Lothian atopic dermatitis study

Herd, Robert M.

MD

1997

Thesis scanned from best copy available: may contain faint or blurred text, and/or cropped or missing pages.

Digitisation notes:

- p.99 missing from original numeration.
The Lothian Atopic Dermatitis Study

Robert M. Herd

Submitted for the degree of Doctor of Medicine of the University of Edinburgh
DECLARATION

I declare that I have written this thesis myself. The study was conceived following conversations with Dr. M. J. Tidman and Professor J. A. A. Hunter. Through my contacts with colleagues in general practice, I identified a suitable community population and chose the method of sampling, the quality of life questionnaires and devised the costing proforma.

The data collection was all my own work. A little guidance was given by Dr. Robin Prescott, Dr. D A Ruta and Dr. A. Y. Finlay in their respective areas of expertise, but the computing and statistical analysis were completed without assistance.

The data was collected between March 1993 and April 1994. I analysed the data and wrote the associated publications thereafter.
# CONTENTS

Acknowledgements ................................................................. v  
Publications .............................................................................. vi  
Abbreviations ........................................................................... vii  
Definitions ............................................................................... viii  
Abstract .................................................................................. ix  
Summary ................................................................................... x  
List of Figures ........................................................................... xi  
List of Tables ............................................................................ xii

## CHAPTER 1: Introduction

1.1 Atopic dermatitis - definition .............................................. 1  
1.1.1 History ......................................................................... 1  
1.1.2 Diagnostic criteria ....................................................... 2  
1.2 Atopic dermatitis the patient's perspective ....................... 4  
1.2.1 The natural history ..................................................... 5  
1.3 Atopic dermatitis prevalence data ..................................... 6  
1.3.1 Trend in prevalence .................................................... 7  
1.3.2 Recent prevalence data ............................................. 8  
1.3.3 Ethnic and Social class differences ............................ 9  
1.4 Economic aspects ............................................................. 10

1.5 Assessment of disability ................................................... 11  
1.5.1 The place of quality of life assessment in medicine ........ 11  
1.5.2 The concept of quality of life .................................... 12  
1.5.3 Quality of life in dermatology .................................. 13

1.6 Summary ........................................................................... 14

1.7 Aims of the study ............................................................... 15

## CHAPTER 2: Methods

2.1 Population .......................................................................... 28

2.2 The General Practice .......................................................... 28

2.3 Sampling ............................................................................. 29

2.3.1 An overview .................................................................. 29

2.3.2 Practical aspects ........................................................... 30

2.4 Assessment of prevalence .................................................. 31

2.5 Assessment of cost .............................................................. 31

2.6 Assessment of quality of life ............................................... 32

2.6.1 Statistical analysis and validation ................................. 34

2.7 Hospital assessment ............................................................ 35

2.8 Statistics ............................................................................. 36

2.8.1 Statistics for the under 2 group .................................. 36

2.8.2 Statistics for the older age groups ............................... 36

2.8.3 Statistics for the costing section ................................. 37

2.8.4 Statistics for the quality of life section ....................... 37

2.9 Pilot study ........................................................................... 38
ACKNOWLEDGEMENTS

I would like to thank my advisors, Dr. M. J. Tidman, and Professor J. A. A. Hunter for their advice and encouragement throughout all stages of the study.

The staff of Howden Health Centre were always courteous and helpful. Dr. Graham Buckley was instrumental in organising my access to the practice computer, to secretarial staff and to patients. His assistance and that of his colleagues was invaluable.

Health economics advice was provided by Dr. J. F. Forbes. I was fortunate to have the enthusiastic support of Dr. D. A. Ruta, a public health medicine specialist, who is at the forefront of quality of life research. He provided information on the newly-introduced Patient Generated Index, and with Mr A. M. Garratt, helped with the analysis of the quality of life data.

A former colleague, Dr. Robin Prescott, gave statistical advice from the start of the project. Both he and another statistician, Dr. G Cohen gave helpful pointers to the analysis of the cluster sample data.

Funding was kindly provided by the Edinburgh Dermatology Research Fund to cover travel expenses, telephone and stationery costs and computing.
Publications


ABBREVIATIONS

AD  Atopic dermatitis
APPG  All party parliamentary group on skin
DLQI  Dermatology Life Quality Index
GP  General practitioner
HHC  Howden Health Centre
LADS  Lothian atopic dermatitis study
OTC  Over the counter
PGI  Patient Generated Index
SCC  Skin care campaign
# Definitions

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Construct validity</td>
<td>The extent to which a new measure relates to established measures of severity.</td>
</tr>
<tr>
<td>Criterion validity</td>
<td>The extent to which a new measure correlates with established measures.</td>
</tr>
<tr>
<td>Incidence rate</td>
<td>The occurrence of new cases of a disease or condition within a specified time frame. Lifetime incidence is the occurrence of new cases at any time previously.</td>
</tr>
<tr>
<td>Prevalence</td>
<td>The overall occurrence of a disease in a specific population at a specific point in time. The one-year period prevalence refers to the occurrence over one year, i.e. includes all individuals who have a disease or condition at any time over a one year period. Age specific prevalence refers to a specific age group.</td>
</tr>
<tr>
<td>Population at risk</td>
<td>Any group of individuals at risk of an event or disease.</td>
</tr>
<tr>
<td>Reliability</td>
<td>The extent to which a test or measurement result is reproducible.</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>The ability of a test to detect a high proportion of true cases.</td>
</tr>
<tr>
<td>Specificity</td>
<td>The ability of a test to identify correctly true negatives.</td>
</tr>
<tr>
<td>Validity</td>
<td>The extent to which a test measures what it is intended to measure.</td>
</tr>
</tbody>
</table>
ABSTRACT

Atopic dermatitis is a chronic, debilitating skin disease. Children have occupied the major part of investigators' time, but cross-sectional community studies, encompassing the whole population, are lacking. This thesis describes an epidemiological study, based on a general practice of 9,786, and assesses, at all ages, the prevalence, the economic burden to patients and the health service, and the quality of life of patients with atopic dermatitis.
SUMMARY

Many studies have examined the prevalence of atopic dermatitis in children. In comparison, little has been written about the prevalence of atopic dermatitis in infants and adults. Diagnostic criteria suitable for use in community surveys have only recently become available with the introduction of the U.K. Working Party's Diagnostic criteria. They are simple and non-invasive and contribute to rigorous community studies.

Atopic dermatitis causes a considerable economic burden to patients and the health service. Only one study has examined the economics of atopic dermatitis. This came from the U.S.A., a country whose health care system bears little resemblance to our own. The Lothian Atopic Dermatitis Study was designed to quantify the economic burden of atopic dermatitis and to measure the impact on the quality of life of patients with this common condition.

The study population was a semi-rural general practice of 9,786. A sampling scheme was devised to identify as many as possible of those in the practice with atopic dermatitis. One-year period prevalences were calculated by standard methods for age groups <2, 2-11, 12-15, 16-24, 25-40, 41+. Expense, estimated over a 2 month period, was attributed to the patient, health service or society according to the source. One unpublished quality of life measure was used for children and two well-validated measures, the Dermatology Life Quality Index and the Patient Generated Index, were completed by adults.

The one year period prevalences were 9.8% for the under 2's, 8.1% age 2-11, 2.2% age 12-15, 2.1% age 16-24, 2.0% age 25-40 and 0.2% over 40's. This pattern shows clearly the sharp decline in the prevalence of atopic dermatitis during teenage and adult years. The largest source of cost to patients was clothing and laundry, and the mean annual cost to patients was £153. Treatments accounted for the largest source of expenditure by the health service giving a mean cost per patient of £97. There were 58 lost working days and 17 lost school days by all patients as a result of atopic dermatitis. If these results were extrapolated to the U.K. population there would represent a total annual expenditure of £172m by patients, £125m by the health service and £168m by society. This adds up to £465m per annum or a per capita cost of £7.38 per annum. The quality of life measures reflected the range of severity of atopic dermatitis in the community. The Dermatology Life Quality Index was not specific for atopic dermatitis but correlated significantly with the Patient Generated Index.

Thirty-eight per cent of all atopic dermatitis patients are over 16 years of age. Few studies of atopic dermatitis in adults exist. Clinical studies are necessary to characterise adult atopic dermatitis and emphasise the pressure from the heavy economic burden and impaired life quality.
| Figure 1.1 | Triggers for atopic dermatitis | 23 |
| Figure 1.2 | Infant with infected facial atopic dermatitis | 24 |
| Figure 1.3 | Loss of eyebrows due to rubbing and scratching in a teenager with facial atopic dermatitis | 25 |
| Figure 1.4 | Severe facial atopic dermatitis in an adult | 26 |
| Figure 1.5 | Pruriginous nodules in an adult with atopic dermatitis | 27 |
| Figure 2.1 | Situation of Livingston | 42 |
| Figure 2.2 | Housing in Livingston | 43 |
| Figure 2.3 | Housing in Livingston | 43 |
| Figure 2.4 | Livingston Kirk | 44 |
| Figure 2.5 | Map of Livingston | 45 |
| Figure 3.1 | One family contained in sample | 52 |
| Figure 3.2 | Sampling groups | 53 |
| Figure 4.1 | Expenditure by patients and NHS | 60 |
| Figure 4.2 | Expenditure by patients on topical OTC preparations | 61 |
| Figure 5.1 | DLQI scores for adults | 71 |
| Figure 5.2 | Scattergram of DLQI vs PGI | 72 |
| Figure 5.3 | Scattergram of mini-DLQI vs PGI | 73 |
LIST OF TABLES

Table 1.1: Hanifin and Rajka's diagnostic criteria for atopic dermatitis........... 16
Table 1.2: The UK Working party's diagnostic criteria.............................................. 17
Table 1.3: Early community studies reporting the prevalence of atopic disease......................................................... 18
Table 1.4: Community studies during period 1970-1982 reporting prevalence of atopic dermatitis......................................................... 19
Table 1.5: Recent community studies reporting the prevalence of atopic dermatitis......................................................... 20
Table 1.6: Sex ratios reported in recent studies from Scandanavia and the U.K......................................................... 21
Table 1.7: Annual per capita cost of treating AE compared with other medical conditions......................................................... 21
Table 1.8: Suggested elements that should be included in a quality of life measure (Fitzpatrick et al, 1992)......................................................... 22
Table 2.1: Age distribution of Livingston compared with that of Scotland (% age)......................................................... 39
Table 2.2: Social class distribution in Livingston compared with the rest of Scotland......................................................... 39
Table 2.3: Details of calculations of cost of consultation with hospital consultant. Costs listed are based on two consultants working in the same session......................................................... 40
Table 2.4: Details of calculation of cost of GP consultation......................................................... 40
Table 2.5: PGI Calculation......................................................... 41
Table 3.1: One year period prevalences with standard errors, point prevalence of visible eczema and sex ratio......................................................... 51
Table 4.1: Mean annual costs of treating AD......................................................... 59
Table 4.2: Annual per capita cost of treating AE compared with other medical conditions......................................................... 59
Table 5.1: The correlation between the PGI and individual questions of the DLQI......................................................... 68
Table 5.2: Areas or activities cited in the PGI as being influenced by the patients' AE......................................................... 69
Table 5.3: Comparison of PGI scores, using a t-test, between those who scored 0 and those who scored 1-3 in individual questions of the DLQI......................................................... 70
Chapter 1
Introduction

1.1 Atopic dermatitis - definition

1.1.1 History

Atopic dermatitis (AD) is a common, debilitating skin condition. Attempts to discover the earliest clinical description have unearthed some interesting possibilities. Perhaps the earliest record of a patient with atopy was the Pharaoh Menes of Memphis who may have succumbed to anaphylaxis in 2,900 BC (Sehgal & Jain, 1993). Later, the Roman Emperor Augustus Caesar (born 69AD) had problems that could have been due to respiratory and skin atopy (Mier, 1975).

Robert Willan constructed a classification of skin diseases (Willan, 1808). He described two types of prurigo: prurigo mitis in younger people and prurigo formicans in adults. Both may have been akin to AD. In 1844, von Hebra noted the flexural distribution of pruritic lesions (Hanifin, 1982), and Brocq and Jaquet, in 1891, introduced the terms localised and disseminated neurodermatitis, used subsequently to describe AD (Brocq & Jaquet, 1891). The next milestone was in 1892 when Besnier described three cases of men who had an itchy skin disease in childhood (Besnier, 1892). He called it 'prurigo diathesique' and in so doing was the first to distinguish AD from other types of dermatitis. It was henceforth known as 'prurigo Besnier'.

The term atopy (meaning a-no, top-place, y-ness, or unclassifiable), was not introduced by Coca and Cooke until 1923 (Coca and Cooke, 1923; Coca et al, 1931). Atopic skin diseases were more clearly delineated in 1932 (Rost & Marchionini, 1932) and the term 'atopic dermatitis' was used first by Wise and Sulzberger in 1933 (Wise & Sultzberger, 1933).
1.1.2 Diagnostic criteria

Firm diagnostic criteria, fundamental in all epidemiological research, were not elaborated until much later. There is no single marker by which patients with AD can be identified. Clinicians agree when the signs and symptoms are characteristic, but mild or atypical disease will give rise to debate. Rigorous criteria are needed to exclude patients with similar conditions such as seborrhoeic eczema in infants or discoid eczema in older patients (Yates et al, 1983). The first diagnostic criteria were suggested independently by Rajka and Hanifin in 1975 and 1977 (Rajka, 1975; Hanifin, 1977), and in 1980 they collaborated on a set of criteria that has represented the gold standard until recently (Table 1.1) (Hanifin & Rajka, 1977). However these cumbersome, invasive and unnecessarily complicated criteria are unsuitable for community studies. Furthermore, they have never been fully validated.

Several attempts have been made to examine the predictive value of Hanifin & Rajka's criteria. Diepgen analysed each separately (Diepgen et al, 1989) but did not analyse all variables simultaneously to determine the best independent predictors. For instance 'flexural eczema' and 'itching when sweating' are both associated significantly with AD, but if all who 'itched when sweating' also have 'flexural eczema', this criterion would make no contribution to the diagnosis of AD. In other words they are not independent and should not both be included. This work, therefore, did not shorten the list of features, nor did the authors construct a more practical diagnostic model.

Attempts have, however, been made to identify the best predictors of AD. The signs in a control group were compared with those in a group with definite AD, and features were identified which were significantly more common in the patients with AD (Svensson et al, 1985). This study had two major shortcomings. First, the independence of individual features was not tested. For instance an association with both 'xerosis' and 'seasonal variation' was highly significant, but if both were present in the same patients, neither would contribute independently to the diagnosis, and both should not be included. Had all variables been tested simultaneously the number of criteria in their model may have been reduced without affecting diagnostic accuracy. The second criticism arises
because they did not take the next logical step which would have been to test the criteria in a separate population at risk to determine their sensitivity and specificity compared with that of experienced clinicians.

Others have looked at the reliability of Hanifin & Rajka’s criteria. Mevorah et al found that two of the so-called 'minor features', anterior neck folds and the Dennie-Morgan infraorbital fold, were not significantly associated with AD (Mevorah et al, 1988). Applied to specific populations, the criteria have been unreliable in infants (Yates et al, 1983), and in a Chinese population possibly due to ethnic differences (Kang & Tian, 1987; Kang & Tian, 1989). Conversely, a study from India found two additional significant features that were not included in Hanifin and Rajka's criteria: diffuse scaling of the scalp and infra-auricular fissuring (Kanwar et al, 1991).

Lack of specificity has also been revealed. Many of the minor features occur in patients with respiratory atopy and so are stigmata of atopy rather than of AD itself (Przybilla et al, 1991). One minor feature, the infraorbital fold, is common in allergic contact dermatitis (Uehara, 1981). Its frequent occurrence may be a result of the lower eyelid being a site of predilection in AD.

Schultz Larsen & Hanifin devised a scheme using a points system which depended on the presence or absence of various features (Schultz Larsen & Hanifin, 1992). Patients fell into three groups: 'definite AD', 'possible AD' or 'not AD', but their scheme did not elucidate the diagnosis in those in the intermediate group, some of whom may have AD. For research purposes a set of criteria was needed that would allow patients to be classified consistently, and in agreement with experienced clinicians, as either having AD or not.

A process of validation that achieves a balance between sensitivity and specificity, is required to establish reliable criteria for use in epidemiological research. If the validation is based on the same population from which the criteria are derived, an over-optimistic separation of cases from controls is produced (Svensson et al, 1985). As the criteria are designed for use in new populations their validity must also be tested on different populations, as has been done for other
dermatological conditions (Tan et al, 1982; International study group for Behcet’s disease, 1990). Williams et al have now described well-validated diagnostic criteria for AD, summarised in Table 1.2, that are sufficiently 'user-friendly' to be applied to community studies (Williams et al, 1994a, 1994b, 1994c). Although there was a small reduction in sensitivity, they were found to be significantly more specific than Hanifin and Rajka’s criteria. Furthermore, they take account of the distinctive pattern of AD in infants and of the inability of young children to give a reliable history. There are three sets of criteria for three age groups (Appendices 1-3). To qualify as a case of AD, an individual must have a history of an itchy skin condition, and satisfy three of the subsequent criteria. These are non-invasive and can be applied easily by an interviewer with no medical training. For the first time community studies can now be carried out, using an appropriate tool for diagnosing AD.

1.2 Atopic dermatitis: the patient’s perspective

AD usually starts in infancy and tends to clear with age (Vickers, 1980). Its main impact is due to its chronicity, to severe itching and to episodes of infection that cause pain, weeping and bleeding. There are many triggers, depicted diagramatically in Figure 1.1, although stress and infection are the most frequent (Morren et al, 1994).

There is no treatment which can be guaranteed to be effective. Some exacerbations settle with simple topical measures but others require intensive treatment in hospital with occlusive dressings and systemic antibiotics. The diagnosis is not always easy in children aged less than 6 months due to lack of scratching and a similarity to viral exanthemata and other inflammatory skin conditions (Bonifazi & Meneghini, 1989) (Figures 1.2-1.5).

The distribution of skin lesions gradually alters from infancy to childhood. The scalp, face and peri-auricular areas are involved at first, but clear progressively and the rash settles in the flexures during the first 2 years of life (Aoki et al, 1992), a pattern unique to AD (Bonifazi, 1992). In later childhood, and early adulthood, pruritus and lichenification are especially distressing, and the face is often affected again, as well as the neck and upper trunk.
1.2.1 The natural history

Too few studies of the natural history of AD have been conducted to permit accurate statements about prognosis. Two retrospective reviews of infants, diagnosed as having AD 20 years previously, have given conflicting rates of resolution. The first found that AD was usually initially noted at age 4 months, and that only 40% with mild eczema and 29% with severe eczema had cleared completely 20 years later (Roth & Kierland, 1964). The second study from Liverpool, included 2,000 cases and found that 87% had cleared by the age of 5, but that in subsequent years the condition returned in some, leading to an overall clearance rate of 89% by the age of 20 (Vickers, 1980). However many patients do not develop AD until their teenage years or adulthood, whereas in others the condition recurs after 20 years of age and would have been missed by these studies (Lammintausta et al, 1991). This point has been referred to but has never been the subject of a long-term follow-up study (Wutrich & Schudel, 1983).

AD usually begins in infancy (Bonifazi & Meneghini, 1989) but diagnosis at this age is difficult both because young infants cannot localise the site of an itch, and because of possible confusion with viral rashes or other inflammatory skin conditions such as seborrhoeic eczema (Yates et al, 1983). As with most AD research, studies of the age of onset have often only included children (Queille-Roussel et al, 1985), excluding those who develop AD later, and thereby falsely reducing the estimated age of onset. This resulted in the high estimate by Queille-Roussel et al of 91.5% of cases occurring before age 2. Rajka’s estimate of 87% developing before 5 may be more realistic and is in keeping with earlier studies (Rajka, 1975; Hellerstrom & Lidman, 1956; Nexmand, 1948).

The likelihood of complete clearance occurring in infants with AD is hard to gauge. Prognostically unfavourable factors include severity, a family history of AD, associated asthma or hay fever, female sex and early age of onset (Rystedt, 1985).

AD may have profound psychological implications. Adults with severe AD can become stigmatised and socially isolated. In an early survey many patients highlighted skin irritation as the worst aspect of AD: it was
described by one as "like sitting on a bed of ants or spiders" (Jowett and Ryan, 1985). Others were principally worried about effects on social and leisure activities, physical appearance, or by the time spent treating their condition. Other frequent concerns were the ignorance of others and difficulties with employment, relationships, anxiety and lack of confidence.

It seems evident that their resources would be drained by laundry bills, by purchasing over-the-counter (OTC) preparations and by repeated changes of clothes soiled by blood or topical treatments, but surprisingly this has never been evaluated.

1.3 Atopic dermatitis: prevalence data

AD makes up a large part of every dermatologist's workload: 13% of new referrals and 15% of review patients (Harris et al, 1990). Inevitably, much effort has been devoted to its complex pathogenesis (Bos et al, 1994). The cellular interactions in the development of an atopic phenotype in the genetically predisposed have slowly become clearer (Hunter & Herd, 1994, Hanifin & Chan, 1995). Progress has also been made in the management of AD and new powerful treatments have been introduced (Przybilla et al, 1994; de Prost, 1992).

In contrast with other atopic diseases, however, there are few good population-based epidemiological studies of AD (Fleming & Crombie, 1987). A list of population-based publications offering a frequency for AD is shown in Tables 1.3-1.5. It is hard to decipher any trend because of the various measures of frequency and different age groups. Most have concentrated on schoolchildren because they are accessible and have a high prevalence of AD. To study infants or adults requires a population study, with its inherent sampling difficulties. The lack of firm diagnostic criteria has usually been glossed over and data have been collected from postal questionnaires, health visitor and GP records, and, rarely, examination by a dermatologist.
1.3.1 Trend in prevalence

The prevalences recorded in early studies were low (Table 1.3). Frequencies often included all atopic diseases, and descriptions of methodology were inadequate. They are of historical interest only, but there is now much evidence suggesting that the prevalence of AD is rising (Taylor et al, 1984; Burr et al, 1989; Sibbald et al, 1990; Ninan & Russell, 1992; Williams, 1992; Schultz Larsen, 1993). Before accepting this as fact, variables that could influence the prevalence of AD have to be taken into account. These include climate and geography (Rajka, 1986), social class (Taylor et al, 1984; Golding & Peters, 1987) and genetics (Williams et al, 1995b). For example, Afro-caribbean children in the U.K. have an increased risk of developing AD when compared with white children in a similar environment (Williams et al, 1995b). Also, many studies originate from Scandinavia, and differences in climate and the genetic pool are likely to invalidate direct comparisons with the U.K. There are also differences between regions in the U.K.: for example, the 1970 national birth cohort suggested that AD is less common in Scotland and Wales than in other parts of the U.K. (Golding & Peters, 1987).

The most persuasive evidence of a rising prevalence comes from studies that have looked at the same population over time. Twin studies are also an attractive model for diseases with environmental and genetic components (World Health Organisation, 1965). Environmental influences, however, cannot exist in isolation. Twin studies from Denmark have shown an increase in prevalence over a 15-year period but not over the last 5 years (Schultz Larsen et al, 1986; Schultz Larsen, 1993). Reports from Aberdeen and Cardiff also showed a rising prevalence over 15 and 25 years respectively (Ninan & Russell, 1992; Burr et al, 1989). But these studies have all relied on questionnaires answered by parents. Publicity leading to increased public knowledge, and the realisation that AD is more common in the upper socio-economic groups, have made AD more socially acceptable, and even fashionable. Perhaps this fashion has contributed to an apparently rising prevalence. Furthermore, prior contact with health visitors may have introduced bias into Taylor’s study (Taylor et al, 1984).
1.3.2 Recent prevalence data

There are now data on the prevalence of AD in various age ranges. In the 1970 birth cohort group, Taylor et al found a lifetime incidence of 12.2% at age 5 (Taylor et al, 1984). The study included 12,982 children, born between 5th and 11th April 1970, and traced in 1975. Interviews were by local health visitors using a standardised questionnaire, but the details of this, and the basis on which the diagnosis of AD was made, were not described.

A study of changing asthma prevalence from 1989 also included data on AD (Burr et al, 1989). They focused on children at schools in a given catchment area, in their first year at high school, and within a year of their 12th birthday. Details given of the criteria used to diagnose AD are minimal, but, by implication, parental recall of 'eczema ever' was used, and a lifetime incidence of 15.9% was found. The frequency of AD among Aberdeen schoolchildren was also estimated as part of a study of asthma and atopy (Ninan & Russell, 1992). Again, no diagnostic criteria are given, but they quote a lifetime incidence in children aged 8-13 of 12%. The latter two might be expected to be higher as older age groups were examined, and in this respect they are consistent. But memory becomes less reliable with passing time and lifetime incidences based on parental recall will be subject to variation even if diagnostic accuracy can be assumed. Furthermore, the lifetime incidence gives no information about age-specific rates. How many had only infantile eczema, and how many were still suffering from active eczema?

This problem can be solved by using one-year age-specific prevalences. In an English general practice, the one-year period prevalence varied from 14.3% in the age group 3-5, to 10.2% in the group 9-11 (Kay et al, 1994). This work can be criticised as data were collected retrospectively from medical records and there was no clear definition of AD.

