	2.78 (3.24)	116 (56.9)	1.89 (2.55)

[a]P<0.05

Table 3.51: Coronal and root surface caries incidence and adjusted increment, by baseline self-care and dental service-use characteristics of the sample

	Coronal caries		*Root surface caries*	
	Incidence (%)	AdjCI (sd)	Incidence (%)	AdjCI (sd)
Usual reason for dental visit				
Problem	171 (60.6)[a]	2.21 (2.84)[a]	164 (58.2)	1.95 (2.77)[b]
Check-up	182 (74.0)	3.15 (3.40)	149 (60.6)	2.51 (2.88)
Age when left school				
<16 years	223 (66.2)	2.65 (3.39)	198 (58.8)	2.25 (2.81)
16+ years	129 (68.3)	2.66 (2.67)	113 (59.8)	2.14 (2.89)
Toothbrushing frequency				
<4 times/week	14 (60.9)	2.31 (2.43)	10 (43.5)	1.29 (1.97)
4+ times/week	339 (67.3)	2.67 (3.17)	303 (60.1)	2.26 (2.86)
Flossing frequency				
Intermittent/never	169 (65.8)	2.54 (3.22)	154 (59.9)	2.08 (2.65)
Occasionally +	183 (68.0)	2.74 (3.06)	158 (58.7)	2.34 (3.00)

[a]P<0.01
[b]P<0.05

Coronal caries incidence was higher among people who were routine users of dental services, and their coronal caries increment was also higher. The adjusted root surface caries increment was higher among individuals who visited the dentist routinely rather than episodically.

3.2.7 Medications and five-year tooth loss, and dental caries incidence and increment

This section describes the associations between medication exposure and (1) tooth-loss incidence and severity, and (2) coronal and root surface caries incidence and increment.

3.2.7.1 Medications and tooth loss over the study period

There was no significant association between the total number of medications taken and the incidence of tooth loss, with 74 (37.0 per cent) of those who were taking no drugs, 72 (34.3 per cent) of those taking one to two different drugs, and 45 (38.1 per cent) of those taking three or more different drugs having lost at least one tooth over the study period ($\chi^2 = 0.58$; 2 df; P = 0.75). The mean number of teeth lost in each of those drug-exposure groups was 0.68 (sd, 1.28), 0.64 (sd,1.21) and 0.82 (sd, 1.52) respectively (ANOVA; 2 df; P = 0.48). The correlation between the total number of drugs taken and the number of teeth lost was extremely low (r = 0.03; P = 0.53).

Data on the bivariate associations of tooth loss and medication exposure at five years are presented in Table 3.52.

Table 3.52: Tooth-loss incidence and mean number of teeth lost over five years among the various medication categories, by five-year medication prevalence

Medication category	Tooth-loss incidence (%)	Mean no. of teeth lost (sd)
Antihypertensives		
Not taken	89 (34.8)	0.66 (1.23)
Taken	102 (37.5)	0.73 (1.38)
	P = 0.51	P = 0.53
β-blockers		
Not taken	167 (36.4)	0.71 (1.34)
Taken	24 (34.8)	0.58 (1.06)
	P = 0.77	P = 0.43
Diuretics		
Not taken	151 (37.4)	0.75 (1.40)
Taken	40 (32.3)	0.52 (0.93)
	P = 0.30	P = 0.08
ACEIs		
Not taken	157 (35.8)	0.69 (1.30)
Taken	34 (38.2)	0.72 (1.36)
	P = 0.66	P = 0.86
CCBs		
Not taken	150 (35.0)	0.64 (1.19)[a]
Taken	41 (41.0)	0.94 (1.72)
	P = 0.27	P = 0.10
Sympatholytics		
Not taken	184 (36.6)	0.70 (1.30)
Taken	7 (28.0)	0.68 (1.44)
	P = 0.38	P = 0.95
Cardiac drugs		
Not taken	171 (34.8)	0.67 (1.30)
Taken	20 (54.1)	1.08 (1.40)
	P = 0.02	P = 0.06
Anginals		
Not taken	173 (35.2)	0.66 (1.26)
Taken	10 (48.6)	1.14 (1.77)
	P = 0.10	P = 0.04
Analgesics		
Not taken	136 (37.3)	0.69 (1.25)
Taken	55 (33.7)	0.72 (1.44)
	P = 0.44	P = 0.81
Simple analgesics		
Not taken	184 (36.0)	0.69 (1.27)
Taken	7 (41.2)	1.00 (2.18)
	P = 0.66	P = 0.33

NSAIDs		
Not taken	169 (37.6)	0.72 (1.32)
Taken	22 (27.8)	0.58 (1.23)
	P = 0.10	P = 0.40
Antigouts		
Not taken	175 (35.7)	0.68 (1.29)
Taken	16 (42.1)	0.87 (1.49)
	P = 0.43	P = 0.40
Narcotics & comb.		
Not taken	172 (36.5)	0.70 (1.31)
Taken	19 (33.3)	0.68 (1.33)
	P = 0.64	P = 0.94
Antiasthma drugs		
Not taken	172 (35.3)	0.66 (1.25)
Taken	19 (46.3)	1.20 (1.81)
	P = 0.16	P = 0.07[a]
HRT		
Not taken	184 (36.7)	0.71 (1.33)
Taken	7 (25.9)	0.41 (0.89)
	P = 0.26	P = 0.24
Antiulcer drugs		
Not taken	162 (36.4)	0.71 (1.33)
Taken	29 (34.9)	0.64 (1.20)
	P = 0.80	P = 0.66
Hypoglycaemics		
Not taken	175 (35.1)	0.59 (1.22)
Taken	16 (53.3)	1.20 (1.83)
	P = 0.04	P = 0.05[a]
Prophylactic aspirin		
Not taken	130 (35.3)	0.72 (1.39)
Taken	61 (38.1)	0.64 (1.10)
	P = 0.54	P = 0.49
Psychotherapeutics		
Not taken	180 (36.6)	0.70 (1.33)
Taken	11 (30.6)	0.56 (1.03)
	P = 0.47	P = 0.50
Antidepressants		
Not taken	181 (35.8)	0.69 (1.30)
Taken	10 (43.5)	0.91 (1.44)
	P = 0.46	P = 0.42
Thyroxine		
Not taken	185 (36.3)	0.70 (1.31)
Taken	6 (33.3)	0.72 (1.45)
	P = 0.80	P = 0.93
Hypolipidaemics		
Not taken	175 (35.9)	0.69 (1.31)
Taken	16 (39.0)	0.76 (1.28)
	P = 0.69	P = 0.76

[a]Independent samples t-test used here; inequality of variances confirmed by Levene's test for homogeneity of variance

The incidence of tooth loss was higher among those who were taking cardiac drugs or hypoglycaemic drugs at the five-year examination. It is also noteworthy that those taking anginals at five years appeared to have had a higher tooth-loss incidence, but this was not statistically significant.

The mean number of teeth lost over the study period was greater among those who were taking cardiac drugs or hypoglycaemic drugs at five years.

Data on the bivariate associations of tooth loss and "continuous" medication exposure are presented in Table 3.53.

Table 3.53: Tooth-loss incidence and mean number of teeth lost over five years among the various medication categories, continuous users compared with the remainder

Medication category	Tooth-loss incidence (%)	Mean no. of teeth lost (sd)
Antihypertensives		
Others	128 (35.8)	0.70 (1.32)
Continuous users	63 (37.1)	0.70 (1.29)
	P = 0.77	P = 0.97
β-blockers		
Others	181 (35.6)	0.68 (1.30)
Continuous users	10 (52.6)	1.05 (1.54)
	P = 0.13	P = 0.23
Diuretics		
Others	167 (36.5)	0.71 (1.34)
Continuous users	24 (34.3)	0.60 (1.06)
	P = 0.72	P = 0.51
ACEIs		
Others	191 (36.4)	0.70 (1.31)
Continuous users	0 (0.0)	0.00 (0.00)
	P = 0.56[a]	P = 0.36
CCBs		
Others	172 (35.3)	0.69 (1.31)
Continuous users	19 (46.3)	0.83 (1.34)
	P = 0.16	P = 0.50
Sympatholytics		
Others	188 (36.4)	0.70 (1.32)
Continuous users	3 (27.3)	0.36 (0.67)
	P = 0.75[a]	P = 0.39
Cardiac drugs		
Others	187 (35.8)	0.68 (1.30)
Continuous users	4 (66.7)	1.00 (1.83)
	P = 0.20[a]	P = 0.03[b]
Anginals		
Others	182 (35.6)	0.69 (1.31)
Continuous users	9 (52.9)	1.00 (1.22)
	P = 0.14	P = 0.33
Analgesics		
Others	167 (36.3)	0.68 (1.28)
Continuous users	24 (35.3)	0.81 (1.50)
	P = 0.87	P = 0.45
Simple analgesics		
Others	190 (36.1)	0.69 (1.31)
Continuous users	1 (100.0)	2.00 (—)
	P = 0.36[a]	P = 0.32

NSAIDs		
Others	179 (36.4)	0.69 (1.29)
Continuous users	12 (33.3)	0.83 (1.56)
	P = 0.71	P = 0.52
Antigouts		
Others	184 (36.1)	0.70 (1.32)
Continuous users	7 (36.8)	0.68 (1.16)
	P = 0.95	P = 0.97
Narcotics & comb.		
Others	188 (36.1)	0.68 (1.28)
Continuous users	3 (42.9)	1.71 (2.63)
	P = 0.71[a]	P = 0.34[c]
Antiasthma drugs		
Others	183 (35.6)	0.68 (1.30)
Continuous users	8 (57.1)	1.21 (1.63)
	P = 0.16[a]	P = 0.13
HRT		
Others	188 (36.4)	0.71 (1.32)
Continuous users	3 (25.0)	0.33 (0.65)
	P = 0.55[a]	P = 0.33
Antiulcer drugs		
Others	187 (36.4)	0.70 (1.31)
Continuous users	4 (28.6)	0.64 (1.39)
	P = 0.78[a]	P = 0.88
Hypoglycaemics		
Others	184 (35.8)	0.68 (1.30)
Continuous users	7 (50.0)	1.14 (1.61)
	P = 0.28	P = 0.20
Prophylactic aspirin		
Others	177 (36.3)	0.69 (1.30)
Continuous users	14 (35.0)	0.83 (1.47)
	P = 0.87	P = 0.52
Psychotherapeutics		
Others	187 (36.5)	0.70 (1.32)
Continuous users	4 (26.7)	0.53 (1.13)
	P = 0.44[a]	P = 0.62
Antidepressants		
Others	188 (36.2)	0.70 (1.31)
Continuous users	3 (37.5)	0.75 (1.39)
	P = 1.00[a]	P = 0.91
Thyroxine		
Others	185 (36.1)	0.69 (1.30)
Continuous users	6 (40.0)	0.87 (1.55)
	P = 0.75[a]	P = 0.61
Hypolipidaemics		
Others	187 (36.5)	0.70 (1.30)
Continuous users	4 (25.0)	0.69 (1.54)
	P = 0.35	P = 0.98

[a]Fisher's Exact test used because one or more expected cell sizes less than 5
[b]Independent samples t-test used here; equality of variances confirmed by Levene's test for homogeneity of variance

[c]Independent samples t-test used here; inequality of variances confirmed by Levene's test for homogeneity of variance

Tooth-loss incidence appeared to be higher among individuals who were "continuously exposed" to antiasthma drugs, cardiac drugs or anginals, but these were not statistically significant. The mean number of teeth lost over the study period was greater among those taking cardiac drugs at baseline and five years.

Data on the five-year tooth-loss of individuals taking the drug combinations which were associated with dry mouth are presented in Table 3.54.

Table 3.54: Tooth loss over the five-year period by the drug combinations which were associated with dry mouth

	Incidence (%)	Mean number of teeth lost (sd)
Anginals at baseline & 5 yrs		
Taken	182 (35.6)	0.70 (1.31)
Not taken	9 (52.9)	1.00 (1.22)
	P = 0.14	P = 0.33
Anginal at 5 yrs only <u>without</u> β-blocker		
Taken	183 (35.6)	0.67 (1.26)
Not taken	8 (57.1)	1.57 (2.41)
	P = 0.10	P = 0.12[b]
Thyroxine & diuretic at 5 years		
Taken	189 (36.3)	0.70 (1.32)
Not taken	2 (28.6)	0.29 (0.49)
	P = 1.00[a]	P = 0.40
Antiasthma drug at baseline & 5 years		
Taken	183 (35.6)	0.68 (1.30)
Not taken	8 (57.1)	1.21 (1.63)
	P = 0.10	P = 0.13
Antidepressants at baseline & 5 years		
Taken	188 (36.2)	0.70 (1.31)
Not taken	3 (37.5)	0.75 (1.39)
	P = 1.00[a]	P = 0.91
Hypolipidaemics at 5 years		
Taken	175 (35.9)	0.69 (1.31)
Not taken	16 (39.0)	0.76 (1.28)
	P = 0.69	P = 0.76

[a]Fisher's Exact test used
[b]Independent samples t-test used (inequality of variances indicated by Levenes test for homogeneity of variance)

There were no significant differences in tooth loss among those medication-exposure groups groups.

Multivariate models

Tooth-loss incidence was modelled using logistic regression. The independent variables used were age at baseline, gender (male = '1'; female = '0'), city of residence (Mt Gambier = '0'; Adelaide = '1'), usual reason for dental visit (regular = '1'; problem = '0'), age when left school (under 16 = '0'; 16+ = '1'), baseline toothbrushing frequency (4 or more times per week = '1'; less frequently = '0'), baseline flossing frequency (occasionally or better = '1'; intermittent or never = '0'), and baseline cigarette smoking status (current smoker = '1'; non-smoker = '0'). Income was not used, as there were too many cases with missing information. Two separate models were developed; the first included the baseline number of missing teeth as a risk predictor, and the second model excluded that characteristic. The taking of cardiac drugs or hypoglycaemic drugs at five years was also entered into the model (taken = '1'; not taken = '0'), as these had shown significant bivariate associations with tooth-loss incidence. The outcome of the procedures is presented in Table 3.55.

Table 3.55: Logistic regression model for five-year tooth-loss incidence

Model (a): Baseline disease characteristic included in model[a]

	B	SE	Odds ratio (95% CI)
Female	-0.383	0.196	0.68 (0.46, 1.00)
Age at baseline	0.027	0.015	1.03 (0.99, 1.06)
Smoker at baseline	0.309	0.430	1.36 (0.59, 3.17)
Adelaide residence	0.100	0.196	1.11 (0.75, 1.62)
Left school at age 16+	-0.134	0.201	0.87 (0.59, 1.30)
Brush 2+ times/day	0.544	0.494	1.72 (0.65, 4.54)
Floss regularly	-0.213	0.190	0.81 (0.56, 1.17)
Regular dental attender	-0.134	0.205	0.87 (0.59, 1.31)
Baseline number of missing teeth	-0.036	0.014	0.96 (0.94, 0.99)
Taking cardiac drugs at 5 years	0.714	0.347	2.04 (1.04, 4.03)
Taking hypoglycaemics at 5 years	0.727	0.389	2.07 (0.96, 4.44)

Model (b): Baseline disease characteristic not included in model[b]

	B	SE	Odds ratio (95% CI)
Female	-0.398	0.194	0.67 (0.46, 0.98)
Age at baseline	0.021	0.014	1.02 (0.99, 1.05)
Smoker at baseline	0.228	0.427	1.26 (0.54, 2.90)
Adelaide residence	0.097	0.195	1.10 (0.75, 1.61)
Left school at age 16+	-0.076	0.198	0.93 (0.63, 1.37)
Brush 2+ times/day	0.491	0.489	1.63 (0.63, 4.26)
Floss regularly	-0.148	0.187	0.86 (0.60, 1.24)
Regular dental attender	0.033	0.194	1.03 (0.71, 1.51)
Taking cardiac drugs at 5 years	0.716	0.347	2.04 (1.04, 4.04)
Taking hypoglycaemics at 5 years	0.737	0.389	2.09 (0.98, 4.46)

[a]Model $\chi^2 = 25.34$; 11 df; 65.84% correctly predicted
[b]Model $\chi^2 = 18.84$; 10 df; 64.89% correctly predicted

In model (a), individuals who were female had lower odds of losing a tooth over the study period. Moreover, the greater the number of missing teeth at baseline, the lower the odds of losing a tooth during the next five years. Those who were taking cardiac inotropics at five years had higher odds of having lost a tooth in the preceding five years. In model (b), being female was associated with lower odds of losing a tooth. Those who were taking cardiac inotropics at five years had higher odds of having lost a tooth in the preceding five years.

The tooth-loss increment was modelled using linear regression. The independent variables used were age at baseline, gender (male = '1'; female = '0'), city of residence (Mt Gambier = '0'; Adelaide = '1'), usual reason for dental visit (regular = '1'; problem = '0'), age when left school (under 16 = '0'; 16+ = '1'), baseline toothbrushing frequency (4 or more times per week = '1'; less frequently = '0'), baseline flossing frequency (occasionally or better = '1'; intermittent or never = '0'), and baseline cigarette smoking status (current smoker = '1'; non-smoker = '0'). Income was not used, as the were too many cases with missing information. Two separate models were developed; the first included the baseline number of missing teeth as a risk predictor, and the second model excluded that characteristic. The taking of (a) cardiac drugs at baseline and five years or (b) hypoglycaemic drugs at five years was also entered into the model (taken = '1'; not taken = '0'), as these variables had shown significant bivariate associations with tooth-loss increment. Income was not used, as there were too many cases with missing information. The outcome of the procedures is presented in Table 3.56.

Table 3.56: Linear regression model of tooth-loss increment over five years

(a) Baseline disease characteristics included in model

	B	Standard error of B	95% CI[a] for B	Significance of T
Female	-0.351	0.118	-0.58, -0.12	P<0.01
Age at baseline	0.0009	0.009	-0.02, 0.02	0.99
Smoker at baseline	0.067	0.263	-0.45, 0.58	0.80
Adelaide residence	0.219	0.117	-0.01, 0.45	0.06
Left school at age 16+	-0.152	0.120	-0.39, 0.08	0.21
Brush 2+ times/day	0.340	0.284	-0.22, 0.90	0.23
Floss regularly	-0.097	0.114	-0.32, 0.13	0.40
Regular dental attender	-0.081	0.124	-0.32, 0.16	0.52
Baseline no. of missing teeth	-0.009	0.009	-0.10, -0.07	0.31
Cardiac drug taken at baseline and 5 years	1.128	0.533	0.08, 2.17	0.04
Hypoglycaemic taken at 5 years	0.733	0.243	0.26, 1.21	P<0.01
Constant	0.595	0.659	-0.70, 1.89	0.37

($R^2 = 0.056$)

(b) Baseline disease characteristics not included in model

	B	Standard error of B	95% CI[a] for B	Significance of T
Female	-0.357	0.117	-0.59, 0.12	P<0.01
Age at baseline	-0.001	0.009	-0.02, 0.02	0.88
Smoker at baseline	0.047	0.262	-0.47, 0.56	0.86
Adelaide residence	0.219	0.117	-0.01, 0.45	0.06
Left school at age 16+	-0.139	0.120	-0.37, 0.10	0.25
Brush 2+ times/day	0.329	0.284	-0.23, 0.89	0.25
Floss regularly	-0.083	0.113	-0.30, 0.14	0.47
Regular dental attender	-0.040	0.117	-0.27, 0.19	0.73
Cardiac drug taken at baseline and 5 years	1.107	0.533	0.06, 2.15	0.04
Hypoglycaemic taken at 5 years	0.739	0.243	0.26, 1.22	P<0.01
Constant	0.547	0.658	-0.74, 1.84	0.41

($R^2 = 0.054$)

[a]Confidence Interval

Model (a) explained 5.6 per cent of the variance in the mean number of teeth lost over the five-year study period, while model (b) explained 5.4 per cent. Females lost fewer teeth than males, and the medication variables were significant predictors in both models: the taking of (a) cardiac drugs at baseline and five years or (b) hypoglycaemic drugs at five years predicted a greater number of teeth lost during the course of the study.

3.2.7.2 Coronal caries

3.2.7.2.1 Medications and five-year coronal caries incidence and adjusted caries increment

There was no association between the total number of medications taken and coronal caries incidence, with 141 (70.5 per cent) of those who were taking no drugs, 134 (63.8 per cent) of those taking 1 to 2 different drugs, and 78 (66.1 per cent) of those taking 3 or more different drugs experiencing coronal caries in at least one surface over the study period (χ^2 = 2.11; 2 df; P = 0.35). The mean adjusted coronal caries increments in each of those drug-exposure groups were 2.72 (sd, 3.32), 2.60 (sd, 3.00) and 2.61 (sd, 3.11) respectively (ANOVA; 2 df; P = 0.93). The correlation between the total number of drugs taken and the adjusted coronal caries increment was extremely low (r = -0.003; P = 0.95).

Data on medications taken at five years and five-year coronal caries incidence and adjusted caries increment are presented in Table 3.57.

Table 3.57: Coronal caries five-year incidence and adjusted caries increment (DFS) among the various medication categories, by five-year medication prevalence

Medication category	Incidence (%)	Adjusted caries increment (sd)
Antihypertensives		
Not taken	174 (68.0)	2.67 (2.84)
Taken	179 (65.8)	2.63 (3.41)
	P = 0.60	P = 0.89
β-blockers		
Not taken	308 (67.1)	2.56 (2.78)
Taken	45 (65.2)	3.22 (4.92)
	P = 0.76	P = 0.28[a]
Diuretics		
Not taken	272 (67.3)	2.73 (3.35)
Taken	81 (65.3)	2.37 (2.34)
	P = 0.68	P = 0.26
ACEIs		
Not taken	284 (64.7)	2.60 (3.06)
Taken	69 (77.5)	2.90 (3.55)
	P = 0.02	P = 0.42
CCBs		
Not taken	289 (67.5)	2.58 (2.80)
Taken	64 (64.0)	2.93 (4.31)
	P = 0.50	P = 0.32
Sympatholytics		
Not taken	339 (67.4)	2.67 (3.16)
Taken	14 (56.0)	2.20 (2.92)
	P = 0.24	P = 0.46
Cardiac drugs		
Not taken	331 (67.4)	2.63 (2.97)
Taken	22 (59.5)	2.90 (4.95)
	P = 0.32	P = 0.62
Anginals		
Not taken	332 (67.6)	2.63 (2.92)
Taken	21 (56.8)	2.86 (5.37)
	P = 0.18	P = 0.67
Analgesics		
Not taken	248 (67.9)	2.72 (3.02)
Taken	105 (64.4)	2.49 (3.41)
	P = 0.43	P = 0.45
Simple analgesics		
Not taken	340 (66.5)	2.66 (3.18)
Taken	13 (76.5)	2.28 (1.82)
	P = 0.39	P = 0.62
NSAIDs		
Not taken	305 (67.9)	2.71 (3.04)
Taken	48 (60.8)	2.30 (3.69)
	P = 0.21	P = 0.28

Antigouts		
Not taken	328 (66.9)	2.69 (3.20)
Taken	25 (65.8)	2.12 (2.17)
	P = 0.89	P = 0.28
Narcotic & comb.analgesics		
Not taken	314 (66.7)	2.64 (3.11)
Taken	39 (68.4)	2.72 (3.45)
	P = 0.79	P = 0.85
Antiasthma drugs		
Not taken	324 (66.5)	2.64 (3.18)
Taken	29 (70.7)	2.79 (2.70)
	P = 0.58	P = 0.77
HRT		
Not taken	334 (66.7)	2.61 (3.11)
Taken	19 (70.4)	3.31 (3.72)
	P = 0.69	P = 0.27
Antiulcer drugs		
Not taken	302 (67.9)	2.72 (3.15)
Taken	51 (61.4)	2.24 (3.10)
	P = 0.25	P = 0.20
Hypoglycaemics		
Not taken	335 (67.3)	2.64 (3.13)
Taken	18 (60.0)	2.78 (3.43)
	P = 0.41	P = 0.81
Prophylactic aspirin		
Not taken	245 (66.6)	2.50 (2.57)
Taken	108 (67.5)	2.99 (4.16)
	P = 0.84	P = 0.10
Psychotherapeutics		
Not taken	331 (67.3)	2.72 (3.20)
Taken	22 (61.1)	1.68 (2.07)
	P = 0.45	P = 0.06[b]
Antidepressants		
Not taken	339 (67.1)	2.71 (3.18)
Taken	14 (60.9)	1.38 (1.63)
	P = 0.53	P = 0.05
Thyroxine		
Not taken	343 (67.3)	2.70 (3.16)
Taken	10 (55.6)	2.33 (2.65)
	P = 0.30	P = 0.67
Hypolipidaemics		
Not taken	327 (67.1)	2.63 (3.16)
Taken	26 (63.4)	2.83 (2.98)
	P = 0.63	P = 0.71

[a]Independent samples t-test used here; inequality of variances confirmed by Levene's test for homogeneity of variance

[b]Independent samples t-test used here; inequality of variances not confirmed by Levene's test for homogeneity of variance

Coronal caries incidence was higher among individuals who were taking ACE inhibitors at five years. The mean AdjCI was lower among those taking antidepressants at five years, and an apparently lower rate among those taking psychotherapeutics at five years did not reach statistical significance.

Data on medications taken at baseline and five years and five-year coronal caries incidence and adjusted caries increment are presented in Table 3.58.

Table 3.58: Coronal caries five-year incidence and adjusted caries increment (DFS) among the various medication categories, continuous users compared with the remainder

	Incidence (%)	Adjusted caries increment (sd)
Medication category		
Antihypertensives		
Others	244 (68.2)	2.64 (3.03)
Continuous users	109 (64.1)	2.66 (3.38)
	P = 0.36	P = 0.96
β-blockers		
Others	340 (66.8)	2.60 (3.04)
Continuous users	13 (68.4)	4.02 (5.20)
	P = 0.88	P = 0.25[b]
Diuretics		
Others	308 (67.2)	2.71 (3.26)
Continuous users	45 (64.3)	2.25 (2.23)
	P = 0.62	P = 0.25
ACEIs		
Others	352 (67.0)	2.66 (3.15)
Continuous users	1 (33.3)	1.00 (1.73)
	P = 0.26[a]	P = 0.36
CCBs		
Others	331 (68.0)	2.66 (3.10)
Continuous users	22 (53.7)	2.56 (3.62)
	P = 0.06	P = 0.86
Sympatholytics		
Others	349 (67.5)	2.65 (3.12)
Continuous users	4 (36.4)	2.55 (4.16)
	P = 0.05[a]	P = 0.91
Cardiac drugs		
Others	350 (67.0)	2.66 (3.16)
Continuous users	3 (50.0)	1.58 (1.03)
	P = 0.32[a]	P = 0.40
Anginals		
Others	345 (67.5)	2.67 (3.16)
Continuous users	8 (47.1)	2.04 (2.61)
	P = 0.08	P = 0.41
Analgesics		
Others	309 (67.2)	2.68 (3.23)
Continuous users	44 (64.7)	2.41 (2.49)
	P = 0.69	P = 0.50
Simple analgesics		
Others	352 (66.8)	2.65 (3.15)
Continuous users	1 (100.0)	2.41 (—)
	P = 1.00[a]	P = 0.95

NSAIDs		
Others	331 (67.3)	2.70 (3.18)
Continuous users	22 (61.1)	1.97 (2.50)
	P = 0.45	P = 0.18
Antigouts		
Others	341 (67.0)	2.65 (3.16)
Continuous users	12 (63.2)	2.71 (2.65)
	P = 0.73	P = 0.93
Narcotic & comb. analgesics		
Others	347 (66.6)	2.66 (3.16)
Continuous users	6 (85.7)	2.08 (1.43)
	P = 0.43[a]	P = 0.63
Antiasthma drugs		
Others	339 (66.0)	2.61 (3.15)
Continuous users	14 (100.0)	3.98 (2.69)
	P = 0.01[a]	P = 0.11
HRT		
Others	345 (66.9)	2.64 (3.16)
Continuous users	8 (66.7)	3.05 (2.34)
	P = 1.00[a]	P = 0.65
Antiulcer drugs		
Others	342 (66.5)	2.66 (3.17)
Continuous users	11 (78.6)	2.10 (1.99)
	P = 0.35	P = 0.51
Hypoglycaemics		
Others	344 (66.9)	2.61 (3.10)
Continuous users	9 (64.3)	4.24 (4.41)
	P = 0.52[a]	P = 0.19[b]
Prophylactic aspirin		
Others	326 (66.8)	2.63 (3.14)
Continuous users	27 (67.5)	2.82 (3.18)
	P = 0.93	P = 0.72
Psychotherapeutics		
Others	345 (67.3)	2.69 (3.16)
Continuous users	8 (53.3)	1.17 (1.88)
	P = 0.27[a]	P = 0.01[c]
Antidepressants		
Others	348 (66.9)	2.67 (3.16)
Continuous users	5 (62.5)	1.46 (1.39)
	P = 0.72[a]	P = 0.28
Thyroxine		
Others	345 (67.3)	2.66 (3.15)
Continuous users	8 (53.3)	2.32 (2.90)
	P = 0.27[a]	P = 0.68
Hypolipidaemics		
Others	342 (66.8)	2.64 (3.16)
Continuous users	11 (68.8)	3.05 (2.82)
	P = 0.87	P = 0.61

[a]Fisher's Exact test used instead of Chi-square test

(Footnotes continue over page)

[b]Independent samples t-test used here; inequality of variances confirmed by Levene's test for homogeneity of variance
[c]Independent samples t-test used here; inequality of variances not confirmed by Levene's test for homogeneity of variance

Coronal caries incidence was higher among individuals who were taking antiasthma drugs at both baseline and five years, and lower among those who were taking sympatholytic antihypertensives at both baseline and five years. The mean AdjCI was lower among individuals who were taking psychotherapeutic drugs at both baseline and five years.

Data on the five-year coronal caries experience of individuals taking the drug combinations which were associated with dry mouth are presented in Table 3.59.

Table 3.59: Coronal caries incidence and adjusted increment over the five-year period by the drug combinations which were associated with dry mouth

	Incidence (%)	AdjCI (sd)
Anginals at baseline & 5 yrs		
Not taken	345 (67.5)	2.67 (3.16)
Taken	9 (47.1)	2.04 (2.61)
	P = 0.08	P = 0.41
Anginal at 5 yrs only without β-blocker		
Not taken	344 (66.9)	2.68 (3.17)
Taken	9 (64.3)	1.57 (1.43)
	P = 0.52[a]	P = 0.20
Thyroxine & diuretic at 5 yrs		
Not taken	350 (67.2)	2.65 (3.15)
Taken	3 (42.9)	2.57 (3.11)
	P = 0.23[a]	P = 0.95
Antiasthma drug at baseline & 5 yrs		
Not taken	339 (66.0)	2.61 (3.15)
Taken	14 (100.0)	3.98 (2.69)
	P = 0.01[a]	P = 0.11
Antidepressants at baseline and at 5 years		
Not taken	348 (66.9)	2.67 (3.16)
Taken	5 (62.5)	1.46 (1.39)
	P = 0.72[a]	P = 0.28
Hypolipidaemics at 5 yrs*		
Not taken	327 (67.1)	2.63 (3.16)
Taken	26 (63.4)	2.83 (2.98)
	P = 0.63	P = 0.71

[a]Fisher's Exact test used

The only significant difference among those medication-exposure groups was the considerably higher coronal caries incidence among people taking antiasthma drugs at baseline and five years.

Multivariate models

Coronal caries incidence was modelled using logistic regression, with the following independent variables initially entered into the model (after Beck, 1987): age at baseline, gender (male = '1'; female = '0'), city of residence (Mt Gambier = '0'; Adelaide = '1'), baseline number of chronic medical conditions, baseline coronal DFS and root surface DFS, usual reason for dental visit at baseline (regular = '1'; problem = '0'), age when left school (under 16 = '0'; 16+ = '1'), baseline toothbrushing frequency (4 or more times per week = '1'; less frequently = '0'), baseline flossing frequency (occasionally or better = '1'; intermittent or never = '0'), and baseline cigarette smoking status (current smoker = '1'; non-smoker = '0'). ACE inhibitors at five years, and the taking of antiasthma drugs or sympatholytics at baseline and five years were also entered into the model (taken = '1'; not taken = '0'), as these had shown significant bivariate associations with the dependent variable. Income was not used, as there were too many cases with missing information.

Two separate models were developed: the first included risk predictors such as baseline disease experience (baseline coronal DFS); and the second model excluded those characteristics on the basis that they were likely to be powerful predictors which may mask other potential risk factors (Beck, 1998). The outcomes of the procedures are presented in Table 3.60.

Table 3.60: Logistic regression model[a] for five-year incidence of coronal caries

(a) Baseline disease characteristics included in model[a]

	B	SE	Odds ratio (95% CI)
Female	-0.185	0.207	0.83 (0.55, 1.25)
Age at baseline	-0.012	0.015	0.99 (0.96, 1.02)
Smoker at baseline	-0.176	0.435	0.84 (0.36, 1.970
Adelaide residence	-0.185	0.208	0.83 (0.55, 1.25)
Left school at age 16+	-0.176	0.218	0.84 (0.55, 1.29)
Brush 2+ times/day	0.231	0.476	1.26 (0.50, 3.20)
Floss regularly	-0.076	0.199	0.93 (0.63, 1.37)
Regular dental attender	0.288	0.223	1.33 (0.86, 2.06)
Baseline coronal DFS	0.036	0.008	1.04 (1.02, 1.05)
Taking ACEIs at 5 years	0.622	0.289	1.86 (1.06, 3.28)
Taking antiasthma drugs at baseline and five years	6.185	9.467	485.20 (0, 6×10^{10})
Taking sympatholytics at baseline and 5 years	-1.554	0.681	0.21 (0.06, 0.80)

(b) Baseline disease characteristics not included in model[b]

Female	-0.139	0.202	0.87 (0.59, 1.29)
Age at baseline	-0.023	0.015	0.98 (0.95, 1.01)
Smoker at baseline	-0.358	0.422	0.70 (0.31, 1.60)
Adelaide residence	-0.215	0.204	0.81 (0.54, 1.20)
Left school at age 16+	0.066	0.206	1.07 (0.71, 1.60)
Brush 2+ times/day	0.219	0.464	1.24 (0.50, 3.09)
Floss regularly	0.030	0.194	1.03 (0.70, 1.51)
Regular dental attender	0.653	0.204	1.92 (1.29, 2.87)
Taking ACEIs at 5 years	0.513	0.284	1.67 (0.96, 2.91)
Taking antiasthma drugs at baseline and five years	6.300	9.674	544.41 (0, 9×10^{10})
Taking sympatholytics at baseline and 5 years	-1.598	0.666	0.20 (0.05, 0.75)

[a]Model $\chi^2 = 56.67$; 13 df; 75.42% correctly predicted
[b]Model $\chi^2 = 39.91$; 12 df; 73.09% correctly predicted

In model (a), higher baseline disease experience predicted greater odds of experiencing a coronal caries increment during the subsequent five years, and the taking of an ACE inhibitor antihypertensive at five years was associated with a higher incidence. In model (b), regular dental attenders had higher odds of experiencing a coronal caries increment. In both models, the taking of sympatholytic antihypertensive medications at

baseline and five years predicted a lower incidence of coronal caries, and the taking of antiasthma medications at baseline and five years predicted a higher incidence of coronal caries.

When the models were rerun with either one of (or both) the XI score or the flow rate as additional independent variables, none of those emerged as a predictor.

The adjusted coronal caries increment was modelled using linear regression, with the following independent variables initially entered into the model (after Beck, 1987): age at baseline, gender (male = '1'; female = '0'), city of residence (Mt Gambier = '0'; Adelaide = '1'), baseline number of missing teeth (continuous), usual reason for dental visit (regular = '1'; problem = '0'), age when left school (under 16 = '0'; 16+ = '1'), baseline toothbrushing frequency (4 or more times per week = '1'; less frequently = '0'), baseline flossing frequency (occasionally or better = '1'; intermittent or never = '0'), and baseline cigarette smoking status (current smoker = '1'; non-smoker = '0'). Psychotherapeutic drugs at baseline and five years, and antidepressants at five years were also entered into the model (taken = '1'; not taken = '0'), as these had shown significant bivariate associations with the dependent variable. As with Table 3.60, two separate models were developed, with the first including baseline disease experience as a risk predictor, and the second model excluding it. The outcome of those procedures is presented in Table 3.61.

Table 3.61: Linear regression model of adjusted coronal caries increment over five years

(a) Baseline disease characteristics included in model[a]

	B	Standard error of B	95% CI[a] for B	Significance of T
Female	-0.552	0.270	-1.08, -0.02	0.04
Age at baseline	0.025	0.020	-0.01, 0.06	0.23
Smoker at baseline	-0.602	0.606	-1.79, 0.59	0.32
Adelaide residence	0.133	0.269	-0.39, 0.66	0.62
Left school at age 16+	-0.546	0.284	-1.10, 0.01	0.06
Brush 2+ times/day	0.214	0.652	-1.06, 1.49	0.74
Floss regularly	-0.139	0.262	-0.65, 0.37	0.60
Regular dental attender	0.141	0.290	-0.43, 0.71	0.63
Baseline coronal DFS	0.072	0.010	0.05, 0.09	P<0.01
Psychotherapeutic drugs at baseline and 5 years	-0.769	0.786	-2.31, 0.77	0.33
Antidepressants at 5 years	-1.199	0.648	-2.47, 0.07	0.07
Constant	-0.164	1.563	-3.23, 2.90	0.92

($R^2 = 0.132$)

(b) Baseline disease characteristics not included in model[b]

	B	Standard error of B	95% CI[a] for B	Significance of T
Female	-0.447	0.282	1.00, 0.11	0.11
Age at baseline	0.011	0.021	-0.03, 0.05	0.99
Smoker at baseline	-0.979	0.633	-2.22, 0.26	0.12
Adelaide residence	0.061	0.282	-0.49, 0.61	0.83
Left school at age 16+	-0.034	0.289	-0.60, 0.53	0.91
Brush 2+ times/day	0.197	0.684	-1.14, 1.54	0.77
Floss regularly	-0.058	0.274	-0.60, 0.48	0.83
Regular dental attender	0.906	0.283	0.35, 1.46	P<0.01
Psychotherapeutic drugs at baseline and 5 years	-1.233	0.822	-2.84, 0.38	0.13
Antidepressants at 5 years	-1.133	0.679	-2.46, 0.20	0.10
Constant	2.296	1.600	-0.84, 5.43	0.15

($R^2 = 0.043$)

[a]Confidence Interval

The first model explained 13.2 per cent of the variance in five-year adjusted coronal caries increment, the second, 4.3 per cent. In the first model, baseline coronal DFS was

a predictor of a higher five-year adjusted coronal caries increment, and being female predicted a lower increment. No medications reached statistical significance, although the taking of antidepressants went close. In the second model, being a regular dental attender was the only predictor of the five-year adjusted coronal caries increment.

3.2.7.3 Root surface caries

3.2.7.3.1 Medications and five-year root surface caries experience

There was no significant association between the total number of medications taken and root surface caries incidence, with 128 (64.0 per cent) of those who were taking no drugs, 119 (56.7 per cent) of those taking 1 to 2 different drugs, and 66 (55.9 per cent) of those taking 3 or more different drugs having experienced root surface caries in at least one surface over the study period ($\chi^2 = 2.99$; 2 df; P = 0.22). The mean root surface adjusted caries increments in each of those drug-exposure groups were 2.52 (sd, 3.11), 2.03 (sd,2.55) and 2.03 (sd, 2.79) respectively (ANOVA; 2 df; P = 0.16). The correlation between the total number of drugs taken and the adjusted root surface caries increment was extremely low (r = -0.06; P = 0.17).

Data on medications taken at five years and five-year root surface caries incidence and adjusted root surface caries increment are presented in Table 3.62.

Table 3.62: Root surface caries five-year incidence and adjusted root surface caries increment (DFS) among the various medication categories, by five-year medication prevalence

Medication category	Incidence (%)	Adjusted root surface caries increment (sd)
Antihypertensives		
Not taken	161 (62.9)	2.52 (3.10)
Taken	152 (55.9)	1.93 (2.53)
	P = 0.10	P = 0.02
β-blockers		
Not taken	275 (59.9)	2.24 (2.83)
Taken	38 (55.1)	2.03 (2.84)
	P = 0.45	P = 0.56
Diuretics		
Not taken	244 (60.4)	2.34 (2.94)
Taken	69 (55.6)	1.81 (2.41)
	P = 0.35	P = 0.07
ACEIs		
Not taken	256 (58.3)	2.20 (2.82)
Taken	57 (64.0)	2.26 (2.90)
	P = 0.32	P = 0.88
CCBs		
Not taken	256 (59.8)	2.20 (2.89)
Taken	57 (57.0)	2.29 (2.57)
	P = 0.90	P = 0.77
Sympatholytics		
Not taken	299 (59.4)	2.26 (2.87)
Taken	14 (56.0)	1.26 (1.83)
	P = 0.73	P = 0.09
Cardiac drugs		
Not taken	294 (59.9)	2.24 (2.85)
Taken	19 (51.4)	1.89 (2.59)
	P = 0.31	P = 0.47
Anginals		
Not taken	294 (59.9)	2.23 (2.82)
Taken	19 (51.4)	1.99 (2.97)
	P = 0.31	P = 0.63
Analgesics		
Not taken	217 (59.5)	2.24 (2.89)
Taken	96 (58.9)	2.16 (2.72)
	P = 0.90	P = 0.76
Simple analgesics		
Not taken	304 (59.5)	2.20 (2.83)
Taken	9 (52.9)	2.75 (2.91)
	P = 0.59	P = 0.43

NSAIDs		
Not taken	265 (59.0)	2.25 (2.94)
Taken	48 (60.8)	2.00 (2.15)
	P = 0.77	P = 0.47
Antigouts		
Not taken	293 (59.8)	2.20 (2.75)
Taken	20 (52.6)	2.38 (3.81)
	P = 0.39	P = 0.71
Narcotic & comb. analgesics		
Not taken	279 (59.2)	2.24 (2.89)
Taken	34 (59.6)	1.98 (2.35)
	P = 0.95	P = 0.51
Antiasthma drugs		
Not taken	290 (59.5)	2.25 (2.88)
Taken	23 (56.1)	1.77 (2.21)
	P = 0.67	P = 0.30
HRT		
Not taken	297 (59.3)	2.19 (2.80)
Taken	16 (59.3)	2.64 (3.39)
	P = 1.00	P = 0.43
Antiulcer drugs		
Not taken	263 (59.1)	2.20 (2.77)
Taken	50 (60.2)	2.27 (3.17)
	P = 0.85	P = 0.85
Hypoglycaemics		
Not taken	292 (58.6)	2.22 (2.00)
Taken	21 (70.0)	2.16 (2.78)
	P = 0.22	P = 0.91
Prophylactic aspirin		
Not taken	220 (59.8)	2.24 (2.85)
Taken	93 (58.1)	2.14 (2.79)
	P = 0.72	P = 0.70
Psychotherapeutics		
Not taken	293 (59.6)	2.24 (2.83)
Taken	20 (55.6)	1.89 (2.90)
	P = 0.64	P = 0.48
Antidepressants		
Not taken	297 (58.8)	2.26 (2.88)
Taken	16 (69.6)	1.25 (1.08)
	P = 0.31	P = 0.10
Thyroxine		
Not taken	302 (54.3)	2.24 (2.86)
Taken	11 (61.1)	1.58 (1.95)
	P = 0.87	P = 0.34
Hypolipidaemics		
Not taken	292 (60.0)	2.24 (2.82)
Taken	21 (51.2)	1.90 (2.96)
	P = 0.27	P = 0.46

Individuals taking an antihypertensive at five years had had a lower root surface caries adjusted increment over the previous five years; those taking diuretics or sympatholytic antihypertensives at five years had apparently lower increments, but these did not reach statistical significance. No medication-exposure groups differed in their root surface caries incidence.

Data on medications taken at baseline and five years and five-year root surface caries incidence and adjusted caries increment are presented in Table 3.63.