Despite these consistently high estimates, the pattern has been disrupted by the finding of a point prevalence of 4.3% in 3-15 year olds in a study from Finland (Poysa et al, 1991).

Recent data on age groups other than young children are few. One infant study from New Zealand estimated a lifetime incidence of 20.3% at 3 years
of age (Fergusson et al, 1981), and another of Norwegian Lapps, quoting an estimated prevalence in 0-4 year olds of 15% (Falk, 1993). Teenagers have been equally neglected but appear to be affected less. The prevalence in 12-16 year olds was 3% in 1980 (Larsson & Liden, 1980). The 20 year old Lambeth study gives prevalences for adults, but their estimates are so high as to suggest the inclusion of many diagnoses other than AD under the banner of 'eczema' (Rea et al, 1976). AD in Danish 'Royal Life Guard' recruits aged 17-24 was estimated to be 3.3% (Svejgaard et al, 1986). The source of information for a more recent U.S. survey was government health statistics (Johnson & Roberts, 1978; Johnson et al, 1984). They covered all ages from one to 74, but quote a low prevalence for age 6-11 of 1.0%, which is not comparable with European studies. The prevalence at age 35-44 was 0.06 but rose to 0.18 at age 55-64. The reliability of poorly controlled national surveys like this one must be questioned.

Differences between populations are also seen in the sex ratio (Table 1.6). The Scandinavian literature finds a predominance of females; that in the UK a male predominance - the difference may be genetic or artefactual.

There are, therefore, gaps in the statistics that delineate AD. Without rigorous research, using consistent methodology, any reports of a rising prevalence must be open to question. Good community data are needed including all age groups and not just those presumed to have the highest prevalence.

1.3.3 Ethnic and Social class differences

The frequency of AD is likely to be influenced by race and socio-economic group.

Racial differences were first highlighted when the rising West Indian population of the U.K. was shown to have a higher prevalence of AD than the native population (Davis et al, 1961). This has been confirmed in a study comparing black Caribbean children born in the U.K. with white children; a prevalence of 16.3% was found in black and of 8.7% in white children (Williams et al, 1995b). Another early survey reported a higher frequency in Chinese than in white children in Honolulu and San Francisco (Worth, 1962).
A hospital study of the Asian population in Leicester initially showed a prevalence apparently different from the white population, but a more detailed community study failed to confirm this difference (Sladden et al, 1991; Neame et al, 1995).

One of the earliest reports of a socio-economic gradient in the prevalence of AD was in a study in Honolulu and San Francisco (Worth, 1962). Differences between socio-economic groups in the U.K. were also found in the 1970 British national cohort study (Golding & Peters, 1987; Peters & Golding 1987). The reasons for this are unclear but may include higher reporting or better recall in some groups. In a well-conducted study of data from the national perinatal mortality study these results were confirmed (Shepherd, 1985; Williams et al, 1994d), with AD significantly more common in social classes I and II than in lower social classes. Suggested reasons for the difference include higher educational status that may have lead to an increased uptake of vaccines or overuse of soaps.

Inheritance and environment are both important determinants of AD. Individuals from different genetic backgrounds in the same environment, and from a similar genetic pool in different environments, can clearly differ in their prevalence of AD.

1.4 Economic aspects

Medical practice in the U.K. is becoming increasingly shackled by economic constraints. Some understanding of the financial implications of different diseases is now necessary, particularly for the most common ones such as AD (Harris et al, 1990).

Two cost-effectiveness studies have shown the benefit of using specific products to treat acne and psoriasis (Cunliffe et al, 1991; Cork, 1993), but the economic aspects of AD have received scant attention. Only one publication in recent years has dealt with the cost of AD (Lapidus et al, 1993). This paper, from the USA, estimated the annual cost of treating children in that country to be $364m, but this figure was derived from a health care system unlike that of the United Kingdom. No mention was made of the cost of AD to sufferers, or to society, and the study was limited to children.
The analysis of the economics of AD in the USA (Lapidus, 1993) was limited for three main reasons: it dealt only with children; treatment in the community was not included; and costs to the patient were omitted. Given the limited need for expensive in-patient treatment, it was all the more surprising that the estimated annual cost of $364 million, equivalent to $1.42 per head of population, was similar to that of conditions which more often need in-patient treatment (Table 1.7). For instance, in 1990 the per capita cost of treating inflammatory bowel disease in the U.S.A. was estimated at between $1.67 and $2.51, and respiratory syncytial virus infection in children $1.26 (Hay & Hay, 1992; Meissner, 1994).

In the U.K., AD clearly causes an enormous social burden. However the cost of treating it is unknown and this is a notable gap in our knowledge. Data on the cost of treating various age groups, different social groups and geographical areas are necessary to raise the profile of AD and spotlight the financial burden to sufferers.

1.5 Assessment of disability

1.5.1 The place of quality of life assessment in medicine

The issues of cost and quality of life are inextricably linked. All clinicians have to play a part in the difficult task of allocating scarce resources within the health services (Lazarus, 1994). To do this properly they need to know which treatments lead to an improved outcome for their patients, and which are cost effective (Detsky & Naglie, 1990; Cunliffe et al, 1991).

Reliable measures of quality of life can help here, by providing an accurate estimate of the benefits conferred by any individual line of treatment. These benefits can then be balanced against costs.

We now live in a purchaser/provider era with an economic approach to setting priorities in the health service. Dermatology services are perhaps at a disadvantage when competing for resources because they deal mainly with illnesses that do not threaten life and are therefore seen as less serious, and of low priority by purchasers of health care. Measures of
quality of life impairment should be incorporated into these assessments of priority (Delamothe, 1994).

Disability due to disease is largely ignored in the medical curriculum (Lancet ed, 1986; Claxton, 1994). Doctors are taught how to take a history, examine a patient, interpret investigations and initiate medical management, but teaching on the impact of disease is often missing.

Where quality of life has been measured it is often added as an afterthought (Bergner, 1989). It is seldom the main variable examined and in a survey of 100 publications using the term 'quality of life', it was seldom defined (van Dam et al, 1981), and this remains a contentious issue (Siegrist & Junge, 1989).

1.5.2 The concept of quality of life

Quality of life has been defined as "the extent to which hopes and ambitions are matched by experience" and the key aim of medical care should be to "narrow the gap between a patient's hopes and aspirations and what actually happens" (Calman, 1984).

'Quality of life' must be distinguished from health status and functional status, concepts that can be measured in a tangible way (Bergner, 1989). Functional status is used for assessing activities of daily living. Two examples of functional status measurements are the Karnofsky Performance Status and the New York Heart Association Classification, which have been used for assessing eligibility for clinical trials (Karnofsky et al, 1980; New York Heart Association, 1979). They are concise and specific to one disease. Two others that assess performance of everyday tasks are the Index of Activities of Daily Living and the Barthel Index which are not specific to any one condition and can be used to evaluate an individual's ability to live independently (Katz & Akpom, 1976; Mahoney & Barthel, 1965).

Health Status measures were developed to improve the care and health of individuals. They include items relating to physical functioning as well as measures of emotional status and perceptions of health (Patrick & Deyo, 1989).
In contrast, quality of life is intangible. Frequently used measures of quality of life such as the Sickness Impact Profile (Bergner et al, 1981) and the SF36 (Ware & Sherbourne, 1992) contain many elements that should be included in a quality of life assessment (Fitzpatrick et al, 1992), and these are listed in Table 1.8. Some desirable characteristics for a quality of life measure have been proposed: that they should rely on the statements of the patient; that they should not be restricted to one moment in time; and that different periods of time should be compared (van Dam et al, 1981).

1.5.3 Quality of life in dermatology

Early measurements of disability in dermatology were based on leprosy (Trautman et al, 1965; Ryan, 1991); then the focus of attention turned to psoriasis (Stankler, 1981; Ginsburg & Link, 1989; Finlay & Kelly, 1987). Compensation claims have increased awareness of the measures needed to assess patients with hand eczema (Meding & Swanbeck, 1990). It is obvious that a chronic condition like AD must also cause massive incapacity. 64% of patients with acne, psoriasis or eczema attending hospital clinics in Oxford, reported that their ability to work was reduced by their disease (Jowett & Ryan, 1985). The effects of severe skin disease are different from those of the other medical conditions used to develop quality of life measures; and the study of life quality in individuals with AD is still in its infancy.

One attempt has been made to develop a measure specific to AD (Eun & Finlay, 1990). Fifty-five AD patients, over 20 years old, completed a questionnaire designed to determine which aspects of their lives were most affected, and a quality of life questionnaire was then constructed using their responses. This may have been the basis for a good quality of life measure but its validity has not been fully proven. Construct validity was significant only at P<0.05, and reliability and criterion validity were not tested.

Indeed, few measures of outcome are valid, reliable and responsive to change, or are practicable for everyday use. The Dermatology Life Quality Index (DLQI) is a simple practical measurement of quality of life in clinical practice (Finlay & Khan, 1994). It was established by studying one
hundred and twenty consecutive patients attending a dermatology out-patient department who were asked to identify how their skin disease affected their lives. From this information, a ten-item questionnaire was constructed, each question scoring 0-3, with high scores representing a severely impaired quality of life (Appendix 4). Reliability was evaluated using the test-retest method which, although it gave a significant correlation (P<0.001), may have been better tested by alternative methods. Further work on external validity testing is underway but has not yet been published.

Patients with AD find that their sleep, work and relationships are all affected by their disease (Jowett & Ryan, 1985), which can also cause psychiatric disturbances (Blomquist & Sakki, 1991; Ginsburg et al, 1993; White et al, 1990). Good qualitative data are needed as a measure of the degree to which patients' lives are altered as well as outcome measures in AD that truly capture its impact and relevance to patients.

The Patient Generated Index (PGI) is an approach to quality of life measurement never previously used for skin conditions (Ruta et al, 1994). It was developed for back pain, and shown to be valid, reliable and to correlate with measures of severity. The elements of life affected by the condition are chosen by the individual completing the questionnaire. Subjects will differ in their living conditions, jobs, hobbies, sports and social activities, and consequently one disease is capable of affecting life in a variety of ways. For instance patients with AD will be more affected if they clean their own house than if they employ a domestic. A nurse is more likely to be affected than a secretary. The PGI not only illustrates the disability attributable to different lifestyles but can theoretically be used for any condition in which quality of life is important. This contrasts starkly with the DLQI that has 10 rigid questions and can only be used for those conditions for which it was developed.

1.6 Summary

AD is a chronic, debilitating disease that has the capacity to drain resources and diminish life quality. Most studies of its prevalence deal only with children and studies of quality of life deal only with adults and these usually take place in a hospital population. Most sufferers do not
attend hospital and are therefore more difficult to contact. To advance our understanding of AD, researchers must resist the temptation to repeat examinations of groups that are easily accessed and analysed and turn their attention to communities and subjects in which our knowledge is lacking. The financial burden on AD patients' families may be heavy and as yet has attracted no attention in the literature. This area is of central importance to sufferers and requires further investigation.

1.7 Aims of the study

The specific aims of the Lothian Atopic Dermatitis Study (LADS) were to answer the following questions:

1. What is the one-year period prevalence at all ages of AD in the community?
2. What is the economic burden on AD patients and their families?
3. What is the cost of AD to the health service and society?
4. What is the impact of AD on the quality of life of patients and their families in a community setting?
5. What is the relative performance of the PGI and DLQI in the measurement of life quality in a community population?
Table 1.1
Hanifin and Rajka's diagnostic criteria for atopic dermatitis.

To qualify as a case of atopic dermatitis, an individual must have three or more basic features and three or more minor features.

<table>
<thead>
<tr>
<th>Basic features</th>
<th>Minor features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pruritus</td>
<td>Xerosis</td>
</tr>
<tr>
<td>Typical distribution - flexural in</td>
<td>Ichthyosis/palmar hyperlinearity/keratosis pilaris</td>
</tr>
<tr>
<td>adults</td>
<td>Immediate skin reactivity</td>
</tr>
<tr>
<td>- facial and extensor in infants</td>
<td>Elevated IgE</td>
</tr>
<tr>
<td>Chronic/relapsing dermatitis</td>
<td>Early age of onset</td>
</tr>
<tr>
<td>Personal/family history of atopy</td>
<td>Cutaneous infections</td>
</tr>
<tr>
<td></td>
<td>Non-specific hand/foot dermatitis</td>
</tr>
<tr>
<td></td>
<td>Nipple eczema</td>
</tr>
<tr>
<td></td>
<td>Cheilitis</td>
</tr>
<tr>
<td></td>
<td>Recurrent conjunctivitis</td>
</tr>
<tr>
<td></td>
<td>Infraorbital fold</td>
</tr>
<tr>
<td></td>
<td>Keratoconus</td>
</tr>
<tr>
<td></td>
<td>Ant. subcapsular cataracts</td>
</tr>
<tr>
<td></td>
<td>Orbital darkening</td>
</tr>
<tr>
<td></td>
<td>Facial pallor/erythema</td>
</tr>
<tr>
<td></td>
<td>Pityriasis alba</td>
</tr>
<tr>
<td></td>
<td>Ant. neck folds</td>
</tr>
<tr>
<td></td>
<td>Itch when sweating</td>
</tr>
<tr>
<td></td>
<td>Intolerance wool &amp; lipid solvents</td>
</tr>
<tr>
<td></td>
<td>Perifollicular accentuation</td>
</tr>
<tr>
<td></td>
<td>Food intolerance</td>
</tr>
<tr>
<td></td>
<td>Influenced by environmental/emotional factors</td>
</tr>
<tr>
<td></td>
<td>White dermographism/delayed blanch</td>
</tr>
</tbody>
</table>
Table 1.2
The UK Working party's diagnostic criteria.

History of an itchy skin condition (or parental report of scratching or rubbing in a child) plus 3 or more of following:-

1. Onset before age 2 (not used in child under 4).
2. History of flexural pattern of disease.
3. History of asthma or hay fever (or atopic disease of first degree relative in children under 4).
4. History of dry skin in the last year
5. Visible eczema in flexures (including cheeks, forehead and outer aspects of limbs if children under 4).
### Table 1.3
Early community studies reporting the prevalence of atopic disease.

<table>
<thead>
<tr>
<th>Author (Country)</th>
<th>Year</th>
<th>Frequency</th>
<th>Methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jimenez (USA)</td>
<td>1934</td>
<td>11.9</td>
<td>Students with atopic diseases</td>
</tr>
<tr>
<td>Service (USA)</td>
<td>1939</td>
<td>2.9</td>
<td>Inclusion criteria uncertain. 56% aged &lt; 10, 71.4% aged &lt; 20.</td>
</tr>
<tr>
<td>Eriksson-Lihr (Finland)</td>
<td>1955</td>
<td>3</td>
<td>Infantile eczema ever Public school children Questionnaire to parents, school health cards, health centre records Point prevalence Children aged 7-14 School nurse health cards &amp; doctor examination</td>
</tr>
<tr>
<td>Walker &amp; Warin (UK)</td>
<td>1956</td>
<td>3.1</td>
<td>Eczema ever Health visitor cards</td>
</tr>
<tr>
<td>Freeman (USA)</td>
<td>1964</td>
<td>'very low'</td>
<td>Prevalence not quoted but &lt; 2.8 8th and 12th grade students</td>
</tr>
<tr>
<td>Arbeiter (USA)</td>
<td>1967</td>
<td>4.4</td>
<td>Prevalence eczema verified by doctor Age 5-15 Questionnaire to parents Even distribution</td>
</tr>
<tr>
<td>Author (Country)</td>
<td>Year</td>
<td>Frequency (age)</td>
<td>Methods</td>
</tr>
<tr>
<td>------------------</td>
<td>------</td>
<td>----------------</td>
<td>---------</td>
</tr>
<tr>
<td>Halpern (USA)</td>
<td>1973</td>
<td>12.4 Age 0-7</td>
<td></td>
</tr>
<tr>
<td>Turner (Australia)</td>
<td>1974</td>
<td>5.6 (age&lt;2), 3.3 (age&gt;2) Lifetime incidence Age 6-17 Questionnaire to parents - history relying on parents memory</td>
<td></td>
</tr>
<tr>
<td>Rea (UK)</td>
<td>1976</td>
<td>12.3 (15-24), 3.5 (25-34), 12.7 (35-54), 6.4 (55-74) Point prevalence Age 15-74 Screening by questionnaire; follow up by trained field workers &amp; doctors</td>
<td></td>
</tr>
<tr>
<td>Johnson (USA)</td>
<td>1977</td>
<td>2.0 (6-11), 1.7 (12-17), 1.5 (18-24), 2.8 (25-34) Prevalence Age 1-74 Health and nutrition examination survey Patients seen by 101 dermatologists</td>
<td></td>
</tr>
<tr>
<td>Kjellman (Sweden)</td>
<td>1977</td>
<td>8.3 Age 0-7</td>
<td></td>
</tr>
<tr>
<td>Larsson (Sweden)</td>
<td>1980</td>
<td>3 Point prevalence Age 12-16 Examined by dermatologists</td>
<td></td>
</tr>
<tr>
<td>Fergusson (NZ)</td>
<td>1981</td>
<td>20.3 Lifetime incidence Age 3 Birth cohort study</td>
<td></td>
</tr>
<tr>
<td>Engbaek (Denmark)</td>
<td>1982</td>
<td>9.1 Point prevalence School age Examination by school medical officer</td>
<td></td>
</tr>
</tbody>
</table>
Table 1.5
Recent community studies reporting the prevalence of atopic dermatitis

<table>
<thead>
<tr>
<th>Author (Country or city)</th>
<th>Year</th>
<th>Frequency</th>
<th>Methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taylor (Bristol)</td>
<td>1984</td>
<td>12.2</td>
<td>Lifetime prevalence Age 5 1970 birth cohort</td>
</tr>
<tr>
<td>Storm (Denmark)</td>
<td>1986</td>
<td>8.9</td>
<td>Point prevalence Age 7 Mailed questionnaire</td>
</tr>
<tr>
<td>Schultz Larsen (Denmark)</td>
<td>1986</td>
<td>10.2</td>
<td>Lifetime prevalence Age 7 Mailed questionnaire followed by examination by dermatologist Genetic-epidemiological twin study</td>
</tr>
<tr>
<td>Svejgaard (Denmark)</td>
<td>1986</td>
<td>3.3</td>
<td>Point prevalence Age 17-24 Danish recruits</td>
</tr>
<tr>
<td>Golding (Cardiff)</td>
<td>1987</td>
<td>12.3</td>
<td>Lifetime prevalence Age 7 1 year period prevalence Questionnaires completed by midwives</td>
</tr>
<tr>
<td>Burr (Cardiff)</td>
<td>1989</td>
<td>15.9</td>
<td>Lifetime prevalence Age 11-12 Mailed questionnaire</td>
</tr>
<tr>
<td>Visscher (USA)</td>
<td>1989</td>
<td>33</td>
<td>Advertisement for 'problem skin'</td>
</tr>
<tr>
<td>Poysa (Finland)</td>
<td>1991</td>
<td>4.3</td>
<td>Point prevalence Age 3-15 Examination by doctor</td>
</tr>
<tr>
<td>Diepgen (Germany)</td>
<td>1992</td>
<td>4.7</td>
<td>Cumulative incidence Young adults</td>
</tr>
<tr>
<td>Ninan (Aberdeen)</td>
<td>1992</td>
<td>12.0</td>
<td>Lifetime prevalence Age 8-13 Questionnaires to parents</td>
</tr>
<tr>
<td>Schultz Larsen (Denmark)</td>
<td>1993</td>
<td>11.5</td>
<td>Lifetime prevalence Age 7 Mailed questionnaire followed by examination by dermatologist Genetic-epidemiological twin study</td>
</tr>
<tr>
<td>Falk (Norway)</td>
<td>1993</td>
<td>2.3%</td>
<td>Lifetime incidence All ages Medical records</td>
</tr>
<tr>
<td>Kay (Birmingham)</td>
<td>1994</td>
<td>11.5</td>
<td>1 year period prevalence Age 3-11 Interview by general practitioner</td>
</tr>
</tbody>
</table>
Table 1.6.
Sex ratios reported in recent studies from Scandanavia and the U.K.

<table>
<thead>
<tr>
<th>Study</th>
<th>M:F ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dotterud (1995)</td>
<td>1:1.3</td>
</tr>
<tr>
<td>Poysa (1991)</td>
<td>1:1</td>
</tr>
<tr>
<td>Ninan (1992)</td>
<td>1:0.7</td>
</tr>
<tr>
<td>Burr (1989)</td>
<td>1:1</td>
</tr>
<tr>
<td>Kay (1993)</td>
<td>1:0.9</td>
</tr>
<tr>
<td>Schultz Larsen (1993)</td>
<td>1:1.4</td>
</tr>
<tr>
<td>Storm (1988)</td>
<td>1:1.5</td>
</tr>
</tbody>
</table>

Table 1.7.
Annual per capita cost of treating AE compared with other medical conditions

<table>
<thead>
<tr>
<th>USA</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atopic eczema</td>
<td>$1.52</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>$1.67-$2.51</td>
</tr>
<tr>
<td>RSV infection</td>
<td>$1.62</td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th></th>
<th>Suggested elements that should be included in a quality of life measure (Fitzpatrick et al, 1992).</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Physical function - e.g. mobility, self care.</td>
</tr>
<tr>
<td>2.</td>
<td>Emotional function - e.g. depression, anxiety.</td>
</tr>
<tr>
<td>3.</td>
<td>Social function - e.g. intimacy, social support, social contact.</td>
</tr>
<tr>
<td>4.</td>
<td>Role performance - e.g. work, housework</td>
</tr>
<tr>
<td>5.</td>
<td>Pain</td>
</tr>
<tr>
<td>6.</td>
<td>Other symptoms - e.g. fatigue, nausea, disease specific symptoms.</td>
</tr>
</tbody>
</table>
Figure 1.1
Triggers for Atopic Dermatitis
Figure 1.2

Infant with infected facial atopic dermatitis.
Figure 1.3

Loss of eyebrows due to rubbing and scratching in a teenager with facial atopic dermatitis.
Figure 1.4
Severe facial atopic dermatitis in an adult.
Figure 1.5
Pruriginous nodules on an adult with atopic dermatitis.
CHAPTER 2
METHODS

2.1 Population

The study population consisted of the 9786 patients in a semi-rural general practice in Livingston, West Lothian (Figures 2.1-2.4). Livingston is one of Scotland’s new towns. It was established about 40 years ago as an overflow from Glasgow and lies 15 miles west of Edinburgh. As a new town its age distribution differs slightly from the rest of Scotland, with fewer over 65 years of age and more between 20 and 39 (Table 2.1). However, the prevalence estimates calculated from this population can be age-adjusted to fit the Scottish population. The distribution of social class is close to that of Scotland as a whole, but with slightly fewer in social classes I and V and more in social class III (Table 2.2) (Livingston Development Corporation, 1994a); this small diversion from the Scottish population should have little influence on the results. To adjust for ethnic differences would be more difficult as no data on the ethnic families in Livingston, or even Scotland, exist, but ethnic minorities make up only a small proportion of the community.

2.2 The General Practice

Livingston is served by four general practices, each dealing with a circumscribed area close to the health centre (Figure 2.5). When patients move from one area to another they are required to register with their local health centre; consequently patients live near to the centre at which they are registered. This arrangement is unusual, but ideal for a community study in which patients must be contacted at home.

Howden Health Centre (HHC), by virtue of its semi-rural location and its manageable list size, was chosen for the study. The eight general practitioners (GPs) have an average list size of just over 1200, which remains in balance as new patients are automatically registered with the GP who has the smallest list at that time. List sizes are considerably less
than the average for Scotland of 1900, because all of the GPs work part-time in a hospital speciality such as paediatrics or obstetrics and gynaecology. This also helps to foster a close relationship with the local hospital, St. John’s at Howden, and makes local doctors aware of the need for good community-based research. This project received the enthusiastic support of all staff at the HHC, medical and office workers alike.

The practice is well organised, with good inter-personal communication and regular staff meetings. A computerised system permits practice records to be cross-referenced, for instance, by age, GP, name and diagnosis.

2.3 Sampling

2.3.1 An overview

Two aims were to assess the cost to, and life quality of patients with AD. Sampling, therefore, had to ensure that as many patients with AD as possible could be identified within the study period of one year. Our chosen method had four separate stages.

1. Patients coded for any type of eczema on the practice computer were selected and subsequently examined, together with their families, to establish their precise diagnosis.

2. Few infants with AD were registered in the diagnostic index, perhaps because of reluctance to diagnose AD so early in life. Therefore all families with a child aged under 2 years were also questioned and examined.

3. The diagnostic index on the practice computer was unlikely to be comprehensive. To estimate the number of cases of AD not included in stages 1 or 2, a random cluster sample was chosen, each cluster being a single family, sampled with probability proportional to size (Cochran, 1977). Families were contacted by telephone; all adult family members were interviewed, and anyone with a history of an itchy skin was examined.
4. One in six of all families which had denied the presence of an itchy member at stage 3 were examined to reduce the chance of cases of AD being omitted.

First contact was through a letter signed by their general practitioner (Appendix 5). Patients were told that they would be contacted by myself, but further information was withheld to reduce bias due to prior knowledge of the study. Two weeks elapsed before patients were telephoned to arrange an interview at their home or at HHC. Those without a telephone were visited at home. Interviews were usually conducted with all family members present.

There were no absolute exclusion criteria, but in the case of recent illness or bereavement contact was delayed.