Table 3.63: Root surface caries five-year incidence and adjusted root surface caries increment (DFS) among the various medication categories, continuous users compared with the remainder

Medication category	Incidence (%)	Adjusted root surface caries increment (sd)
Antihypertensives		
Others	216 (60.3)	2.38 (3.00)
Continuous users	97 (57.1)	1.87 (2.41)
	P = 0.47	P = 0.05
β-blockers		
Others	302 (59.3)	2.19 (2.78)
Continuous users	11 (57.9)	2.82 (4.09)
	P = 0.90	P = 0.34
Diuretics		
Others	273 (59.6)	2.29 (2.90)
Continuous users	40 (57.1)	1.74 (2.31)
	P = 0.70	P = 0.14
ACEIs		
Others	311 (59.2)	2.22 (2.84)
Continuous users	2 (66.7)	0.67 (0.58)
	P = 1.00[a]	P = 0.34
CCBs		
Others	291 (59.8)	2.26 (2.89)
Continuous users	22 (53.7)	1.63 (1.94)
	P = 0.45	P = 0.17
Sympatholytics		
Others	304 (58.8)	2.21 (2.85)
Continuous users	9 (81.8)	2.17 (2.22)
	P = 0.21[a]	P = 0.96
Cardiac drugs		
Others	310 (59.4)	2.21 (2.83)
Continuous users	3 (50.0)	2.17 (2.99)
	P = 0.69[a]	P = 0.97
Anginals		
Others	305 (59.7)	2.22 (2.81)
Continuous users	8 (47.1)	2.00 (3.66)
	P = 0.30	P = 0.75
Analgesics		
Others	275 (59.8)	2.21 (2.80)
Continuous users	38 (55.9)	2.25 (3.08)
	P = 0.54	P = 0.91
Simple analgesics		
Others	313 (59.4)	2.21 (2.84)
Continuous users	0 (0.0)	2.00 (—)
	P = 0.41[a]	P = 0.94

NSAIDs		
Others	292 (59.3)	2.23 (2.89)
Continuous users	21 (58.3)	1.94 (1.97)
	P = 0.91	P = 0.55
Antigouts		
Others	301 (59.1)	2.16 (2.73)
Continuous users	12 (63.2)	3.66 (4.76)
	P = 0.73	P = 0.19[b]
Narcotic & comb. analgesics		
Others	309 (59.3)	2.22 (2.84)
Continuous users	4 (57.1)	1.38 (2.45)
	P = 1.00[a]	P = 0.45
Antiasthma drugs		
Others	305 (59.3)	2.23 (2.85)
Continuous users	8 (57.1)	1.67 (1.96)
	P = 0.87	P = 0.47
HRT		
Others	304 (58.9)	2.19 (2.82)
Continuous users	9 (75.0)	3.10 (3.49)
	P = 0.38	P = 0.28
Antiulcer drugs		
Others	305 (59.3)	2.20 (2.80)
Continuous users	8 (57.1)	2.61 (3.93)
	P = 0.87	P = 0.60
Hypoglycaemics		
Others	302 (58.8)	2.19 (2.82)
Continuous users	11 (78.6)	3.06 (3.14)
	P = 0.14	P = 0.26
Prophylactic aspirin		
Others	297 (60.9)	2.28 (2.88)
Continuous users	16 (40.0)	1.40 (2.08)
	P = 0.01	P = 0.06
Psychotherapeutics		
Others	307 (59.8)	2.24 (2.86)
Continuous users	6 (40.0)	1.25 (1.60)
	P = 0.12	P = 0.18
Antidepressants		
Others	307 (59.0)	2.22 (2.85)
Continuous users	6 (75.0)	1.85 (0.96)
	P = 0.48[a]	P = 0.72
Thyroxine		
Others	304 (59.3)	2.23 (2.85)
Continuous users	9 (60.0)	1.63 (1.96)
	P = 0.95	P = 0.42
Hypolipidaemics		
Others	304 (59.4)	2.22 (2.85)
Continuous users	9 (56.3)	1.89 (2.46)
	P = 0.80	P = 0.64

[a]Fisher's Exact test used because one or more expected cell sizes less than 5
[b]Independent samples t-test performed here because of inequality of variances in the two exposure groups

Root surface caries incidence was lower among individuals who were taking prophylactic aspirin at both baseline and five years. Those taking an antihypertensive at baseline and five years had a lower root surface caries adjusted increment, but there were no significant differences in any of the antihypertensive subclasses.

Data on the five-year root surface caries experience of individuals taking the drug combinations which were associated with dry mouth are presented in Table 3.64.

Table 3.64: Root surface caries five-year incidence and adjusted root surface caries increment (DFS) by the drug combinations which were associated with dry mouth

	Incidence (%)	Adjusted root surface caries increment (sd)
Anginals at baseline & 5 yrs		
Not taken	305 (59.7)	2.22 (2.81)
Taken	8 (47.1)	2.00 (3.66)
	P = 0.30	P = 0.75
Anginal at 5 yrs only without β-blocker		
Not taken	305 (54.5)	2.22 (2.85)
Taken	8 (57.1)	1.84 (2.36)
	P = 0.87	P = 0.62
Thyroxine & diuretic at 5 yrs		
Not taken	309 (59.3)	2.22 (2.84)
Taken	4 (57.1)	1.39 (1.80)
	P = 1.00[a]	P = 0.44
Antiasthma drug at baseline & 5 yrs		
Not taken	305 (59.3)	2.23 (2.85)
Taken	8 (57.1)	1.67 (1.96)
	P = 0.87	P = 0.47
Antidepressants at baseline and at 5 years		
Not taken	307 (59.0)	2.22 (2.85)
Taken	6 (75.0)	1.85 (0.96)
	P = 0.48[a]	P = 0.72
Hypolipidaemics at 5 yrs*		
Not taken	304 (59.4)	2.22 (2.85)
Taken	9 (56.3)	1.89 (2.46)
	P = 0.80	P = 0.64

[a]Fisher's Exact test used because one or more expected cell sizes less than 5
[b]Independent samples t-test performed here because of inequality of variances in the two exposure groups

There were no significant differences among those medication-exposure groups groups.

Multivariate models

Root surface caries incidence was modelled using logistic regression, with the following independent variables initially entered into the model (after Beck, 1987): age at baseline, gender (male = '1'; female = '0'), city of residence (Mt Gambier = '0'; Adelaide = '1'), baseline number of chronic medical conditions, baseline coronal DFS and root surface DFS, baseline number of missing teeth (continuous), usual reason for dental visit (regular = '1'; problem = '0'), age when left school (under 16 = '0'; 16+ = '1'), baseline toothbrushing frequency (4 or more times per week = '1'; less frequently = '0'), baseline flossing frequency (occasionally or better = '1'; intermittent or never = '0'), and baseline cigarette smoking status (current smoker = '1'; non-smoker = '0'). Prophylactic aspirin ("continuous" use) was also entered into the model (taken = '1'; not taken = '0'), as it had shown significant bivariate associations with the dependent variable. Income was not used, as there were too many cases with missing information. Two separate models were developed; the first included baseline root DFS as a risk predictor, and the second model excluded that characteristic on the basis that it was likely to be powerful predictors which may mask other potential risk factors (Beck, 1998). The outcomes of the procedures are presented in Table 3.65.

Table 3.65: Logistic regression models for five-year incidence of root surface caries

(a) Baseline disease characteristics included in model[a]

	B	SE	Odds ratio (95% CI)
Female	0.007	0.190	1.00 (0.69, 1.46)
Age at baseline	0.014	0.014	1.01 (0.99, 1.04)
Smoker at baseline	0.401	0.436	1.49 (0.64, 3.51)
Adelaide residence	-0.337	0.190	0.71 (0.49, 1.04)
Left school at age 16+	0.0003	0.192	1.00 (0.69, 1.46)
Baseline root DFS	-0.004	0.028	1.00 (0.94, 1.05)
Brush 2+ times/day	0.697	0.452	2.01 (0.83, 4.87)
Floss regularly	-0.067	0.182	0.94 (0.65, 1.34)
Regular dental attender	0.166	0.193	1.18 (0.81, 3.72)
Prophylactic aspirin taken at baseline and 5 years	-0.905	0.348	0.40 (0.20, 0.80)

(b) Baseline disease characteristics not included in model[b]

	B	SE	Odds ratio (95% CI)
Female	0.102	0.189	1.01 (0.70, 1.46)
Age at baseline	0.013	0.014	1.01 (0.99, 1.04)
Smoker at baseline	0.405	0.436	1.50 (0.64, 3.52)
Adelaide residence	-0.338	0.190	0.71 (0.49, 1.03)
Left school at age 16+	0.000[c]	0.192	1.00 (0.69, 1.46)
Brush 2+ times/day	0.693	0.451	2.00 (0.83, 4.83)
Floss regularly	-0.068	0.182	0.93 (0.65, 1.34)
Regular dental attender	0.160	0.188	1.17 (0.81, 1.70)
Prophylactic aspirin taken at baseline and 5 years	-0.903	0.347	0.41 (0.21, 0.80)

[a]Model $\chi^2 = 13.44$; 10 df; 61.04% correctly predicted
[b]Model $\chi^2 = 14.58$; 9 df; 61.83% correctly predicted
[c]Rounded from 0.0000022

In both models, the only significant predictor was the taking of prophylactic aspirin at baseline and 5 years, whereby those individuals had lower odds of being an incident case of root surface caries.

When models (a) and (b) were rerun with either one of (or both) the XI score or the flow rate as additional independent variables, none of those emerged as a predictor.

The adjusted root surface caries increment was modelled using linear regression, with the following independent variables initially entered into the model (after Beck, 1987): age at baseline, gender (male = '1'; female = '0'), city of residence (Mt Gambier = '0'; Adelaide = '1'), usual reason for dental visit (regular = '1'; problem = '0'), age when left school (under 16 = '0'; 16+ = '1'), baseline toothbrushing frequency (4 or more times per week = '1'; less frequently = '0'), baseline flossing frequency (occasionally or better = '1'; intermittent or never = '0'), and baseline cigarette smoking status (current smoker = '1'; non-smoker = '0'). The taking of one or more antihypertensives at baseline and five years ("continuous use"; taken = '1'; not taken = '0') was also entered into the model, as this had shown significant bivariate associations with the dependent variable. Income was not used, as there were too many cases with missing information. Two separate models were developed; the first included baseline root DFS as a risk predictor, and the second model excluded that characteristic. The outcome of the procedures is presented in Table 3.66.

Table 3.66: Linear regression model of adjusted root surface caries increment over five years

(a) Baseline disease characteristics included in model

	B	Standard error of B	95% CI[a] for B	Significance of T
Female	-0.161	0.258	-0.67, 0.35	0.53
Age at baseline	-0.016	0.019	-0.05, 0.02	0.40
Smoker at baseline	-0.370	0.574	-1.50, 0.76	0.52
Adelaide residence	-0.171	0.256	-0.67, 0.33	0.50
Left school at age 16+	-0.188	0.261	-0.70, 0.32	0.47
Baseline root DFS	0.104	0.038	0.03, 0.18	P<0.01
Brush 2+ times/day	0.797	0.623	-0.42, 2.02	0.20
Floss regularly	0.157	0.248	-0.33, 0.64	0.53
Regular dental attender	0.401	0.262	-0.11, 0.92	0.13
Antihypertensive taken at baseline and 5 years	-0.442	0.266	-0.96, 0.08	0.10
Constant	2.371	1.439	-0.45, 5.19	0.10

($R^2 = 0.040$)

(b) Baseline disease characteristics not included in model

	B	Standard error of B	95% CI[a] for B	Significance of T
Female	-0.235	0.258	-0.74, 0.27	0.36
Age at baseline	-0.011	0.019	-0.05, 0.03	0.56
Smoker at baseline	-0.476	0.577	-1.61, 0.65	0.41
Adelaide residence	-0.157	0.257	-0.66, 0.35	0.54
Left school at age 16+	-0.179	0.263	-0.69, 0.34	0.50
Brush 2+ times/day	0.914	0.625	-0.31, 2.14	0.14
Floss regularly	0.187	0.250	-0.30, 0.68	0.45
Regular dental attender	0.548	0.258	0.04, 1.05	P<0.05
Antihypertensive taken at baseline and 5 years	-0.433	0.268	-0.96, 0.09	0.11
Constant	2.169	1.446	-0.67, 5.00	0.13

($R^2 = 0.026$)

[a]Confidence Interval

The baseline root surface DFS was the sole predictor of the five-year adjusted root surface caries increment in model (a), which explained 4.0 per cent of the variance in five-year adjusted root surface caries increment. When baseline root DFS was omitted,

being a regular user of dental services was (positively) associated with the outcome variable (in model (b), which explained 2.6 per cent of the variance). When the models were rerun with either one of (or both) the XI score or the flow rate as additional independent variables, neither of those emerged as a predictor.

3.2.8 Summary: medications and five-year disease experience

The detailed approach taken in the above analyses may have produced the situation where the reader is in need of a summary which presents all the statistically-significant associations of medications with the range of outcome measures from the longitudinal analyses in order to facilitate the reading of the Discussion section. Such a summary is presented in Table 3.67.

Table 3.67: Summary of statistically-significant associations of medication exposure with five-year tooth-loss and dental caries outcomes

Outcome of bivariate analyses

	Medication	Confirmed by multivariate analysis?
Tooth loss		
Incidence	Cardiac drugs at 5 years (↑)	Yes
	Hypoglycaemics at 5 years (↑)	No
Increment	Cardiac drugs at 5 years (↑)	Yes
	Hypoglycaemics at 5 years (↑)	Yes
Coronal caries		
Incidence	Antiasthma drugs at baseline and 5 years (↑)	Yes
	ACEI antihypertensives at 5 years (↑)	Yes
	Sympatholytic antihypertensives at 5 years (↓)	Yes
Adjusted increment	β-blockers at 5 years (↑)	No
	Antidepressants at 5 years (↓)	No
	Psychotherapeutics at baseline and 5 years (↑)	No
Root surface caries		
Incidence	Prophylactic aspirin at baseline and 5 years (↓)	Yes
Adjusted increment	Antihypertensive at 5 years (↓)	No

[a]Arrows indicate direction of the effect: ↑ indicates a positive association; ↓ indicates a negative association

Of the 11 significant bivariate associations which were observed, seven were strong enough to persist after other potential confounders were controlled using multivariate analysis.

4. Discussion

The Discussion section is organised as a series of loosely linked parts. First, the baseline findings are briefly discussed; this is followed by discussion of the retention of the SADLS baseline sample at five years; and then the medications taken by the SADLS sample are considered. Both aspects of dry mouth are then dealt with in turn, and then the five-year dental caries experience of the SADLS sample is examined with the ultimate aim of determining whether certain medications are associated with tooth-loss or dental caries experience among older people.

4.1 Discussion of baseline findings

There are two major concerns about the baseline medication data. First, to what extent is the prevalence of the various medication types in SADLS representative of the older population at large; and, second, what was the duration of exposure to each medication type likely to have been, given that data on exposure duration were not collected in SADLS? The latter is a particularly critical issue, given that the development of root surface caries is not a particularly rapid process: although no data have been reported on the *progression* of root surface caries in older populations, the *increment* has been recently reported to be approximately 0.5 new surfaces affected over a five-year period among older people in the Piedmont study (Lawrence *et al*, 1996). This is lower than the 18-month increment rate reported for a population of older Iowans (Hunt *et al*, 1989), and suggests that older populations may differ substantially in their root surface caries increment rates. However, it is likely that the duration of exposure would have to be of the order of *years* for a medication to be seriously considered as a potential modifier of the caries process.

A useful source of confirmation (or otherwise) that the medication patterns observed in the SADLS dataset are generally representative of those which existed in the wider population of older South Australians is the baseline data set from the Australian Longitudinal Study on Ageing (ALSA), for which the sampling strategy and data collection are described in Section 2.2.1. The ALSA sample was drawn from the

Adelaide statistical division. While comparisons are available only for dentate people aged 70 and over (862 individuals in ALSA; 315 in SADLS)—because weights were only available in the ALSA for individuals who were aged 70 or more—those which are possible should be sufficient to indicate whether the SADLS sample and medication patterns appear to be representative of older people in South Australia. This is examined in the following two sections.

4.1.1 Socio-demographic characteristics and overall medication levels

The distributions of a number of key socio-demographic, dental and medication characteristics of dentate participants aged 70+ in the SADLS and ALSA studies are compared in Table 4.1.

Table 4.1: Comparison of dentate individuals aged 70+ in the SADLS (Adelaide participants only) and ALSA samples (weighted data)

	ALSA	SADLS
Number of participants	862	315
Socio-demographic attributes		
Female	52.1%	51.1%
Mean age (sd)	76.0 (5.3)	75.5 (5.2)
Annual income > $20,000	22.0%	22.3%
Dental characteristics		
Episodic dental visiting pattern	54.1%	50.6%
Mean no. of teeth[a] (sd)	21.7 (6.0)	16.2 (6.9)
Medication		
No. of prescribed drugs being taken (sd)	3.0 (2.4)	2.3 (2.4)
Range of prescribed drugs being taken	0 to 9	0 to 12

[a]Self-reported for ALSA; examiner-determined for SADLS

The ALSA and SADLS samples differed substantially in only two respects. First, participants in the ALSA reported greater numbers of teeth remaining than were observed in the SADLS sample. The import of this finding is unknown; it could reflect

an actual difference between the two samples, or it may reflect the tendency for older people to over-estimate their number of remaining teeth which was reported by Heloe (1972). On the other hand, Douglass *et al* (1991) found no such evidence of such a systematic bias.

Second, the ALSA sample took more medications than the SADLS one, even in comparison with the Adelaide-only component of the SADLS sample. Again, the import of this difference is unclear.

4.1.2 Detailed medication comparisons - SADLS and ALSA

The ALSA study provides supporting data with respect to two areas on which data were not collected in the SADLS study. First, a distinction was made in the ALSA between doctor-prescribed and self-prescribed medications. In the SADLS baseline study, only data on prescription medications were collected. Second, the ALSA also collected some data on the duration of exposure to each medication. Data on the prevalence of doctor-prescribed and self-prescribed medications are presented in Table 4.2, where the medication categories are presented in the same order as in the SADLS results, for ease of comparison.

Table 4.2: Prevalence of medication types in ALSA, by prescription source

Medication category	Medically-prescribed Number taking (%)	Self-prescribed Number taking (%)	Both sources combined Number taking (%)
Antihypertensives[a]	422 (44.8)		422 (44.8)
Analgesics[b]	377 (40.1)	72 (7.7)	428 (45.5)
Antiangina drugs	72 (7.7)		72 (7.7)
Prophylactic aspirin[c]	113 (12.0)	28 (3.0)	141 (15.0)
Psychotherapeutics	112 (11.9)		112 (11.9)
Cardiac preparations	64 (6.8)		64 (6.8)
Antiasthma drugs	79 (8.4)	1 (0.1)[e]	79 (8.4)
Hypoglycaemics	44 (4.7)		44 (4.7)
Antiulcer drugs	121 (12.9)	9 (1.0)	128 (13.6)
Hypolipidaemics	33 (3.5)		33 (3.5)
Antidepressants	53 (5.6)		53 (5.6)
Nutrient agents	68 (7.2)	75 (8.0)	134 (14.2)
Antithrombotics	47 (5.0)		47 (5.0)
Uncodables[d]	9 (1.0)	16 (1.7)	25 (2.7)
Non-thyroid hormones	66 (7.0)		66 (7.0)
Thyroxines	0 (0.0)		0 (0.0)
Antibiotics	45 (4.8)		45 (4.8)
Potassium preparations	24 (2.6)	1 (0.1)[f]	25 (2.7)
Anticonvulsants	16 (1.7)		16 (1.7)
Miscellaneous others	64 (6.8)	8 (0.9)	71 (7.5)
Antiinflammatory, steroid	28 (3.0)		28 (3.0)
Antipsychotics	19 (2.0)		19 (2.0)
Anticholinergics[e]	27 (2.9)		27 (2.9)
Antihistamines	26 (2.8)	3 (0.3)	29 (3.1)
Anti-neoplastics	14 (1.5)		14 (1.5)
Laxatives	42 (4.5)	48 (5.1)	89 (9.5)
Topical agents	27 (2.9)	2 (0.2)	29 (3.1)
Antidiarrhoeals	8 (0.9)	1 (0.1)	9 (1.0)
Other CV agents	1 (0.1)	1 (0.1)[g]	2 (0.2)
Antimigraine agents	4 (0.4)		4 (0.4)
Antinauseants	7 (0.7)		7 (0.7)
Antipruritics	3 (0.3)		3 (0.3)
Antituberculotics	1 (0.1)		1 (0.1)

[a] Includes diuretics

[b] Includes antigout drugs

[c] Low-dose aspirin was counted separately from the analgesics in order to reflect its current use in the prevention of stroke and myocardial infarction.

[d] These are medication names which were recorded and which proved unclassifiable.

[e] This person was taking bisolvon, a non-prescription antiasthma drug.

[f] This person was taking Slow-K, a non-prescription potassium preparation

[g] These persons were taking Paroven, a non-prescription preparation used to reduce peripheral oedema

It is possible that, in only including information on prescription medications, the SADLS baseline data may have underestimated the prevalence of preparations such as the analgesics, laxatives, antiulcer drugs, nutrient supplements and prophylactic aspirin.

Medication prevalence among among dentate people aged 70 and over in the baseline ALSA and SADLS samples is compared in Table 4.3.

Table 4.3: Comparison of prescription medication prevalence among participants aged 70+ - ALSA and SADLS samples (weighted data; percentages in brackets)

Medication category	ALSA (N = 862)	SADLS (N = 315) Adelaide only
Antihypertensives[a]	412 (47.8)	142 (45.2)
Analgesics	365 (42.4)	68 (21.6)[b]
Anginals	68 (7.9)	49 (15.5)[b]
Prophylactic aspirin	98 (11.4)	46 (14.6)
Psychotherapeutics	97 (11.2)	19 (6.0)[b]
Antiasthma drugs/antiasthmatics	60 (7.0)	22 (6.9)
Cardiac preparations	58 (6.7)	16 (5.2)
Antiulcer drugs	120 (13.9)	18 (5.6)
Hypoglycaemics	35 (4.1)	13 (4.0)
Antidepressants	46 (5.3)	26 (8.2)
Antithrombotics	43 (5.0)	18 (5.6)
Hypolipidaemics	32 (3.7)	19 (6.0)
Nutrient agents	67 (7.8)	15 (4.9)
Non-thyroid hormones	61 (7.1)	12 (3.7)[c]
Antibiotics	36 (4.2)	15 (4.7)
Uncodables	4 (0.5)	12 (3.7)[b]
Thyroxine	0 (0.0)	9 (2.7)
Anticonvulsants	7 (0.8)	4 (1.2)
Potassium preparations	24 (2.8)	9 (2.7)
Topical agents	23 (2.7)	5 (1.7)
Antipsychotics	18 (2.1)	4 (1.4)
Miscellaneous others	53 (6.2)	5 (1.7)[b]
Anti-neoplastics	16 (1.8)	6 (1.8)
Anticholinergics	28 (3.2)	2 (0.6)
Antiinflammatory, steroid	22 (2.5)	5 (1.7)
Antihistamines	22 (2.5)	3 (1.0)
Laxatives	37 (4.3)	4 (1.3)[c]
Antidiarrhoeals	10 (1.2)	1 (0.3)
Other CV agents	0 (0.0)	2 (0.6)
Antirheumatics	0 (0.0)	1 (0.3)
Antinauseants	3 (0.4)	0 (0.0)
Antimigraine agents	5 (0.6)	0 (0.0)
Anorectics	0 (0.0)	2 (0.6)
Peripheral vasodilators	0 (0.0)	2 (0.6)

[a]Includes diuretics
[b]$P<0.01$
[c]$P<0.05$

For the most part, the prevalences of different medications in the two samples were similar. However, substantial differences existed for some, with ALSA having greater

proportions of participants who were taking: analgesics, psychotherapeutics, antiulcer drugs, non-thyroid hormones, anticholinergics, laxatives, or preparations which fell into the "miscellaneous" category. The SADLS sample had greater proportions of participants who were taking anginals, thyroxine or preparations for which no code could be allocated (the latter is assumed to be due to errors in writing drug names down at the time of the baseline data collection). It is difficult to account for these differences, although, as mentioned above, it is possible that the lower prevalence of analgesics, laxatives, nutrient agents and antiulcer drugs may have been due to the non-recording of self-prescribed drugs in SADLS at baseline. However, there is no evidence of this with respect to prophylactic aspirin, as its prevalence in the SADLS sample was still somewhat higher than in the ALSA sample.

4.1.3 Duration of exposure to particular medication categories (ALSA)

Assessing the duration of exposure to each medication in the ALSA study was done by asking participants whether they had been taking it for weeks, months or years. While this does not give detailed information on medication duration, it does give some indication of the scale of the exposure to a particular drug. This can be useful; certainly, it is better than having no information at all on the length of exposure. Data for the 15 most common prescription medications which were taken by dentate participants aged 70+ are presented in Table 4.4.

Table 4.4: Self-reported duration of exposure for the 15 most prevalent medication types being taken by the 862 dentate participants aged 70+ in ALSA

Medication category	No. taking	Percent taking for:		
		Weeks	Months	Years
Antihypertensives	411	2.2	18.5	79.3
Analgesics	287	10.6	15.6	73.8
Anginals	68	3.0	25.4	71.6
Prophylactic aspirin	99	6.2	20.6	73.2
Psychotherapeutics	97	4.4	15.4	80.2
Antiasthma drugs	61	8.2	23.0	68.9
Cardiac preparations	57	0.0	10.7	89.3
Antiulcer drugs	119	6.8	11.9	81.4
Hypoglycaemics	35	0.0	22.9	77.1
Antidepressants	45	8.9	28.9	62.2
Antithrombotics	29	3.4	27.6	67.0
Hypolipidaemics	33	3.0	24.2	72.7
Nutrient agents	67	6.0	17.9	76.1
Non-thyroid hormones	61	0.0	23.3	76.7
Antibiotics	35	54.3	11.4	34.3

For most medications, the great majority of people taking them reported having been on them for "years" (which it is reasonable to interpret as one or more years), reflecting chronic exposure. By contrast, the duration data for antibiotics tend to reflect the acute nature of most infections which require antibiotic therapy: 65.7 percent had been taking antibiotics for "weeks" or "months", although just over one-third had been taking them for "years".

4.1.4 Medications and caries at baseline

The results of the baseline analysis must be viewed in the light of the overall aim of this investigation, which is to elucidate the relationship between and the taking of medications in older people and their dental caries *incidence and increment*. The baseline associations necessarily pertain to the taking of particular medications and caries *prevalence* only, and examination of those associations is, of course, fraught with all the customary problems of prevalence studies. Most notable among the latter is the problem of being unable to determine the time-ordering in any associations

observed between the dependent and independent variables, meaning that any particular medications which emerge as contenders must be regarded merely as "risk indicators", rather than "risk factors" (Beck, 1998). Nevertheless, examination of the baseline associations can provide what may be useful indications of potential areas of interest. At worst, it may serve to once again highlight the weaknesses of prevalence studies of dental caries in older populations. At best, the outcome might demonstrate (once the outcomes of incidence studies are known) that the prevalence study approach has some utility in this sort of investigation. This, in itself, would be a useful outcome given that, to date, only prevalence studies have been conducted (or at least, reported) in examining the associations between dental caries and medications. Ultimately, what is interesting is whether the same drugs showing significant associations with baseline caries levels are also associated with caries incidence and increment.

It follows that the baseline analysis of medications and caries was not intended to be other than an exploratory investigation, and its findings should be treated with caution. Despite such a caveat, however, there is the very real issue of whether there was anything of interest in the baseline analysis. Before that is discussed, it may be more appropriate to briefly justify the largely *post hoc* approach which was taken to generating the medication-caries prevalence data. The information on medications was collected at baseline with the aim of later conducting an analysis of the associations of medications and oral health/disease. There was, at that stage, no suitable method for coding and analysing the medication information, and it was not until another researcher (WMT, who had a particular interest in that area) joined the team that the study's potential in this area was seriously examined. However, that the data were collected is undeniable, and it would have been an unfortunate waste of resources (if not a breach of research ethics) not to explore the baseline data from the medication-caries perspective.

Methodological purists would argue that to proceed in examining the data-set with what is, essentially, an *a posteriori* approach is untenable, and that it also exposes the analysis to the possibility of Type I error. Such criticisms are not without a degree of justification. However, a more pragmatic approach is argued by Savitz and Olshan

(1995), who reason that more flexible searches for risk indicators (and risk factors) are warranted, given our ignorance of the biologically-relevant exposure to agents which might be implicated in the process which is under study. They point out that epidemiological data are independent of any *a priori* or *a posteriori* hypotheses which may be involved in their collection and analysis, and that each specific hypothesis should be examined independently. Indeed, a further reason for not impugning hypotheses which are generated after data collection is that failure to fully explore an expensively (and invasively) obtained dataset is ethically untenable. If this latter point is accepted, then there is little basis for considering *a posteriori* hypotheses to be somehow inferior to *a priori* ones.

Recent support for such a view has come from Perneger (1998), who argued that the Bonferroni adjustment is unnecessary and may, in fact, be detrimental to sound statistical inference, chiefly because it is concerned with the general null hypothesis (that is, that all null hypotheses for all tests performed are true simultaneously), and this is very seldom useful to the investigator. In the current study, the Bonferroni adjustment would mean that a statistically significant relationship between (say) low flow rate and the taking of antidepressants would be rejected because anticholinergics and antihistamines were examined and tested too, and the required alpha value would have been too low. This is clearly absurd. Instead, Perneger recommended that the best approach is simply to describe what tests have been performed on the data, and why. However, he also did advise that one situation where Bonferroni adjustments might be necessary is when significant associations are being sought without pre-established hypotheses; this just happens to be the situation encountered in the current study (particularly with the medication-dry mouth associations). This is explored further in the discussion of the CART analysis approach to the polypharmacy problem.

These considerations aside, there were definite indications that certain medications—most notably the antiulcer drugs (specifically, the H_2-receptor antagonist subclass), and the anginals—were associated with greater baseline root surface caries experience. H_2-receptor antagonists are often prescribed for individuals with gastro-oesophageal reflux disease, which is a chronic condition characterised by frequent relapse and the necessity to maintain a long-term therapeutic strategy for sufferers (Klinkenberg-Knol

et al, 1995). For older individuals in particular, maintenance therapy with an H_2-receptor antagonist is the preferred course of action (Crotty and Smallwood, 1995). It may be that, as a consequence of this process, individuals who suffer gastro-oesophageal reflux disease have an intra-oral pH which is lower than normal, and this might contribute to an increased rate of root surface caries attack. It may be that the process involved is a combination of caries susceptibility and a superimposed erosive process occasioned by the depressed oral pH. However, the null finding with respect to five-year root surface caries increment and exposure to antiulcer drugs suggests that the purported association probably does not exist, and that the association observed at baseline was probably a chance finding. However, the issue of Type II error is important when considering these findings; it is discussed further in Section 4.2.6.2.

One final observation deserves mention: that regular dental attendance was positively associated with the outcome in each of the multivariate analyses of baseline caries suggests strongly that dental providers have an inordinately large influence on the outcome of dental epidemiological studies such as the current one. While no analytical strategy can allow for the tendency for dentists to overtreat, it is assumed that the effect will be greatest when disease experience is examined in a cross-sectional analysis (such as that at baseline), and it is hoped that it is less apparent when disease experience over five years is examined.

4.2 SADLS findings at five years

4.2.1 Sample retention at five years

The longitudinal design is a powerful one; being able to make repeated observations on the same individuals allows the researcher to examine the time-ordering of exposure and outcome with a far greater degree of certainty than is possible with the cross-sectional approach. However, a common problem in cohort studies is the loss of participants over time leading to the non-representativeness of the study sample, irrespective of how meticulously the baseline sample was drawn. In the current study,

this is a major issue: to what extent did the general loss of participants between baseline and five years compromise the sample's representativeness. Moreover, there is the secondary problem of the extent to which the different participation rates for the various aspects of the dry-mouth study at five years may have further compromised the generalisability of those findings.

In considering the first issue, the data in Table 3.17 indicate that there were indeed some systematic differences between those who participated and those who were lost to follow-up. While the baseline sample was representative of non-institutionalised South Australians aged 60 or more, it is evident from those data that the participants remaining at five years were no longer so, being younger, less highly medicated, and having better dental self-care and service-use patterns than the baseline sample and, by inference, the general population of community-dwelling older South Australians. Regarding the second issue, proportionately more of those for whom saliva samples were not taken were female, and a similar relationship was apparent for the medication data. There were no significant differences with the XI data. Similar relationships were apparent among the examined dentate individuals. Thus, it can be concluded that there is a definite—but hopefully minor—risk of bias resulting from the differential participation in those parts of the study at five years.

Both issues mean that the generalisability of the current study's findings is somewhat compromised, as does the fact that the data were unweighted: the calculation of the weights was based on the sampling strategy at baseline, and ensured that the baseline data were able to be generalised to the population of older South Australians. However, the non-random loss of participants over the five years since baseline means that it can no longer be assumed that those weights are accurate, and the decision was made not to use them in the analysis of the five-year follow-up data. It is acknowledged that this is not ideal practice, but no statistician has been able to advise the author on the procedure to be followed in this situation, despite a number of people being consulted.

Similar considerations prevail for the dentate sample, and the patterns are largely the same. Thus, it would be unwise to generalise to the universe of South Australian older people from the five-year findings of this study.

4.2.2 Medications and their changes over the five-year SADLS period

Section 4.1 has already discussed the issue of how 'typical' the baseline SADLS sample was of the general population of older South Australians, and it appears that this aspect was satisfactory, assuming that the ALSA baseline sample was indeed a representative one.

When examining the time trends in medication prevalence, there are difficulties in distinguishing (1) the age-associated changes which arise from changes in morbidity across the sample, and (2) the changes which have occurred because of changes in medical practitioners' prescribing practices which may have resulted from the development of new drugs (and pharmaceutical companies' marketing practices) or changes in therapeutic approaches. The former can be characterised as *age effects*, whereas the latter can be characterised as *period effects* (Costa and McCrae, 1982). An example of the former might be the substantial increase in prevalence of hypoglycaemic drugs over the course of the study, from 4.0 per cent to 6.8 per cent. This could be interpreted as suggesting that the five-year net incidence of diagnosed diabetes among the sample was 2.8 per cent, assuming that there were no changes in medical practitioners' therapeutic approaches to that condition during the course of the study. An example of the changes in prescribing practices which have occurred is the dramatic increase in usage of the ACE Inhibitor drugs.

4.2.3 Salivary flow rate

Several issues need to be explored with respect to the flow rate data. First, how appropriate was it to only measure unstimulated salivary flow? Second, was it appropriate to measure whole saliva, or should glandular flow have been assessed too?

Third, having measured unstimulated flow rate, were the estimates obtained typical of older populations which have been studied elsewhere?

4.2.3.1 Why only unstimulated flow?

Unstimulated saliva flow was measured in this study because it was considered to be more relevant to the study hypotheses; that is, unstimulated salivary flow confers oral protection for the majority of the time, and where the aim of the investigation is to examine the association between medications, dry mouth and dental caries, it can be argued that it is the more relevant of the two flows. Galan and Lynch (1993) have also suggested that unstimulated salivary flow rate may be a more appropriate measurement to make when investigating caries rates in older people. There are also pragmatic considerations: when approximately 700 individuals are to have salivary flow measured, the ease of saliva collection must be taken into account when selecting the type of flow to be measured and the method of doing so. It would have been nice to have estimates of both flows for each participant, but this would have greatly reduced the efficiency of data collection. In any case, the measurement of dry mouth was not the primary aim of the study, and it was difficult to justify taking any more time than had already been allocated in an extremely tight assessment programme.

4.2.3.2 Whole saliva versus glandular saliva

Salivary flow was estimated by collecting whole saliva. This method is more common and far less invasive than collecting the flow of individual glands, and more closely approximates the *in vivo* situation (Navazesh and Christensen, 1982). This is certainly the case in respect of both saliva's caries-protective function and the fact that dry mouth is considered to be a multi-glandular condition (Sreebny and Broich, 1987). The "drain method" has been suggested as the most suitable one for large-scale collection of whole saliva, but the "spit method" is certainly easier for the participants. It should be borne in mind that, in making these measurements, researchers are making a considerable imposition on study participants, and it is important to use a method which is acceptable to them. SADLS study members often had to be persuaded to take

part in the saliva collection; for most of them, the notion of spitting in front of a stranger was unthinkable, and many had to be gently persuaded to do so. The use of humour to lighten the situation was often effective.

4.2.3.3 How "typical" were the observed flow rates?

"Typical" flow rate estimates are difficult to determine, partly due to the range of flow rates which is observed in studies, and partly due to the convenience samples used in most studies of salivary flow. However, Edgar and O'Mullane's review (1996) noted the following "typical" whole-salivary flow rates: 1.00-2.00 ml/min for stimulated flow, and 0.3 ml.min for unstimulated flow. The estimated mean unstimulated flow rate observed in the SADLS study (0.27 ml/min) appears acceptably close to the latter, and its range (0.00 to 1.84 ml/min) is certainly typical of the wide variation that has been reported. This suggests not only that the "spit method' of sialometry used in the SADLS study was reasonably accurate, but that the range of collection times used was not inappropriate. Certainly, the latter point is borne out by the finding (Section 3.2.3.1) that the correlation between flow rate and collection time was very low (and not significant). An issue which begs examination is that of intra-individual variation: it may be that, a more important issue than flow rate at a particular time is the extent to which salivary flow changes over time for a given individual. It is possible that the individuals most at risk—whether it be dental caries or the symptoms of dry mouth—are not those with low flow rates *per se*, but those whose flow rate is reducing rapidly over time. Unfortunately, the current study did not permit examination of that aspect of the cohort's salivary flow rates, and so it is impossible to identify those participants who were in that situation. Nevertheless, it is a possibility which should be considered for future longitudinal research in this field, with sialometry being used in both the baseline and follow-up data collections.

4.2.4 Xerostomia

4.2.4.1 Measurement issues

The decision to measure xerostomia and flow rate separately in the five-year data collection was made with little support from previous studies. If it had turned out that xerostomia and SGH coincided in all (or, at least, the great majority of) participants, then it could clearly have been seen as a waste of scarce resources and of participants' time. Whatever the outcome, however, there had been no satisfactory reports from population-based samples of the degreee of concurrence of those two aspects of dry mouth, and merely to have confirmed their concurrence in that event would have been a useful contribution to the scientific literature on dry mouth. It had been expected that perhaps the relationship was not that straightforward, despite the almost universal assumption implicit in the existing literature that "dry mouth was dry mouth", whichever way it was measured. In the final analysis, the small amount of overlap which emerged certainly vindicated the decisions to (1) measure both aspects separately, and (2) develop a method for measuring the severity of dry mouth.

Aside from the study by Narhi (1994), this is the only report from a population-based study on the occurrence of both xerostomia and salivary gland hypofunction, and this study's findings were somewhat surprising. Although xerostomia and SGH had very similar prevalence estimates—at roughly one in five individuals—the conditions occurred together in only 5.7 per cent of the overall sample; this was equivalent to only one in six of those who had either condition. The data support the contention that, in this population of community-dwelling older South Australians at least, low unstimulated salivary flow accounts for only a small proportion of the xerostomia experienced. It could be argued that the concurrence between the two conditions might have been greater if stimulated salivary flow had been measured, but the unstimulated flow is a more important determinant of oral dryness (Dawes, 1987). Moreover, no association between stimulated flow and xerostomia was observed by Sreebny and Valdini (1988).

The current study observed a lack of concurrence between the two conditions, and there is support for this in the findings of another recent study (Billings *et al*, 1996), where xerostomia among younger members of a convenience sample of 710 adults (ranging in age from 19 to 88 years) appeared to be more closely related to the flow rate than among older persons in that study, in whom it appeared to be a more complex phenomenon. The lack of concurrence is further borne out by the low correlation between salivary flow and the responses to the standard xerostomia question in the SADLS study, indeed suggesting that xerostomia is largely determined by factors other than flow rate *per se*. It has been suggested previously that differences in either saliva quality or individuals' perceptions of oral wetness are at least partly responsible for this phenomenon, and this is suggested by the current findings. The sex difference in the degree of concurrence of the two conditions was marked, and suggests that the aetiology of dry mouth may differ between males and females.

Any estimate of the prevalence of a disease or condition is dependent on the case definition which is used. Where that used for SGH is concerned, the unstimulated flow rate cut-off of 0.1ml.min has been defined (Edgar and O'Mullane, 1990) and reported previously (Osterberg *et al*, 1984; Sreebny, 1996). It can be considered to be well-established. For xerostomia, however, it may be that the single question which was used to define the condition in the current study was inappropriate. Comparison with the findings of other population-based studies may assist in clarifying this issue: the estimate for xerostomia prevalence which was obtained from our study (20.5%) is remarkably close to the 20.8% reported from a population-based sample of Swedes aged 70 and over (Osterberg *et al*, 1984), and to the 20.0% reported from a study of institutionalised older New Zealanders (Thomson *et al*, 1993) which used the same question. It is a little higher than the 17.7% found in a population of Toronto people aged 50 and over (Locker, 1993), but that difference may reflect the younger age distribution of the Toronto sample. It is certainly higher than the 12% reported for older Finns by Narhi (1994), but that is possibly a reflection of Narhi's rigorous approach to defining dry mouth, whereby oral dryness had to be consistently reported for three different times of the day. The 39% estimated in the Florida study using the question "Is your mouth sometimes dry?" (Gilbert *et al*, 1993) is rather higher than the others, and can be attributed to the nature of the question used. It is debatable whether

that question identifies true xerostomics; perhaps if "often" had been used instead of "sometimes', their estimate would have been more consistent with the others reported. That particular study aside, the comparisons made here suggest that, despite considerable differences in their content and orientation, most "global" questions about xerostomia result in broadly similar prevalence estimates, and that there is reason for confidence that the standard question used here was appropriate (from a phenomenological perspective, at least).

4.2.4.2 The Xerostomia Inventory

The purpose behind the development of the Xerostomia Inventory was to enable an estimate of xerostomia to be made (on an ordinal scale) for each individual so that it could be included as a continuous covariate in the modelling of coronal and root surface caries incidence among older people in the South Australia Dental Longitudinal Study. Measuring xerostomia symptoms on a continuous scale in this way is intended to reduce the risk of misclassification error which can occur when individuals are labelled as "xerostomic" on the basis of an arbitrary cut-off point, as with previous attempts to measure the condition. Those earlier attempts to objectively measure the symptoms of xerostomia have been relatively crude, and have not employed an analytical approach which, first, confirmed that a discrete xerostomia dimension did exist and was actually being measured, and second, acknowledged (and satisfactorily included) the wider constellation of symptoms which are thought to comprise the condition. It appears therefore that the XI may offer considerable advantages over previous approaches to xerostomia symptomatology.

The two discrete dimensions revealed by the factor analysis were intuitively appropriate. The 11 items upon which Factor 1 loaded did indeed appear to represent a xerostomia dimension which included both experiential and behavioural aspects of sufferers' experiences of the condition. For example, it is considered that the MOUTHDRY (*my mouth feels dry when eating a meal*), DRYFOOD (*I have difficulty in eating dry foods*) and DIFFSWAL (*I have difficulties swallowing certain foods*) statements relate directly to the individual's awareness of xerostomia, while the SIPLIQ (*I sip liquids to aid in swallowing food*), NITDRINK (*I get up at night to*

drink) and SUCK (*I suck sweets or cough lollies to relieve dry mouth*) statements reflect the consequences of xerostomia symptoms. The inclusion of both aspects strengthens the case for the XI being a valid representation of xerostomia symptoms.

Factor 2 suggested the presence of what has been described as Burning Mouth Syndrome (Savage, 1996), with the four significant items pertaining to sensations of burning or itching of the gums and tongue. It is worthy of note that the mean scores on that scale were higher for individuals who answered "Always" to the standard question, confirming previous observations of the association of severe xerostomia and burning mouth (Grushka, 1987). The scale for Factor 2 may therefore offer useful insights into the occurrence and associations of a condition which may be closely related to xerostomia, and warrants further investigation which is beyond the scope of this thesis. It is recommended that those items not be included in future use of the Xerostomia Inventory unless the research is to specifically examine the occurrence of Burning Mouth Syndrome as well.

Validity is a key issue in considering the merits of an instrument which purports to measure subjective symptoms, and relates to whether it is really measuring what the researcher intends to measure. There are several types of validity which can be considered. *Content validity* is held to be acceptable when the instrument adequately samples the domain which is supposed to measure. This depends, in part, on demonstrating that all relevant dimensions have been used in defining the domain, and that the domain was appropriately and adequately sampled (Kaplan *et al*, 1976). Valid content requires that it must positively and exhaustively define the dimensions of the construct which it is to measure. The combined empirical-theoretical approach taken to deriving the items for the pretest version—together with the factor structure which was revealed—suggests that it did indeed represent a distinct, authentic xerostomia dimension.