2.3.2 Practical aspects

The study period was chosen as one year, in an attempt to eliminate seasonal variation. Lists of patients registered with each of the eight GPs were sampled sequentially, in random order. Every 6-7 weeks, appropriate 'listings' of all patients in the care of a specific GP, and separate lists of all children under 2, and all patients with a diagnosis of eczema, were printed. Case records for each GP are filed separately and by address, so that members of one household are filed together. Individual notes were counted sequentially from the first address, and, using random number tables, these individuals and their families were included in the random sample. Those already on the list of eczema patients or the list of under 2's were excluded. In this way the likelihood of a family being chosen depended on its size, thereby achieving sampling with 'probability proportional to size'. Most AD patients are children. Because larger families are more likely to include children, the sample encompassed more of those likely to be affected than would a straightforward random sample.

Each week one sixth of all eczema patients, and a sixth of all families with a member aged below 2, registered with one GP, were contacted along with 6 families selected for the random sample. In 6 weeks, all patients in the sample of a given GP could be contacted. An unbiased selection of patients was achieved randomly over a one year period, and included
some infants born during the period of the study, included in the under 2 category.

2.4 Assessment of prevalence

The population was divided into the following age groups: <2, 2-11, 12-15, 16-24, 25-40 and over 40. The younger ranges correspond to those used for the U.K. Working Party's diagnostic criteria, whereas the older groupings were chosen empirically.

A diagnosis of AD was assigned to all patients who fulfilled the criteria of the U.K. Working Party. The protocol was adhered to strictly using the exact wording of each criterion. At the outset of this study these criteria had not been published but Dr Hywel Williams provided information on the most recent developments and the most likely format of the final version. The criteria we used differed slightly from the final version: the cut off for family history of atopy, infantile pattern and onset was age 2 rather than age 4. A protocol for the diagnosis of flexural eczema that was being developed for research assistants, a final form of which has now been published (Williams et al, 1995a), was followed.

All families with children under 2 years were contacted, and so prevalence could then be calculated as the proportion of those seen who were affected. The situation with the older groups was more complicated. To calculate the prevalence in each age group, individuals sampled from the eczema families, those from the under 2 families, and those from the random cluster sample had to be considered separately. The statistics are outlined below.

2.5 Assessment of cost

AD patients identified as above were all included in an estimate of cost.

Individuals who are the subjects of studies may become more focused on their skin and as a result may visit their doctor more often or apply their treatment more assiduously, thus introducing a possible source of bias. To minimise this effect, the initial visit was kept as short as possible; attempts by patients to discuss their treatment were avoided with an
explanation that this might bias the results and that an opportunity for a prolonged discussion would be given at a second visit. All sources of cost were recorded on a proforma (Appendix 6), and a yellow plastic bag was provided, in which to collect treatments used during the study period. Patients were also given an information sheet explaining the purpose of the survey (Appendix 7).

Cost was assessed over two months. At a second visit at the end of this period the proforma was scrutinised and responses were elucidated where necessary. The cost of OTC items were recorded where possible or the manufacturer, size and location of purchase were noted and the price ascertained later. Similarly the cost of clothing and laundry in excess of normal use was recorded. After discussion with a representative of the South of Scotland Electricity Board, the cost of depreciation of a washing machine was estimated as £1.54 per week and the cost per wash of electricity and soap powder was judged to be £0.13 and £0.20 respectively.

Expenditure could then be apportioned to the patient (eg prescription charges and over-the-counter preparations), to the health service (eg drugs, and doctor and nurse time) and to society (lost working days). The unit cost to the health service of each prescribed item can be calculated by adding £1.40 onto the basic cost listed in the British National Formulary: £0.70 dispensing fee and £0.70 for professional registration is charged by the pharmacist. The cost of doctor and nurse time included their salaries and the running costs of the hospital or health centre, and were calculated by standard methods (Hughes, 1991), as was the cost to society of lost working days which was calculated using quoted estimates of £8.42 per hour (Robinson, 1993) (Table 2.3). For a visit to hospital, on the basis that 25 patients are seen per consultant session, the cost per patient visit would be £7.21. The cost of a visit to a GP was calculated to be £9.05 (Table 2.4).

2.6 Assessment of quality of life

Two validated questionnaires were used to assess adults. The first was the Dermatology Life Quality Index (DLQI) developed by Dr A Finlay (Finlay & Khan, 1994). It consists of ten questions designed to assess various skin diseases and has been used to measure quality of life in AD.
Each question contributes a score of 0-3 ('not at all'=0, 'a little'=1, 'a lot'=2, 'very much'=3), giving totals of from 0 to 30. All questions refer to the impact of the condition over the previous week. AD varies with seasons (Morren et al, 1994) and so too may the answers to the questions asked. In an additional questionnaire the same questions were asked as in the DLQI, but referring to the previous year. The impact on patients' lives at all times of year can then be encompassed.

The second questionnaire was the PGI (Ruta et al, 1994) which is completed in three stages (Appendix 8). These are illustrated in Table 2.5, which demonstrates an example of a 32 year old woman with AD. First, patients identify the five areas or activities most influenced by their disease: for instance work, socialising, swimming, housework and sleep are nominated in the example. Second, each of these areas is given a score of from 0-100. The lower the score the greater the impairment of quality of life: in the example 'sleep', is judged to be most profoundly affected by AD and is given the lowest score of 10. A sixth line is provided for areas or activities other than those already mentioned, which may or may not be related to the subject's skin disease. Finally the patient is given 60 points 'to spend', with most points being given to those areas they most want to improve: sleep and work were the areas to which the subject in our example attached most importance. From this information an overall score of from 0-100 is calculated, by weighting the scores at the second stage of the PGI according to the priorities assigned at the third stage.

Although an activity such as 'swimming' may be considerably impaired, it may not be an area that would be a priority to improve because it can be bypassed easily. It does not, therefore contribute to the final tally. The resulting score represents the extent to which reality falls short of expectation for those areas of life in which they would most value improvement. In contrast to the DLQI, poor life quality is indicated by low PGI scores. This questionnaire was designed for adults suffering from a medical condition, but was also given to parents in this study to assess the impact on their lives of their children's disease.

Any community study of AD will include many children. Measurement of life quality in the young is at an early stage. Few measures exist or are
even being developed. The quality of life questionnaire used here for children aged 5-15 is currently being developed (Appendix 9). It consists of three parts. Section A asks patients about their own disease, Section B asks a parent about their child's disease, and Section C is an assessment by one parent of the impact of the child's disease on the family. The scoring system is similar to that of the DLQI: each question scores 0-3 (or 0-2 in question 9) resulting in a maximum possible score of 26 for Section A and 27 for Section B. The maximum for Section C is 39, but this is only attainable if the patient has brothers and sisters because questions 4, 9a and 9c ask about sibling relationships. It is therefore imperfect but was the only questionnaire for children available at the start of this study.

2.6.1 Statistical analysis and validation

Descriptive statistics of the DLQI and PGI were computed individually. Any new measure of quality of life must be tested to show that it does genuinely measure changes in the quality of life for individuals in their particular situation. This is validity and the concept has been refined by research workers in public health medicine. A rigorous definition is that 'validity is the extent to which a questionnaire measures what is intended' (Streiner & Norman, 1990). Two aspects of validity were tested in this study: criterion validity and construct validity. Criterion validity is the extent to which a new measure correlates with established measures; whereas construct validity is the extent to which a new measure relates to specified variables that reflect severity in accordance with established assessments of severity.

To assess criterion validity, the correlations between the PGI and DLQI, and between the PGI and individual questions of the DLQI, were calculated (Armitage & Berry, 1987). As this was a community study scores in the individual DLQI questions were likely to be low, and those who scored 0 in each question may form a group distinct from those who scored 1 or more. Hence, the mean PGI scores of those who scored 0 were compared, using a t-test, with the scores of those who scored 1-3 in each item of the DLQI.

The results of the cost evaluation, described in Chapter 4, were used to test construct validity, by correlating cost and quality of life. It was
postulated that patients with a poor quality of life measured by the PGI and DLQI, incur high total costs, health service costs and patient costs. Although personal costs may in some part be dictated by income, health service costs, other than prescription costs are more likely to correlate with severity.

The idea that the open-ended nature of the PGI might confer greater validity as a quality of life measure in AD, over and above the DLQI, was tested by the hypothesis that patients would include a broader range of affected areas in their responses to the PGI than those included in the DLQI. As a further test of construct validity, patients were divided into 2 groups: group 1 consisted of those who mentioned in the PGI only areas that are part of the DLQI; and group 2 contained those who mentioned in the PGI areas outwith the DLQI. If both these groups yield a significant correlation between the PGI and the DLQI then there is evidence that the areas outwith the DLQI are also valid for the measurement of quality of life in AD.

2.7 Hospital assessment

This study was primarily of AD in the community, and only a few of the patients had severe disease. To compare the cost to, and quality of life of, more severely affected patients, a cohort attending the Royal Infirmary of Edinburgh for dressings or admitted to the ward there, was appraised in a similar way. All patients with AD admitted for in-patient treatment or accepted for daily dressings, during four two-week periods evenly spaced throughout the study, were invited to participate.

They were first seen at the time of their admission to the daily dressings service or to the ward. When the 2 month interview was carried out, all treatments used in hospital and at home were recorded. Costs were calculated in a way similar to that for patients in the community, but included the cost of nurse time and in-patient treatment where appropriate. Quality of life questionnaires were identical to those used in the community part of the study.
2.8 Statistics

Data were coded, loaded onto computer and analysed using the statistical package SPSS-PC. Calculations of prevalence were carried out by hand, using standard methods for cluster samples with probability proportional to size (Cochran, 1977).

2.8.1 Statistics for the under 2 group

There were very few families with more than one child aged less than 2 which allowed this group to be analysed using the normal approximation to the binomial distribution. If

\[ p = \text{proportion affected} \]
\[ q = 1-p \]
\[ n = \text{sample size} \]

Then the standard error of the estimate of the proportion affected is

\[ SE = \sqrt{\frac{pq}{n}} \]

2.8.2 Statistics for the older age groups

Each sampling group was considered separately. For each age group the estimate of the number with AD in each group and the variance of this estimate are

\[ Y = \frac{M_0 (\sum y)}{n} \]

\[ \text{Variance}(Y) = \frac{M_0^2 \sum (y_i - \bar{y})^2}{n(n-1)} \]

where \( M_0 = \text{total number in the population} \)
\( n = \text{number of families in sample} \)
\( y_i = \text{proportion of family i who are affected} \)
\( Y = \bar{y}M_0 \)
The total estimated number is calculated by adding together the estimates of Y in all three sampling groups and the variance of this total is the sum of the separate variances. The prevalence is calculated as a percentage of the total number in that age group and the variance of the prevalence is calculated from the variance of the total estimated number. i.e.

\[
\text{Prevalence} = \frac{\sum Y}{\sum N} \times 100\%
\]

where \( N \) = total number in that group

\[
\text{Variance of prevalence} = \frac{(\sum \text{Variance} \times 100\%)}{\sum N}
\]

Age groups can be combined by adding the numbers and variances to estimate, for example, the prevalence for those over 16.

The sex ratios were calculated by considering the sexes separately and calculating the prevalence in the same way within each age group. The sex ratios were calculated from these prevalences.

2.8.3 Statistics for the costing section

The Chi square statistic was used for comparing the proportion of those aged under 16 with those aged over 16, who had no expenditure.

Mean annual costs were computed by multiplying the 2 monthly costs by 6, which gives an unbiased representation of the total costs over one year. Extrapolation of costs and lost working days were calculated on the basis that those with AD who had not been identified had expenditure similar to those identified in the random sample. In other words it was assumed that those not captured by our sampling method would be represented in terms of economic burden by those in the random sample. The per capita cost assumed a U.K. population of 58,191,230.

2.8.4 Statistics for the quality of life section

The DLQI asking about life quality over the previous 2 weeks and 1 year were compared using the paired Wilcoxon two sample test, and the scores of the Children's questionnaire were compared using the Wilcoxon summed rank test. Correlations were calculated using Pearson's (Armitage, 1987).
2.9 Pilot study

Before data collection started a pilot study was carried out at Dedridge Health Centre, a general practice neighbouring HHC in Livingston. It proved suitable because of its similarity to HHC in terms of population and organisation. Forty patients were seen in one month to establish the methodology.

Initially the intention was to see all patients who had been prescribed topical steroids as well as those with a diagnosis of eczema, but the size of such a sample proved to be unmanageable. As a consequence, the numbers included in the random sample were increased.

The design of the study was intended to keep bias to a minimum. The possibility of being contacted before a visit from the investigator might change patients' responses. To avoid this, patients were contacted by telephone if possible, or failing this, by a visit. Predictably, a stranger telephoning or visiting without warning sometimes met with suspicion or even aggression. Therefore, about 2 weeks prior to the proposed visit, all households in the main protocol were sent a letter on headed notepaper, signed by their GP (a copy of which is shown in appendix 5). It gave limited information about the study. This method also allowed GPs to screen out families they thought were unsuitable because of illness or bereavement.

Otherwise the protocol was considered sound and yielded no unexpected obstacles. Neither the costing nor the quality of life questionnaires caused any difficulties.
Table 2.1.
Age distribution of Livingston compared with that of Scotland (% age)

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Livingston</th>
<th>Scotland</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-19</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>20-39</td>
<td>36</td>
<td>28</td>
</tr>
<tr>
<td>40-64</td>
<td>28</td>
<td>28</td>
</tr>
<tr>
<td>65+</td>
<td>6</td>
<td>14</td>
</tr>
</tbody>
</table>

Table 2.2
Social class distribution in Livingston compared with the rest of Scotland

<table>
<thead>
<tr>
<th>Social class</th>
<th>Livingston</th>
<th>Scotland</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Professional</td>
<td>3.3</td>
<td>4.5</td>
</tr>
<tr>
<td>2. Managerial/technical</td>
<td>21.1</td>
<td>25.2</td>
</tr>
<tr>
<td>3. Skilled</td>
<td>47.6</td>
<td>43.3</td>
</tr>
<tr>
<td>4. Partly skilled</td>
<td>18.3</td>
<td>15.9</td>
</tr>
<tr>
<td>5. Unskilled</td>
<td>6.8</td>
<td>7.7</td>
</tr>
</tbody>
</table>
Table 2.3.
Details of calculations of cost of consultation with hospital consultant. Costs listed are based on two consultants working in the same session.

<table>
<thead>
<tr>
<th>Source</th>
<th>Cost per session</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cleaning</td>
<td>£24.51</td>
</tr>
<tr>
<td>Portering</td>
<td>£4.23</td>
</tr>
<tr>
<td>Heating</td>
<td>£5.04</td>
</tr>
<tr>
<td>Power and light</td>
<td>£4.32</td>
</tr>
<tr>
<td>Other fuel</td>
<td>£0.47</td>
</tr>
<tr>
<td>Building</td>
<td>£3.26</td>
</tr>
<tr>
<td>Engineering</td>
<td>£3.30</td>
</tr>
<tr>
<td>Grounds</td>
<td>£0.20</td>
</tr>
<tr>
<td>Rent and rates</td>
<td>£7.41</td>
</tr>
<tr>
<td>Consultants' salaries</td>
<td>£162.80</td>
</tr>
<tr>
<td>Nurses, aux, records etc</td>
<td>£146.00</td>
</tr>
<tr>
<td>Total</td>
<td>£361.54</td>
</tr>
</tbody>
</table>

Table 2.4.
Details of calculation of cost of GP consultation

<table>
<thead>
<tr>
<th>Source</th>
<th>Charge per quarter</th>
<th>Charge per patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gross charge</td>
<td>£13,769</td>
<td></td>
</tr>
<tr>
<td>Admin &amp; clerical</td>
<td>£21,756.36</td>
<td></td>
</tr>
<tr>
<td>GP salary</td>
<td>£53,600</td>
<td>£5.15</td>
</tr>
<tr>
<td>Total</td>
<td>£89,125.36</td>
<td>£9.05</td>
</tr>
</tbody>
</table>

Assuming each GP sees 100 patients per week the cost of a consultation per patient is £9.05. Practice nurses are paid £9.73 per hour which results in a cost of £5.36 per nurse consultation.
<table>
<thead>
<tr>
<th>Activity</th>
<th>Score</th>
<th>Points</th>
<th>Total Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Work</td>
<td>20</td>
<td>20 / 60 = 6.7</td>
<td></td>
</tr>
<tr>
<td>Socialising</td>
<td>20</td>
<td>10 / 60 = 3.3</td>
<td></td>
</tr>
<tr>
<td>Swimming</td>
<td>30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Housework</td>
<td>20</td>
<td>10 / 60 = 3.3</td>
<td></td>
</tr>
<tr>
<td>Sleep</td>
<td>10</td>
<td>20 / 60 = 3.3</td>
<td></td>
</tr>
<tr>
<td>Other aspects of life</td>
<td>30</td>
<td></td>
<td>16.7</td>
</tr>
</tbody>
</table>
Figure 2.1
Livingston, situated west of Edinburgh
Figure 2.2 & 2.3
Housing in the new town of Livingston
Figure 2.4
Livingston Kirk, part of the original Livingston Village
Figure 2.5

Map of Livingston. The area served by Howden Health Centre is outlined in black.
Chapter 3
Prevalence of Atopic Dermatitis in the Community.

3.1 Methods in practice

The identification and collection of patient details took one full year, and follow-up a further two months. The bulk of the work was planned to take place one full day per week but it soon became clear that more time would be needed. Individuals in the community, some with mild disease, had to be allowed flexibility in arranging appointment times, which necessitated spending three or four evenings per week and several hours at weekends visiting patients. For every individual with AD identified, many families with no affected members had to be seen. Generally, women with young children were at home during the day and could be contacted easily, but adults with full-time jobs had to be accommodated outside normal working hours. Most patients cooperated, but some seemed reluctant to participate: one 20 year old man failed to attend four appointments and was never seen for follow-up.

The sampling scheme described in Chapter 2 produced three sampling groups: families with a member recorded on computer as having eczema (the computer group), families with a member aged below 2 (the under 2 group), and families included in the random cluster sample (the random group). Those in the fourth stage of the sampling procedure, which consisted of individuals who had denied the presence of an itchy rash, yielded no further cases and this group was therefore incorporated into the random group.

None of those approached refused to answer the questions pertaining to the diagnostic criteria, nor did any refuse to be examined. Nevertheless, over the subsequent 2 months, nine patients could not be recalled or preferred to drop out of the survey.

As mentioned previously, the population is primarily indiginous, and
therefore a language barrier was not anticipated. However a Japanese family who spoke very little English had two members with AD and would have proved a linguistic challenge for any investigator (Figure 3.1)

3.2 Results

The breakdown of the age distribution within the three groups described above is shown in Figure 3.2 and the composition of all families sampled is given in appendices 11-16. The contact rate was 93% for the computer group, 89% for the under 2 group, and 87% for the random group, and in total 2,365 subjects were sampled, 24% of the practice population.

The one year period prevalences of AD for the different age groups are shown in Table 3.1 and demonstrate a steady decline with increasing age. The overall prevalence age-standardised to the Scottish population for all age groups was 2.3%. Only 52% of patients with AD were aged between 2 and 15, leaving almost half of AD patients in the poorly studied groups below the age of 2 and over the age of 16. Thirty-eight per cent of all patients with AD were over 16. The one year period prevalence in this group was 1.2% dropping to 0.2% in the over 40's. The mathematical calculations involved in arriving at these results are detailed in Appendix 10 and the raw data are contained in Appendices 11-16.

The prevalences of active eczema are also displayed. While 66% of individuals below the age of 16 were in remission at the time of examination, only 47% of adults over 16 were in remission. Sixty-five per cent of patients diagnosed as having AD had active eczema at the time the diagnosis was made. The male predominance with a ratio to females of 1.5:1 among infants under 2, was reversed in older age groups.

3.3 Discussion

3.3.1 Methods

Community studies are ideal target populations in several respects. They represent a complete cross-section of society and are therefore unbiased if sampled correctly. However, they are laborious, time-consuming and at times demoralising. The intrinsic problems of contacting subjects is a
source of many frustrations.

The present study has some clear benefits. All patients were seen by, and the data collected and analysed by one investigator, a dermatologist in training. This eliminates the possibility of bias from non-specialist workers or variation in methods of data recording.

Further attributes of the design are that social class, age distribution and seasonal variation were all accounted for, and any bias arising from these sources should be minimal.

Two minor criticisms are that the population may not be entirely representative of the U.K. because the Livingston community is predominantly white, and it is semi-rural and cannot be compared directly to a city population.

The contact rates achieved in this study are very high for a population survey. Any bias in our estimates will be small and the results will stand comparison with any other population survey. As reported above, using our sampling scheme we identified 155 patients with AD from an estimated 225 in the whole practice, despite only seeing 24% of the practice population. Had we used a simple random sample of 24% we would have expected to identify only 56 patients with AD. This would have reduced the number available for the costing and quality of life parts of the study by two thirds, and detracted from the accuracy of these results.

The U.K. Working Party's diagnostic criteria proved ideal for use in a community setting. There were not thought to be any cases of AD that were missed by the criteria. Two adult patients who fulfilled the diagnostic criteria did not have AD; one had nickel dermatitis causing active eczema on her neck while the other was a man with pityriasis versicolor. Both these patients were excluded.

3.3.2 Infants

The one year period prevalence for infants under 2 was 9.8%. The epidemiology of AD in infants has been neglected possibly because, until now, there has been no reliable means of separating those with AD from other skin problems such as seborrheic eczema. Reports from New
Zealand of a lifetime incidence of 20.4% in the under 3's seem unrealistically high and suggest that the inclusion criteria used were not robust (Fergusson et al, 1981). Falk, using medical records in a retrospective study, did not separate infants and estimated the lifetime incidence of children aged 0-4 as 15% but the diagnosis was made retrospectively from medical records (Falk, 1993). These figures may be comparable with ours because the lifetime incidence will be higher than the 1 year period prevalence, but without a detailed knowledge of the natural history of AD a direct comparison is invalid.

3.3.3 Children

Measurement of AD frequency in children has been the aim of many research projects. Schoolchildren provide an accessible, well-defined and stable population that contains a large proportion of sufferers, and consequently, many researchers have focused on this age-group to the exclusion of others. Among the many recent studies, the most reliable are the twin studies from Denmark and a recent study from Sheffield, which cover the 2-11 year age groups (Schultz larsen et al, 1986; Schultz Larsen, 1993; Kay et al, 1994). Given the lower prevalence in Scotland compared with the rest of the U.K., and the differing methodology, these studies yield similar prevalences to ours and confirm the high prevalence in the 2-11 year age group.

Older children have proved much less popular as a target of concern but have a reported point prevalence of 3% in the 12-16 year age group and a detailed study from Finland has found a prevalence of 3% in 17 year olds (Larsson & Liden, 1980; Saarinen & Kajosaari, 1995). It appears from these data and our own that the prevalence of AD declines after the age of 12.

The sex ratios found in this study are at variance with previous reports (Table 1.6). They indicate that AD is more common in male infants in whom there is a M:F ratio of 1:0.6, while in the over 2s the ratio is reversed with an overall figure of 1:1.4. However, other published reports have been based on children rather than infants, and as such, our results for the over 2s correspond to previous reports.
Information on the prevalence of AD in adults is almost non-existent. The Lambeth study, now almost 20 years old, gave a prevalence of 12.5% for ages 35 to 54, suggesting that many conditions other than AD must have been included under the banner of 'eczema' (Rea et al, 1976). Norwegian Lapps have been studied throughout their age range (Falk, 1993). The results, however are inconsistent, possibly as a result of the methodology. The author used medical records to assess 'eczema ever', a method that may be suitable for examining children, but the lifetime medical records of adults are unlikely to be complete or accurate. For example, a lifetime incidence of 0.4% in the 50-59 year age group suggests that AD among children 50 years ago was very uncommon. This would be a dangerous assumption to make and casts doubt on the prevalence figures. The only other adult figures published in the USA used national health statistics and cannot be considered reliable data (Johnson & Roberts, 1978).

We have shown in this cross-sectional, community study that AD is most common in infants and becomes progressively less common in the older age groups until over the age of 40 when it becomes relatively uncommon. Other studies suggest a rising prevalence in children and if this shows a cohort effect it will be reflected in the adult population, resulting in a commensurate increase in the proportion of adults affected (Williams, 1992). Young adults with severe, disabling disease form an expanding proportion of the community. It is clear from the prevalence figures of active eczema in table 3.1 that an adult with AD is more likely to have active disease than a child which lends weight to the argument for further research focused on the many young adults with AD.

We are therefore left with no studies on AD in adults with sound methodology that can be compared with ours. The finding of 37% of AD sufferers are over the age of 16 and that the proportion of adults with active disease is higher than among children serves to emphasise the burden of disease in adults.
Table 3.1.
One year period prevalences with standard errors, point prevalence of visible eczema and sex ratio.