Concurrent validity pertains to the inventory's performance against an existing standard; such a criterion-related approach requires that it show a similar gradient in scores to an alternative method of measurement which is assumed to be valid. One of the problems in xerostomia research is the wide range of items which studies have used

to ask individuals about their experience of the condition (Table 1.2). The choice of the particular question used in the current study was not a reflection of any perceived lack of utility of the other questions which have been used; rather, it reflected the researchers' familiarity with the use of that particular item in investigating xerostomia. Perhaps, in retrospect, one or two more should have been used to gain a more complete picture of the XI's performance against existing standards. Comparison of the increasing XI scores with the increasing severity categories of the standard single-item inventory in Table 3.31 suggests that this aspect of validity was also satisfactory, particularly in view of the difference in scores across all four response groups for the standard question. The outcome of the validation study offered further evidence for the concurrent validity of the XI: it was hypothesised that scores in the *Onset* group would increase in concert with those from the standard question; moreover, as the standard-question responses remained essentially the same in the *Normal* group, so too would the XI scores essentially not change. Both of these hypotheses were confirmed, supporting the concurrent validity of the XI.

Construct validity pertains to the extent to which the instrument appears to conform to theoretically-derived predictions about it; in other words, construct validation involves assembling empirical evidence to support the inference that the XI has meaning. The Xerostomia Inventory's ability to assign higher scores to individuals who complain of frequent dry mouth suggests that it does indeed show this, but the degree of overlap (as represented by the standard deviations in Table 3.31) among XI score distributions and "gold standard" categories indicates that further examination of this characteristic in other populations would be advisable before making a definitive statement on the construct validity of the XI. As with the XI's concurrent validity, the outcome of the validation study offered further evidence for its construct validity: it was hypothesised that scores would increase greatly in the *Onset* group and remain essentially the same in the *Normal* group, and both of these were confirmed.

Some aspects of validity were not examined in the pretest phase. *Convergent validity* is apparent where several dissimilar methods of measurement of the concept correlate well with the test being investigated; in the case of the Xerostomia Inventory, this was unable to be examined, as only one alternative method was used to assess xerostomia.

However, a sufficient number of alternatives exist (Table 1.2) for this to be undertaken in subsequent studies among older people.

Discriminant validity is apparent when the test does not correlate well with measures of other concepts; in other words, it is able to distinguish the xerostomia experience from other symptom sets; this was only superficially examined in the current study: although the two factor scales were moderately correlated, their different relationship to the standard question (Table 3.31) suggests that they would be adequate in discriminating xerostomia sufferers from BMS sufferers.

Temporal stability (reliability) is another desirable characteristic of such an instrument, whereby the developer should be able to demonstrate that scores do not change over time when the characteristic which is being measured does not itself change. Slade *et al* (1996) reported on the stability of OHIP scores among a subsample of the SADLS participants, but theirs was a phenomenological approach, documenting the actual variations over time, rather than the OHIP's stability relative to an alternative method of measuring the same entity. In this, they had no choice, as no alternative method of measuring the social impact of oral conditions was available. By contrast, XI scores in the validation study were able to be compared over time to scores on the standard dry-mouth question. The stability of the scores among the *Normal* group in that study suggests that this aspect of the XI is also acceptable, although further confirmation of this feature would be desirable. Over the six months of the validation study, there appeared to be a slight increase in the proportion of people with xerostomia in the *Normal* group: it is a moot point whether this is the increase that would be expected due to the true incidence of the condition in that largely older group, or whether it is actually due to some property of the measurement methods used. Thus, confirmation of the XI's temporal stability should be conducted at future stage using a group of younger adults.

Future research efforts in the development and testing of the Xerostomia Inventory will need to examine its reliability, as well as its convergent and discriminant validity before it can be held up as a truly viable alternative method of measuring xerostomia. The relationship between Xerostomia Inventory scores and existing psychometric

scales also needs to be clarified, particularly in view of a recent report of a higher prevalence of depressive symptoms in individuals with xerostomia (Bergdahl *et al*, 1997).

4.2.5 Medications and dry mouth

In the investigation of the relationship between medications and dry mouth in the SADLS study, two main questions presented themselves. First, which drugs were associated with dry mouth prevalence at five years, and, for those, were the observed associations plausible, both in terms of biological knowledge and of what has been reported previously about drugs and dry mouth? Second, given the associations observed at five years, was the association more marked for those who were also taking the drugs five years previously?

4.2.5.1 The utility of the approach which was used

This study has used a number of approaches which are new to the field of drugs and dry mouth. First, the method of capturing and analysing medication data has enabled more ready analysis of medication exposure than alternative systems such as the WHO Anatomic Therapeutic Classification (WHO, 1995), which may be more comprehensive but is analytically far more cumbersome because it employs alphanumeric codes, as discussed in Section 1.5.1.

Second, xerostomia has been measured as a continuous variable which purports to represent the condition's severity. This has allowed the exploration of subtle associations between xerostomia severity and medication exposure while avoiding the risk of misclassification which was a very real issue in previous studies, which have usually examined xerostomia prevalence using a single-item dichotomous classification. However, one of the limitations of this study is concern about the validity and reliability of the Xerostomia Inventory, and further research is needed before it can be accepted as a truly viable alternative method of measuring xerostomia. Was the almost complete absence of overlap in the predictor medications for xerostomia and SGH due to real differences between the two conditions, or did it result from unresolved

problems with the XI? Antidepressants were the only medication category to emerge as a predictor for both; for xerostomia, their effect was apparent only for individuals who were using them at both data collections, and that group had the very low mean flow rate of 0.12 ml/min (sd, 0.08), indicating that the two conditions do tend to concur when flow rate is very low.

Third, a longitudinal approach to medication exposure has been taken, and appears to have been useful. The validity of that particular approach rests heavily on the assumption that a medication taken at baseline and at follow-up was, in fact, taken throughout the intervening period. Such an assumption has been used previously (Psaty *et al*, 1995), although only in describing temporal changes in medication prevalence, and not in modelling the occurrence of side-effects such as dry mouth. While it is not possible to state categorically that the assumption is valid, the current study's findings—for example, the strong association between a low flow rate and antidepressant use at baseline and five years—bear it out, and it appears to be intuitively satisfactory. In a dental longitudinal study, the continuous monitoring of medication exposure over the course of the investigation is not usually feasible; thus, the assumption of continuous exposure is necessary. However, where the same medication has been recorded at baseline and five years, two possibilities exist: (1) it may have been taken continuously throughout the intervening period; or (2) it may have not been taken for a time during that period. In the latter case, the time that the medication was not being taken could be anything up to five years, and the question is raised of what occurred while the drug was not being taken—was it substituted by another of a different type, or was medication not taken? This chronicity will vary for different medication categories. For example, an antihypertensive or an antiarthritic is more likely to have been taken continously over the five-year period than an antibiotic or an antineoplastic would have been. The issue of chronicity of exposure is no less critical for the baseline analysis, in which it must be assumed that current medications have been taken for sufficiently long to have had detectable oral side-effects. Current information is often too recent to have aetiological meaning, but its use is occasionally justified, such as where either there is good correlation between current and past exposure, or where recall of previous exposure is likely to be unreliable (Rothman, 1986). In the age group under study, both of these are likely to apply, in which case

current exposure is able to be used as a proxy for previous exposure, but may adversely affect the validity of exposure classification. The analysis also makes the assumption that dosage and pharmacological effects (including side-effects) are equivalent for all individuals who are taking that particular drug: of necessity, no concession is made to the wide variation that may exist among older people in the pharmacokinetics and pharmacodynamics of a given medication (Bressler and Katz, 1993), as this is very difficult (if not impossible) to determine in an epidemiological study. It is therefore necessary to assume that the effects of such inter-individual variation are randomly distributed among the population under study, and that they have no bearing upon the outcome of the investigation.

Fourth, this study has attempted to allow for polypharmacy in the investigation of medications and dry mouth by using an analytical strategy which has been previously reported only once in this field (Johnson *et al*, 1984). Whether it has been successful or not is difficult to say, as the approach is novel and there are no comparable data. However, some intriguing associations and interactions were uncovered which were not found in preliminary analyses using conventional *a priori* methods. A major justification for using the CART analysis approach was the plethora of confusing and contradictory information on medications and dry mouth which was available, and it was hoped that using a more empirically-driven analytical approach with no *a priori* assumptions would be useful in arriving at the real situation. It is questionable whether using CART analysis has entirely solved the polypharmacy problem, but it appears to have allowed more opportunity for the researcher to uncover the more obvious (and hopefully) important interactions present among the medications in the data-set. It also goes some way toward appeasing the "statistical purists" who insist that the risk of Type I error must be minimised wherever possible (Section 4.1.5 contains further discussion of this particular point). For these reasons, the use of CART analysis in this study must be regarded as a methodological step forward in the analysis of complex medication-dry mouth data-sets. The aim of the linear regression analyses in this study was to help assess the robustness of the associations revealed by the CART analysis. Neither was primarily intended to completely explain the occurrence of either flow rate or xerostomia severity (and that was borne out by neither model explaining much of the variance in either of the two dependent variables), but to control effect

confounding by different medications, and to see which of the associations uncovered in the CART analysis were robust enough to persist as predictors in the outcome of the multivariate analyses. It could be argued that potential "non-medication" predictors—such as age group, sex, smoking and drinking status—should also have been included in this study's CART analysis, but the aim was to examine the medication-dry-mouth associations free of any other potential confounding variables, and also at two different medication-exposure levels (at five years, and baseline and five years). There was the strong possibility that an early split on a variable such as gender would have greatly reduced the numbers in subsequent splits, with the consequence that important predictor medications might have been missed. Thus, the decision was made not to introduce the other potential predictors until the regression analysis stage. The generally close agreement between the two approaches suggests that the essentially data-driven CART method can be useful for investigating the association of medications and dry mouth, but it is prudent to supplement it with an alternative approach.

Fifth, both xerostomia prevalence and severity were modelled in this study. Different medication associations were found with each. Narcotic analgesics, diuretics, sympatholytic antihypertensives or antiulcer drugs taken at five years were all associated with a higher prevalence of xerostomia, as were antiulcer drugs taken "continuously", and being female was also a predictor. Of those, only being female was a predictor for xerostomia severity, and diuretics were only involved as an interaction effect with thyroxine.

Generalising about medications and dry mouth among older populations from the findings of this study is problematic. While the baseline sample was representative of non-institutionalised South Australians aged 60 or more, it is evident from the data in Table 3.17 that those remaining at five years were no longer so, being younger, less highly medicated, and having better dental self-care and service-use patterns than the general population of community-dwelling older South Australians. However, it can certainly be stated that, among participants in this study, unstimulated flow rate was higher among current users of hypolipidaemic drugs and among current cigarette smokers, and lower among people who were exposed to antidepressants at both data

collections. Xerostomia symptoms were more severe among: those taking anginals at five years without a concomitant β-blocker, and among those taking either thyroxine and a diuretic or HRT at five years; and those who were exposed to antidepressants or antiasthma drugs at both data collection stages. Xerostomia symptoms were more severe among those taking (1) anginals without a concomitant β-blocker, (2) thyroxine and a diuretic, (3) hormone replacement therapy at five years, or (4) those who were "continuous users" of either antidepressants or antiasthma drugs.

4.2.5.1 Comparison of findings with those of previous studies

It is remarkable that none of the published epidemiological studies of the association between medications and dry mouth has reported using multivariate analysis to test the observed associations. It is only through multivariate analysis that possible confounding by age, gender or the effects of other medications can be ruled out. However, because all previous reports have been from bivariate analyses, an initial brief comparison of the current study's bivariate findings with those from previous studies (Table 1.6) is warranted. The SADLS bivariate findings on dry mouth support the associations reported previously between xerostomia and antihypertensives (Narhi *et al*, 1992), diuretics (Atkinson *et al*, 1989), analgesics (Narhi, 1994), some cardiac agents (Narhi *et al*, 1992; Loesche *et al*, 1995) and antiulcer drugs (Loesche *et al*, 1995). However, close examination of the SADLS bivariate findings reveals that the overall antihypertensive effect appears largely due to the effect of the diuretic agents. Moreover, anginals were included in the broad category of 'cardiac agents' by Narhi *et al* (1992) and Loesche *et al* (1995), and the SADLS findings suggest that the effect is more specific than that, being due to the anginals. Where lowered flow rate is concerned, the SADLS findings support those of Johnson *et al* (1984) and Loesche *et al* (1995), and offer strong supporting evidence for the negative effect of antidepressant medications on flow rate. Antipsychotics, antihistamines and anticholinergics are discussed below. No previous study has reported the apparent positive association of hypolipidaemic drugs with salivary flow.

4.2.5.3 Explaining the findings

Several medication types were observed to be predictors of either reduced unstimulated salivary flow or dry mouth. However, the observed associations were not always in the expected direction, and, other than the antidepressants, no medication type was predictive of both lowered flow rate and increased xerostomia severity. Explaining the medication findings is a challenge: while some are relatively simple—for example, the association between antidepressants and low unstimulated salivary flow rate has long been hinted at in cross-sectional studies and in reviews of the literature (for example: Ettinger, 1981; Friedlander *et al*, 1993), and their emergence as predictors was consistent with those results (and particularly with those of the other study to have used the CART approach (Johnson *et al*, 1984))—others are considerably less so. The apparent positive effect of hypolipidaemic medications on flow rate was an unexpected finding which cannot be explained on the basis of our current knowledge of the physiology of salivation, but points to a possible therapeutic use for these preparations among people with low salivary flow rates. They may also have a role in the prevention of lowered flow rates in individuals or groups who are known to be at high risk of developing the condition. However, replication of this study's findings and more research into the apparent sialogenic properties of those preparations (such as simvastatin and pravastatin) are indicated before this can be seriously considered. Determining whether hypolipidaemics cause unstimulated flow rate to increase or if individuals taking them are likely to have higher flow rates anyway is not possible with this study.

Possible reasons for some of the associations with xerostomia severity are relatively easy to find. For example, the thyroxine-diuretic interaction may be due to a dehydrating effect of both of those medication types, although neither produced the effect independently. The antidepressant-xerostomia association has been discussed above. The increased severity of xerostomia symptoms among individuals taking antiasthma drugs at baseline and five years may possibly be due to the dehydrating effect of the mouthbreathing which is a common feature of their everyday breathing. The association of xerostomia and HRT is intriguing; the published literature in this area is equivocal, with one recent study reporting no difference (Streckfus *et al*, 1998)

but another reporting higher salivary flow rates among women in a longitudinal study who began using HRT (Laine *et al*, 1996). The latter study measured the symptoms of dry mouth, but did not report on whether they had improved or worsened since the commencement of HRT. Finally, it is difficult to account for the association of anginal use and xerostomia, but it is a strong relationship which merits further research.

There were a number of drug categories for which cross-sectional studies have reported an association with dry mouth but for which none was apparent in the current study. These include anti-ulcer drugs, anxiolytics (Loesche *et al*, 1995), anticholinergics (Osterberg *et al*, 1984; Thomson *et al*, 1993) and antihistamines (Johnson *et al*, 1984). There were insufficient numbers of the latter for the approach taken in this study to be successfully used: antihistamine prevalence was only 1.6 per cent at baseline and 1.5 per cent at five years. The other categories did not have an association with either dependent variable, which suggests either that the putative relationships do not exist, or that perhaps they may be more apparent when stimulated salivary flow is being measured. Certainly, the studies reported by Johnson *et al* (1984), Persson *et al* (1991) and Loesche *et al* (1995) all examined only the stimulated flow rate; moreover, the first-mentioned study only measured parotid salivary flow, while the other two measured whole saliva. Only the study by Osterberg *et al* (1984) examined unstimulated whole-salivary flow (in addition to the stimulated flow), but the numbers in that study were relatively low: only 111 individuals had their salivary flow rate measured.

Finally, the small R-squared values of the multivariate models indicate that the models failed to account for most of the variance in the dependent variables, and much remains to be explained about the occurrence of dry mouth.

4.2.6 Dental caries experience over the five years of the SADLS study

4.2.6.1 Comparison of caries incidence findings with those from previous studies

The coronal and root surface caries incidence and increment of the SADLS participants was comparable to that which has been reported from other cohort studies of older people. At 66.9 per cent, the five-year incidence of coronal caries in SADLS was in the region of the three-year estimates of 64.9 per cent and 53.2 per cent respectively in the Iowa (Hunt *et al*, 1988) and Ontario studies (Hawkins *et al*, 1997), and the 45 and 59 per cent (respectively) for whites and blacks in the Piedmont study (Drake *et al*, 1997), despite the obvious difficulty of comparing incidence estimates for periods of different duration. The incidence rate for root surface caries (59.3 per cent) appeared to be consistent with the other studies' findings.

A better idea of the comparability of the caries rates is obtained when caries increment is compared (caries data from the other studies are presented in Section 1.6.2.1). After conversion to annual rates to aid comparison, the coronal caries increment rates from the Iowa (mean 0.8 surfaces affected per year), Piedmont (0.7 surfaces per year for whites, and 0.5 for blacks) and Ontario (0.5 surfaces per year) studies were very similar to the current study's estimate of a five-year mean (adjusted) increment of 2.65 surfaces, or about 0.53 surfaces per year. Comparison of the current study's root surface caries increment rate (2.21 surfaces, or just over 0.4 surfaces per year) with those from the other studies (Iowa, 0.4 surfaces per year; Ontario 0.2 surfaces per year) further confirms the impression that the South Australian coronal and root surface caries rates appear to approximate those reported from other longitudinal studies of community-dwelling older people.

4.2.6.2 Medications and five-year disease experience

The fundamental question which this investigation set out to examine was: *does the alleged medication-caries relationship exist?* In other words, can certain medications (or combinations of medications) be considered to be risk factors for dental caries on the strength of this study's findings?

Previous workers have specified three criteria which need to be satisfied before a characteristic can be considered to be a risk factor for a particular disease (Kleinbaum *et al*, 1982; cited in Beck, 1998). First, it must be observed to co-vary with the disease outcome; that is, it must be statistically associated with disease development, or the occurrence of disease must be observed to differ by category or level of the characteristic. In the current context, that means that either a "dose-response" relationship between exposure and outcome must be observed, or there is a predictive relationship with disease incidence or increment. Second, the putative risk factor must precede disease occurrence; in the current study's context, this requires that "continuous" exposure is associated with greater caries development between baseline and five years. Third, there must be no other tenable hypotheses (such as chance, sampling error, or competing risk factors) to explain the observed relationship. It follows that multivariate analysis is necessary (but not necessarily sufficient) for this criterion to be satisfied, and the current investigation has taken this approach. Beck added a fourth criterion, that of biological plausibility. That is, the putative relationship must be able to be explained in the light of (a) current knowledge of the mechanisms involved in the occurrence of dental caries among older people, and (b) current knowledge of the pharmacology of the putative (medication) risk factor.

The investigation has not resulted in a long list of medication types which were predictors for five-year dental caries incidence or increment, or even tooth-loss incidence over the study period. Thus, while the task of critically examining the outcome in the light of the criteria established by Kleinbaum *et al* (1982) and Beck (1998) is a demanding one, it is not particularly onerous because its extent is limited by the small number of statistically significant associations which were observed. The following discussion concentrates mainly on the findings with respect to medication

exposure—as this was the primary focus of the investigation—but other predictors which emerged from the multivariate models are briefly discussed where appropriate.

Medications and tooth loss

The taking of a cardiac drug at five years was a predictor for both the incidence and increment of tooth loss, and the taking of hypoglycaemic drugs was a predictor for tooth-loss increment. While the second criterion mentioned above (that of exposure being shown to have preceded outcome) was not strictly met for either of these medication types, the ALSA finding that 89.3 per cent of those taking cardiac drugs (and 77.1 per cent of those taking hypoglycaemic drugs) had been taking them for 'years' (Table 4.4) suggests that at least some of the individuals who were taking those preparations at five years may perhaps have been taking them for long enough for any associated increase in oral disease to manifest itself as tooth loss. Moreover, it is probable that a lack of statistical power was at least partly responsible for the "continuous use" of cardiac drugs not staying in the model; had more than 6 individuals been taking those preparations at baseline and at five years, it is possible that that medication class would have emerged as a predictor: two-thirds (N = 4) of those participants lost one or more teeth over the study period, and the mean number of teeth lost in that group was higher than that of the remainder of the sample. The self-reported reasons for tooth loss which were recorded at the time of the five-year examinations of those individuals were as follows:

- participant #14696 - tooth 36 extracted due to an abscess; tooth 31 extracted for periodontal reasons, tooth 15 added to partial denture since baseline but can't remember having it extracted;
- participant #28837 - teeth 35 and 43 extracted because they ached;
- participant #42804 - teeth 22, 27 and 28 extracted because they were broken down; and
- participant #51698 - tooth 48 extracted because it was very painful.

It appears that most (if not all) lost teeth because of the sequelae of caries, although this is not conclusive. Cardiac inotropics should therefore be considered as putative

risk factors for tooth loss, although it appears that people taking those drugs were more unhealthy overall than those who were not. Of the four individuals who lost teeth and who were taking cardiac drugs at both baseline and five years, two were taking eight different prescription drugs, one was taking nine, and the fourth was taking 11. The two individuals who were taking cardiac drugs at both baseline and five years and who did not lose a tooth were taking five and six different drugs respectively. Thus, cardiac drugs should not be regarded as risk factors for tooth loss (*ceteris paribus*), but as risk markers, whereby they can serve as indicators of those who are likely to lose teeth over time.

The observed association of hypoglycaemic drugs with tooth-loss increment is noteworthy because of the status of diabetes as a known risk indicator for periodontal loss of attachment (Nelson *et al*, 1990). It is possible that at least part of this association is due to teeth lost because of periodontal disease; however, it may also be due to caries, given the significantly higher coronal caries increment observed (at the bivariate analysis level, at least) in those who were "continuously exposed" to hypoglycaemics over the five-year period.

Being female predicted a lower incidence and increment of tooth-loss. This has been observed elsewhere (Caplan and Hunt, 1996), and is probably a reflection of older females' less episodic use of dental services and tending to place more value on an intact dentition than among males (MacEntee *et al*, 1993).

Slade *et al* (1997) reported that the baseline number of missing teeth was not a predictor of tooth-loss incidence over two years in the SADLS study. The current study's finding that the baseline number of missing teeth was a negative predictor of losing a tooth over the five-year period supports a similar finding from a five-year longitudinal study of Melbourne adults by Wright *et al* (1991). However, given that the effect in the current study was not a strong one, and the baseline number of missing teeth was not a predictor of the tooth-loss increment, the importance of the number of teeth missing at baseline remains unclear, especially when it is considered that it was not reported from the Piedmont and Ontario studies to be a predictor (Drake *et al*, 1995; Locker *et al*, 1996).

How valid was the choice of tooth loss as one of the outcomes of interest in this investigation? Implicit in the analysis of medication exposure and tooth loss has been the assumption that dental caries was the predominant reason for the tooth loss which was experienced by the sample over the five years of the study. It has been pointed out that tooth loss is the outcome of a set of complex decisions which are made by both the individual and the dentist (Locker *et al*, 1996), and disease-related characteristics are only one element in the decision. However, there is a precedent: Caplan and Hunt (1996) examined the role of lowered baseline salivary flow as a predictor for three-year tooth loss incidence in the Piedmont study, and found that individuals with low stimulated flow had a higher incidence of tooth loss (after potential confounders had been controlled by multivariate analysis). Their justification for examining tooth loss was that lowered salivary flow may be an antecedent of not only dental caries but also periodontal disease—although supporting evidence for the latter contention is even more scarce than that for the former—based on the assertion that there is a theoretical risk of more severe periodontal disease in individuals with lowered salivary flow because of their reduced secretory antibodies and mechanical debridement of the gums and teeth. This rationale is not entirely convincing, but a stronger case for tooth loss as an outcome variable in the current study comes from the report by Chauncey *et al* (1989) that dental caries was the predominant cause of tooth loss in a sample of older males in the US. Nevertheless, the possibility should be borne in mind that a proportion of the tooth loss observed in the current study may have resulted from periodontal diseases, and that this may, in fact, be masking an association with exposure to one or more medications. Another argument in favour of including tooth loss is that an increased caries rate due to a particular medication may have been so great as to result in considerable tooth loss, and so the examination of tooth loss over the study period is an essential part of such an analysis. Finally, a more pragmatic viewpoint is that the analysis of medications and tooth loss has uncovered more intriguing and perhaps biologically plausible associations than the caries analysis has, thus providing some interest to the resultant discussion.

Medications and dental caries

The finding that the taking of sympatholytic antihypertensive medication at five years was a predictor of a lowered coronal caries incidence rate is not possible to explain in the light of current knowledge; there is no biologically plausible mechanism to explain the association. Therefore, the possibility of Type I error must be acknowledged in this case. At the same time, it is possible that Type II error is responsible for the antiasthma drugs failing to emerge from the multivariate analysis as predictors of coronal caries incidence: there were only 14 dentate individuals taking those preparations at baseline and five years who were examined at both data collections. It is an intriguing outcome, given that they were also (but only just) significantly associated with more severe xerostomia symptoms (represented by higher XI scores) at five years. This offers some support for the second pathway in the proposed medication-caries model (Figure 1.3), whereby individuals with more severe dry-mouth symptoms caused by the medication take steps to relieve their mouth dryness (such as using cough lollies or frequent sweet drinks) which themselves threaten the integrity of the dentition. An association between antiasthma drugs and coronal caries prevalence in children has been previously reported (Bjerkeborn *et al*, 1987), and that the current study has uncovered a similar association among older people supports the case for considering those medications to be risk factors for coronal caries.

Given the constraints of the theoretical model (Figure 1.3), it is difficult to account for the observations that (1) the taking of ACEI antihypertensives at five years was associated with a higher incidence of coronal caries, and (2) those who were taking psychotherapeutic drugs had a higher coronal caries increment. Neither of those drug types was associated with dry mouth, and it may be that those associations are attributable to Type I error.

The bivariate finding that antidepressant use at five years predicted a lower coronal caries increment is distinctly counter-intuitive, given the hypothesised pathway (Figure 1.3) and the strong association of those drugs with a lowered unstimulated salivary flow rate at five years. That it did not survive the multivariate analysis suggests that confounding by other characteristics may have been responsible for the apparent association.

With root surface caries, there was the somewhat intriguing finding that individuals who were taking prophylactic aspirin at baseline and at five years had a lower *incidence* of the condition. It may be that (a) the association of these drugs with a lowered disease occurrence was a chance finding, (b) one (or both) somehow exerts a caries-protective effect (for which there is currently no evidence, and the biological plausibility of such a relationship is tenuous), or (c) it may be that individuals who are motivated enough to take prophylactic measures for the prevention of cardiovascular disease are a more "elite" group in terms of their health behaviour anyway, and the taking of those sorts of drugs is merely an indicator of such behaviour. There is support for the latter hypothesis when the aspirin data are examined more closely: the medical practitioner was the prescription source for only 7.7 per cent of the group on daily aspirin at baseline and five years; the other 92.3 per cent had self-prescribed their aspirin, perhaps indicating a more health-conscious individual than someone who does not practise such preventive health behaviour. Thus, not taking daily aspirin could be considered to be a "risk marker" (Beck, 1998) for root surface caries.

No medications emerged as predictors of an increased root surface caries increment. At the commencement of the study, the investigator's intuition was that, if anything substantive was to emerge from an investigation of medications as predictors of caries in a longitudinal study of older people, it would be with the root surface caries increment data, given the condition's much later onset than coronal caries and its more variable presentation. Unfortunately, this did not eventuate, and it appears that medications *per se* are not risk factors for the occurrence of coronal or root surface caries among older people in the current study.

It is noteworthy that the only other predictor of the five-year root surface caries increment was being a regular user of dental services. The latter finding may be associated with the receipt of root-surface restorations for abrasion, or it may indicate that some "over-servicing" of regular attenders may have been occurring.

It is, of course, not surprising that dry mouth measured at five years—whether estimated as symptom severity (XI scores) or as unstimulated flow rate—did not

predict any of the three disease outcome variables. It would have been far more useful to have had baseline estimates of those parameters, and too little is known of their natural history among older people for any confidence to be placed in the utility of the estimates at five years as 'retrospective predictors". To date, only one study (Locker, 1995) has reported on five-year changes in dry mouth; aside from that report, there remains a general shortage of data on the natural history of salivary secretion from cohort studies of older people. As discussed in Section 4.2.4, there is the possibility that intra-individual change in salivary flow may be more important than the absolute level, at least where dental caries is concerned.

An interesting point is whether an association between dental caries and one or more medication types may have been uncovered if only the D component of the DFS increment had been examined, on the basis that many restorations are placed for reasons other than dental caries. This is particularly apparent for root surfaces, where abrasion defects are often restored. Repeating the bivariate analyses using only the D component did reveal that the coronal caries increment was greater among continuous users of antigout medication. The root surface caries increment was greater among continuous users of antiulcer drugs or beta-blockers. Where caries incidence is concerned, there were no significant differences for either type. There were no differences by any of the medication combinations which had been found to be associated with dry mouth. Interpretation of these findings is not straightforward. Although it could be argued that the D component of the caries increment is a more "pure" representation than the combined DF component because the placement of restorations for reasons other than caries may obscure the "real" relationship between caries and medication exposure, restricting the analysis to the D component only is also highly problematic. Individuals A and B may take the same medication and have had identical DS increments, but A may have had hers recently treated by her dentist (and thereby converted to an FS increment) and, in effect, have no DS increment, while B may not have been to a dentist in the preceding five years and have a considerable DS increment as a consequence. Using the dental visiting pattern as a predictor in a multivariate analysis would therefore be a useful strategy in any examination of the DS component. This is an issue which should be examined in future analyses of the SADLS data-set.

Was it worth presenting the associations between dental caries experience at five years and medication exposure in this report, given that incidence and increment data were available and arguably more useful in examining the study hypotheses? The answer is "yes", if only on the basis that the bulk of our current knowledge of the association of medications and dental caries comes from prevalence studies, and it is therefore important for comparison purposes that other workers—who may only have been able to conduct a cross-sectional investigation—are able to compare their findings with those of the current study.

Overview of the findings on medication, tooth loss and caries

The study hypotheses were that certain categories of medication would emerge as risk factors for five-year tooth-loss incidence, five-year coronal caries incidence and increment, and five-year root surface caries incidence and increment among community-dwelling older South Australians. Because it was further hypothesised that, if such associations were to be demonstrated, they would be observed to occur through the pathways specified in Figure 1.3, the investigator has resisted the temptation to use the CART analytical approach to directly examine the medication-caries relationships, because to do so would have circumvented a vital link in the putative causal chain. It was acceptable to use CART to explore the medication-dry mouth associations because so much of what had been previously written was contradictory or confusing (and developing a theoretical model was a daunting task because of that), but because nothing substantial had been published on the medication-caries relationship, it was deemed appropriate to use a structured hypothetical pathway.

In the final outcome, the study hypotheses have generally not been borne out. Prior to this study, there was very little evidence to support even the notion that medication was a risk indicator for dental caries, although there had been considerable speculation that individuals taking particular drugs were at higher risk of the disease. Aside from the association between cardiac inotropic drugs and tooth-loss incidence (and increment), the outcomes of interest were not associated with any particular class of medication, whether alone or in combination. It should also not be forgotten that some

classes of drugs such as the anticholinergics and antihistamines (both of which have been shown to be associated with dry mouth) were not present in sufficient numbers to be adequately investigated.

The possibility of Type II error has been mentioned above and should be further acknowledged. It is indeed a strong possibility that there may have been occasions in the study when the null hypothesis was accepted when it was, in fact, false. The failure to reach statistical significance does not necessarily mean that the particular medication-exposure groups being compared were identical in their caries experience; it may have been that the number in the medication-exposure subgroup was too small to ensure that an observed association was statistically significant (Freiman *et al*, 1978). As discussed above (Section 4.1.4), the purposive examination of medications and their oral health associations commenced some time after the initial power calculations for the study (in fact, after the baseline data collection had been completed), and it was simply not possible to ensure adequate numbers in many of the medication-exposure subgroups. Thus, while null findings predominate in the medication-caries analyses, it is appropriate to bear in mind that Type II error may account for at least a proportion of those (Chalmers, 1981). Unfortunately, it is not possible to nominate those for which this caveat applies.

It may be, therefore, that if the original sample size had been twice the number examined at baseline, some stronger associations may have emerged. This may be so, but then, if considerably larger numbers are required to investigate it, then perhaps the putative effect isn't that great in the first place. On the other hand, it should not be forgotten that, of the dentate people examined at baseline, 39.9 per cent were lost to follow-up, and that group tended to be more medicated, and have a greater proportion of males and people with worse self-care and dental service-use behaviours. This highlights one of the dilemmas of the cohort study design: sample attrition over time is not a random process, and those who are lost to follow-up generally have worse health and health practices than those who remain. Beck *et al* (1997) demonstrated with the Piedmont study data that the three-year root caries increment was actually much higher among whites who had been lost to follow-up by five years. This suggests that the Piedmont study's reported five-year increments actually underestimated what

happened over that period, as the individuals with the greatest disease experience had been lost. It is highly probable that there has been a similar occurrence in the current study, and that perhaps those with the greatest disease increment had been lost by five years; when it is considered that they were also more highly medicated (Table 3.41), it is tempting to speculate that some medications may have emerged as risk factors if the sample retention rate had been greater. Nevertheless, the only conclusion that it is possible to draw from the current study is that, among the sample examined, exposure to medications (other than antiasthma drugs or ACEI antihypertensives) was not a risk factor for dental caries (although it was for tooth loss).

4.2.7 Clinical implications of the investigation

No dental epidemiological investigation is complete without an examination of the clinical implications of its outcome. This is best achieved by asking the question: what should our message to clinicians be, based on this study's findings? Alternatively, how would the study's outcome be explained to an old dental classmate who is in general dental practice in rural Australia or New Zealand? Considering the outcome in this way forces the investigator to place the findings in a "real-world" context. Using this approach, the study's outcomes can be listed as follows:

- most older people with dry mouth symptoms do not have a reduced salivary flow rate, and most older people with a reduced salivary flow rate do not have the symptoms of dry mouth;
- older females and people taking long-term antidepressants are at risk of low salivary flow;
- the symptoms of dry mouth are more severe in older people taking either anginals without an associated β-blocker, thyroxine and a diuretic, or a long-term antidepressant; and
- contrary to the "conventional wisdom", there is little evidence (from this study, at least) that particular medications are risk factors for dental caries, although older people taking cardiac drugs appear to be at higher risk for

tooth loss, and those taking ACEIs or antiasthma drugs appear to be at higher risk for coronal caries).

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(*Indicates publications which have resulted from the work done in this thesis project)

Appendix 1: Medication codes by therapeutic category

(NB: For coding of medications prior to data entry, a version of this Appendix was used which lists the medications in alphabetical order. This is accomplished by a simple sort procedure in Microsoft Word)

41. Antidepressants

antidepressant, un-named 41000
desipramine 41001
pertofran 41002
imipramine 41003
imipramin (imipramine HCl) 41004
melipramine 41005
tofranil 41018
clomipramine 41006
anafranil 41007
opipramol 41008
trimipramine 41009
tripress (trimipramine) 41010
surmontil 41011
lofepramine 41012
dibenzepin 41013
amitriptyline 41014
amitrip 41015
endep 41016
tryptanol 41017
laroxyl (amitriptyline HCl) 41018
nortriptyline 41019
norpress (nortriptyline HCl) 41020
allegron 41021
protriptyline 41022
doxepin 41026
deptran 41023
sinequan 41025
anten (doxepin) 41024
iprindole 41027
melitracen 41028
butriptyline 41029
dosulepin 41030
amoxapine 41031
asendin (amoxapine) 41032
dimetacrine 41033
amineptine 41034
maprotiline 41035
venlafaxine 41036
ludiomil (maprotiline HCl) 41037

prozac 41101
fluoxetine 41102
bupropion 41103
zoloft 41104
zimeldine 41105
citalopram 41107
paroxetine 41108
aropax 41109
sertraline 41110
alaproclate 41111
fluvoxamine 41112
etoperidone 41113
dothiepin 41114
dothep 41115
prothiaden 41116

marplan 41201
nardil 41202
aurorix 41203
isocarboxazid 41204
nialamide 41205
phenelzine 41206
tranylcypromine 41207
parnate 41208
moclobemide 41209
toloxatone 41210
parstelin 41211

oxitriptan 41301
tryptophan 41302
lerivon 41303
mianserin 41304
lumin 41305
tolvon 41306
nomifensine 41307
trazodone 41308
mefazodone 41309
minaprine 41310
bifemelane 41311
viloxazine 41312
oxaflozane 41313
mirtazapine 41314
amfebutamone 41315

42. Anticholinergics, antispasmodics, antiparkinsonian drugs

anticholinergic un-named 42000
atropine 42004
monodral 42014
pro-banthine 42016
robinul 42017
Darbid (isopropamide iodide) 42019
propantheline 42022
glycopyrrolate 42027
glycopyrronium 42028
merbentyl 42049
isopropamide 42061
Tyrimide (isopropamide) 42068
oxyphencyclimine 42029
camylofin 42030
mebeverine 42031
trimebutine 42032
rociverine 42033

3. Antipsychotics

serenace 43101
haldol 43102
bromperidol 43103
benperidol 43104
droperidol 43105
droleptan 43106

thiothixene 43200
navane (thiothixene) 43201
flupentixol 43202

pimozide 43300
orap 43301

remoxipride 43400

lithium 43500
lithicarb 43501

risperidone 43601

4. Antihypertensives, cardiovascular preparations, diuretics, Ca++ antagonists, antiarrhythmics, antiangina drugs

"blood pressure pills" (un-named) 44000
"heart tablets" 44700
"water tablets" 44100
"angina tablets" 44800

beta-blocker (unspec.) 44001
alprenolol 44002
aptin 44003
oxprenolol 44004
trasicor 44005
pindolol 44006
visken 44006
barbloc 44007
propranolol 44008
inderal 44008
cardinol 44009
deralin 44010
timolol 44011
blocadren 44012
sotalol 44013
nadolol 44014
mepindolol 44015
carteolol 44016
tertatolol 44017
bupranolol 44018
penbutolol 44019
cloranolol 44020
practolol 44021
metoprolol 44022
minax 44022
lopresor 44023
betaloc 44024
atenolol 44025
noten 44026
tenormin 44027
acebutolol 44028
betaxolol 44029
bevantolol 44030
bisoprolol 44031
celiprolol 44032
esmolol 44033
brevibloc 44034
epanolol 44035
S-atenolol 44036
labetolol 44037
presolol 44038
trandate 44039
carvedilol 44040
sotacor 44041

bendroflumethiazide 44101
bendrofluazide 44102
aprinox 44103
hydroflumethiazide 44104
hydrochlorothiazide 44105
dichlotride 44106
dyazide 44107
chlorothiazide 44108
chlotride 44109
polythiazide 44110
chlorthalidone 44111
hygroton 44112
trichlormethiazide 44113
cyclopenthiazide 44114
navidrex 44115
methyclothiazide 44116
enduron 44117
cyclothiazide 44118
mebutizide 44119
quinethazone 44120
clopamide 44121
mefruside 44123
clofenamide 44124
metolazone 44125
diulo 44126
meticrane 44127
xipamide 44128
indapamide 44129
clorexolone 44130
fenquizone 44131
mersalyl 44132
cicletanine 44136
furosemide 44137
frusemide 44138
Lasix (frusemide) 44139
uremide 44140
urex 44141
urex forte 44142
bumetanide 44143
burinex 44144

5. Antihistamines

antihistamine, un-named 45000

benadryl 45001
benatuss 45002
benyphed 45003
bromazine 45004
clemastine 45005
diphenhydramine 45006
diphenylpyraline 45007
histalert 45008
hydroxyethylpromethazine 45009
isothipendyl 45010
phenergan 45011
phensedyl 45012
promethazine 45013
prothazine 45014
tixylix 45015

buclizine 45100
cetirizine 45101
chlorcyclizine 45102
cyclizine 45103
meclozine 45104
oxatomide 45105

acrivastine 45200
actifed 45201
antazoline 45202
astemizole 45203
azatadine 45204
azelastine 45205
bamipine 45206
claratyne 45207
cyproheptadine 45208
periactin 45209
deptropine 45210
ebastine 45211
fabahistin 45212
hismanal 45213
ketotifen 45214
loratadine 45215
mebhydrolin 45216
phenindamine 45217
pyrrobutamine 45218
teldane 45219
terfenadine 45220

thenalidine 45300
triprolidine 45301
tritoqualine 45302
zadine 45303

action 45320
alimemazine 45321
atarax 45322
avil 45323
brompheniramine 45324
carbinoxamine 45325
chloropyramine 45326
chlorpheniramine 45327
chlorphenoxamine 45328
day and night 45329
demazin 45330
dexbrompheniramine 45331
dexchlorpheniramine 45332
dilosyn 45333
dimetapp 45334
dimetindene 45335
doxylamine 45336
fenamine 45337
headclear 45338
histapyrrodine 45339
hycomine 45340
mepyramine 45341
mequitazine 45342
methapyrilene 45343
methdilazine 45344
neo-diophen 45345
orthoxicol 45346
oxomemazine 45347
panadol allergy sinus 45348
pheniramine 45349
piriton 45350
polaramine 45351
sinutab 45352
sudafed 45353
sudagesic 45354
talastine 45355
thiethylperazine 45356
thiazinam 45357
thonzylamine 45358
tripelenamine 45359
tylenol allergy sinus 45360
tylenol cold & flu 45361
vallergan 45362

6. Simple analgesics, antigout drugs, NSAIDs and narcotic analgesics

"painkiller" (unnamed) 46000
ASA arthritis strength aspirin 46007
Alka-Seltzer 46012
aloxiprin 46019
choline salicylate 46020
sodium salicylate 46021
salicylamide 46022
salicyloylsalicylic acid 46023
ethenzamide 46024
morpholine salicylate 46025
dipyrocetyl 46026
benorilate 46027
diflunisal 46028
dolobid 46028

potassium salicylate 46029
lysine acetylsalicylate 46030
guacetisal 46031
imidazole salicylate 46033
phenazone 46034
metamizole sodium 46035
aminophenazone 46036
propyphenazone 46037
nifenazone 46038
paracetamol 46039
panadol 46040
paralgin 46041
paraspen 46042
setamol 46043
tempra 46044
tylenol preparations 46045
phenacetin 46046
bucetin 46047
rimazolium 46048
glafenine 46049
floctafenine 46050
viminol 46051
nefopam 46052
flupirtine 46053

phenylbutazone 46101
butazolidin 46102
mofebutazone 46103
oxyphenbutazone 46104
clofezone 46105
kebuzone 46106
indomethacin 46107
indocid 46108
arthrexin 46109
sulindac 46110
aclin 46111
Clinoril (sulindac) 46112
Daclin (sulindac) 46113
tolmetin 46114
zomepirac 46115
diclenofac 46116
fenac 46117
voltaren 46118
alclofenac 46119
bumadizone 46120
etodolac 46121
lonazolac 46122
fentiazac 46123
acemetacin 46124
difenpiramide 46125
oxametacin 46126
proglumetacin 46127
ketorolac 46128
toradol inj 46129
piroxicam 46130
feldene 46131
tenoxicam 46136
tilcotil 46137
droxicam 46138
lornoxicam 46139
ibuprofen 46140
brufen 46141
ACT-3 46142
ACT-3C 46143
nurofen 46144
rafen 46145
naproxen 46146
Naprosyn (naproxen) 46147
Naxen (naproxen) 46148
Noflam (naproxen) 46149
inza 46150
synflex 46151
ketoprofen 46152
Oruvail (ketoprofen) 46153
orudis 46154
fenoprofen calcium 46155
fenopron 46156
fenbufen 46157
benoxaprofen 46158
suprofen 46159
pirprofen 46160
flurbiprofen 46161
indoprofen 46162
tiaprofenic acid 46163
surgam 46164
oxaprozin 46165
ibuproxam 46166
dexibuprofen 46167
flunoxaprofen 46168
mefenamic acid 46169
mefic 46170
ponstan 46171
tolfenamic acid 46172
flufenamic acid 46173
meclofenamic acid 46174
nabumetone 46175
niflumic acid 46176
azapropazone 46177
glucosamine 46178
benzydamine 46179
glucosaminoglycan polysulfate 46180
proquazone 46181
orgotein 46182
nimesulide 46183
feprazone 46184
diacerein 46185
morniflumate 46186
tenidap 46187

"gout pills" 46201
allopurinol 46202
capurate 46203
progout 46205
zyloprim 46206
alinol 46207
allorin 46209