<table>
<thead>
<tr>
<th>Age</th>
<th>One Year Period Prevalence (Se)</th>
<th>Point Prevalence Of Visible Eczema</th>
<th>Sex Ratio (M:F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2</td>
<td>9.8% (0.5)</td>
<td>7.5%</td>
<td>1:0.6</td>
</tr>
<tr>
<td>2-11</td>
<td>8.1% (1.5)</td>
<td>2.5%</td>
<td>1:1.5</td>
</tr>
<tr>
<td>12-15</td>
<td>2.2% (0.8)</td>
<td>1.1%</td>
<td></td>
</tr>
<tr>
<td>16-24</td>
<td>2.1% (0.5)</td>
<td>1.3%</td>
<td>1:1.7</td>
</tr>
<tr>
<td>25-40</td>
<td>2.0% (0.7)</td>
<td>0.9%</td>
<td></td>
</tr>
<tr>
<td>over 40</td>
<td>0.2% (0.15)</td>
<td>0.1%</td>
<td>1:1.3</td>
</tr>
</tbody>
</table>
Figure 3.1

Japanese family, two of whom fulfilled the criteria for atopic dermatitis
Figure 3.2

Sampling groups

Numbers by age in each sampling group with those who could not be contacted in brackets. Group A represents the whole practice population. Group B is the group seen and sampled from those families containing a member with GP diagnosed eczema, and group C comprises the families of the under 2s who were examined. Group D includes those who were not sampled in groups B and C. Group E is a random cluster sample of group D. Boxes B, C and E represent individuals who were sampled.
CHAPTER 4.
FINANCIAL CONSIDERATIONS.

4.1 Results

One hundred and fifty five of those examined in the community fulfilled the diagnostic criteria for AD and were studied in detail: 103 from sampling stage 1, 38 from stage 2, 14 from stage 3. Sampling stage 4 produced no further cases. Of these the costing assessment was completed by 146 patients or parents: 19 subjects were aged less than 2, 58 aged 2-16 and 69 aged 16 and over.

Personal costs and Health Service costs are shown in Table 4.1, and the raw data are shown in Appendix 17. The skewed distribution of the costs illustrated in Figure 4.1 makes it difficult to quote summary statistics. Means are useful for extrapolations while medians are representative averages. The mean or median is quoted where appropriate. 58 lost working days and 17 lost school days were attributable to AD in this population of 146 patients over a 2 month period.

4.1.1 Personal costs

Over a 2 month period, the mean personal expenditure was £25.90 and the maximum spent was £546, the majority due to salary loss. Three patients spent over £300 and ten spent over £100. Some patients in remission had no expenditure attributable to AD, and this included 45% of those aged less than 16, compared with 26% of those over 16, a difference that was statistically significant ($X^2=7.47$, $P<0.01$). Expenditure in the under 2 group was significantly lower than that in the older age groups with a ceiling of £40. There was a difference between the 2-15 age group and over 16 age group (medians £0.50 and £6.73).

Prescriptions accounted for 7% of patient costs. Patients below the age of 16 are not required to pay prescription charges, and of the 69 aged over 16 years, only 28 paid for a prescription.
Treatments bought OTC comprised 21% of the total. These consisted mainly of emollients, bath additives, shampoo and evening primrose oil, and the percentage spent on these items by age is shown in Figure 4.2. Very little was spent by adults on bath additives and more was spent on shampoo compared with younger groups. There was no sex difference.

There was a substantial salary loss but the largest part of expenditure by patients was on clothing and laundry. Other expenses consisted of visits to the Royal Homeopathic Hospital, Glasgow by 2 children, herbalist advice to one adult and a visit to London for Chinese herbal treatment by one child and his mother.

4.1.2 Health Service Costs

The mean 2 month cost to the Health Service was £16.20 and the maximum attributable to one patient was £177.07. Ten patients cost the Health Service over £50 but only 2 cost over £100. The median cost in the 2-15 age group was significantly higher than that in the over 16 age group (£10.86 and £6.22) while that in the under 2 group had a median of £0.00, but this was not significantly different.

Treatments accounted for the largest part of health service costs: 38% were on emollients or bath additives, 32% were on topical steroids, 10% on bandages and the remaining 20% on antihistamines, shampoo, antibiotics and evening primrose oil.

Topical corticosteroids can be separated into four potency categories: very potent, potent, moderately potent and mildly potent. 89% of prescribed steroids were mildly potent or potent; 68% of that prescribed to adults were potent while 69% prescribed to the younger age group were mildly potent.

GP consultations accounted for almost 30% of costs, and hospital consultations comprised only 6% of costs.

4.1.3 Hospital costs

The 2 monthly mean cost to the Health Service of the more severely affected cohort attending the RIE was £415 (up to £1,500 for one patient), 63% of which was incurred by the hospital and 34% by the GP's. The
maximum personal cost was £1,225 (mean £325) over 2 months, 75% of which was due to loss of salary.

4.2 Extrapolation to the wider population

The information provided by the sampling scheme, detailed above, can be extrapolated to the whole practice population of approximately 225 AD patients. The estimated total annual cost of treating AD in this practice of 9,786 was £50,005; 58% was incurred by patients and 42% by the Health Service. An estimated 427 working days and 170 school days were lost annually.

Any projection to a wider population is subject to greater error, but if these results were representative of the whole country they would add up to a total annual expenditure in the U.K. of £297m, 58% of which would be borne personally by patients. The estimated annual cost to the Health Service would be £125m. If the cost to society of lost working days is included, the total cost in the U.K. is £465m, a per capita cost of £7.38 per annum.

4.3 Discussion

Several aspects of economic assessment are of central importance to clinicians. Knowledge of therapeutic cost-effectiveness must become an essential part of the national allocation of scarce resources, and may be used to identify areas where savings can be made (Detsky & Naglie, 1990; Evans, 1990; Robinson, 1993). Furthermore this knowledge should demonstrate the value of certain treatments which might appear to be expensive and inefficient. Any assessment of costs should include those borne by the Health Service, by the sufferers and their families, and any other costs borne by the rest of society (Robinson, 1993). This appears to be particularly important for patients with AD, and perhaps other dermatological disorders, as an estimated £297m per annum is borne by patients themselves.

Extrapolation of these data to the wider population of the U.K. should be interpreted cautiously, but the final estimate of the cost is likely to be an underestimate for the following reasons:-.
1. The prevalence of AD in Scotland is less than in the rest of the U.K. according to the 1970 National Child Development Study (Golding & Peters, 1987).

2. The general practitioners in the study practice are low prescribers (Scottish Prescribing Analysis, 1994).

3. None of the patients in the study population had required hospital treatment during the course of the study.

4. All patients lived within walking distance of the health centre, and this minimised travel costs.

5. The cost to society of time spent by carers looking after dependants is not included.

The data do, however, give some indication of the magnitude of the problem with an estimated national cost of £465m.

Chronic skin diseases differ from most other medical conditions when their costs are being assessed. A plethora of OTC preparations is available for problems ranging from acne to warts. Remedies for treating dry skin conditions like AD are particularly numerous, and vary greatly in their price. Articles in the media often advertise new expensive 'holistic' treatments that claim to cure eczema or psoriasis, but at a price. A further drain on patients' resources comes from the need for new clothing or bedding, and from the laundry costs which accounted for 45% of expense to patients in the whole study, and 63% of the costs to families with children aged less than 16. One ten year old boy, for example, needed new cotton sheets every 2 months, partly because of repeated washing, but also because nocturnal scratching led to extra wear and tear on the sheets.

Only a few attempts have been made to quantify the cost to the health service of medical treatments in the UK and direct comparisons are impossible due to differences in methodology and in spectrum of disease. The cost of treating venous ulceration has been estimated to be £400m, or £6.73 per head of population, a figure close to that for AD (Bosanquet, 1993). The total annual per capita cost of treating benign prostatic hypertrophy has been estimated at £1.04-£1.53 (Drummond et al, 1993).
The per capita cost of treating strokes, which usually require prolonged in-patient therapy, was recently estimated to be £18.78 annually in Scotland (Isard & Forbes, 1992). Accurate evaluation of the economic impact of AIDS has proved to be impossible (Postma et al, 1993). Few would have expected the economic burden of these systemic conditions so closely to resemble that of AD.

The financial impact of severe AD has considerable repercussions on sufferers. Adults with AD have to pay for prescriptions and are further saddled by loss of salary and high clothing and laundry expenses. We have shown that an individual attending hospital can spend as much as £1,225 (mean £325) over a 2 month period; the financial burden is clearly heavy.

The continuing rise in the cost of providing health care calls for a more rigorous examination of clinical effectiveness. When treatment outcomes are shown to be similar, cost effectiveness becomes a central variable in drawing conclusions about clinical practice. Costing is important to help clinicians make rational decisions about resource allocation, and it is therefore important that clinicians have an understanding of the significance of costing and the methods involved in calculating these costs.
Table 4.1.
Mean annual costs of treating AD.

<table>
<thead>
<tr>
<th></th>
<th>Under 2</th>
<th>Cost to patient (% age)</th>
<th>Over 16</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Treatments-prescriptions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-OTC preparations</td>
<td>£1.60</td>
<td>£9.90</td>
<td>£19.50</td>
<td>£31</td>
</tr>
<tr>
<td>2. GP consultations</td>
<td>£0.06</td>
<td>£0.04</td>
<td>£0.15</td>
<td>£0.25</td>
</tr>
<tr>
<td>3. Hospital consultations</td>
<td>£0.24</td>
<td>£11.28</td>
<td>£0.48</td>
<td>£12</td>
</tr>
<tr>
<td>5. Salary loss</td>
<td>£0.92</td>
<td>£22.08</td>
<td>£23</td>
<td></td>
</tr>
<tr>
<td>6. Clothing/laundry</td>
<td>£3.50</td>
<td>£45.50</td>
<td>£21.00</td>
<td>£70</td>
</tr>
<tr>
<td>7. Other expenses</td>
<td>£1.20</td>
<td>£4.80</td>
<td>£6</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>£5.40</td>
<td>£68.84</td>
<td>£79.01</td>
<td>£153</td>
</tr>
</tbody>
</table>

Table 4.2.
Annual per capita cost of treating AD compared with other medical conditions

<table>
<thead>
<tr>
<th></th>
<th>UK</th>
<th>Atopic eczema (this study) £7.83</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Venous ulceration £6.73</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Stroke in Scotland £18.78</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Benign prostatic hypertrophy £1.04-£1.53</td>
<td></td>
</tr>
</tbody>
</table>
Figure 4.1
Expenditure by Patients and NHS in 2 months
Figure 4.2

Percentage spent by patients broken down by age, on topical OTC treatments

![Bar chart showing percentage spent by age groups on different products.](image-url)
CHAPTER 5
QUALITY OF LIFE IN ATOPIC DERMATITIS

5.1 Methods in practice

Both the DLQI and PGI were interviewer administered. It generally took no longer than 5 minutes to complete both questionnaires.

After several individuals had completed the PGI, a list of core areas or activities most commonly cited could be used as a prompt for subsequent patients. There is a stark contrast between the approaches of the DLQI and the PGI to the measurement of quality of life. The essential difference is that the DLQI is a rigid questionnaire consisting of 10 fixed items while the PGI is generated by the respondents who select the items they believe are most important and these will vary between patients with the same skin disease according to their circumstances.

5.2 Results

Of the 155 patients identified with AD, 146 completed the quality of life part of the survey. This included 56 adults on whom most data were collected. The raw data are shown in Appendices 18 and 19.

5.2.1 Dermatology Life Quality Index

The DLQI scores varied from 0-27 out of a possible maximum of 30, but only 2 patients scored over 15, the mid-point in the scale (Figure 5.1). This distribution reflects the range of severity of AD in the community, most patients having a low score and only a few with severe AD having high scores. The mean scores for individual questions are shown in Table 5.1. Question 1, which asked about symptoms of itch, pain and stinging, yielded the highest score of any individual question, followed by Questions 2 and 4, which deal with embarrassment and clothing.
The results of the one-year DLQI were compared with those of the standard DLQI using a paired Wilcoxon Test. The one-year questionnaire yielded significantly higher scores than the standard DLQI (P<0.001).

5.2.2 Patient Generated Index

The total scores were distributed inversely to the DLQI, over the whole range of 0-100. The eighteen areas or activities, cited by patients in the PGI as being influenced by their AD, are shown in Table 5.2. The first 10 items listed, correspond to the ten questions of the DLQI but several other activities, particularly sleep and swimming, were cited often and are clearly relevant to AD patients.

5.2.3 Children

The questionnaire used for children is shown in Appendix 9. There were 47 children aged 5-15. Two were withdrawn by their parents with no reason being given, and a further six could not be interviewed with their parents during the study period. Some were too young to understand the questions. That left 39 children, three of whom were unable to complete Section A. Sections B and C were all completed by parents of all 39 patients, Section B referring to the child's disease and Section C referring to the effect on the family.

The median score in Section A was 3 while that in Section B was 5 and that difference was significant using the paired Wilcoxon summed rank test. The median for Section C was 2 with a possible total of 39.

Eleven parents responded to the PGI about the way their lives were affected by their children's AD. The most frequently cited effect was sleep, followed by necessity for nagging about applying topical treatments and the inconvenience of regular treatment. The median score was 60 with a range of 0-95.

5.2.4 Validation of the DLQI with the PGI

The correlation between results from the DLQI and PGI was -0.52 (P<0.001). The value is negative because low scores in the PGI and high scores in the DLQI represent poor quality of life and this significant value means there is a strong relationship between the two. However the value
is not so high as to suggest that the PGI and DLQI have identical properties.

A definite pattern emerged on the scattergram displayed on Figure 5.2. The PGI scores (median 38.5) are spread more evenly over the complete range than the DLQI scores (median 5.5); in the latter, only two individuals yielded scores of over 15, the mid-point of the scale. Nevertheless one might expect those with low scores in the DLQI to have high scores in the PGI. In fact many scored low on both measures, and this suggests that the apparently poor life quality registered by the PGI is not reflected consistently by the DLQI.

Correlations between scores in the PGI and scores in individual questions of the DLQI are shown in Table 5.1, and indicate that the PGI correlates with Questions 1-5 of the DLQI, with significance levels shown. In questions 2-5 of the DLQI the PGI scores of patients who scored 0 were significantly greater than those who scored 1-3. In questions 1 and 9, numbers precluded the test from being carried out, and in the remaining questions there was no significant difference (Table 5.3).

In the light of these results, a 'mini-DLQI' was constructed using only questions that showed a significant correlation with the PGI, questions 1-5, yielding a possible total score of 0-15. Results from this 'mini-DLQI' were also significantly correlated with the PGI (r=-0.57, P<0.001) and the scattergram with those from the PGI is shown in Figure 5.3.

Thirty six individuals mentioned areas or activities that were not part of the DLQI, while 20 patients identified only areas included in the DLQI. The correlation coefficients for these groups with the PGI were -0.41 and -0.58 respectively, both of which were significant (P<0.01).

The data evaluating the economic burden of AD patients and on the health service are detailed in Chapter 4. The DLQI was significantly correlated with total cost (r=-0.34, P<0.01) but the PGI was not (r=-0.23, NS). Health service costs alone were significantly correlated with both the DLQI (r=-0.47, P<0.001) and the PGI (r=-0.36, P<0.01), but the patient costs did not correlate significantly with either.
5.3 Discussion

The DLQI has been validated in general dermatology patients, but not specifically in those with AD. In one sense, therefore, it is a suitable criterion of validity against which an untried quality of life measure like the PGI can be assessed (Streiner & Norman, 1990). Patients' PGI scores correlated moderately well with their overall DLQI scores. In addition, those features measured by the DLQI which one would expect to have the greatest impact on perceived quality of life - itch, embarrassment, choice of clothes, social life - had the highest correlations with the PGI. This strongly supports the validity of the PGI as a quality of life measure in dermatology.

Perhaps more important were a number of areas mentioned in responses to the PGI which may be highly relevant to AD, such as sleep and swimming, but which are not included in the DLQI. Conversely, the DLQI includes questions unlikely to be of great relevance to patients with mild to moderate AD. This is borne out by the low mean scores for four of the DLQI questions, their poor correlation with the PGI, and the higher correlation of the 'mini-DLQI' with the PGI.

Results from the two groups of patients (outlined in the methods section), one quoting only areas contained within the DLQI, and the other quoting areas outwith the DLQI, both showed significant correlation with the PGI, although the latter group showed a lower correlation. This suggests that some areas included in the DLQI are not necessary for assessing disability in AD, and others not included in the DLQI are important to AD patients. These results are echoed by the distribution of DLQI and PGI scores on Figure 5.2: the five questions in the DLQI that correlated with the PGI can contribute a score ranging from 0-15 which, with the exception of two individuals, was the range of scores achieved on the DLQI (Figure 5.3). In contrast, the PGI scores were more widely spread throughout the range of 0-100, which perhaps implies that the PGI is a more meaningful and relevant interpretation of life quality for patients with AD in the community in the context of patients' daily lives.

The WHO has published a model of disability based on three elements. These are: loss or abnormality- i.e. impairment; its consequence on
performance of an activity—i.e. disability; and the disadvantage in fulfilment of a role—i.e. handicap. In a sense these form a spectrum ranging from impairment to handicap, from the objective to the subjective, and from the functional to the social (WHO, 1980; Ebrahim, 1990). Impairment can be measured purely on clinical or laboratory criteria, but handicap must be assessed by the patient. The DLQI and PGI, because of their nature are measuring health and quality of life at different parts of this spectrum. The DLQI concentrates on features that include physical symptoms and so is placed closer to 'impairment'. On the other hand the PGI is a subjective valuation, initiated by the patient, and is therefore closer to 'handicap'. This is reflected by the results of the validation with cost as an objective measure of impairment: the DLQI correlates more highly with it than the PGI. It may also be true that the DLQI is more responsive to small, but clinically significant changes in health or health-related quality of life, which makes it more suitable for routine use, especially if self-administered. However a more concise, user-friendly version of the PGI has been developed, and if fully validated in the dermatological setting, may be a good measure of handicap (Cotton et al, 1995).

What are the implications here for clinicians assessing the value of treatment for patients with AD? It must be remembered first that our patients were selected from a community population, and in general had less severe disease than in a hospital-based sample. However, the DLQI is not a specific measure of quality of life in these patients. Certain questions could be discarded, or replaced with questions about sleep, contact with animals etc., to produce a more valid, condition-specific instrument. In contrast, the individualistic, patient-centred PGI is a measure with considerable pertinence for patients with AD.

If the PGI is to be recommended to evaluate treatments for AD, further research is required to assess its responsiveness to changes in perceived health or quality of life over time. The numerous skin conditions cause a wide variety of changes in patient's lives. As an open-ended questionnaire, the PGI may be suitable for use over a range of dermatological conditions, but it must also be shown to be reliable, and adaptable.
The conclusions one can draw from the children's quality of life results are limited. Validity cannot be tested on one questionnaire, but it is interesting to observe the difference between parts A and B that children score their disease higher than their parents. The implication is that parents' perception of the effect on their childrens' lives is greater than the child's perception. Perhaps children grow up with AD being such an intrinsic part of their lives that it becomes 'normal'. The parents, however, appreciate the abnormality of their child's skin.

The effect of a child's disease on the family has always been recognised. The PGI singled out sleep loss and the psychological stress of constant reminding about topical treatments as being the worst aspects of having a child with AD. This topic clearly deserves to be the focus of further research.
Table 5.1.
The correlation between the PGI and individual questions of the DLQI.

<table>
<thead>
<tr>
<th>Question No. in DLQI</th>
<th>Mean score</th>
<th>Correlation with PGI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.7</td>
<td>-0.36 *</td>
</tr>
<tr>
<td>2</td>
<td>1.1</td>
<td>-0.51 **</td>
</tr>
<tr>
<td>3</td>
<td>0.5</td>
<td>-0.39 *</td>
</tr>
<tr>
<td>4</td>
<td>0.86</td>
<td>-0.42 **</td>
</tr>
<tr>
<td>5</td>
<td>0.41</td>
<td>-0.40 *</td>
</tr>
<tr>
<td>6</td>
<td>0.32</td>
<td>-0.27</td>
</tr>
<tr>
<td>7</td>
<td>0.64</td>
<td>-0.20</td>
</tr>
<tr>
<td>8</td>
<td>0.27</td>
<td>-0.19</td>
</tr>
<tr>
<td>9</td>
<td>0.05</td>
<td>-0.13</td>
</tr>
<tr>
<td>10</td>
<td>0.48</td>
<td>-0.32</td>
</tr>
</tbody>
</table>

* P<0.01
** P<0.001
Table 5.2.
Areas or activities cited in the PGI as being influenced by the patients' AD.

<table>
<thead>
<tr>
<th>Area or activity</th>
<th>No. of citations (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DLQI1</td>
<td>0</td>
</tr>
<tr>
<td>DLQI2 - Embarrassment</td>
<td>15 (27%)</td>
</tr>
<tr>
<td>DLQI3 - Home and garden</td>
<td>25 (45%)</td>
</tr>
<tr>
<td>DLQI4 - Clothes</td>
<td>7 (13%)</td>
</tr>
<tr>
<td>DLQI5 - Social &amp; leisure</td>
<td>4 (7%)</td>
</tr>
<tr>
<td>DLQI6 - Sport</td>
<td>7 (13%)</td>
</tr>
<tr>
<td>DLQI7 - Work</td>
<td>19 (34%)</td>
</tr>
<tr>
<td>DLQI8 - Relationships</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>DLQI9 - Sexual</td>
<td>0</td>
</tr>
<tr>
<td>DLQI10 - Treatments</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Swimming</td>
<td>18 (32%)</td>
</tr>
<tr>
<td>Sleep</td>
<td>15 (27%)</td>
</tr>
<tr>
<td>Pets</td>
<td>7 (13%)</td>
</tr>
<tr>
<td>Washing/bathing</td>
<td>6 (11%)</td>
</tr>
<tr>
<td>Warm weather</td>
<td>3 (5%)</td>
</tr>
<tr>
<td>Cold weather</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Scratching causing embarrassment</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Rubber products</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Make-up</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Dust</td>
<td>1 (2%)</td>
</tr>
</tbody>
</table>
Table 5.3.
Comparison of PGI scores, using a t-test, between those who scored 0 and those who scored 1-3 in individual questions of the DLQI.

<table>
<thead>
<tr>
<th>DLQI Score</th>
<th>No of patients</th>
<th>Mean PGI score and significance level</th>
</tr>
</thead>
<tbody>
<tr>
<td>DLQI1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>1-3</td>
<td>54</td>
</tr>
<tr>
<td>DLQI2</td>
<td>0</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>1-3</td>
<td>36</td>
</tr>
<tr>
<td>DLQI3</td>
<td>0</td>
<td>37</td>
</tr>
<tr>
<td></td>
<td>1-3</td>
<td>19</td>
</tr>
<tr>
<td>DLQI4</td>
<td>0</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>1-3</td>
<td>25</td>
</tr>
<tr>
<td>DLQI5</td>
<td>0</td>
<td>38</td>
</tr>
<tr>
<td></td>
<td>1-3</td>
<td>18</td>
</tr>
<tr>
<td>DLQI6</td>
<td>0</td>
<td>45</td>
</tr>
<tr>
<td></td>
<td>1-3</td>
<td>11</td>
</tr>
<tr>
<td>DLQI7</td>
<td>0</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>1-3</td>
<td>25</td>
</tr>
<tr>
<td>DLQI8</td>
<td>0</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>1-3</td>
<td>38</td>
</tr>
<tr>
<td>DLQI9</td>
<td>0</td>
<td>55</td>
</tr>
<tr>
<td></td>
<td>1-3</td>
<td>1</td>
</tr>
<tr>
<td>DLQI10</td>
<td>0</td>
<td>38</td>
</tr>
<tr>
<td></td>
<td>1-3</td>
<td>18</td>
</tr>
</tbody>
</table>

NS = not significant
Figure 5.1
DLQI scores for adults
Figure 5.2
Scattergram of DLQI vs PGI
Figure 5.3

Scattergram of mini-DLQI vs PGI

![Scattergram of mini-DLQI vs PGI](image)
6.1 The Prevalence of Atopic Dermatitis

6.1.1 The place of epidemiology in atopic dermatitis research

AD research is advancing on many fronts. These range from genetics and molecular biology at one end of the spectrum to epidemiology at the other. Genetic studies indicate that atopic diseases run true to type within families: those whose relatives have AD, for instance, are more likely to have AD (Diepgen & Fartasch, 1992; Dold et al, 1992). Atopic diseases are also more likely to be inherited from maternal atopy than paternal atopy whichever atopic disease is implicated (Ruiz et al, 1992; Savin, 1993). Genetic linkage of atopic IgE responses to chromosome 11q13 was first proposed in 1989 and has since been confirmed by other workers (Cookson et al, 1989; Young et al, 1992; Collee et al, 1993; Shirakawa et al, 1994a). Examination of polymorphisms of the chain gene of the high affinity receptor for IgE are associated with atopy and, when inherited maternally, identifies a risk factor for atopy (Sandford et al, 1993; Shirakawa et al, 1994b; Hill et al, 1995).

Immunocytochemistry has given us the tool to separate two T helper cell subsets, TH1 and TH2, on the basis of their cytokine production (Zachary et al, 1985; Mosmann & Coffman, 1989; Sowden et al, 1992). Active disease in patients with severe AD is associated with activation of lymphocytes that are predominantly TH2. There is now evidence that abnormalities in monocytes and Langerhans cells alter the function of T cells to influence the immunological defects associated with AD (Hanifin & Chan, 1995).

In parallel with this revolution in the genetics and immunology of AD, progress in epidemiology has continued (Schmied & Saurat, 1991). New methods like immunocytochemistry have their counterparts in epidemiology. Researchers have struggled with serum IgE and other invasive diagnostic tests (Hanifin & Rajka, 1980). However the whole concept of AD being an allergic disease has been thrown into disarray by a
literature review that analysed thoroughly the evidence for and against a role for IgE mediated hypersensitivity reactions in AD (Halbert et al, 1995). The conclusion was that allergy may be an aggravating factor in some patients, but is not central to the pathogenesis of AD. It should occasion little surprise that serum IgE has proved to be unnecessary for diagnosing AD and has been found to be significant in only 20% of patients with AD (Svensson & Mansson, 1985). The U.K. Working Party's diagnostic criteria are non-invasive and have paved the way for community studies that can now have consistent methods of diagnosis and this will reduce sources of error in estimates of prevalence. They have opened the way for uniformity in community studies.

New discoveries are helping to elucidate the aetiology. Research has shown a difference in the prevalence of AD between East and West Berlin which narrowed after the Wall was destroyed (Diepgen, 1995). Prevalences differ between urban and rural communities (Lynch et al, 1984) and between different ethnic groups in the same environment (Williams, 1995b). The further epidemiological work required to pinpoint the reasons for these differences promises to provide major advances in our understanding of AD.

6.1.2 Prevalence data in perspective

The community studies of AD were listed in chronological order in Chapter 1. The number of prevalence studies in the last decade has grown but there has been no attempt to introduce uniformity of design. The impression is of haphazard planning with very little consideration of the best methods to use. It is only by applying consistent methodology, similar age groups, diagnostic tools and measures of frequency that populations can be compared with a reasonable degree of certainty. There seems little point in publishing successive reports of prevalence of AD without improving and standardising methods.

For purposes of comparison with the LADS the best recent prevalence studies in the U.K. have been those from Birmingham and Aberdeen (Kay et al, 1994; Ninan & Russell, 1992).

The first of these examined a general practice of 13,314 on the outskirts of Birmingham. The parents of all children aged 3-11 were sent a letter
asking if they would like to participate in a health survey. This produced an excellent response rate of 97.6%. An interview was conducted by one of the GPs, referring to the case notes to determine the one-year period prevalence and lifetime incidence. Social class, ear-piercing and associated asthma were also recorded.

AD was defined as "an itchy, often relapsing and lichenified dermatitis that tends to affect the face and limbs in infants and also the popliteal fossae in children 18 months and over". This is the first major shortcoming of this report. Every aspect of this definition is vague, and with words like 'often' and 'tends to', the possibility of misclassification is enormous. There is no clear demarcation to discriminate 'cases' from 'non-cases' of AD.

Kay and colleagues quoted one-year period prevalences and lifetime incidences. The former are less liable to variation due to memory distortion. Not only might a parent have forgotten mild AD during a child's infancy but other diseases might have been interpreted as AD. Memory plays a small part in the estimation of the one-year period prevalence which is consequently more reliable. However, they state the following: "Although we have presented the age structure of our population, in most other studies it is not known, and hence a true comparison on the basis of age adjusted prevalence rates is not possible". The age structure of a population is unnecessary for comparison if age-specific rates are known, as long as the age structure of the population under study is known. To rephrase this, if the prevalence of a disease at every age is known, it is possible to calculate the prevalence of a new population of known age structure. This is the attraction of an age-specific one-year period prevalence.

In the Aberdeen study 3,942 children aged 8-13 were targeted (Ninan & Russell, 1992). Questionnaires were sent to parents and replies were received from 85.3%. However the questions used and the details of diagnostic methods were not published.

The measure of frequency quoted is not discussed but is likely to be point prevalence, and is reported to be 12.0% with M:F ratio of 1.6:1. Unfortunately not enough information is given to allow a detailed
assessment. It can only be assumed that if the information was not recorded then it was not carefully considered.

Work from Scandinavia which traditionally has contributed much to the literature on AD and where the prevalence is reportedly high, is worth considering. Falk attempted to calculate prevalence figures for atopic disease at all ages (Falk, 1993) but the ten line methods section contains very little detail rendering analysis of the methodology impossible.

A twin study from Denmark concentrated on the 0-7 group (Schultz Larsen, 1993). Even this respected study used empirical criteria that had not been tested or validated. It also depended on a mailed questionnaire, and parents' positive responses from a brief description of AD in an accompanying letter before subjects were finally seen by a dermatologist. Twins were categorised according to year of birth. There was no significant increase found in the groups born during the years 1970-1974 and 1975-1979 and the cumulative incidence aged 0-7 was 11.5%. The comparison of the prevalences of these groups is valid because similar methods were used, but as a guide to the prevalence in the community, the results are less valuable.

The design of the LADS has clear advantages over these studies in terms of the definition of AD and confirmation of diagnosis. In the LADS one investigator, a dermatologist, saw all subjects and followed a strict protocol. The methods allow for seasonal variation (not mentioned in any of the above reports) and were designed to estimate the prevalence at all ages. This community study has advanced knowledge of the prevalence of AD and should help to promote a standard approach for future researchers.

6.1.3 Suggestions for the future

Prevalence studies should conform to certain basic requirements:

1. Methodological details should be described in full.

2. At present there is only one set of diagnostic criteria that has been validated and is suitable for use in a community setting, the U.K. Working Party's Diagnostic Criteria for AD. Until an equivalent or
better set of criteria is available these should be used in future population surveys.

3. The age-specific one-year period prevalence estimates are free from the problems of memory distortion, smooth out seasonal variation and, no matter what age is studied, allow computation of age-adjusted prevalences.

Two areas should be developed. As patients age, the classical flexural pattern might change and the features necessary to confirm a diagnosis of AD may differ from those in childhood. There is also a group of patients who, with no previous history of AD, first present in later life with a generalised pattern that is often labelled as AD. A clinical and immunological study of adults is necessary to clarify this.

6.2 The economics of atopic dermatitis

6.2.1 Costing in today's health service

Priorities in today's health service are changing. Rising costs have prompted decision makers to identify ways of streamlining efficiency and to put them into practice directly. In 1995-96 purchasers have been asked to increase investment in at least two interventions that are known to be effective and to reduce investment in at least two interventions that evidence suggests are ineffective (Hayward, 1994; NHS Executive, 1994). Directives like these create a climate of urgency to reduce costs and to choose areas of intervention where savings can be made. It does not eliminate choice but expensive treatments can only be justified if they are shown to be more cost-effective than existing therapies, thus introducing the concept of efficiency (Freemantle et al, 1995).

From these pressures there arise a demand for data to show that clinicians' interventions are evidence-based (Smith, 1994). There is a wealth of research in all areas of medicine but it is a cause of concern that the information it contains has failed to influence clinical practice (Haines & Jones, 1994). The root cause of this failure of translation to clinical practice may be a failure of training at medical school in scientific
methods and critical appraisal of medical research but it has led to a recognition of the need for systematic review of existing data.

One project established in 1992 to address this problem is the Cochrane Collaboration (Godlee, 1994). Its principal objective is to amass available evidence from randomised controlled trials to produce guidelines for the best treatment options from published articles. Using systematic review and meta-analysis the information generated is distributed to practitioners for implementation in clinical practice.

Showing efficacy alone is not sufficient. Clinical interventions must also be shown to be effective in terms of cost, outcome and acceptability to society (Department of Health, 1994; Robinson, 1993b). Cost-effectiveness evaluation and a knowledge of economic analyses should be within the grasp of all clinicians. Outcome measures are also important for evaluating effectiveness. Traditional outcome measures are often related to lives saved or life years gained, which may be appropriate when dealing with surgical procedures or the management of myocardial infarction but are not suitable in the domain of dermatology. Other ways of spotlighting skin disease must be found. Two approaches are to count the cost-of-illness (Rice, 1994) and to assess the impact of the disease on the patient by measuring quality of life, both of which form the core of data collected in the LADS.

6.2.2 Evidence of cost of atopic dermatitis

It is surprising that, until now, the assessment of cost of AD has been ignored by dermatologists in this country. AD is known to be common and, by nature, it provokes individuals into spending large sums on OTC preparations. Skin disease is almost unique in this respect.

Beauty is only skin deep: by implication, beauty is dependant on attractive skin. A whole industry thrives on this concept and patients strive to conform to the society's ideal of 'a perfect complexion', displayed on the cover of every woman's magazine. This tempts individuals to buy expensive cosmetics where cheaper alternatives may be equally good. In the assessment of the economic burden of skin disease this factor must be accounted for and the personal cost to patients must be included (Robinson, 1993a).
Treatments are not the only drain on resources. The nature of AD leads to high laundry bills. Blood and secretions cause soiling of sheets and clothes resulting in high laundry expenses. Clothing wears out more quickly and this results in a total estimated annual expenditure by patients of £172m. Why, therefore, has the issue of patient costs never been addressed?

A central organisation in the debate about costs is the National Eczema Society (NES) which is a high profile support group for AD sufferers. In 1993 the NES entered into discussion with other dermatological patient support groups: the Acne Support Group, Dystrophic Epidermolysis Bullosa Research Association, Melanoma network and the Vitiligo Society. This led to the establishment of the Skin Care Campaign (SCC) which began in February 1994, to gather data to heighten awareness of skin disease. The stated objectives of the group are

1. To raise awareness about the importance of skin.
2. To educate the general public and opinion formers.
3. To establish the cost of skin disorders to employers, the health service and the community.
4. To promote the need for more and improved resources for treating skin disorders.

One of its successes has been to encourage the foundation of an All Party Parliamentary Group (APPG) of interested members of parliament and peers. The inaugural meeting was in April 1994 and, during its first year, under the chairmanship of David Congdon MP, it had six meetings with an average attendance of 50 per meeting, one of the best for an all party group. The first meeting concentrated on school education about skin cancer, a common and emotive skin disorder that appeals to the media.

A current inquiry of the APPG is entitled "an investigation into the adequacy of service provision and treatments for patients with skin diseases in the U.K.". It has planned three oral evidence sessions to gather information that is relevant to their areas of interest.
Cost is a central issue to both the APPG and SCC. The data generated by the LADS should provide invaluable information for campaigns such as these and can now be used as part of the evidence required by both groups.

The National Eczema Society has also recently highlighted another problem that patients with severe AD encounter. Individuals with skin disease can be so severely affected that they are unable to work or carry out everyday household tasks yet there have been problems gaining a Disability Living Allowance. It is only by bringing results of studies such as this one into the public arena that skin disease will be given priority in the health service.

6.2.3 Progress in the costing issue

The results presented in Chapter 4 are unexpectedly high and bound to attract publicity. It is the first study that counts the personal cost to patients as a direct result of AD. The momentum should not be lost and further studies extending these results are necessary.

A large study in Nottingham is looking at AD in the under 5's in four general practices. One of the aims of this survey is to assess the cost to patients and the health service in a way similar to that in the LADS. Although it is restricted to a narrow age band, it should provide accurate figures that can be compared with those from our study. Another study based at the Royal London Hospital is looking at children with AD. The investigators have planned to use the same proforma as in the LADS but at present it is only at the planning stage.

Our survey is primarily community based. It would be possible to obtain more reliable figures for those attending hospital by studying a larger number of hospital patients over a prolonged period. This could include measures of severity and take account of repeated attendances at the Day Treatment Centre and admissions to hospital by individual patients, instead of simply including the most severe patients, at times of exacerbation of their disease, as we have done. Such a study could include all those attending hospital whether or not they are admitted for treatment at the Day Treatment Centre or in the ward. This would provide a different type of data, equally valuable for publicising the burden of skin disease.
Costs may be used as a measure of impairment during treatment and can be calculated in a standard acceptable manner (Hall & Mooney, 1990). Do costs reduce when patients skin condition improves? Further work on the relationship between severity, cost and quality of life would also be illuminating.

6.3 Quality of life

As implied previously the issues of cost and quality of life are closely related. They can both be used as a barometer of the impact of AD. The SCC aims to bring skin diseases closer to the public consciousness and includes a strong emphasis on both these areas. To strengthen the case it is vital to have a database of reliable statistics.

6.3.1 Implications of results

The results generated by the LADS have quantified the disability experienced by AD patients in the community. Both the DLQI and the PGI indicated a range of disability and imply that many patients in the community who seldom see their own doctor, have a significant degree of quality of life impairment. Equally the effect of children with AD on parents and the family has been shown by our assessment of life quality in children and parents.

The most important areas affecting sufferers were work in the home, effect on employment, swimming, embarrassment and loss of sleep. These are vitally important to individuals' well-being and will therefore affect the way they function at home and in society at large. In the WHO model of disability ranging from 'impairment' to 'handicap', these factors are all at the 'handicap' end of the spectrum: the only way of identifying these sources of handicap is to question sufferers using sound, well-validated questionnaires. The ideal questionnaire should be suitable for comparison with other conditions to focus on the importance of skin diseases to patients.

The DLQI was published as recently as 1994, but it has already been embraced as the standard quality of life measure in dermatological practice. At the meeting of the British Association of Dermatologists in
1995, three poster presentations used the DLQI to assess the quality of life in patients with Acne, Darier's disease and Bechet's disease (Mallon et al., 1995; Harris et al., 1995; Blackford et al., 1995), conditions in which it has not been validated and which had few representatives in the original patients on whom the DLQI was based. Yet even in AD, one of the most common skin diseases, we have shown it to have deficiencies. There is a danger that the measurement of quality of life in dermatology will fall into disrepute because inappropriate questionnaires are being used. Skin diseases are diverse and cause a spectrum of disability that may not be captured by a ten-item questionnaire. There are two possible solutions. One is to use a measure that contains a sufficiently large number of questions to cover all possible areas of disability. Such a questionnaire would be cumbersome and unsuitable for everyday clinical practice. The alternative is to use a quality of life measure that is flexible and allows the patients to choose the areas or activities of their lives that are predominantly affected. The PGI would satisfy this condition.

The PGI has not previously been used to assess dermatological conditions. When the science of quality of life measurement was first developed, it was not distinguished from health status measures. Quality of life was initially promoted as a measure of outcome in 1986, as an alternative to more traditional end points like death or myocardial infarction (Croog et al., 1986). However, this early attempt to assess quality of life included physical, cognitive, emotional and social function and would be better considered a measure of health status. Quality of life should be a uniquely personal perception of the way an individual reacts to their health status (Gill, 1995). A review of 75 quality of life articles found the majority deficient in several ways: they did not define quality of life; they did not identify the specific areas of life on which they intended to focus; and did not aggregate their results into a composite score (Gill & Feinstein, 1994). The PGI was given special mention, along with two other articles, for "showing promise" (Ruta et al., 1994; O'Boyle et al., 1992; Joyce, 1994). Three attributes were suggested that a quality of life measure should possess, based on the hypothesis that quality of life comprises many different characteristics that are the province of the individual. First, patients should identify the areas that are important to them.
Second, the severity should be rated. Third, patients should be invited to rate the relative importance of these items to their quality of life.

The PGI fulfils all these requirements. It is gaining wider acceptance and has been shown in this study to encompass the areas that are important to patients with AD in the general population and a new user-friendly version of the PGI now exists (Cotton et al, 1995). When measuring handicap rather than impairment it also has an advantage over the DLQI. There are techniques of measuring severity, for example, in AD and psoriasis (European Task Force on Atopic Dermatitis, 1993; Fredriksson & Pettersson, 1978) and these are one indication of impairment, but it is measures of handicap that are necessary for raising the profile of dermatology.

Death is often used as the yardstick in other branches of medicine, but this is inappropriate in dermatology where many diseases cause severe morbidity but not mortality. For assimilating the consequence of skin disease on the population as a whole the area of quality of life assessment needs to be expanded.

6.3.2 Advances since the Lothian Atopic Dermatitis Study began

Unlike the counting of cost, quality of life assessment is developing rapidly. Inevitably since planning the LADS there have been some advances. One article, describing a survey of 11,500 members of the National Eczema Society, yielded a response rate of 29% (Long et al, 1993). The results contained in this paper may be biased on two accounts: the population may not have been representative of all patients with AD, and the response rate was low. They did however confirm the important effect on work, household activities and personal relationships and a survey of parents of children with AD demonstrated that sleep loss was the most important area.

A follow-up study one year later targeting individuals with severe AD, generated some interesting data (Finlay, 1994). The DLQI scores were high. There was an average of £5,000 lost income and five lost working days per annum. Subjects were given a brief description of bronchitis and asked whether they considered it to be worse than AD: the majority would rather have had AD. However, the few individuals who had both
AD and bronchitis felt that AD was worse. 50% were willing to spend 2 hours per day on treatment to make their skin normal, and 70% would spend one hour. Half would pay £10,000 for a cure and 75% would pay £1,000, but when these results were corrected for income, patients were prepared to pay up to 75% of their annual income for a cure.

A similar survey of patients with severe psoriasis included larger numbers (Finlay & Coles, 1995). When compared with diabetes, asthma and bronchitis, 46%, 42% and 32% thought that psoriasis would be worse, but among those who had these conditions the percentages change to 87%, 80% and 77%.

At present prevalence studies are generally restricted to children while quality of life studies relate to adults. This may be convenient for research workers but is illogical. The former need more community studies of the whole cross-section of the population. Children's quality of life assessment is difficult, but there is now a Children's Dermatology Life Quality Index that allows an entry into the world of disability measurement in children (Lewis-Jones & Finlay, 1995).

6.3.3 The future

Further data on the morbidity of skin disease are needed urgently. The PGI has provided a new and exciting avenue down which to proceed in the pursuit of the ideal quality of life index. In the light of the results of the LADS, we have designed a study to extend the use of the PGI to other common skin disorders. Measures of severity will be included to validate it fully as a measure of quality of life in a hospital-based population.

Measures of disability are required to assess new treatments or compare existing treatments from the patient's perspective. Cyclosporin treatment has been shown to improve quality of life, and in-patient has been shown to be superior to out-patient treatment when patients' quality of life is measured (Salek et al, 1993; Kurwa & Finlay, 1995). Treatment comparisons have also been incorporated into our new study. If the PGI performs as well in a hospital population as it has done in a general practice then it may provide the quality of life measure we need, that is sufficiently flexible for use across the range of skin conditions, sufficiently
user-friendly for routine clinical use, and may give us a method of comparing skin diseases with other medical conditions.


Coca AF, Cooke RA. (1923) On the classification of the phenomena of hypersensitiveness. *Journal of Immunology*, 8, 163-82.


Halpern SR, Sellars WA, Johnson RB, Anderson DW, Saperstein S, Reisch JS. (1973) Development of childhood allergy in infants fed breast, soy or cow milk. *Journal of Allergy and Clinical Immunology*, 51, 139.


Livingston Development Corporation. (1994b) 1991 census results for the Scottish new towns. Planning Department, LDC.


Mosmann TR, Coffman RL. (1989) TH1 and TH2 cells: different patterns of lymphokine secretion lead to different functional properties. Annual Review of Immunology, 7, 145-173.


Nexmand PH. (1948) Clinical studies of prurigo Besnier. Rosenkilde and Bagger, Copenhagen.


Ruta DA, Garratt AM, Leng M, Russell IT, MacDonald LM. (1994) A new approach to the measurement of quality of life. The Patient-Generated Index. Medical Care, 32, 1109-1126.


Siegrist J, Junge A. (1989) Background material for the workshop on QALYs. Social Science Medicine, 29, 463-468.


## APPENDICES

<table>
<thead>
<tr>
<th>APPENDICES 1-3</th>
<th>Observers' response sheets for diagnostic criteria</th>
<th>99</th>
</tr>
</thead>
<tbody>
<tr>
<td>APPENDIX 4</td>
<td>Dermatology Life Quality Index</td>
<td>102</td>
</tr>
<tr>
<td>APPENDIX 5</td>
<td>Letter to patients</td>
<td>104</td>
</tr>
<tr>
<td>APPENDIX 6</td>
<td>Proforma for assessing cost</td>
<td>105</td>
</tr>
<tr>
<td>APPENDIX 7</td>
<td>Patient information sheet</td>
<td>106</td>
</tr>
<tr>
<td>APPENDIX 8</td>
<td>Patient Generated Index</td>
<td>107</td>
</tr>
<tr>
<td>APPENDIX 9</td>
<td>Children's quality of life questionnaire</td>
<td>110</td>
</tr>
<tr>
<td>APPENDIX 10</td>
<td>Prevalence calculation</td>
<td>114</td>
</tr>
<tr>
<td>APPENDIX 11-16</td>
<td>Families listed by sampling group</td>
<td>118</td>
</tr>
<tr>
<td>APPENDIX 17</td>
<td>Costing data</td>
<td>157</td>
</tr>
<tr>
<td>APPENDIX 18</td>
<td>Adult quality of life data</td>
<td>161</td>
</tr>
<tr>
<td>APPENDIX 19</td>
<td>Children's quality of life data</td>
<td>163</td>
</tr>
</tbody>
</table>
Appendix 2

OBSERVER'S RESPONSE SHEET FOR CHILDREN AGED 2-12 YRS

Name: Age:

A. Questions
1. Has your child had an itchy skin condition in the last year - by 'itchy' we mean scratching or rubbing the skin a lot?
   Yes/No

2. At what age did this skin problem begin?
   Under 2
   2 - 5 years
   5 - 10 years

3. Has this skin condition ever affected any of the following areas in the past - fronts of elbows, behind the knees, fronts of ankles, sides or front of the neck or around the ears or eyes?
   Yes/No

4. Has your child ever suffered from asthma (bouts of wheezing with coughing) or hay fever (bouts of sneezing with a runny nose or itchy eyes in the summer)?
   Yes/No

5. In the last year has your child suffered from dry skin?
   Yes/No

B. Signs
1. Visible flexural eczema or eczema on cheeks.
   Yes/No
APPENDIX 3

OBSERVER'S RESPONSE SHEET FOR ADULTS (AGE > 12 YRS)

Name:  
Age:  

A. Questions

1. Have you had an itchy skin condition in the last year?
   Yes/No

2. How old were you when your skin problem began?
   - Under 2
   - 2 - 5 years
   - 5 - 10 years
   - Over 10

3. Has this skin condition ever affected the skin creases in the past - by skin creases I mean fronts of elbows, behind the knees, fronts of ankles, sides or front of neck, or around the ears or eyes?
   Yes/No

4. Do you, or have you ever suffered from asthma (bouts of wheezing with coughing) or hay fever (bouts of sneezing with runny nose or itchy eyes in the summer)?
   Yes/No

5. In the last year have you suffered from dry skin?
   Yes/No

B. Signs

1. Visible flexural eczema?
   Yes/No
**Appendix 4**

**DERMATOLOGY LIFE QUALITY INDEX**

<table>
<thead>
<tr>
<th>Name:</th>
<th>Date:</th>
<th>TOTAL SCORE:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Address:</td>
<td>Age:</td>
<td></td>
</tr>
</tbody>
</table>

The aim of this questionnaire is to measure how much your skin has affected your life OVER THE LAST WEEK. Please circle one answer for each question.

1. **Over the last week, how itchy, sore, painful or stinging has your skin been?**
   - Very much
   - A lot
   - A little
   - Not at all

2. **Over the last week, how embarrassed or self conscious have you been because of your skin?**
   - Very much
   - A lot
   - A little
   - Not at all

3. **Over the last week, how much has your skin interfered with you going shopping or looking after your home or garden?**
   - Very much
   - A lot
   - A little
   - Not at all
   - not relevant

4. **Over the last week, how much has your skin influenced the clothes you wear?**
   - Very much
   - A lot
   - A little
   - Not at all
   - not relevant

5. **Over the last week, how much has your skin affected any social or leisure activities?**
   - Very much
   - A lot
   - A little
   - Not at all
   - not relevant

6. **Over the last week, how much has your skin made it difficult for you to do sport?**
   - Very much
   - A lot
   - A little
   - Not at all
   - not relevant

PLEASE TURN SHEET OVER............
7. Over the last week, has your skin prevented you for working or studying?  
   Yes
   No
   If "no", over the last week how much has your skin been a problem at work or studying?
   A lot
   A little
   Not at all

8. Over the last week, how much has your skin created problems with your partner or any of your close friends or relatives?  
   Very much
   A lot
   A little
   Not at all
   not relevant

9. Over the last week, how much has your skin caused any sexual difficulties?  
   Very much
   A lot
   A little
   Not at all
   not relevant

10. Over the last week, how much of a problem has the treatment for your skin been, for example by making your home messy, or by taking up time?  
    Very much
    A lot
    A little
    Not at all
    not relevant

PLEASE CHECK YOU HAVE ANSWERED EVERY QUESTION - THANK YOU
Dear

Dr Robert Herd of the skin department at the Royal Infirmary of Edinburgh is carrying out a survey of skin conditions at Howden Health Centre. He would be delighted if you were willing to participate and will be contacting you in the next two weeks to explain what is required. He will either telephone or visit you at home.

Many thanks for your co-operation.

Kind regards

Yours sincerely

Dr
TO BE RECORDED BY PATIENT

Over the next two months:

1. Please keep containers for all creams or ointments, bandages and all tablets for your skin which you buy from the chemist or are prescribed by your doctor.

2. Please record the dates of all consultations with a doctor or nurse because of your skin and all expenses involved in these.

3. Please record the dates of all visits to hospital because of your skin and expenses involved in these visits.

4. Please record the dates of all days off work or school because of your skin condition.

5. Please record any loss of salary as a result of your skin condition.

6. Have you required any new clothing because of your skin condition? Have there been any extra laundry expenses as a result of your skin condition? Could you please record the cost of these over the next two months.