Z 300 46210
probenecid 46211
benemid 46212
sulfinpyrazone 46213
anturan 46214
benzbromarone 46215
isobromindione 46216
colchicine 46217
colgout 46218
cinchophen 46219
urate oxidase 46220

morphine sulfate 46301
morphalgin 46302
morphine mixtures 46303
morphine tartrate 46304
MS Contin 46305
MST continus (morphine sulphate) 46306
anamorph 46307
mersyndol forte 46308
opium 46309
hydromorphone 46310
nicomorphone 46311
oxycodone 46312
endone 46315
percodan 46314
proladone 46315
dihydrocodeine 46316
codate 46317
codeine 46318
codcomol 46318
codral forte 46319
ketobemidone 46320
pethidine 46321
fentanyl 46322
sublimaze 46323
dextromoramide 46324
palfium 46325
methadone 46326
physeptone 46330
piritramide 46331
dextropropoxyphene 46332
digesic 46333
doloxene 46334
capadex 46335
paradex 46336
bezitramide 46337
pentazocine 46338
fortral 46339
phenazocine 46340
buprenorphine 46341
temgesic 46342
butorphanol 46343
nalbufine 46344
tilidine 46345
tramadol 46346
dezocine 46347
operidine 46348
papaveretum 46349

aspalgin 46401
codalgin 46402
codiphen 46403
pirophen 46403
codis 46404
codox 46405
codral 46406
decrin 46407
disprin forte 46408
dymadon 46409
dymadon forte 46419
fiorinal 46410
mersyndol 46411
painstop syrup 46412
panadeine 46413
panalgesic 46414
panamax 46415
tyledeine 46416
solcode 46417
veganin 46418

panquil 46500
panadol elixir with promethazine 46501
seda-gel 46502

7. Antidiarrhoeals

antidiarrhoeal unnamed 47000
diareze 47002
dia-chek 47003
pectin 47005
kaolin 47006
kaofort 47007
kaomagna 47008
kaopectate 47009
diphenoxylate 47010
lomotil 47011
loperamide 47012
imodium (loperamide Hcl) 47013
gastro-stop 47014
sulfasalazine 47015
salazoprin 47016
mesalazine 47017
mesasal 47018
olsalazine 47019
dipentum 47020
albumin tannate 47021
tannalbin 47022
ceratonia 47023
veracolate 47024

8. Antinauseants

antinauseant, unamed 48000
benacine 48001
kwells 48002
scop 48003
travacalm 48004
andrumin 48006
avomine 48007
dramamine 48008
emetrol 48009
instant carobel 48010
maxolon 48011
metoclopramide 48012
motilium 48013
pramin 48014
zofran 48015
maxolon high dose 48016
metaclopramide HCl 48017
Metamide (metaclopramide HCl) 48018
Paramax (metaclopramide HCl) 48019
domperidone 48013

9. Antineoplastics

"cancer tablets" unnamed 49000
cyclophosphamide 49001
cycloblastin 49002
endoxan-asta 49003
chlorambucil 49004
melphalan 49006
chlormethine 49007
ifosfamide 49008
trofosfamide 49009
prednimustine 49010
busulfan 49011
treosulfan 49012
mannosulfan 49013
thiotepa 49014
triaziquone 49015
carboquone 49016
carmustine 49017
lomustine 49018
semustine 49019
streptozocin 49020
fotemustine 49021
nimustine 49022
ranimustine 49021
etoglucid 49022
mitobronitol 49023
pipobroman 49024
methotrexate 49100
tioguanine 49101
cladribine 49102
fludarabine 49103
cytarabine 49104
fluorouracil 49105
tegafur 49106
carmofur 49107
gemcitabine 49108
hydrea 49193
hydroxyurea 49193
vinblastine 49200
vincristine 49201
vindesine 49202
etoposide 49203
vepesid 49204
teniposide 49205
vumon 49206
demecolcine 49207
paclitaxel 49208
dactinomycin 49300
cosmegen 49301
doxorubicin 49302
adriamycin inj. 49303
daunorubicin 49304
epirubicin 49305
pharmorubicin 49306
aclarubicin 49307
zorubicin 49308
idarubicin 49309
zavedos 49310
mitoxantrone 49311
novantrone 49312
bleomycin 49313
blenoxane 49314
plicamycin 49315
mitomycin 49316
cisplatin 49400
carboplatin 49401
paraplatin 49402
procarbazine 49403
natulan 49404
amsacrine 49405
amsidyl 49406
asparaginase 49407
altretamine 49408
hydroxycarbamide 49409
lonidamine 49410
pentostatin 49411
miltefosine 49412
masaprocol 49413
estramustine 49414
dacarbazine 49415
DTIC 49416
tretinoin 49417
porfimer sodium 49418
diethylstilbestrol 49500
ethinylestradiol 49501
fosfestrol 49502
megestrol 49503
medroxyprogesterone 49504
provera 49504
gestonorone 49505
buserelin 49506
leuprorelin 49507

goserelin 49508
zoladex implant
triptorelin 49509
tamoxifen 49510
tamofem 49511
genox 49512
nolvadex 49513
tormifene 49514
flutamide 49515
eulexin 49516
nilutamide 49517
aminogluthetimide 49518
formestane 49519
interleukin-2 49600
filgrastim 49601
molgramostim 49602
interferon alfa 49603
poly I:C 49604
poly ICLC 49605
thymopentin 49606
interferon gamma 49607
sargramostim 49608
lenograstim 49609
interferon beta 49610
lentinan 49611
roquinimex 49612
BCG vaccine 49613
ciclosporin 49700
muromonab-CD3 49701
antilymphocyte immunoglobulin 49702
antithymocyte immunoglobulin 49703
azathioprine 49704
Imuran (azathioprine) 49705

10. Antipruritics

Antipruritic, unnamed 10000
betnov 10000
Pinetarsol 10001
hydrocortisone cream/lotion 10002
cortef 10002
locoid 10002
pine tar/triethanolamine lauryl sulphate 10003
alpha-keri lotion 10004
alpha-keri oil 10005
anthisan cream 10006
aveeno prep 10007
BFI powder 10008
caladryl 10009
calistaflex 10010
dermocaine 10011
eczema cream 10012
egoderm cream 10013
egoderm ointment 10014
eurax 10015
formicare bath/shower solutions 10016
formicare skin relief 10017
oilatum prep 10018
paraderm 10019
polytar ointment 10020
QV bathoil 10021
QV skin lotion 10022
QV tar 10023
rikoderm lotion 10024
rikoderm bath oil 10025
sarna lotion 10026
stingose 10027
sigmacort 10028

11. Antiulcer drugs

"ulcer tablets", unnamed 11000
amfamox 11001
pepcidine 11002
cimetidine 11003
tagamet 11003
ranitidine 11004
Zantac (ranitidine Hcl) 11005
magicul 11006
tazac 11007
famotidine 11008
nizatidine 11009
niperotidine 11010
roxatidine 11011
dijene 11012

misoprostol 11101
cytotec 11102
enprostil 11103

roter 11201
SCF 11202
Carafate (sucralfate) 11203
sucralfate 11204
ulcyte 11205
de-nol tabs 11206

zoton 11301
lansoprazole 11301
losec 11302
omeprazole 11302

gaviscon 11402
mylanta 11403
simethicone 11414
titralac 11417
amphojel 11419
ad-sorb 11420
algicon 11421
almacarb 11422
alu-tab 11423
charcoal 11424
charcocaps 11425
de-gas 11426

dexsal 11427
eno powder 11428
gastrogel 11429
gastrobrom 11430
gavigrans 11431
gelusil 11432
medefoam-2 11434
meracote 11435
mucaine 11436
no gas 11437
rennie 11438
prepulsid 11439
cisapride 11439
salvital 11440
simeco 11441

12. Psychotherapeutics

"sleeping tabs/sedatives" 12000

diazepam 12001
diazemuls 12002
ducene 12003
valium 12004
antenex 12005
chlordiazepoxide 12006
librium 12007
medazepam 12008
oxazepam 12009
Serepax (oxazepam) 12010
murelax 12011
alepam 12012
clorazepate potassium 12013
tranxene 12014
lorazepam 12015
ativan 12016
emoten 12017
adinazolam 12018
bromazepam 12019
lexotan 12020
clobazam 12021
frisium 12022
ketazolam 12023
prazepam 12024
alprazolam 12025
xanax 12026
kalma 12027
halazepam 12028
pinazepam 12029
camazepam 12030
nordazepam 12031
fludiazepam 12032
ethyl loflazepate 12033
etizolam 12034
clotiazepam 12035
cloxazolam 12036

hydroxyzine 12100
captodiame 12101

meprobamate 12200
equanil 12201
emylcamate 12202
mebutamate 12203
benzoctamine 12204

buspirone 12300
buspar 12301
mefenoxalone 12302
gedocarnil 12303

pentobarbital 12400
pentobarbitone 12401
carbrital 12402
amobarbital 12403
amylobarbitone 12404
amytal sodium 12405
neur-amyl 12406
butobarbital 12407
soneryl 12408
barbital 12409
aprobarbital 12410
secobarbital 12411
talbutal 12412
vinylbital 12413
vinbarbital 12414
cyclobarbital 12415
heptabarbital 12416
reposal 12417
methohexital 12418
hexobarbital 12419
thiopental 12420
etallobarbital 12421
allobarbital 12422

chloral hydrate 12500
dormel 12501
noctec 12502
chloralodol 12503
acetylglycinamide chloral hydrate 12504
dichloralphenazone 12505
paraldehyde 12506

flunitrazepam 12600
rohypnol 12601
hypnodorm 12602
estazolam 12603
flurazepam 12604
dalmane 12605
midazolam 12606
brotizolam 12607
quazepam 12608
loprazolam 12609
doxefazepam 12610
nitrazepam 12611

alodorm 12612
mogadon 12613
lormetazepam 12614
noctamid (lormetazepam) 12615
temazepam 12616
euhypnos 12617
normison 12618
temaze 12619
triazolam 12620
halcion (triazolam) 12621
glutethimide 12622
methyprylon 12623
pyrithyldione 12624
zopiclone 12625
zolpidem 12626
methaqualone 12627

chlormethiazole 12700
hemineurin (chlormethiazole) 12701
bromisoval 12702
carbromal 12703
scopolamine 12704
propiomazine 12705
triclofos 12707
ethchlorvynol 12708
valerian 12709
hexapropymate 12710
bromides 12711
apronal 12712
valnoctamide 12713
relaxa-tabs 12714
restavit 12715
oxpentifyline 12716

13. Laxatives

"laxative", unnamed 13000
paraffin 13001
agarol 13002
parachoc 13003
docusate sodium 13004
Coloxyl (docusate sodium) 13006
acetphenolisatin 13007
bisacodyl 13008
bisalax 13009
durolax 13010
dantron 13011
phenolphthalein 13012
alophen 13013
figsen 13014
castor oil 13015
senna 13016
senokot 13017
laxettes 13018
cascara 13019
sodium picosulfate 13020
ispaghula 13021
fybogel 13021
agiolax 13022
ethulose 13023
sterculia 13024
granocol 13025
normacol plus 13026
agiofibe 13027
effersylium 13028
psyllium hydrocolloid 13029
Metamucil (psyllium) 13030
linseed 13031
methylcellulose 13032
triticum 13033
magnesium carbonate 13034
magnesium oxide 13035
magnesium peroxide 13036
magnesium sulphate 13037
lactulose 13038
Duphalac 13039
Laevolac (lactulose) 13040
actilax 13041
lactitol 13042
sodium sulphate 13043
enema (type to be recorded separately) 13044
glycerol 13045
ipecacuanha 13046

14. Antibiotics

antibiotic un-named 14000

demeclocycline 14001
ledermycin 14002
doxycycline 14003
doryx 14004
doxylin 14005
vibra-tabs 14006
vibramycin 14007
chlortetracycline 14008
aureomycin 14009
lymecycline 14010
methacycline 14011
rondomycin 14012
oxytetracycline 14013
tetracycline 14014
achromycin 14015
mysteclin 14016
tetrex 14017
minocycline 14018
minomycin 14019
rolitetracycline 14020
reverin 14021
penimepicycline 14022
clomocycline 14023

chloramphenicol 14100

chloromycetin 14101
thiamphenicol 14102

ampicillin 14200
alphacin 14201
ampicyn 14202
austrapen 14203
penbritin 14204
pivampicillin 14205
carbenicillin 14206
amoxycillin 14207
amoxycillin/clavulanic acid 14208
amoxil 14209
alphamox 14210
augmentin 14211
cilamox 14212
fisamox 14213
moxacin 14214
ibiamox 14215
carindacillin 14216
bacampacillin 14217
epicillin 14218
pivmecillinam 14219
azlocillin 14220
securopen 14221
mezlocillin 14222
mecillinam 14223
piperacillin 14224
pipril 14225
ticarcillin 14226
tarcil 14227
ticillin 14228
timentin 14229
metampicillin 14230
talampicillin 14231
sulbenicillin 14232
temocillin 14233
hetacillin 14234

benzylpenicillin 14235
penicillin 14236
clinacaine 14236
phenoxymethylpenicillin 14237
abbocillin 14238
LPV 14239
PVK 14240
propicillin 14241
azidocillin 14242
phenethicillin 14243
pensig 14244
penamecillin 14245
clometocillin 14246
benzathine benzylpenicillin 14247
procaine penicillin 14248
cilicaine 14249
benzathine phenoxymethylpenicillin 14250
bicillin 14251
dicloxacillin 14252
cloxacillin 14253
alclox 14254
austrastaph 14255
methicillin 14256
oxacillin 14257
flucloxacillin 14258
flopen 14259
floxapen 14260
flucil 14261
staphylex 14262

cefalexin 14301
ceporex 14302
ibilex 14303
keflex 14304
cefaloridine 14305
cefalothin 14306
keflin 14307
cefazolin 14308
cefamezin 14309
kefzol 14310
cefoxitin 14311
mefoxin 14312
cefuroxime 14313
cefamandole 14314
mandol 14315
cefaclor 14316
ceclor 14317
cefadroxil 14318
cefazidime 14319
fortum 14320
cefsulodin 14321
ceftriaxone 14322
rocephin 14323
cefotetan 14324
apatef 14325
cefazedone 14326
cefmenoxime 14327
cefonicide 14328
latamoxef 14329
cefotiam 14330
cefatrizine 14331
ceftizoxime 14332
cefixime 14333
cefepime 14334
cefodizime 14335
cefetamet 14336
cefpiramide 14337
cefapirin 14338
cefradine 14339
cefoperazone 14340
cefpodoxime 14341
cefacetrile 14342
cefroxadine 14343
ceftezole 14344
cefpirome 14345
loracarbef 14346

ceftibuten 14347
cefinetazole 14348
aztreonam 14349
azactam 14350
meropenem 14351
imipenem 14352
primaxin 14353
claforan 14354

trimethoprim 14401
triprim 14402
alprim 14403
brodimoprim 14404
sulfaisodimidine 14405
sulfamethizole 14406
urolucosil 14407
sulfadimidine 14408
sulfapyridine 14409
sulfafurazole 14410
sulfaniliamide 14411
sulfathiazole 14412
sulfathiourea 14413
sulfamethoxazole 14414
sulphadiazine 14415
sulfamoxole 14416
sulfadimethoxine 14417
sulfalene 14418
sulfamethomidine 14419
sulfamethoxydiazine 14420
sulfamethoxypyridazine 14421
sulfaperin 14422
sulfamerazine 14423
sulfaphenazole 14424
sulfamazon 14425
sulfamethoxazole and trimethoprim 14426
co-trimoxazole 14427
resprim 14428
septrin 14429
sulphadiazine and trimethoprim 14430
sulfametrole and trimethoprim 14431
sulfamoxole and trimethoprim 14432
sulfadimidine and trimethoprim 14433

erythromycin 14501
EES 14502
EMU-V 14503
Eryc 14504
erythrocin 14505
ilosone 14506
spiramycin 14507
midecamycin 14508
pristinamycin 14509
oleandomycin 14510
roxithromycin 14511
rulide 14512
josamycin 14513
troleandomycin 14514
clarithromycin 14515
azithromycin 14516
miocamycin 14517
rokitamycin 14518
clindamycin 14519
clindatech 14520
dalacin 14521
lincomycin 14522
lincocin 14523

streptomycin 14601
streptoduocin 14602
tobramycin 14603
nebcin 14604
gentamycin 14605
septopal 14606
cidomycin 14607
kanamycin 14608
neomycin 14609
minims, neomycin 14610
neosulf 14611
amikacin 14612
amikin 14613
netilmicin 14614
netromycin 14615
sosmicin 14616
dibekacin 14617
ribostamycin 14618

ofloxacin 14701
ciprofloxacin 14702
pefloxacin 14703
enoxacin 14704
temafloxacin 14705
norfloxacin 14706
lomefloxacin 14707
fleroxacin 14708
sparfloxacin 14709
rosoxacin 14710

vancocin 14801
vancomycin 14802
vancoled 14803
teicoplanin 14804
colistin 14805
polymyxin 14806
fucidic acid 14807
fucidin 14808
metronidazole 14809
rozex 14809
flagyl 14810
metrogyl 14811
tinidazole 14812
omidazole 14813
fosfomycin 14814
xibornol 14815
clofoctol 14816
spectinomycin 14817

trobicin 14818
furadantin 14819
macrodantin 14820
mifuran 14821
nitrofurantoin 14822
pentacarinat 14823
pentamidine 14824
nalidixic acid 14825
Negram (nalidixic acid) 14826

amphotericin 14901
fungilin 14902
fungizone 14903
hachimycin 14904
miconazole 14905
daktarin 14906
ketoconazole 14907
nizoral 14908
fluconazole 14909
diflucan 14910
itraconazole 14911
flucytosine 14912
ancotil 14913
ciproxin 14914
noroxin 14915
griseofulvin 14916
fulcin 14917
griseostatin 14918
grisovin 14919
nystatin 14920
mycostatin 14921
nilstat 14922

15. Hypoglycaemics

insulin 15001
actrapid 15002
lente MC 15003
novo nordisk 15004
novo MC insulin prep 15005
humulin 15006
hypurin 15007
insulatard 15008
isotard 15009
mixtard 15010
monotard 15011
protamine zinc insulin mc 15012
protaphane hm preps 15013
ultralente mc 15014
ultratard hm 15015
velosulin human preps 15016

"diabetes tablets", unnamed 15100

metformin 15101
diaformin 15102
diabex 15103
glucophage 15104

chlorpropamide 15201
diabinese 15202
glibenclamide 15203
daonil 15204
euglucon 15205
Gliben (glibenclamide) 15206
glimel 15207
Semi-euglucon (glibenclamide) 15208
Semi-daonil (glibenclamide) 15209
gliclazide 15210
Diamicron (gliclazide) 15211
glipizide 15212
minidiab 15213
tolbutamide 15214
Diatol (tolbutamide) 15215
rastinon 15216

16. Nutrient agents

multivitamin &/or mineral (unnamed) 16000
Healtheries women's multivitamins 16001
Kordel's multivitamins 16002
Kordel's women's multivitamins 16003
Multivitamins 16004
Women's Multivitamins 16005
Multivitamins (bought in USA) 16006
Nature's Life multivitamins 16007
Megavit 2 16007
Synovus multivitamins 16008
Immunoforte multivitamins 16009
Cenova's multivitamins 16010
Boost vitamins multivitamins 16011
Energy in a Tablet 16012
Accomin 16013
Bioglan Hemofactor 16014
Myadec 16015
Multivitamin with extra calcium and iron 16016
Nutraway daily multivitamin tablets 16017
Chewable kids' multivitamins 16018
Healtheries multivitamins 16019
Blackmores multivitamins 16020
Horleys multivitamin for men 16021
Usana vitamins nutritional systems 16022
Nutrisport multivitamins 16023
Berocca vit B + vit C 16024
Multivitamin with cod liver oil 16025
Multivitamin with antioxidants 16026
Natural Nutrition Women's multivit. with Se 16027

***Other multinutrient preparations 16030**
Blackmore's Vitamin C & Garlic & Echinacea 16031
Kordel's Cold Sore relief 16032
Ester C and Echinacea 16033
Healtheries Echinacea, Zinc, Vit C, Garlic 16034

New Era Hayfever and allergic rhinitis tablets 16035

***Antioxidant nutrient preparations 16060**
Healtheries antioxidant 16061
Selenium Ace 16062
Kordel's antioxidant 16063
Bodyguard antioxidant 16064
Unclassifiable multivitamin or mineral prep 16099

***Mineral supplements 16100**

Calcium 16100
Calcium supplement 16101
Calcium carbonate 16102
Calcium and magnesium 16103
Calcium and vitamin D 16104

Iron 16110
Natural Health Red Seal Iron plus tablets 16111
Iron tablets 16112
Thompson's Organic Iron 16113
Ferrum 16114
Nature's Own Iron Plus 16115
Nutraway Iron tablet 16116
Iron + Vitamin C

Magnesium 16130
Potassium 16140
Selenium 16150

Zinc 16160
Zinc tablets 16161

Pharmacological dose calcium 16170
Cal-Sup 16171
Calcium-Sandoz 16172
Caltrate 16173
Oscal 16174
Sandocal 16175

Pharmacological dose iron 16180
Ferrogradumet 16181
Fergon 16182
Fespan 16183

***Other mineral supplements 16190**

***Fat-soluble vitamin and beta-carotene supplements 16200**
Vitamin A 16200

Vitamin D 16210
Calcitriol 16211
Calciferol 16212
Ostelin (ergocalciferol) 16213
Ergocalciferol 16213
Rocaltrol (calcitriol) 16214
Vitamin E (tocopherol) 16220
Vitamin E 16221
Cenovis Vitamin E 16222

Beta-carotene 16230

***Water-soluble vitamin supplements 16300**
Thiamin 16300
Thiamine 16301
Betamin 16302
Beta-Sol 16303
Riboflavin 16310
Niacin 16320
Pantothenic acid 16330
Vitamin B6 16340
Golden Globe Vitamin B6 16341
Gold Globe Vitamin B6 + Apple Cider Complex 16342

Vitamin B12 (Cobalamin) 16350
Vitamin B12 16351
Cyanacobalamin 16352
Hydroxocobalamin 16353
Neo-Cytamen (hydroxocobalamin) 16354
Country Life Vitamin B12 tablets 16355

***Folic Acid 16360**
Folic Acid 16361
Pregnacare (folic acid, vits B & C, minerals) 16362
Fefol (folic acid & iron) 16363
FGF (folic acid & iron) 16364
Megafol 16365
Ferrogradfolic (ferrous sulphate + folic acid) 16366

***Vitamin B Complex 16370**
Vitamin B Complex 16371
Healtheries Vitamin B Complex 16372
Blackmores Vitamin B 16373

***Vitamin C 16380**
Vitamin C (ascorbic acid) Tablet 16381
Healtheries Vitamin C 16382
Roxdale Vitamin C 16383
Nature's Way Vitamin C 16384
Bioglan Cal C Tablets (ascorbic acid) 16383
Flavettes 16387
Macro C (ascorbic acid & calcium ascorbate) 16388
Haliborange Vitamin C tablets 16389
Vitamin C drink 16390