7. Have there been any other expenses incurred directly or indirectly as a result of your skin condition?
Thank you for agreeing to participate in this survey of skin disease.

In order to estimate the cost of your skin condition to yourself and to Howden Health Centre we would like you to keep a record over the next two months of all treatments and other expenses as listed on the attached sheet.

We will also ask you to complete a short questionnaire about the other ways in which your skin condition affects you at the end of the two month period.
This questionnaire is in three stages. The part you have to fill in is on page three and is marked 'stage one', 'stage two' and 'stage three'. The instructions on how to fill it in are also divided into three stages. You might find it easiest to read through the instructions for stage one, then go to page three and fill in stage one, and then do the same for stage two and stage three.

When you are filling in each stage, we would like you to think about when you were at your worst with your eczema in the last month. If you are at your worst now, then think about how you feel now.

**STAGE ONE** (please refer to page three as you read this page)

At this stage, we would like you to think of the different areas of your life, or activities in your life that have been affected by your eczema in the last month. When you think of areas or activities, you might think of some small area or activity which may be quite personal and special to you like 'I can't play with my kids'.

We would like you to write the FIVE most important areas or activities of your life that are affected by your eczema in the boxes provided in STAGE ONE on page three. Put one area or activity in each box.

You may be able to think of more than five areas but you can only write down the five most important ones.

You don't have to write down five areas of your life if you don't feel that five areas of your life have been affected. If you have less than five, you can write 'none' in the empty boxes and move on to stage two.

If you feel that your life is not affected by your eczema AT ALL, then just send back the questionnaire with 'none' in each box. In this case you don't need to go on to stages two and three.

Once you have written down the most important areas or activities that have been affected by your eczema, you can move on to stage two.

**STAGE TWO** (please refer to page eight as you read this page)

Looking at page three, you will see a scale going from 0-100 in multiples of 10. This scale is supposed to show you how badly affected you are for each of the areas or activities you
have mentioned. A score of zero would mean that then you were at your worst in the last month, you felt that this was really the worst you would imagine for yourself. The score of 100 is meant to represent exactly how you would like to be, in that area or activity of your life (even if it is impossible for you to reach).

For each area or activity that you have mentioned, write down a score out of 100 that you would give to reflect how you were affected when you were at your worst in the last month.

You will notice that we have filled in 'all other aspects of your life' as the final 'area or activity'. This is meant to include all the other areas of your life affected by your eczema, but which are not important enough to go in the top five boxes. It will also include areas in your life which might be totally unaffected, like the size of your house.

You might suffer from another illness as well as your eczema, and any other areas that are affected by this illness would be included in this box.

Please give a score out of 100 to the 'All other areas of your life' box in the same way that you scored the other 'areas and activities'. Even if you leave other boxes empty you must fill in this box.

**STAGE THREE** (please refer to page eight as you read this page)

For the final stage, we would like you to imagine that we can grant you a wish to improve ANY area of your life, including the areas that have nothing to do with your eczema.

Imagine that you are given 60 POINTS to improve your score in any of the areas you have mentioned. You cannot have more than 60 points in total but you can spend them anyway you like. For example, you could give 10 points to each area or you might give 60 points to one area. The choice is yours to split the points up any way you like, but you cannot have more than 60 points in total.

If you don't give any points to an area of your life, you must try to imagine that this area will stay exactly as it is.
Go through the boxes in stage three and distribute your points to those areas or activities in which you would most like to improve. You can keep changing your mind until you feel that you have reached the best distribution of points. Remember that the total across all areas has to add up to 60.

<table>
<thead>
<tr>
<th>STAGE 1 area/activity (eg sport)</th>
<th>STAGE 2 score each area/activity out of 100</th>
<th>STAGE 3 spend your 60 points between the different areas</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

You must fill in this box

All other aspects of your life not mentioned above

100 exactly as you would like to be
90 close to how you would like to be
80 very good but not how you would like to be
70 good but not how you would like to be
60 between fair and good
50 fair
40 between poor and fair
30 poor but not the worst you could imagine
20 very poor but not the worst you could imagine
10 close to the worst you could imagine
0 the worst you could imagine

You have finished this section. It will tell us how your eczema has affected your life and also which aspects of your life you would most like to see improved.
Children's quality of life questionnaire

QUALITY OF LIFE QUESTIONNAIRE IN CHILDREN WITH ATOPIC ECZEMA

SECTION A: Effect of eczema on child

Questionnaire for 5-16 year olds with Atopic Eczema

Section A will be completed by the interviewer

All questions relate to the LAST FEW DAYS

<table>
<thead>
<tr>
<th>Question</th>
<th>Very Much</th>
<th>A Lot</th>
<th>A Little</th>
<th>Not At All</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. How itchy, sore, painful or stinging has your skin been?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. How much has the skin problem affected you playing or socialising with your friends?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. How much has your skin problem affected you doing any sports?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. How much has the skin problem interfered with your school work?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. How much has the skin problem interfered with any of your other interests or hobbies, apart from the ones already mentioned?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. How much has the skin problem interfered with your sleep?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. How much do you get teased because of your skin trouble or how much do people make comments about your skin?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. How much does having the ointment or cream treatments put on affect you?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. How happy have you been over the last few days?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. Are there any other ways in which having the skin problem affects you?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**SECTION B: Effect of eczema on child**

Questionnaire for parent or guardian of 5-16 year olds with Atopic Eczema.

Section B will be completed by the parent or guardian.

Please could you answer each question, describing your view of how your child has been affected by having eczema and how this has affected you. The questions relate to the LAST FEW DAYS.

Relationship to child: Mother Father Other (please specify)

<table>
<thead>
<tr>
<th>Question</th>
<th>Very Much</th>
<th>A Lot</th>
<th>A Little</th>
<th>At All</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. How itchy, sore, painful or stinging has the child's skin been?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. How much has the skin problem affected the child playing or socialising with their friends?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. How much has the child's skin problem affected them doing any sports?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. How much has the skin problem interfered with the child's school work?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. How much has the skin problem interfered with any of the child's other interests or hobbies, apart from the ones already mentioned?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. How much has the skin problem interfered with the child's sleep?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. How much do you think the child gets teased or made comments about because of their skin trouble?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. How much does having the ointment or cream treatments put on upset the child?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. How embarrassed or self conscious has the child been because of the skin problem?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. Are there any other ways in which you feel the child's life has been affected by having eczema?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
SECTION C: Affect of child's eczema on family

Section C will be completed by the parent/guardian.

<table>
<thead>
<tr>
<th></th>
<th>Very Much</th>
<th>A Lot</th>
<th>A Little</th>
<th>Not At All</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>How much has the eczema interfered with any family social events?</td>
<td>□ □ □ □</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>How much has the eczema interfered with plans for food preparation?</td>
<td>□ □ □ □</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>How much has having a child with eczema cost over the last two months?</td>
<td>□ □ □ □</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>a) clothes</td>
<td>□ □ □ □</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>b) beds</td>
<td>□ □ □ □</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>c) cleaning</td>
<td>□ □ □ □</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>d) dressings</td>
<td>□ □ □ □</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>e) prescriptions</td>
<td>□ □ □ □</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>f) non prescription treatment</td>
<td>□ □ □ □</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>g) other (please specify)</td>
<td>□ □ □ □</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>How much has your child having eczema affected brothers or sisters?</td>
<td>□ □ □ □</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>How much has having a child with eczema affected the mother socially?</td>
<td>□ □ □ □</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>How much has having the eczema affected the mother's work or career?</td>
<td>□ □ □ □</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>How much has having a child with eczema affected the father socially?</td>
<td>□ □ □ □</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8.</td>
<td>How much has having a child with eczema affected the father's work or career?</td>
<td>□ □ □ □</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9.</td>
<td>How much has having eczema affected the following relationships within the family:</td>
<td>□ □ □ □</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>a) child to brothers and sisters</td>
<td>□ □ □ □</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>b) child to parents</td>
<td>□ □ □ □</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>c) brothers and sisters to parents</td>
<td>□ □ □ □</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>d) parent to parent</td>
<td>□ □ □ □</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
10. How big an effect has the process of treating the child had on the home (e.g. mess from ointments)?

11. How much embarrassment or guilt has been felt by you, the parent/guardian concerning having a child with eczema?
APPENDIX 10

Calculation of the prevalence and standard error

The statistical methods are contained in standard textbooks (Cochran, 1977). The calculations for the 2-11 year age group are as follows where the notation is

\[ M_0 = \text{Total number in population} \]

\[ n = \text{number of families in sample} \]

\[ y_i = \text{proportion affected in family } i \]

\[ \bar{y} = \frac{Y}{M_0} \]

The estimated number with AD in the group obtained from the practice computer is

\[ \hat{Y} = \frac{M_0 \cdot \sum y_i}{n} \]

\[ = \frac{164 \cdot (24.55)}{97} \]

\[ = 41.5 \]

\[ \text{Var} (\hat{Y}) = \frac{M_0^2 \cdot \sum (y_i - \bar{y})^2}{n(n-1)} \]
with finite population correction.

The estimated number in the families of the under 2s is

\[ \hat{Y} = \frac{M_0 \sum y_i}{n} \]

\[ = \frac{122 \cdot (10.5)}{80} \]

\[ = 16.0 \]

\[ \text{Var}(\hat{Y}) = \frac{M_0^2 \sum (y_i - \bar{y})^2}{n(n-1)} \]

\[ = \frac{122^2 \cdot 6.11}{80.79} \]

\[ = 14.4 \]
1.53

with finite population correction.

The estimated number from the remainder of the population is obtained from the random sample

\[ \hat{y} = \frac{M_0 \sum y_i}{n} \]

\[ = \frac{1111 \cdot (4.25)}{84} \]

\[ = 56.2 \]

\[ \text{Var} (\hat{y}) = \frac{M_0^2 \sum(y_i - \bar{y})^2}{n(n-1)} \]

\[ = \frac{1111^2 \cdot 2.76}{84.83} \]

\[ = 488.9 \]

\[ = 424.2 \]
with finite population correction.

The estimated prevalence of AD in the population is

\[
\frac{41.5 + 16.0 + 56.2}{1397} \times 100\% = 8.1\%
\]

The overall variance is the sum of the individual groups

\[
\text{Variance} = 428.76
\]

\[
\text{Standard error} = \sqrt{428.76} \times 100\% = 1.5
\]

The prevalences and standard errors in the older age groups were calculated in a similar way. Where there were no individuals with AD it was assumed that \( y_1 = 0.5 \) to estimate the variance.
# APPENDIX 11

Ages in families with a member with AD. Each line represents a family and those with AD are underlined.

<table>
<thead>
<tr>
<th>Family</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>13, 46</td>
<td>45</td>
</tr>
<tr>
<td>2</td>
<td>12, 37</td>
<td>10, 36</td>
</tr>
<tr>
<td>3</td>
<td>24, 28</td>
<td>53</td>
</tr>
<tr>
<td>4</td>
<td>3, Z, 16, 37</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>37</td>
<td>17</td>
</tr>
<tr>
<td>6</td>
<td>20, 50</td>
<td>48</td>
</tr>
<tr>
<td>7</td>
<td>11, 36</td>
<td>2, 30</td>
</tr>
<tr>
<td>8</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>2, 12, 28</td>
<td>28</td>
</tr>
<tr>
<td>10</td>
<td>19, 45</td>
<td>45</td>
</tr>
<tr>
<td>11</td>
<td>31</td>
<td>0, 29</td>
</tr>
<tr>
<td>12</td>
<td>2, 42</td>
<td>41</td>
</tr>
<tr>
<td>13</td>
<td>11, 42</td>
<td>2, 39</td>
</tr>
<tr>
<td>14</td>
<td>8, 33</td>
<td>0, 30</td>
</tr>
<tr>
<td>15</td>
<td>39</td>
<td>13, 35</td>
</tr>
<tr>
<td>16</td>
<td>30</td>
<td>2, 29</td>
</tr>
<tr>
<td>17</td>
<td>30</td>
<td>29</td>
</tr>
<tr>
<td>18</td>
<td>3, 5, 11, 42</td>
<td>0, 5, 33</td>
</tr>
<tr>
<td>19</td>
<td>4</td>
<td>0, 27</td>
</tr>
<tr>
<td>20</td>
<td>18, 45</td>
<td>44</td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>----------</td>
<td>--------</td>
</tr>
<tr>
<td>21</td>
<td>2, 36</td>
<td>33</td>
</tr>
<tr>
<td>22</td>
<td>2, 23</td>
<td>4, 26, 57</td>
</tr>
<tr>
<td>23</td>
<td>30</td>
<td>2, 30</td>
</tr>
<tr>
<td>24</td>
<td>6, 14, 46</td>
<td>2, 7, 16, 36</td>
</tr>
<tr>
<td>25</td>
<td>17, 25</td>
<td>8, 22, 48</td>
</tr>
<tr>
<td>26</td>
<td>15, 19, 45</td>
<td>19, 41</td>
</tr>
<tr>
<td>27</td>
<td>3, 30</td>
<td>26</td>
</tr>
<tr>
<td>28</td>
<td>1, 58</td>
<td>22, 36, 56</td>
</tr>
<tr>
<td>29</td>
<td></td>
<td>4, 6, 11, 30</td>
</tr>
<tr>
<td>30</td>
<td>22, 45</td>
<td>20, 44</td>
</tr>
<tr>
<td>31</td>
<td>14, 16, 39</td>
<td>16, 37</td>
</tr>
<tr>
<td>32</td>
<td>11, 43</td>
<td>14, 36</td>
</tr>
<tr>
<td>33</td>
<td>1, 4, 35</td>
<td>32</td>
</tr>
<tr>
<td>34</td>
<td>7, 11, 13, 39</td>
<td>5, 15, 36</td>
</tr>
<tr>
<td>35</td>
<td>23</td>
<td>22</td>
</tr>
<tr>
<td>36</td>
<td>26</td>
<td>27</td>
</tr>
<tr>
<td>37</td>
<td>13, 34</td>
<td>14, 5, 28</td>
</tr>
<tr>
<td>38</td>
<td>15, 36</td>
<td>5, 33</td>
</tr>
<tr>
<td>39</td>
<td>23</td>
<td>3, 22</td>
</tr>
<tr>
<td>40</td>
<td>30</td>
<td>28</td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>--------------</td>
<td>--------------</td>
</tr>
<tr>
<td>41</td>
<td>1, 3, 4, 24</td>
<td>22</td>
</tr>
<tr>
<td>42</td>
<td>6, 7, 33</td>
<td>4, 12, 33</td>
</tr>
<tr>
<td>43</td>
<td>2, 2, Z, 11, 31</td>
<td>30</td>
</tr>
<tr>
<td>44</td>
<td></td>
<td>24</td>
</tr>
<tr>
<td>45</td>
<td>3, 30</td>
<td>5, 29</td>
</tr>
<tr>
<td>46</td>
<td>36</td>
<td>12, 36</td>
</tr>
<tr>
<td>47</td>
<td>5, 37</td>
<td>1, 9, 11, 33</td>
</tr>
<tr>
<td>48</td>
<td></td>
<td>21</td>
</tr>
<tr>
<td>49</td>
<td>11, 13, 18, 70</td>
<td>44</td>
</tr>
<tr>
<td>50</td>
<td>12, 40</td>
<td>15, 41</td>
</tr>
<tr>
<td>51</td>
<td>10, 14, 19, 46</td>
<td>44</td>
</tr>
<tr>
<td>52</td>
<td>69</td>
<td>32, 71</td>
</tr>
<tr>
<td>53</td>
<td>7, 35</td>
<td>10, 33</td>
</tr>
<tr>
<td>54</td>
<td>40</td>
<td>45</td>
</tr>
<tr>
<td>55</td>
<td>38</td>
<td>14, 36</td>
</tr>
<tr>
<td>56</td>
<td>Z, 9, 13</td>
<td>32</td>
</tr>
<tr>
<td>57</td>
<td>2, 4</td>
<td>26</td>
</tr>
<tr>
<td>58</td>
<td>47</td>
<td>21, 47</td>
</tr>
<tr>
<td>59</td>
<td>26</td>
<td>25</td>
</tr>
<tr>
<td>60</td>
<td>6, 32</td>
<td>4, 30</td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>--------------</td>
<td>--------------</td>
</tr>
<tr>
<td>61</td>
<td>1, 3, 5, 7</td>
<td>28</td>
</tr>
<tr>
<td>62</td>
<td>0, 53</td>
<td>23</td>
</tr>
<tr>
<td>63</td>
<td>13, 17, 52</td>
<td>20, 47</td>
</tr>
<tr>
<td>64</td>
<td>54</td>
<td>25, 55</td>
</tr>
<tr>
<td>65</td>
<td>15, 33</td>
<td>4, 13, 34</td>
</tr>
<tr>
<td>66</td>
<td>43</td>
<td>12, 39</td>
</tr>
<tr>
<td>67</td>
<td>4, 49</td>
<td>15, 16, 22, 38</td>
</tr>
<tr>
<td>68</td>
<td>4, 33</td>
<td>30</td>
</tr>
<tr>
<td>69</td>
<td></td>
<td>21</td>
</tr>
<tr>
<td>70</td>
<td>15, 18, 45</td>
<td>42</td>
</tr>
<tr>
<td>71</td>
<td>Z, 27</td>
<td>26</td>
</tr>
<tr>
<td>72</td>
<td>Z, 29</td>
<td>0, 3, 28</td>
</tr>
<tr>
<td>73</td>
<td>27</td>
<td>1, 26</td>
</tr>
<tr>
<td>74</td>
<td></td>
<td>2, 4, 26</td>
</tr>
<tr>
<td>75</td>
<td>0, 25</td>
<td>0, 22</td>
</tr>
<tr>
<td>76</td>
<td>45</td>
<td>14, 17, 45</td>
</tr>
<tr>
<td>77</td>
<td>19</td>
<td>12, 18, 39</td>
</tr>
<tr>
<td>78</td>
<td>26</td>
<td>16, 23, 46</td>
</tr>
<tr>
<td>79</td>
<td>17, 44</td>
<td>39</td>
</tr>
<tr>
<td>80</td>
<td>24</td>
<td>22</td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>------------</td>
<td>--------------</td>
</tr>
<tr>
<td>81</td>
<td>1, 5, 30</td>
<td>6, 27</td>
</tr>
<tr>
<td>82</td>
<td>14, 54</td>
<td>54</td>
</tr>
<tr>
<td>83</td>
<td>39</td>
<td>6, 9, 30</td>
</tr>
<tr>
<td>84</td>
<td>4, 34</td>
<td>24, 43</td>
</tr>
<tr>
<td>85</td>
<td>20, 54</td>
<td>24, 51</td>
</tr>
<tr>
<td>86</td>
<td>21, 50</td>
<td>23, 43</td>
</tr>
<tr>
<td>87</td>
<td>3, 23</td>
<td>0, 4, 23</td>
</tr>
<tr>
<td>89</td>
<td>6, 15, 32, 45</td>
<td>6, 10, 14, 35</td>
</tr>
<tr>
<td>90</td>
<td>20, 48</td>
<td>47</td>
</tr>
<tr>
<td>91</td>
<td>29, 54</td>
<td>52</td>
</tr>
<tr>
<td>92</td>
<td>21, 24, 29</td>
<td>44</td>
</tr>
<tr>
<td>93</td>
<td>18, 43</td>
<td>14, 37</td>
</tr>
<tr>
<td>94</td>
<td>42</td>
<td>13, 18, 40</td>
</tr>
<tr>
<td>95</td>
<td>14, 52</td>
<td>15, 16, 49</td>
</tr>
<tr>
<td>96</td>
<td>30</td>
<td></td>
</tr>
</tbody>
</table>
**APPENDIX 12**

Families with one member under 2 and also containing a member with AD, listed in the same way as in Appendix 11.

<table>
<thead>
<tr>
<th>Family</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0, 1, 24</td>
<td>2, 19</td>
</tr>
<tr>
<td>2</td>
<td>27</td>
<td>0, 3, 25</td>
</tr>
<tr>
<td>3</td>
<td>26</td>
<td>1, 3, 24</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>9, 11, 31</td>
</tr>
<tr>
<td>5</td>
<td>10, 37</td>
<td>1, 3, 36</td>
</tr>
<tr>
<td>6</td>
<td>33</td>
<td>0, 2, 5, 33</td>
</tr>
<tr>
<td>7</td>
<td>0, 2, 31</td>
<td>35</td>
</tr>
<tr>
<td>8</td>
<td>1, 28</td>
<td>28</td>
</tr>
<tr>
<td>9</td>
<td>0, 30</td>
<td>4, 25</td>
</tr>
<tr>
<td>10</td>
<td>1, 2, 37</td>
<td>7, 36</td>
</tr>
<tr>
<td>11</td>
<td>4, 33</td>
<td>1, 31</td>
</tr>
<tr>
<td>12</td>
<td>1, 6, 31</td>
<td>4, 29</td>
</tr>
<tr>
<td>13</td>
<td>1, 4, 25</td>
<td>2, 23</td>
</tr>
<tr>
<td>14</td>
<td>2, 45</td>
<td>0, 22, 26, 47</td>
</tr>
<tr>
<td>15</td>
<td>10, 43</td>
<td>1, 11, 33</td>
</tr>
<tr>
<td>16</td>
<td>1</td>
<td>4, 29</td>
</tr>
<tr>
<td>17</td>
<td>1, 25</td>
<td>28</td>
</tr>
<tr>
<td>18</td>
<td>1, 4</td>
<td>7, 26</td>
</tr>
<tr>
<td>19</td>
<td>0, 27</td>
<td>27</td>
</tr>
<tr>
<td>20</td>
<td>0, 28</td>
<td>2, 28</td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>-------</td>
<td>--------</td>
</tr>
<tr>
<td>21</td>
<td>1, 6, 29</td>
<td>30</td>
</tr>
<tr>
<td>22</td>
<td>0, 35</td>
<td>2, 34</td>
</tr>
<tr>
<td>23</td>
<td>1, 48</td>
<td>6, 32</td>
</tr>
<tr>
<td>24</td>
<td>7, 34</td>
<td>1, 31</td>
</tr>
<tr>
<td>25</td>
<td>1, 5, 31</td>
<td>8, 30</td>
</tr>
<tr>
<td>26</td>
<td>1, 21, 49</td>
<td>18, 44</td>
</tr>
<tr>
<td>27</td>
<td>L, 9</td>
<td>7, 27</td>
</tr>
<tr>
<td>28</td>
<td>32</td>
<td>L, 33</td>
</tr>
</tbody>
</table>
### Appendix 13

Families from the random sample containing a member with AD, listed as in Appendix 11.

<table>
<thead>
<tr>
<th>Family</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>32</td>
<td>2, 5, 6, 8, 34</td>
</tr>
<tr>
<td>2</td>
<td>9, 36</td>
<td>10, 33</td>
</tr>
<tr>
<td>3</td>
<td>6, 8, 9</td>
<td>31</td>
</tr>
<tr>
<td>4</td>
<td>33</td>
<td>7, 34</td>
</tr>
<tr>
<td>5</td>
<td>8, 31</td>
<td>2, 28</td>
</tr>
<tr>
<td>6</td>
<td>2, 3, 10</td>
<td>5, 10, 35, 78</td>
</tr>
<tr>
<td>7</td>
<td>3, 9, 26</td>
<td>30</td>
</tr>
</tbody>
</table>
## APPENDIX 14

Computer families without AD

<table>
<thead>
<tr>
<th>Family</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>28, 56</td>
<td>25, 56</td>
</tr>
<tr>
<td>2</td>
<td>30, 61</td>
<td>28, 61</td>
</tr>
<tr>
<td>3</td>
<td>32, 66</td>
<td>25</td>
</tr>
<tr>
<td>4</td>
<td>4, 25, 26, 32</td>
<td>9</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>62</td>
</tr>
<tr>
<td>6</td>
<td>64</td>
<td>62, 64</td>
</tr>
<tr>
<td>7</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>24, 27, 52</td>
<td>21, 48</td>
</tr>
<tr>
<td>9</td>
<td>23, 45</td>
<td>44</td>
</tr>
<tr>
<td>10</td>
<td>44</td>
<td>14, 17, 43</td>
</tr>
<tr>
<td>11</td>
<td>54</td>
<td>21, 50</td>
</tr>
<tr>
<td>12</td>
<td>14, 18, 44</td>
<td>44</td>
</tr>
<tr>
<td>13</td>
<td>22, 48</td>
<td>46</td>
</tr>
<tr>
<td>14</td>
<td>10, 48</td>
<td>17, 45</td>
</tr>
<tr>
<td>15</td>
<td>18, 22, 50</td>
<td>45</td>
</tr>
<tr>
<td>16</td>
<td>17, 49</td>
<td>46</td>
</tr>
<tr>
<td>17</td>
<td>10, 16, 41</td>
<td>41</td>
</tr>
<tr>
<td>18</td>
<td>18, 24, 51</td>
<td>47</td>
</tr>
<tr>
<td>19</td>
<td>21, 50</td>
<td>50</td>
</tr>
<tr>
<td>20</td>
<td>69</td>
<td>66</td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>-------</td>
<td>-----------------</td>
</tr>
<tr>
<td>21</td>
<td></td>
<td>60</td>
</tr>
<tr>
<td>22</td>
<td>27</td>
<td>2, 5, 27</td>
</tr>
<tr>
<td>23</td>
<td>50</td>
<td>35</td>
</tr>
<tr>
<td>24</td>
<td>26, 45, 53</td>
<td>53</td>
</tr>
<tr>
<td>25</td>
<td>59</td>
<td>18, 21, 58</td>
</tr>
<tr>
<td>26</td>
<td></td>
<td>14, 38</td>
</tr>
<tr>
<td>27</td>
<td>65</td>
<td>65</td>
</tr>
<tr>
<td>28</td>
<td>51</td>
<td>54</td>
</tr>
<tr>
<td>29</td>
<td>51</td>
<td>22, 53</td>
</tr>
<tr>
<td>30</td>
<td>15</td>
<td>12</td>
</tr>
<tr>
<td>31</td>
<td>2, 32</td>
<td>32</td>
</tr>
<tr>
<td>32</td>
<td>45</td>
<td>21, 45</td>
</tr>
<tr>
<td>33</td>
<td>74</td>
<td>71</td>
</tr>
<tr>
<td>34</td>
<td></td>
<td>44</td>
</tr>
<tr>
<td>35</td>
<td>16</td>
<td>43</td>
</tr>
<tr>
<td>36</td>
<td></td>
<td>44</td>
</tr>
<tr>
<td>37</td>
<td>19, 22</td>
<td>42</td>
</tr>
<tr>
<td>38</td>
<td>11, 15, 34</td>
<td>35</td>
</tr>
<tr>
<td>39</td>
<td>30</td>
<td>0, 29</td>
</tr>
<tr>
<td>40</td>
<td>15, 45</td>
<td>18, 20, 40</td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>--------</td>
<td>---------</td>
</tr>
<tr>
<td>41</td>
<td></td>
<td>73</td>
</tr>
<tr>
<td>42</td>
<td>7</td>
<td>3, 11, 34</td>
</tr>
<tr>
<td>43</td>
<td>2, 32</td>
<td>35</td>
</tr>
<tr>
<td>44</td>
<td>5, 33</td>
<td>8, 33</td>
</tr>
<tr>
<td>45</td>
<td>70</td>
<td>63</td>
</tr>
<tr>
<td>46</td>
<td>28</td>
<td>3, 26</td>
</tr>
<tr>
<td>47</td>
<td>42</td>
<td>43</td>
</tr>
<tr>
<td>48</td>
<td>25, 50</td>
<td>49</td>
</tr>
<tr>
<td>49</td>
<td>22, 46</td>
<td>7, 42</td>
</tr>
<tr>
<td>50</td>
<td>12, 43</td>
<td>15, 45</td>
</tr>
<tr>
<td>51</td>
<td>21, 56</td>
<td>49</td>
</tr>
<tr>
<td>52</td>
<td>24, 56</td>
<td>54</td>
</tr>
<tr>
<td>53</td>
<td></td>
<td>19, 60</td>
</tr>
<tr>
<td>54</td>
<td></td>
<td>74</td>
</tr>
<tr>
<td>55</td>
<td>41</td>
<td></td>
</tr>
<tr>
<td>56</td>
<td></td>
<td>72</td>
</tr>
<tr>
<td>57</td>
<td>78</td>
<td></td>
</tr>
<tr>
<td>58</td>
<td>56</td>
<td>29, 52</td>
</tr>
<tr>
<td>59</td>
<td></td>
<td>21</td>
</tr>
<tr>
<td>60</td>
<td>2, 3, 7, 36</td>
<td>33</td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>------------</td>
<td>-----------</td>
</tr>
<tr>
<td>61</td>
<td>5, 7, 40</td>
<td>12, 33</td>
</tr>
<tr>
<td>62</td>
<td>19, 41</td>
<td>14, 42</td>
</tr>
<tr>
<td>63</td>
<td>60</td>
<td>61</td>
</tr>
<tr>
<td>64</td>
<td>1, 43</td>
<td>3, 41</td>
</tr>
<tr>
<td>65</td>
<td>60</td>
<td>21, 52</td>
</tr>
<tr>
<td>66</td>
<td>53</td>
<td>51</td>
</tr>
<tr>
<td>67</td>
<td>14, 42</td>
<td>42</td>
</tr>
<tr>
<td>68</td>
<td>14, 46</td>
<td>43</td>
</tr>
<tr>
<td>69</td>
<td>13</td>
<td>39</td>
</tr>
<tr>
<td>70</td>
<td>34</td>
<td>2, 11, 14, 32</td>
</tr>
<tr>
<td>71</td>
<td>17, 45</td>
<td>45</td>
</tr>
<tr>
<td>72</td>
<td>36</td>
<td>1, 5, 30</td>
</tr>
<tr>
<td>73</td>
<td>27, 62</td>
<td>60</td>
</tr>
<tr>
<td>74</td>
<td>10, 39</td>
<td>12, 36</td>
</tr>
<tr>
<td>75</td>
<td></td>
<td>82</td>
</tr>
<tr>
<td>76</td>
<td>52</td>
<td>28, 50</td>
</tr>
<tr>
<td>77</td>
<td>15, 32</td>
<td>10, 32</td>
</tr>
<tr>
<td>78</td>
<td>58</td>
<td>59</td>
</tr>
<tr>
<td>79</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td>80</td>
<td>29</td>
<td>0, 29</td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>--------</td>
<td>-----------------</td>
</tr>
<tr>
<td>81</td>
<td>53</td>
<td>24, 49</td>
</tr>
<tr>
<td>82</td>
<td>24</td>
<td>54</td>
</tr>
<tr>
<td>83</td>
<td>30</td>
<td>28</td>
</tr>
<tr>
<td>84</td>
<td>22, 53</td>
<td>15, 47</td>
</tr>
<tr>
<td>85</td>
<td>42</td>
<td></td>
</tr>
<tr>
<td>86</td>
<td>17, 20, 44</td>
<td>45</td>
</tr>
<tr>
<td>87</td>
<td></td>
<td>19</td>
</tr>
<tr>
<td>88</td>
<td>60</td>
<td>5, 10, 30, 60</td>
</tr>
<tr>
<td>89</td>
<td>31</td>
<td>24</td>
</tr>
<tr>
<td>90</td>
<td>23, 44</td>
<td>44</td>
</tr>
<tr>
<td>91</td>
<td>58</td>
<td>23, 56</td>
</tr>
<tr>
<td>92</td>
<td>3, 37</td>
<td>12, 36</td>
</tr>
<tr>
<td>93</td>
<td>15, 35</td>
<td>16, 47</td>
</tr>
<tr>
<td>94</td>
<td>7, 38</td>
<td>5, 34</td>
</tr>
<tr>
<td>95</td>
<td>33, 59, 61</td>
<td>62</td>
</tr>
<tr>
<td>96</td>
<td>55</td>
<td>58</td>
</tr>
<tr>
<td>97</td>
<td></td>
<td>69</td>
</tr>
<tr>
<td>98</td>
<td>42</td>
<td>16, 18, 49</td>
</tr>
<tr>
<td>99</td>
<td>10, 37</td>
<td>7, 34</td>
</tr>
<tr>
<td>100</td>
<td>7</td>
<td>32</td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>----------</td>
<td>----------</td>
</tr>
<tr>
<td>101</td>
<td>24, 48</td>
<td>23, 48</td>
</tr>
<tr>
<td>102</td>
<td>73</td>
<td>73</td>
</tr>
<tr>
<td>103</td>
<td>26, 28</td>
<td>22</td>
</tr>
<tr>
<td>104</td>
<td>6, 7, 34</td>
<td>3, 32</td>
</tr>
<tr>
<td>105</td>
<td>43</td>
<td>18, 43</td>
</tr>
<tr>
<td>106</td>
<td></td>
<td>21</td>
</tr>
<tr>
<td>107</td>
<td>53</td>
<td>51</td>
</tr>
<tr>
<td>108</td>
<td>15, 43</td>
<td>18, 47</td>
</tr>
<tr>
<td>109</td>
<td>5, 10, 12, 33</td>
<td>32</td>
</tr>
<tr>
<td>110</td>
<td>15, 35</td>
<td>35</td>
</tr>
<tr>
<td>111</td>
<td>31</td>
<td>23</td>
</tr>
<tr>
<td>112</td>
<td>6, 25</td>
<td>4, 44, 47</td>
</tr>
<tr>
<td>113</td>
<td></td>
<td>27</td>
</tr>
<tr>
<td>114</td>
<td>44</td>
<td>14, 19, 42</td>
</tr>
<tr>
<td>115</td>
<td>19, 54</td>
<td>51</td>
</tr>
<tr>
<td>116</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>117</td>
<td>53</td>
<td>50</td>
</tr>
<tr>
<td>118</td>
<td>0</td>
<td>3, 29</td>
</tr>
<tr>
<td>119</td>
<td>60</td>
<td>61</td>
</tr>
<tr>
<td>120</td>
<td>33, 69</td>
<td>67</td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>-------</td>
<td>--------</td>
</tr>
<tr>
<td>121</td>
<td>16, 36</td>
<td>13, 38</td>
</tr>
<tr>
<td>122</td>
<td>21, 47</td>
<td>19, 43</td>
</tr>
<tr>
<td>123</td>
<td>41, 78</td>
<td>18, 40</td>
</tr>
<tr>
<td>124</td>
<td>19, 45</td>
<td>44</td>
</tr>
<tr>
<td>125</td>
<td>17, 18</td>
<td>41</td>
</tr>
<tr>
<td>126</td>
<td>26, 28</td>
<td>24, 61</td>
</tr>
<tr>
<td>127</td>
<td>23, 45</td>
<td>25, 44</td>
</tr>
<tr>
<td>128</td>
<td>4, 30</td>
<td>28</td>
</tr>
<tr>
<td>129</td>
<td>25, 51</td>
<td>21, 22, 48</td>
</tr>
<tr>
<td>130</td>
<td>43</td>
<td>19, 43</td>
</tr>
<tr>
<td>131</td>
<td>10, 40</td>
<td>19, 48</td>
</tr>
<tr>
<td>132</td>
<td></td>
<td>8, 26</td>
</tr>
<tr>
<td>133</td>
<td></td>
<td>38</td>
</tr>
<tr>
<td>134</td>
<td>12, 39</td>
<td>8</td>
</tr>
<tr>
<td>135</td>
<td>55</td>
<td>57</td>
</tr>
<tr>
<td>136</td>
<td></td>
<td>0, 4, 11, 24, 30</td>
</tr>
<tr>
<td>137</td>
<td>9, 35</td>
<td>11, 12, 35</td>
</tr>
<tr>
<td>138</td>
<td>1, 27</td>
<td>25</td>
</tr>
<tr>
<td>139</td>
<td>6</td>
<td>34</td>
</tr>
<tr>
<td>140</td>
<td>46</td>
<td>18, 41</td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>----------</td>
<td>----------</td>
</tr>
<tr>
<td>141</td>
<td>31</td>
<td>6, 29</td>
</tr>
<tr>
<td>142</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>143</td>
<td>14, 21, 24, 47</td>
<td>50</td>
</tr>
<tr>
<td>144</td>
<td>61</td>
<td>55</td>
</tr>
<tr>
<td>145</td>
<td>65</td>
<td>29, 66</td>
</tr>
<tr>
<td>146</td>
<td>55</td>
<td>24, 50</td>
</tr>
<tr>
<td>147</td>
<td>33</td>
<td>6, 29</td>
</tr>
<tr>
<td>148</td>
<td>12, 42</td>
<td>14, 16, 37</td>
</tr>
<tr>
<td>149</td>
<td>10, 13, 39</td>
<td>40</td>
</tr>
<tr>
<td>150</td>
<td>61</td>
<td>59</td>
</tr>
<tr>
<td>151</td>
<td></td>
<td>30</td>
</tr>
<tr>
<td>152</td>
<td>21, 26, 53</td>
<td>5, 32, 55</td>
</tr>
<tr>
<td>153</td>
<td>14, 18, 41</td>
<td>41</td>
</tr>
<tr>
<td>154</td>
<td>19, 21, 42</td>
<td>44</td>
</tr>
<tr>
<td>155</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>156</td>
<td>17, 42</td>
<td>14, 38</td>
</tr>
<tr>
<td>157</td>
<td>15, 50</td>
<td>18, 49</td>
</tr>
<tr>
<td>158</td>
<td></td>
<td>12, 43</td>
</tr>
<tr>
<td>159</td>
<td>33</td>
<td>26</td>
</tr>
<tr>
<td>160</td>
<td>50</td>
<td>46</td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>----------</td>
<td>----------</td>
</tr>
<tr>
<td>161</td>
<td>17, 41</td>
<td>15, 36</td>
</tr>
<tr>
<td>162</td>
<td>32</td>
<td>24</td>
</tr>
<tr>
<td>163</td>
<td>20</td>
<td>17, 43</td>
</tr>
<tr>
<td>164</td>
<td>18, 54</td>
<td>20, 42</td>
</tr>
<tr>
<td>165</td>
<td>9, 37</td>
<td>12, 15, 35</td>
</tr>
<tr>
<td>166</td>
<td>31</td>
<td>29</td>
</tr>
<tr>
<td>167</td>
<td>34</td>
<td>32</td>
</tr>
<tr>
<td>168</td>
<td>2, 32</td>
<td>31</td>
</tr>
<tr>
<td>169</td>
<td>19</td>
<td>12, 49</td>
</tr>
<tr>
<td>170</td>
<td>25, 52</td>
<td>22, 57</td>
</tr>
<tr>
<td>171</td>
<td>13, 15, 18, 45</td>
<td>42</td>
</tr>
<tr>
<td>172</td>
<td>9, 39</td>
<td>8, 37</td>
</tr>
<tr>
<td>173</td>
<td>20</td>
<td>24</td>
</tr>
<tr>
<td>174</td>
<td>45</td>
<td>22, 23, 45</td>
</tr>
<tr>
<td>175</td>
<td>15, 40</td>
<td>12, 41</td>
</tr>
<tr>
<td>176</td>
<td>8, 30</td>
<td>4, 29</td>
</tr>
<tr>
<td>177</td>
<td>22, 52</td>
<td>50</td>
</tr>
<tr>
<td>178</td>
<td>29</td>
<td>29</td>
</tr>
<tr>
<td>179</td>
<td>54</td>
<td>20, 56</td>
</tr>
<tr>
<td>180</td>
<td>26, 63</td>
<td>61</td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>----------</td>
<td>----------</td>
</tr>
<tr>
<td>181</td>
<td>48</td>
<td>18, 21, 41</td>
</tr>
<tr>
<td>182</td>
<td>21, 24, 46</td>
<td>48</td>
</tr>
<tr>
<td>183</td>
<td>1, 37</td>
<td>28</td>
</tr>
<tr>
<td>184</td>
<td></td>
<td>65</td>
</tr>
<tr>
<td>185</td>
<td>4, 33</td>
<td>43</td>
</tr>
<tr>
<td>186</td>
<td>9, 13, 18, 42</td>
<td>40</td>
</tr>
<tr>
<td>187</td>
<td>23</td>
<td>20, 41</td>
</tr>
<tr>
<td>188</td>
<td>52</td>
<td>52</td>
</tr>
<tr>
<td>189</td>
<td>24, 62</td>
<td>57</td>
</tr>
<tr>
<td>190</td>
<td>20, 40</td>
<td>0, 13, 18, 39</td>
</tr>
<tr>
<td>191</td>
<td>30</td>
<td>5, 27</td>
</tr>
<tr>
<td>192</td>
<td>22</td>
<td>0, 22</td>
</tr>
<tr>
<td>193</td>
<td>34</td>
<td>40</td>
</tr>
<tr>
<td>194</td>
<td></td>
<td>22</td>
</tr>
<tr>
<td>195</td>
<td>4, 49</td>
<td>15, 16, 38</td>
</tr>
<tr>
<td>196</td>
<td>32</td>
<td>32</td>
</tr>
<tr>
<td>197</td>
<td>1, 23</td>
<td>20</td>
</tr>
<tr>
<td>198</td>
<td>10</td>
<td>1, 30</td>
</tr>
<tr>
<td>199</td>
<td></td>
<td>22, 47</td>
</tr>
<tr>
<td>200</td>
<td>64</td>
<td></td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>----------</td>
<td>----------</td>
</tr>
<tr>
<td>201</td>
<td>13, 52</td>
<td>26, 56</td>
</tr>
<tr>
<td>202</td>
<td>19</td>
<td>14, 38</td>
</tr>
<tr>
<td>203</td>
<td></td>
<td>0, 26</td>
</tr>
<tr>
<td>204</td>
<td></td>
<td>4, 39</td>
</tr>
<tr>
<td>205</td>
<td>29, 62</td>
<td>62</td>
</tr>
<tr>
<td>206</td>
<td>25</td>
<td>24, 47</td>
</tr>
<tr>
<td>207</td>
<td></td>
<td>26</td>
</tr>
<tr>
<td>208</td>
<td>34</td>
<td>33</td>
</tr>
<tr>
<td>209</td>
<td>54</td>
<td>48</td>
</tr>
<tr>
<td>210</td>
<td>59</td>
<td>53</td>
</tr>
<tr>
<td>211</td>
<td>34</td>
<td>9, 13, 34</td>
</tr>
<tr>
<td>212</td>
<td></td>
<td>77</td>
</tr>
<tr>
<td>213</td>
<td>19, 43</td>
<td>17, 42</td>
</tr>
<tr>
<td>214</td>
<td>13, 37</td>
<td>18, 37</td>
</tr>
<tr>
<td>215</td>
<td>8, 42</td>
<td>8, 13, 39</td>
</tr>
<tr>
<td>216</td>
<td>10, 41</td>
<td>10, 34</td>
</tr>
</tbody>
</table>
### Appendix 15