***Other Dietary Supplement Groups**

***BRAN/FIBRE 16400**
Oat Bran, Wheat Bran and Wheat Germ 16400
Fibre Powders (eg. Metamucil, isogel etc) 16420
Livatone (psyllium husk powder) 16421

***Fibre tablets (eg. chitosan) 16440**

Chitosan 16441

***OILS 16500**
Evening Primrose Oil 16500
Evening Primrose Oil 16501
Healtheries Evening Primrose Oil 16502
Epomega Flax Seed and Evening Primrose Oil 16503

***Cod Liver Oil and Halibut Liver Oil 16520**
Cod Liver Oil 16521

***Other Oils - omega 3 fish oil, wheatgerm oil, starflower oil, flaxseed oil, linseed 16530**
Omega 16531
Starflower Oil 16532

***GARLIC SUPPLEMENTS 16600**
(incl. use of raw garlic)
Garlic Tablets 16601
Garlic and Parsley Tablets 16602
Kyolic Garlic 16604
Garlic and Licorice 16605

***BOTANICAL, MICRO-ORGANISM AND BEE PRODUCTS 16700**
Acidophilus 16700
Acidophilus bifidus 16701

***Herbal remedies and other plant extracts (incl. kelp and echinacea) 16710**
Echinacea 16711
Garlic and Echinacea 16712
Ginseng/Ginsana 16713
St John's Wort (*Hypericum perforatum)* 16714
KIRA-*Hypericum perforatum* 16715
Ephedra 16716
Guarana Lift 16717
Bach Flower Rescue Remedy 16718
Kordel's Garlic and Echinacea 16719
Healtheries Echinacea and Garlic 16720
Gino Tincture 16721
Echinacea Lozenges 16722
Nodoze 16723
Cranberry Concentrate tablets 16724

Brewer's Yeast 16730

***Spirulina 16740**
Spirulina 16741
Lifestream Spirulina 16742

Bee Products (bee pollen, royal jelly, propolis etc) 16750
Propolis and Garlic 16751

***OTHER SUPPLEMENTS 16800**
***Complete and/or Supplementary Nutrition 16800**
Calogen (triglycerides) 16801
Complan 16802
Elemental 16803
Ensure 16804
Generaid 16805
Glucerna 16806
Isocal 16807
Liquigen (triglycerides) 16808
Maxijul L.E. 16809
MCT Duocal 16810
Neocate 16811
Osmolite 16812
Paediatric seravit 16813
Pediasure 16814
Polycal 16815
Polycose 16816
Poly-Joule 16817
Promod 16818
Pulmocare 16819
Sanatogen 16820
Seravit 16821
Super Soluble Maxipro 16822
Sustacal Pudding 16823
Sustagen Hospital Forumula 16824
Traumacal 16825
Two Cal HN 16826
Vital 16827
Lifestream Food Supplement (seafood) 16828

***Milk Substitutes and/or Supplements 16840**
Enfamil Human Milk Fortifier 16841
FM 85 16842
Super Soluble Duocal 16843

Silica Supplements 16850

Homeopathic Salts 16860

Lecithin 16870

***Miscellaneous (incl. fat mobilisers/slimming products, deer velvet, 16880**
shark cartilage, single amino acids, chomium, coenzyme Q10/ubiquinone)
Natural Energy Co-enzyme Q 10 16881
Thompson's Fat Blockers 16882
Liver 10,000 (liver extract 550 mg) 16883

***SPORTS SUPPLEMENTS 16900**
Carbohydrate supplements 16900

Protein Powders 16920
Protein 16921

Carnitine and Creatinine 16940
Creatine 16941

Other sports supplements 16960
Bulk (energy drink) 16961

Vitamin prep, un-codable or unnamed 16999

17. Potassium preparations

Potassium preparation (unspec.) 17000
Potassium chloride 17001
Slow K 17002

18. Bronchodilators/antiasthmatics

"asthma drug" 18000
epinephrine 18001
medihaler Epi 18002
isoprenaline 18003
medihaler Iso 18004
orciprenaline 18005
alupent metered aerosol 18006
salbutamol 18007
salbutamol respirator 18008
ventolin 18009
asmol 18010
respax 18011
respolin inhaler 18012
terbutaline 18013
bricanyl 18014
fenoterol 18015
berotec metered aerosol 18016
rimiterol 18017
hexoprenaline 18018
isoetarine 18019
pirbuterol 18020
procaterol 18021
tretoquinol 18022
carbuterol 18023
tulobuterol 18024
bambuterol 18025
salmeterol 18026
serevent 18027
formoterol 18028
clenbuterol 18029
reproterol 18030
bitolterol 18032

beclomethasone 18101
becodisk 18101
respocort-100 18101
aldecin inhaler 18102
becloforte inhaler 18108
becotide 18109
budesonide 18110
pulmicort 18111
flunisolide 18112
rhinalar 18112
betamethasone inhalant 18113
fluticasone 18114
flixotide 18115
ipratropium 18116
atrovent metered aerosol 18117
oxitropium 18118
stramoni prep 18119
cromoglycic acid 18120
rynacrom 18120
intal 18121
intal forte 18122
nedocromil 18123
fenspiride 18124

diprophylline 18201
choline theophyllinate 18202
brondecon 18203
choledyl 18204
proxyphylline 18205
theophylline 18206
elixophyllin 18207
slo-bid 18209
theo-dur 18210
nuelin 18211
austyn 18212
aminophylline 18213
cardophyllin 18214
etamiphylline 18215
theobromine 18216
bisolvon 18217
bamifylline 18218
acefylline piperazine 18219
bufylline 18220
doxofylline 18221
amlexanox 18222
eprozinol 18223
mucomyst 18224
dopram 18225

19. Topical agents

eye drops (not found elsewhere) 19001
propine 19002
pilocarpine 19003
timoptol 19004
eppy/n 19005
tenopt 19006
flarex 19007
chlorsig 19008
genoptic 19009
latycin 19010
tobrex 19011
acetazolamide 19012
diamox (acetazolamide) 19012

ear drops (not found elsewhere) 19100
soframycin 19101
coly-mycin 19102

sofradex 19103
auralgan otic 19104
nose, oropharynx sprays/drops (not found elsewhere) 19200
nyal 19201
pyralvex 19202
SM-33 19203
tuscodin 19204
dequadin 19205
beconase 19206
rhinocort 19207
difflam 19208
bactroban 19209
xylometazoline 19215
otrivine 19215
topical, other (not found elsewhere) 19300
neosporin 19301
cicatrin 19302
garamycin 19303
graneodin 19304
mycitracin 19305
spersin 19306
diprosone 19307
nemdyn 19308
sofra-tulle 19309
aristocomb 19310
celestone 19311
kenacomb 19312
dermovate 19313
dermol 19314
anusol 19351
colifoam 19352
hemocane 19353
predsol 19354
preparation H 19355
proctocort 19356
proctosedyl 19357
rectinol 19358
scheriproct 19359
ultraproct 19360
xyloproct 19361

20. Hormonal preparations

"hormone tabs" 20000

testosterone 20001
andriol 20002
primoteston 20004
sustanon 20006
halotestin 20007
fluoxymesterone 20008
mesterolone 20009
proviron tabs 20010

oestrogen 20100
oestradiol 20101
vagifem 20101
dienoestrol cream 20102
estigyn 20103
estraderm 20104
premarin 20105
primodian depot 20106
primogyn 20107
progynova 20108
trisequens 20109
ogen 20110
ovestin cream 20111
ovestin tabs 20112

ethinyloestradiol with ethynodiol diacetate 20151
ovulen 0.5/50 20151
ovulen 1/50 20152
ethinyloestradiol with desogestrel 20155
mercilon 21 20155
mercilon 28 20156
marvelon 21 20157
marvelon 28 20158
ethinyloestradiol with gestodene 20160
minulet 21 20160
femodene 21 20160
minulet 28 20161
femodene 28 20161
ethinyloestradiol with norethisterone 20165
brevinor 21 20165
norimin 20166
brevinor 28 20166
synphasic 28 20167
brevinor 1/21 20168
brevinor 1/28 20169
levonorgestrel with ethinyloestradiol 20170
triphasil 20170
biphasil 21 20171
biphasil 28 20172
triphasil 28 20173
triquilar ED 20173
microgynon 50 ED 20174
nordette 21 20175
microgynon 30 20175
monofeme 20175
nordette 28 20176
microgynon 30 ED 20176
nordiol 21 20177
nordiol 28 20178
norethisterone with mestranol 20180
norinyl-1/21 20180
norinyl-1/28 20181
norgestrel with ethinyloestradiol 20185
ovral 20185
ethynodiol diacetate 20190
femulen 20190
levonorgestrel 20191
microval 20191
microlut 20191
medroxyprogesterone acetate 20192

depo provera 20192
norethisterone 20193
noriday 28 20193

primolut 20198

oestradiol with testosterone 20200

cyproterone acetate 20300
Diane-S 20300
androcur (cyproterone acetate) 20301

danocrine 20400
azol 20401

tetracosactrin 20500
synacthen 20501
pitressin 20502
desmopressin 20503
ornipressin 20504

thyroxine 20600
liothyronine 20601
oroxine 20602
tertroxin 20603
triiodothyronine 20604
propylthiouracil 20605
carbimazole 20606
neo-mercazole 20607

glucagon 20700
viokase 20701
pancreatin 20701

calcitonin 20800
salcatonin 20801
didronel 20802
didrocal 20803
cibacalcin 20804
miacalcic 20805

21. Anticonvulsants

"epileptic pills", unnamed 21000

phenobarbitone 21001
mysoline 21002
prominal 21003

phenytoin 21101
dilantin 21102

milontin 21201
celontin 21202
zarontin 21203

clonazepam 21301
rivotril 21302

carbamazepine 21401
tegretol 21402
Tegreton (carbamazepine) 21403
teril 21404

epilim 21501
valpro 21502
vigabatrin 21503

sulthiame 21601
ospolot 21602
lamotrigine 21603
gabapentim 21604

22. Antispasticity agents

baclofen 22001
Lioresal (baclofen) 22002
Nitoman (tetrabenazine) 22003
Pacifen (baclofen) 22004
clofen 22006
dantrium 22007

23. Anorectics

"diet pills", unnamed 23000
adifax 23001
duromine 23002
ponderax pacaps 23003
sanorex 23004
tenuate 23005
tenuate dospan 23006

24. Antirheumatics

oxycinchophen 24001
nivaquine 24002
plaquenil 24003
sodium aurothiomalate 24101
myocrisin 24102
sodium aurothiosulphate 24103
auranofin 24104
ridaura 24105
aurothioglucose 24106
gold-50 24107
penicillamine 24201
D-penamine 24202
bucillamine 24203

25. Antiinflammatory, steroid

"steroid" 25000
aldosterone 25001
fludrocortisone 25002
florinef 25003
desoxycortone 25004
betamethasone 25100
dexamethasone 25001
fluocortolone 25002
methylprednisolone 25003
paramethasone 25004
prednisolone 25005
panafcortelone 25005
prednisone 25006
triamcinolone 25007
hydrocortisone 25008
cortisone 25009
prednylidene 25010
rimexolone 25011
deflazacort 25012
cloprednol 25013

26. Hypolipidaemic agents

"cholesterol pills", unnamed 26000
simvastatin 26001
lipex 26002
zocor 26003
lovastatin 26004
pravastatin 26005
pravachol 26006
fluvastatin 26007
atorvastatin 26008
clofibrate 26100
atromid-S 26101
col 26102
bezafibrate 26103
aluminium clofibrate 26104
gemfibrozil 26105
lopid 26106
fenofibrate 26107
simfibrate 26108
ronifibrate 26109
cholestyramine 25200
colestipol 26201
colestid granules 26202
questran lite 26203
detaxtran 26204
niceritrol 26300
nicotinic acid 26301
nicofuranose 26302
aluminium nicotinate 26303
nicotinyl alcohol 26304
dextrothyroxine 26400
probucol 26401
lurselle 26402
acipimox 26403
sulodexide 26404
tiadenol 26405
benfluorex 26406
meglutol 26407

27. Antiviral agents

cymevene 27003
ganciclovir 27004
hivid 27005
zalcitabine 27006
interferon 27007
intron inj 27008
retrovir 27009
ribavirin 27010
zidovudine 27011
roferon-A 27012
videx 27014
virazide 27015
zovirax 27016
acyclovir 27017

28. Antituberculosis, antileprotics

dapsone 28001
ethambutol 28002
isoniazid 28003
lamprene 28004
myambutol 28005
pyrazinamide 28006
rifadin 28007
rifampicin 28008
rimycin 28009
zinamide 28010

29. Antithrombotics

anticoagulant, unnamed 29000
dicoumarol 29001
phenindione 29002
dindevan 29003
warfarin 29004
marevan 29005
phenprocoumon 29006
acenocoumarol 29007
ethyl biscoumacetate 29008
clorindione 29009
diphenadione 29010
heparin 29100
calcihep 29101
uniparin-ca 29102
calciparine 29103
caprin 29104
caprin forte 29105
coumadin 29106
uniparin 29107
antithrombin 29108

dalteparin 29109
fragmin 29110
enoxaparin 29111
nadroparin 29112
parnaparin 29113
reviparin 29114
danaparoid 29115
tinzaparin 29116
ditazole 29200
cloricromen 29201
picotamid 29202
clopidogrel 29203
ticlopidine 29204
ticlid 29204
dipyridamole 29206
persantin (dipyridamole) 29206
carbasalate calcium 29207
epoprostenol 29208
indobufen 29209
iloprost 29210
abciximab 29211
streptokinase 29300
alteplase 29301
anistreplase 29302
urokinase 29303
ukidan 29304
fibrinolysin 29305
brinase 29306
defibrotide 29400

30. Antimigraine agents

"migraine tablets", unnamed 30000
dihydroergotamine 30001
dihydergot 30002
ergotamine 30003
cafergot 30004
ergodryl 30005
ergodryl mono 30006
migral 30007
methysergide 30008
lisuride 30009
flumedroxone 30100
pizotifen 30200
sandomigran 30201
iprazochrome 30202
sumatriptan 30203
imigran 30204
dimetotiazine 30205

31. Peripheral vasodilators

dibenyline 31001
duvadilan 31002
priscoline 31003
regitine 31004
serc 31005

32. Vasopressors

adrenaline 32001
aramine 32002
dobutrex 32003
dopamine HCl 32004
intropin 32005
isuprel parenteral 32007
levophed 32008
talusin 32009

33. Other cardiovascular agents

rutoside 33000
cirflo 33001
paroven 33003
varemoid 33008
monoxeruterin 33009
diosmin 33010
troxerutin 33011
oxpentifylline 33012
trental-400 33020

34. Neuromuscular agents

mestinon 34001
neostigmine 34002
physostigmine salicylate 34003
prostigmin 34004
ubretid 34005

35. Miscellaneous others

quinine 35001
quinsul 35001
quinate 35002
quinoctal 35001
biquinate 35003
quinbusil 35003
ural 35006
hiprex 35007
myoquin 35019
urocarb 35022
urecholine 35023
bethanechol 35024
chenodeoxycholic acid 35025
durotuss 35060
pholcodine 35060
coldrex 35060
vicks cough lozenges 35061
vicks cough syrup 35061
senagar 35062
orased gel 35066

rawleigh cough mixture 35069
cough mixture 35069
strepsils 35070
ritalin 35090
deca-durabolin 35091
nandrolone 35091
fluoride tablets 35099

prostate drug 35100
proscar 35101
finasteride 35102
alprostadil 35103
phenazopyridine 35104
tamsulosin 35105
acetohydroxamic acid 35106
pygeum africanum 35107

acne medication 35200
tretinoin 35201
Roaccutane 35202
retinol 35205
adapalene 35210
isotretinoin 35215

39. Prophylactic aspirin

acetylsalicylic acid 39205
aspirin 39205
cardiprin 39205
cartia 39205
ecotrin 39205
solprin 39205

40. Uncodables

unreadable/uncodable 40001

Appendix 2: SADLS medication capture form

SADLS 96 Medication Information

SUBJECT ID :

EXAM DATE:

Do you have any prescribed medicines or medicines bought over the counter with you today, that you have taken or were supposed to take regularly in the past 2 weeks?

1 = YES (complete this form)
2 = NO I do not take any medicines
3 = NO I have not bought them today

	DRUG NAME	DRUG CODE	SOURCE *1=container 2=memory 3=follow-up*	PRESCRIBER *1=doctor/dentist 2=self 8=don't know*	TYPE *1=prescription 2=OTC*	NAME (on container) *1=subject's name 2=other name 8=don't know/no name*	DATE *(on container)*	STRENGTH *(number) (mg/ml) (form)*	FREQUENCY *(units) (frequency)*
1									
2									
3									
4									
5									
6									
7									
8									
9									

SADLS 96 Medication Information

		DRUG CODE	SOURCE *1=container* *2=memory* *3=follow-up*	PRESCRIBER *1=doctor/dentist* *2=self* *8=don't know*	TYPE *1=prescription* *2=OTC*	NAME (on container) *1=subject's name* *2=other name* *8=don't know/no name*	DATE *(on container)*	STRENGTH *(number) (mg/ml) (form)*	FREQUENCY *(units) (frequency)*
10									
11									
2									
3									
4									
5									
6									
7									
3									
9									
0									

This questionnaire will take you a few minutes to complete. Please circle the answer which best applies to you during the last year, as shown in this example:

EXAMPLE: If your throat felt dry occasionally during the last year, then circle "occasionally".

Q16	My throat feels dry	NEVER	HARDLY EVER	(OCCAS-IONALLY)	FAIRLY OFTEN	VERY OFTEN

HOW OFTEN HAS THIS APPLIED TO YOU DURING THE LAST YEAR?
Please circle your answer.

Q1	I sip liquids to aid in swallowing food	(NEVER)	HARDLY EVER	OCCAS-IONALLY	FAIRLY OFTEN	VERY OFTEN
Q2	My mouth feels dry when eating a meal	(NEVER)	HARDLY EVER	OCCAS-IONALLY	FAIRLY OFTEN	VERY OFTEN
Q3	I have too much saliva in my mouth	(NEVER)	HARDLY EVER	OCCAS-IONALLY	FAIRLY OFTEN	VERY OFTEN
Q4	My lips feel dry	NEVER	(HARDLY EVER)	OCCAS-IONALLY	FAIRLY OFTEN	VERY OFTEN
Q5	I have difficulties swallowing certain foods	(NEVER)	HARDLY EVER	OCCAS-IONALLY	FAIRLY OFTEN	VERY OFTEN
Q6	My mouth feels dry	NEVER	(HARDLY EVER)	OCCAS-IONALLY	FAIRLY OFTEN	VERY OFTEN
Q7	I get up at night to drink	(NEVER)	HARDLY EVER	OCCAS-IONALLY	FAIRLY OFTEN	VERY OFTEN
Q8	My gums itch	(NEVER)	HARDLY EVER	OCCAS-IONALLY	FAIRLY OFTEN	VERY OFTEN
Q9	I have a burning sensation in my gums	(NEVER)	HARDLY EVER	OCCAS-IONALLY	FAIRLY OFTEN	VERY OFTEN

HOW OFTEN HAS THIS APPLIED TO YOU DURING THE LAST YEAR?
Please circle your answer.

Q10	My tongue itches	(NEVER)	HARDLY EVER	OCCAS-IONALLY	FAIRLY OFTEN	VERY OFTEN
Q11	I have a burning sensation in my tongue	(NEVER)	HARDLY EVER	OCCAS-IONALLY	FAIRLY OFTEN	VERY OFTEN
Q12	I chew gum to relieve dry mouth	(NEVER)	HARDLY EVER	OCCAS-IONALLY	FAIRLY OFTEN	VERY OFTEN
Q13	My eyes feel dry	(NEVER)	HARDLY EVER	OCCAS-IONALLY	FAIRLY OFTEN	VERY OFTEN
Q14	I have difficulty in eating dry foods	(NEVER)	HARDLY EVER	OCCAS-IONALLY	FAIRLY OFTEN	VERY OFTEN
Q15	I have difficulty in swallowing	NEVER	(HARDLY EVER)	OCCAS-IONALLY	FAIRLY OFTEN	VERY OFTEN
Q16	My throat feels dry	NEVER	(HARDLY EVER)	OCCAS-IONALLY	FAIRLY OFTEN	VERY OFTEN
Q17	The inside of my nose feels dry	(NEVER)	HARDLY EVER	OCCAS-IONALLY	FAIRLY OFTEN	VERY OFTEN
Q18	I suck sweets or cough lollies to relieve dry mouth	NEVER	(HARDLY EVER)	OCCAS-IONALLY	FAIRLY OFTEN	VERY OFTEN
Q19	The skin of my face feels dry	(NEVER)	HARDLY EVER	OCCAS-IONALLY	FAIRLY OFTEN	VERY OFTEN

Thank you for completing this questionnaire.

Please return it to the attending dental staff.

Appendix 4: De Paola grids for tooth-surface transitions over the study period

1. Coronal surfaces

		FIVE YEARS				
		Sound	Decayed	Filled	Crowned	Missing
BASELINE	Sound	25783	81	1379	154	1186
	Decayed	22	10	69	4	54
	Filled	284	24	8437	267	684
	Crowned	1[a]	0	12	1468	153
	Missing	45	0	12	9	37649

[a]This individual had tooth 15 recorded as crowned at baseline but it was recorded as only having the mesial, occlusal, distal and lingual surfaces filled at five years

Summary of coronal transitions

	Baseline	Five years
Sound	28593	26141
Filled	9573	9715
Filled unsatisfactory	124	225
Decayed	118	100
Recurrent decay	41	15
Crowned	1634	1912
Missing	37672	40013

2. Root surfaces

		FIVE YEARS				
		Unexposed	Sound	Decayed	Filled	Missing
BASELINE	Unexposed	13485	7185	173	365	1453
	Sound	1467	9044	283	551	727
	Decayed	30	35	28	50	64
	Filled	83	214	48	947	125
	Missing	27	42	8	0	30818

Summary of root surface transitions

	Baseline	Five years
Unexposed	22661	15135
Sound	12072	16525
Filled	1387	1872
Filled unsatisfactory	30	49
Decayed	192	450
Recurrent decay	15	82
Missing	30895	33471