Random families without atopic dermatitis

<table>
<thead>
<tr>
<th>Family</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>63</td>
<td>59</td>
</tr>
<tr>
<td>2</td>
<td>29</td>
<td>29</td>
</tr>
<tr>
<td>3</td>
<td>10, 36</td>
<td>13, 35</td>
</tr>
<tr>
<td>4</td>
<td>19, 20, 47</td>
<td>45</td>
</tr>
<tr>
<td>5</td>
<td>15, 53</td>
<td>21, 50</td>
</tr>
<tr>
<td>6</td>
<td>49</td>
<td>45</td>
</tr>
<tr>
<td>7</td>
<td>6</td>
<td>25</td>
</tr>
<tr>
<td>8</td>
<td>5, 28</td>
<td>7, 28</td>
</tr>
<tr>
<td>9</td>
<td>4, 5</td>
<td>25</td>
</tr>
<tr>
<td>10</td>
<td>13, 48</td>
<td>45</td>
</tr>
<tr>
<td>11</td>
<td>21, 24, 49</td>
<td>53</td>
</tr>
<tr>
<td>12</td>
<td>45</td>
<td>18, 23, 44</td>
</tr>
<tr>
<td>13</td>
<td>70</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>67</td>
<td>66</td>
</tr>
<tr>
<td>15</td>
<td>21, 55</td>
<td>46</td>
</tr>
<tr>
<td>16</td>
<td>38</td>
<td>13, 41</td>
</tr>
<tr>
<td>17</td>
<td>48</td>
<td>16, 20, 48</td>
</tr>
<tr>
<td>18</td>
<td>36</td>
<td>2, 33</td>
</tr>
<tr>
<td>19</td>
<td>4, 33</td>
<td>3, 33</td>
</tr>
<tr>
<td>20</td>
<td>72</td>
<td>71</td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>----------</td>
<td>----------</td>
</tr>
<tr>
<td>21</td>
<td>31</td>
<td>29</td>
</tr>
<tr>
<td>22</td>
<td></td>
<td>18</td>
</tr>
<tr>
<td>23</td>
<td>6, 8, 31</td>
<td>5, 29</td>
</tr>
<tr>
<td>24</td>
<td>24</td>
<td>2, 21</td>
</tr>
<tr>
<td>25</td>
<td>68</td>
<td>9, 51</td>
</tr>
<tr>
<td>26</td>
<td>8, 10, 12, 41</td>
<td>40</td>
</tr>
<tr>
<td>27</td>
<td>36</td>
<td>10, 14, 34</td>
</tr>
<tr>
<td>28</td>
<td>10</td>
<td>34</td>
</tr>
<tr>
<td>29</td>
<td>25, 48</td>
<td>45</td>
</tr>
<tr>
<td>30</td>
<td></td>
<td>74</td>
</tr>
<tr>
<td>31</td>
<td>49</td>
<td>49</td>
</tr>
<tr>
<td>32</td>
<td>24, 49</td>
<td>45</td>
</tr>
<tr>
<td>33</td>
<td>8, 35</td>
<td>33, 55</td>
</tr>
<tr>
<td>34</td>
<td>20, 46</td>
<td>23, 47</td>
</tr>
<tr>
<td>35</td>
<td>4, 27</td>
<td>2, 63</td>
</tr>
<tr>
<td>36</td>
<td>59</td>
<td>59</td>
</tr>
<tr>
<td>37</td>
<td>62</td>
<td></td>
</tr>
<tr>
<td>38</td>
<td>22</td>
<td>23</td>
</tr>
<tr>
<td>39</td>
<td>48</td>
<td>47</td>
</tr>
<tr>
<td>40</td>
<td>15</td>
<td>12, 45</td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>----------------</td>
<td>------------</td>
</tr>
<tr>
<td>41</td>
<td>2, 41</td>
<td>32</td>
</tr>
<tr>
<td>42</td>
<td>19, 21, 43</td>
<td>43</td>
</tr>
<tr>
<td>43</td>
<td>26</td>
<td>35, 81</td>
</tr>
<tr>
<td>44</td>
<td>3, 50</td>
<td>32</td>
</tr>
<tr>
<td>45</td>
<td></td>
<td>84</td>
</tr>
<tr>
<td>46</td>
<td>2, 10, 13, 30</td>
<td>34</td>
</tr>
<tr>
<td>47</td>
<td>59</td>
<td>14, 59</td>
</tr>
<tr>
<td>48</td>
<td>46</td>
<td>20, 46</td>
</tr>
<tr>
<td>49</td>
<td>47</td>
<td>50</td>
</tr>
<tr>
<td>50</td>
<td>22, 56</td>
<td>55</td>
</tr>
<tr>
<td>51</td>
<td>10, 19, 53</td>
<td>47</td>
</tr>
<tr>
<td>52</td>
<td>3, 29</td>
<td>26</td>
</tr>
<tr>
<td>53</td>
<td>68</td>
<td>64</td>
</tr>
<tr>
<td>54</td>
<td>7, 30</td>
<td>5, 34</td>
</tr>
<tr>
<td>55</td>
<td>33</td>
<td>41</td>
</tr>
<tr>
<td>56</td>
<td>50</td>
<td>19, 45</td>
</tr>
<tr>
<td>57</td>
<td>7, 7, 16, 37</td>
<td>13, 27</td>
</tr>
<tr>
<td>58</td>
<td>7, 35</td>
<td>30</td>
</tr>
<tr>
<td>59</td>
<td>15, 18, 43</td>
<td>12, 43</td>
</tr>
<tr>
<td>60</td>
<td>15, 42</td>
<td>12, 17, 42</td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>--------</td>
<td>----------</td>
</tr>
<tr>
<td>61</td>
<td>13</td>
<td>5, 37</td>
</tr>
<tr>
<td>62</td>
<td>42</td>
<td>48</td>
</tr>
<tr>
<td>63</td>
<td>10</td>
<td>13, 43</td>
</tr>
<tr>
<td>64</td>
<td></td>
<td>51, 78</td>
</tr>
<tr>
<td>65</td>
<td>19, 40, 44</td>
<td>14, 40</td>
</tr>
<tr>
<td>66</td>
<td>63</td>
<td>65</td>
</tr>
<tr>
<td>67</td>
<td>56</td>
<td>52</td>
</tr>
<tr>
<td>68</td>
<td>8, 15, 37</td>
<td>33</td>
</tr>
<tr>
<td>69</td>
<td>2, 4, 27</td>
<td>25</td>
</tr>
<tr>
<td>70</td>
<td>56</td>
<td>54</td>
</tr>
<tr>
<td>71</td>
<td>19, 39</td>
<td>16, 38</td>
</tr>
<tr>
<td>72</td>
<td>68</td>
<td>68</td>
</tr>
<tr>
<td>73</td>
<td>9, 12, 38</td>
<td>14, 44</td>
</tr>
<tr>
<td>74</td>
<td>46</td>
<td>19, 44</td>
</tr>
<tr>
<td>75</td>
<td>55</td>
<td>45</td>
</tr>
<tr>
<td>76</td>
<td>25, 53</td>
<td>50</td>
</tr>
<tr>
<td>77</td>
<td>39</td>
<td>69</td>
</tr>
<tr>
<td>78</td>
<td>2, 5, 6, 26</td>
<td>27</td>
</tr>
<tr>
<td>79</td>
<td>30, 63</td>
<td>67</td>
</tr>
<tr>
<td>80</td>
<td>48</td>
<td>13, 18, 38</td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>------------</td>
<td>----------------</td>
</tr>
<tr>
<td>81</td>
<td>2, 30</td>
<td>30</td>
</tr>
<tr>
<td>82</td>
<td>27</td>
<td>25</td>
</tr>
<tr>
<td>83</td>
<td>48</td>
<td>13, 18, 38</td>
</tr>
<tr>
<td>84</td>
<td>15</td>
<td>14, 35</td>
</tr>
<tr>
<td>85</td>
<td>48</td>
<td>49</td>
</tr>
<tr>
<td>86</td>
<td>66</td>
<td>65</td>
</tr>
<tr>
<td>87</td>
<td>24, 47</td>
<td>49</td>
</tr>
<tr>
<td>88</td>
<td>51, 73</td>
<td>48, 69</td>
</tr>
<tr>
<td>89</td>
<td>3, 11, 12, 43</td>
<td>39</td>
</tr>
<tr>
<td>90</td>
<td>77</td>
<td>40</td>
</tr>
<tr>
<td>91</td>
<td></td>
<td>78</td>
</tr>
<tr>
<td>92</td>
<td>26</td>
<td>2, 25</td>
</tr>
<tr>
<td>93</td>
<td>60</td>
<td>59</td>
</tr>
<tr>
<td>94</td>
<td>9, 36</td>
<td>6, 32</td>
</tr>
<tr>
<td>95</td>
<td>14, 42</td>
<td>19, 21, 43</td>
</tr>
<tr>
<td>96</td>
<td>19, 45</td>
<td>16, 44</td>
</tr>
<tr>
<td>97</td>
<td>21, 25, 52</td>
<td>50</td>
</tr>
<tr>
<td>98</td>
<td></td>
<td>61</td>
</tr>
<tr>
<td>99</td>
<td>6, 13, 17, 19, 30</td>
<td>3, 11, 37</td>
</tr>
<tr>
<td>100</td>
<td>18, 43</td>
<td>20, 41</td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>------------</td>
<td>--------</td>
</tr>
<tr>
<td>101</td>
<td></td>
<td>83</td>
</tr>
<tr>
<td>102</td>
<td>63</td>
<td>71</td>
</tr>
<tr>
<td>103</td>
<td>57</td>
<td>54</td>
</tr>
<tr>
<td>104</td>
<td>17, 55</td>
<td>53</td>
</tr>
<tr>
<td>105</td>
<td>24</td>
<td>23</td>
</tr>
<tr>
<td>106</td>
<td>14, 38</td>
<td>10, 32</td>
</tr>
<tr>
<td>107</td>
<td>3</td>
<td>2, 6, 35</td>
</tr>
<tr>
<td>108</td>
<td>48</td>
<td>48</td>
</tr>
<tr>
<td>109</td>
<td>4, 31</td>
<td>8, 27</td>
</tr>
<tr>
<td>110</td>
<td>44, 44</td>
<td>21, 45</td>
</tr>
<tr>
<td>111</td>
<td>6, 23</td>
<td>30</td>
</tr>
<tr>
<td>112</td>
<td>56</td>
<td>51</td>
</tr>
<tr>
<td>113</td>
<td>10, 39</td>
<td>12, 35</td>
</tr>
<tr>
<td>114</td>
<td>13, 43</td>
<td>25, 49</td>
</tr>
<tr>
<td>115</td>
<td>31, 55</td>
<td>7, 17, 30, 51</td>
</tr>
<tr>
<td>116</td>
<td>67</td>
<td>65</td>
</tr>
<tr>
<td>117</td>
<td>17, 23, 48</td>
<td>48</td>
</tr>
<tr>
<td>118</td>
<td>26</td>
<td>24</td>
</tr>
<tr>
<td>119</td>
<td>54</td>
<td>14, 51</td>
</tr>
<tr>
<td>120</td>
<td>11, 37</td>
<td>35</td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>--------------</td>
<td>-----------------</td>
</tr>
<tr>
<td>121</td>
<td>26, 61</td>
<td>57</td>
</tr>
<tr>
<td>122</td>
<td>10, 19, 19, 32</td>
<td>27</td>
</tr>
<tr>
<td>123</td>
<td>43</td>
<td>11, 15, 18, 37</td>
</tr>
<tr>
<td>124</td>
<td>32, 62</td>
<td></td>
</tr>
<tr>
<td>125</td>
<td>58</td>
<td>22, 49</td>
</tr>
<tr>
<td>126</td>
<td>5, 5, 42</td>
<td>2, 31</td>
</tr>
<tr>
<td>127</td>
<td>37</td>
<td>29</td>
</tr>
<tr>
<td>128</td>
<td>21, 45</td>
<td>18, 43</td>
</tr>
<tr>
<td>129</td>
<td>52</td>
<td>48</td>
</tr>
<tr>
<td>130</td>
<td>26</td>
<td>2, 4, 24</td>
</tr>
<tr>
<td>131</td>
<td>50</td>
<td>23, 47</td>
</tr>
<tr>
<td>132</td>
<td></td>
<td>35</td>
</tr>
<tr>
<td>133</td>
<td>8, 12, 17, 40</td>
<td>15, 19, 39</td>
</tr>
<tr>
<td>134</td>
<td>7, 39</td>
<td>8, 31</td>
</tr>
<tr>
<td>135</td>
<td>58</td>
<td>54</td>
</tr>
<tr>
<td>136</td>
<td>26</td>
<td>61</td>
</tr>
<tr>
<td>137</td>
<td>7, 22, 23, 47</td>
<td>21, 44</td>
</tr>
<tr>
<td>138</td>
<td>14, 24</td>
<td>14, 17, 47</td>
</tr>
<tr>
<td>139</td>
<td>43</td>
<td>14, 43</td>
</tr>
<tr>
<td>140</td>
<td>20, 48</td>
<td>15, 45</td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>--------------</td>
<td>--------</td>
</tr>
<tr>
<td>141</td>
<td>18, 20, 39</td>
<td>38</td>
</tr>
<tr>
<td>142</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>143</td>
<td>34</td>
<td>26</td>
</tr>
<tr>
<td>144</td>
<td>16, 20, 37</td>
<td>41</td>
</tr>
<tr>
<td>145</td>
<td>16, 36</td>
<td>15, 34</td>
</tr>
<tr>
<td>146</td>
<td>25</td>
<td>24</td>
</tr>
<tr>
<td>147</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>148</td>
<td></td>
<td>84</td>
</tr>
<tr>
<td>149</td>
<td>3, 30</td>
<td>5, 31</td>
</tr>
<tr>
<td>150</td>
<td>10, 31</td>
<td>4, 13, 30</td>
</tr>
<tr>
<td>151</td>
<td>29</td>
<td>29</td>
</tr>
<tr>
<td>152</td>
<td>55</td>
<td>24, 50</td>
</tr>
<tr>
<td>153</td>
<td></td>
<td>76</td>
</tr>
<tr>
<td>154</td>
<td></td>
<td>76</td>
</tr>
<tr>
<td>155</td>
<td>10, 17, 43</td>
<td>4, 15, 39</td>
</tr>
<tr>
<td>156</td>
<td>10, 16, 42</td>
<td>39</td>
</tr>
<tr>
<td>157</td>
<td>51</td>
<td>51</td>
</tr>
<tr>
<td>158</td>
<td>28</td>
<td>25</td>
</tr>
<tr>
<td>159</td>
<td>68</td>
<td>68</td>
</tr>
<tr>
<td>160</td>
<td>10</td>
<td>12, 40</td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>------------</td>
<td>------------</td>
</tr>
<tr>
<td>161</td>
<td>8, 10, 56</td>
<td></td>
</tr>
<tr>
<td>162</td>
<td>18</td>
<td>14, 16</td>
</tr>
<tr>
<td>163</td>
<td>7, 34</td>
<td>8, 35</td>
</tr>
<tr>
<td>164</td>
<td>18, 49</td>
<td>21, 25, 45</td>
</tr>
<tr>
<td>165</td>
<td>23, 68</td>
<td>53</td>
</tr>
<tr>
<td>166</td>
<td>47</td>
<td>51</td>
</tr>
<tr>
<td>167</td>
<td>13</td>
<td>43</td>
</tr>
<tr>
<td>168</td>
<td></td>
<td>19, 58</td>
</tr>
<tr>
<td>169</td>
<td>60</td>
<td>5, 18, 47</td>
</tr>
<tr>
<td>170</td>
<td>34</td>
<td>13, 15, 32</td>
</tr>
<tr>
<td>171</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>172</td>
<td>22, 51</td>
<td>20, 51</td>
</tr>
<tr>
<td>173</td>
<td>13, 22, 47</td>
<td>47</td>
</tr>
<tr>
<td>174</td>
<td>13, 40</td>
<td>16, 39</td>
</tr>
<tr>
<td>175</td>
<td>7, 29</td>
<td>3, 26</td>
</tr>
<tr>
<td>176</td>
<td>3, 23</td>
<td>23</td>
</tr>
<tr>
<td>177</td>
<td>26</td>
<td>2, 32</td>
</tr>
<tr>
<td>178</td>
<td>11, 34</td>
<td>8, 35</td>
</tr>
<tr>
<td>179</td>
<td>7, 33</td>
<td>4, 30</td>
</tr>
<tr>
<td>180</td>
<td>31, 70</td>
<td>65</td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>----------</td>
<td>----------</td>
</tr>
<tr>
<td>181</td>
<td>2, 42</td>
<td></td>
</tr>
<tr>
<td>182</td>
<td>20, 43</td>
<td>22, 40</td>
</tr>
<tr>
<td>183</td>
<td>29</td>
<td>26</td>
</tr>
<tr>
<td>184</td>
<td>2</td>
<td>9, 11, 29</td>
</tr>
<tr>
<td>185</td>
<td>36</td>
<td>4, 6, 8, 32</td>
</tr>
<tr>
<td>186</td>
<td>17</td>
<td>49</td>
</tr>
<tr>
<td>187</td>
<td>7, 9, 11, 38</td>
<td>32</td>
</tr>
<tr>
<td>188</td>
<td></td>
<td>85</td>
</tr>
<tr>
<td>189</td>
<td>11, 38</td>
<td>16, 37</td>
</tr>
<tr>
<td>190</td>
<td>3, 32</td>
<td>6, 31</td>
</tr>
<tr>
<td>191</td>
<td>33</td>
<td>26</td>
</tr>
<tr>
<td>192</td>
<td>36</td>
<td>33</td>
</tr>
<tr>
<td>193</td>
<td>5, 30</td>
<td>2, 33</td>
</tr>
<tr>
<td>194</td>
<td>56</td>
<td>54</td>
</tr>
<tr>
<td>195</td>
<td>7, 54</td>
<td></td>
</tr>
<tr>
<td>196</td>
<td>4</td>
<td>12, 14, 30</td>
</tr>
<tr>
<td>197</td>
<td>3, 10, 58</td>
<td>33</td>
</tr>
<tr>
<td>198</td>
<td>12, 53</td>
<td>51</td>
</tr>
<tr>
<td>199</td>
<td>47</td>
<td>46</td>
</tr>
<tr>
<td>200</td>
<td>39</td>
<td>9, 14, 36</td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>--------------</td>
<td>---------------</td>
</tr>
<tr>
<td>201</td>
<td>10, 33</td>
<td>2, 31</td>
</tr>
<tr>
<td>202</td>
<td>16, 50</td>
<td>19, 44</td>
</tr>
<tr>
<td>203</td>
<td>35</td>
<td>2, 31</td>
</tr>
<tr>
<td>204</td>
<td>49</td>
<td>14, 49</td>
</tr>
<tr>
<td>205</td>
<td>51</td>
<td>51</td>
</tr>
<tr>
<td>206</td>
<td>4, 35</td>
<td>8, 12, 31</td>
</tr>
<tr>
<td>207</td>
<td>9, 36</td>
<td>10, 33</td>
</tr>
<tr>
<td>208</td>
<td>25, 64</td>
<td>59</td>
</tr>
<tr>
<td>209</td>
<td>9, 39</td>
<td>20, 40</td>
</tr>
<tr>
<td>210</td>
<td></td>
<td>23, 51</td>
</tr>
<tr>
<td>211</td>
<td>17, 45</td>
<td>16, 49</td>
</tr>
<tr>
<td>212</td>
<td>13, 16, 21, 36</td>
<td>38</td>
</tr>
<tr>
<td>213</td>
<td>21</td>
<td>54</td>
</tr>
<tr>
<td>214</td>
<td>11</td>
<td>13, 32</td>
</tr>
<tr>
<td>215</td>
<td>7</td>
<td>5, 25</td>
</tr>
<tr>
<td>216</td>
<td>20</td>
<td>46</td>
</tr>
<tr>
<td>217</td>
<td>20, 48</td>
<td>24, 43</td>
</tr>
<tr>
<td>218</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>219</td>
<td>71</td>
<td>71</td>
</tr>
<tr>
<td>220</td>
<td>18, 21, 26, 51</td>
<td>53</td>
</tr>
</tbody>
</table>

147
<table>
<thead>
<tr>
<th>Family</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>221</td>
<td>20, 23, 44</td>
<td>6, 44</td>
</tr>
<tr>
<td>222</td>
<td>12, 19, 44</td>
<td>43</td>
</tr>
<tr>
<td>223</td>
<td>62</td>
<td>59</td>
</tr>
<tr>
<td>224</td>
<td>9, 13</td>
<td>38</td>
</tr>
<tr>
<td>225</td>
<td>10, 31</td>
<td>3, 7, 30</td>
</tr>
<tr>
<td>226</td>
<td>20, 45</td>
<td>22, 45</td>
</tr>
<tr>
<td>227</td>
<td>62</td>
<td>59</td>
</tr>
<tr>
<td>228</td>
<td>35, 59</td>
<td>28, 60</td>
</tr>
</tbody>
</table>
## Appendix 16

Families with a member under 2 without AD

<table>
<thead>
<tr>
<th>Family</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>1, 27</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>34, 57</td>
</tr>
<tr>
<td>3</td>
<td>0, 29</td>
<td>30</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>28</td>
</tr>
<tr>
<td>5</td>
<td>5, 30</td>
<td>0, 24</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>1, 23</td>
</tr>
<tr>
<td>7</td>
<td>0, 9, 32</td>
<td>4, 30</td>
</tr>
<tr>
<td>8</td>
<td>0, 14, 47</td>
<td>45</td>
</tr>
<tr>
<td>9</td>
<td>24</td>
<td>0, 2, 21</td>
</tr>
<tr>
<td>10</td>
<td>1, 33</td>
<td>34</td>
</tr>
<tr>
<td>11</td>
<td>6</td>
<td>1, 23</td>
</tr>
<tr>
<td>12</td>
<td>1, 26</td>
<td>30</td>
</tr>
<tr>
<td>13</td>
<td>32</td>
<td>1, 9, 31</td>
</tr>
<tr>
<td>14</td>
<td>1, 56</td>
<td>56</td>
</tr>
<tr>
<td>15</td>
<td>28</td>
<td>1, 20</td>
</tr>
<tr>
<td>16</td>
<td>25</td>
<td>1, 5, 6, 24</td>
</tr>
<tr>
<td>17</td>
<td>1, 28</td>
<td>5, 6, 27</td>
</tr>
<tr>
<td>18</td>
<td>11</td>
<td>1, 28</td>
</tr>
<tr>
<td>19</td>
<td>29</td>
<td>0, 36</td>
</tr>
<tr>
<td>20</td>
<td>24</td>
<td>1, 23</td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>------</td>
<td>--------</td>
</tr>
<tr>
<td>21</td>
<td></td>
<td>1, 26</td>
</tr>
<tr>
<td>22</td>
<td>1, 35</td>
<td>28</td>
</tr>
<tr>
<td>23</td>
<td>26</td>
<td>1, 25</td>
</tr>
<tr>
<td>24</td>
<td>24</td>
<td>0, 8, 29</td>
</tr>
<tr>
<td>25</td>
<td>1, 28</td>
<td>6, 27</td>
</tr>
<tr>
<td>26</td>
<td>33</td>
<td>0, 41</td>
</tr>
<tr>
<td>27</td>
<td>22</td>
<td>0, 23</td>
</tr>
<tr>
<td>28</td>
<td>1, 46</td>
<td>20, 46</td>
</tr>
<tr>
<td>29</td>
<td>1, 29</td>
<td>29</td>
</tr>
<tr>
<td>30</td>
<td></td>
<td>0, 3, 28</td>
</tr>
<tr>
<td>31</td>
<td>37</td>
<td>0, 3, 28</td>
</tr>
<tr>
<td>32</td>
<td>0, 24</td>
<td>19</td>
</tr>
<tr>
<td>33</td>
<td>30</td>
<td>1, 38</td>
</tr>
<tr>
<td>34</td>
<td>25</td>
<td>0, 3, 25</td>
</tr>
<tr>
<td>35</td>
<td>25</td>
<td>0, 29</td>
</tr>
<tr>
<td>36</td>
<td>24</td>
<td>1, 23</td>
</tr>
<tr>
<td>37</td>
<td>1, 44</td>
<td>7, 34</td>
</tr>
<tr>
<td>38</td>
<td>1, 23</td>
<td>21</td>
</tr>
<tr>
<td>39</td>
<td></td>
<td>0, 80</td>
</tr>
<tr>
<td>40</td>
<td>0, 34</td>
<td>11, 11, 34</td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>------</td>
<td>--------</td>
</tr>
<tr>
<td>41</td>
<td></td>
<td>1, 35</td>
</tr>
<tr>
<td>42</td>
<td>30</td>
<td>0, 3, 25</td>
</tr>
<tr>
<td>43</td>
<td>0, 3, 30</td>
<td>31</td>
</tr>
<tr>
<td>44</td>
<td>39</td>
<td>1, 12, 36</td>
</tr>
<tr>
<td>45</td>
<td>1, 31</td>
<td>4, 32</td>
</tr>
<tr>
<td>46</td>
<td>0, 3, 25</td>
<td>25</td>
</tr>
<tr>
<td>47</td>
<td>28</td>
<td>0, 24</td>
</tr>
<tr>
<td>48</td>
<td>0, 25</td>
<td>26</td>
</tr>
<tr>
<td>49</td>
<td>1, 4, 32</td>
<td>30</td>
</tr>
<tr>
<td>50</td>
<td></td>
<td>1, 23</td>
</tr>
<tr>
<td>51</td>
<td>0, 5, 10</td>
<td>33</td>
</tr>
<tr>
<td>52</td>
<td>1, 6, 32</td>
<td>32</td>
</tr>
<tr>
<td>53</td>
<td>3, 23</td>
<td>0, 22</td>
</tr>
<tr>
<td>54</td>
<td>27</td>
<td>0, 27</td>
</tr>
<tr>
<td>55</td>
<td>0, 31</td>
<td>2, 32</td>
</tr>
<tr>
<td>56</td>
<td>1, 24</td>
<td>7, 9, 29</td>
</tr>
<tr>
<td>57</td>
<td>1, 27</td>
<td>23</td>
</tr>
<tr>
<td>58</td>
<td>64</td>
<td>0, 20, 54</td>
</tr>
<tr>
<td>59</td>
<td>0</td>
<td>25, 48</td>
</tr>
<tr>
<td>60</td>
<td>7, 22</td>
<td>0, 21</td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>---------------</td>
<td>--------</td>
</tr>
<tr>
<td>61</td>
<td>0, 7, 12, 26</td>
<td>33</td>
</tr>
<tr>
<td>62</td>
<td>0</td>
<td>29</td>
</tr>
<tr>
<td>63</td>
<td>28</td>
<td>0, 29</td>
</tr>
<tr>
<td>64</td>
<td>0, 4</td>
<td>31</td>
</tr>
<tr>
<td>65</td>
<td>29</td>
<td>0, 27</td>
</tr>
<tr>
<td>66</td>
<td>0, 13, 30</td>
<td>31</td>
</tr>
<tr>
<td>67</td>
<td>1, 37</td>
<td>33</td>
</tr>
<tr>
<td>68</td>
<td>29</td>
<td>1, 29</td>
</tr>
<tr>
<td>69</td>
<td>0, 26</td>
<td>2, 25</td>
</tr>
<tr>
<td>70</td>
<td>1, 3</td>
<td>2, 6, 35</td>
</tr>
<tr>
<td>71</td>
<td>3, 27</td>
<td>0, 28</td>
</tr>
<tr>
<td>72</td>
<td>0, 2, 26</td>
<td>25</td>
</tr>
<tr>
<td>73</td>
<td>1, 9, 12, 37</td>
<td>35</td>
</tr>
<tr>
<td>74</td>
<td>0, 30</td>
<td>30</td>
</tr>
<tr>
<td>75</td>
<td>1, 28</td>
<td>6, 25</td>
</tr>
<tr>
<td>76</td>
<td>0, 30</td>
<td>4, 30</td>
</tr>
<tr>
<td>77</td>
<td>1</td>
<td>5, 29</td>
</tr>
<tr>
<td>78</td>
<td>1, 25</td>
<td>21, 23, 58</td>
</tr>
<tr>
<td>79</td>
<td></td>
<td>0, 27</td>
</tr>
<tr>
<td>80</td>
<td>29</td>
<td>0, 27</td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>----------</td>
<td>----------</td>
</tr>
<tr>
<td>81</td>
<td>1</td>
<td>21</td>
</tr>
<tr>
<td>82</td>
<td>0</td>
<td>22</td>
</tr>
<tr>
<td>83</td>
<td>1, 32</td>
<td>22</td>
</tr>
<tr>
<td>84</td>
<td>2, 32</td>
<td>0, 35</td>
</tr>
<tr>
<td>85</td>
<td>35</td>
<td>1, 3, 34</td>
</tr>
<tr>
<td>86</td>
<td>2, 25</td>
<td>0, 9, 30</td>
</tr>
<tr>
<td>87</td>
<td>4</td>
<td>0, 29</td>
</tr>
<tr>
<td>88</td>
<td>0, 6, 33</td>
<td>32</td>
</tr>
<tr>
<td>89</td>
<td></td>
<td>0, 30</td>
</tr>
<tr>
<td>90</td>
<td>28</td>
<td>1, 26</td>
</tr>
<tr>
<td>91</td>
<td>1, 31</td>
<td>30</td>
</tr>
<tr>
<td>92</td>
<td>32</td>
<td>1, 31</td>
</tr>
<tr>
<td>93</td>
<td>10, 33</td>
<td>1, 37</td>
</tr>
<tr>
<td>94</td>
<td>1, 23</td>
<td>0, 21</td>
</tr>
<tr>
<td>95</td>
<td>34</td>
<td>1, 26</td>
</tr>
<tr>
<td>96</td>
<td>1</td>
<td>0, 22</td>
</tr>
<tr>
<td>97</td>
<td>0, 7, 39</td>
<td>8, 31</td>
</tr>
<tr>
<td>98</td>
<td>1, 40</td>
<td>10, 13, 41</td>
</tr>
<tr>
<td>99</td>
<td>0, 28</td>
<td>26</td>
</tr>
<tr>
<td>100</td>
<td>1, 21</td>
<td>14, 19, 21</td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>---------</td>
<td>--------</td>
</tr>
<tr>
<td>101</td>
<td>0, 25</td>
<td>27</td>
</tr>
<tr>
<td>102</td>
<td></td>
<td>0, 12, 35</td>
</tr>
<tr>
<td>103</td>
<td>0, 31</td>
<td>3, 38</td>
</tr>
<tr>
<td>104</td>
<td>28</td>
<td>0, 28</td>
</tr>
<tr>
<td>105</td>
<td>13</td>
<td>0, 9, 14, 33</td>
</tr>
<tr>
<td>106</td>
<td>26</td>
<td>1, 24</td>
</tr>
<tr>
<td>107</td>
<td>5</td>
<td>1, 31</td>
</tr>
<tr>
<td>108</td>
<td>0, 5, 7, 25</td>
<td>25</td>
</tr>
<tr>
<td>109</td>
<td>40</td>
<td>0, 16, 18, 39</td>
</tr>
<tr>
<td>110</td>
<td>50</td>
<td>0, 18, 74</td>
</tr>
<tr>
<td>111</td>
<td>1, 3</td>
<td>23</td>
</tr>
<tr>
<td>112</td>
<td>0, 26</td>
<td>26</td>
</tr>
<tr>
<td>113</td>
<td>1, 29</td>
<td>6, 8, 30</td>
</tr>
<tr>
<td>114</td>
<td>24</td>
<td>1, 5, 21</td>
</tr>
<tr>
<td>115</td>
<td>0, 35</td>
<td>7, 26</td>
</tr>
<tr>
<td>116</td>
<td>24</td>
<td>0, 1, 24</td>
</tr>
<tr>
<td>117</td>
<td>0, 23</td>
<td>23</td>
</tr>
<tr>
<td>118</td>
<td>23</td>
<td>0, 22</td>
</tr>
<tr>
<td>119</td>
<td>1</td>
<td>9, 31</td>
</tr>
<tr>
<td>120</td>
<td>33</td>
<td>1, 35</td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>------------</td>
<td>--------</td>
</tr>
<tr>
<td>121</td>
<td>0, 3, 29</td>
<td>28</td>
</tr>
<tr>
<td>122</td>
<td>0, 29</td>
<td>29</td>
</tr>
<tr>
<td>123</td>
<td>34</td>
<td>0, 29</td>
</tr>
<tr>
<td>124</td>
<td>20</td>
<td>0, 2, 20</td>
</tr>
<tr>
<td>125</td>
<td>1, 29</td>
<td>5, 29</td>
</tr>
<tr>
<td>126</td>
<td>23, 40</td>
<td>0, 43</td>
</tr>
<tr>
<td>127</td>
<td></td>
<td>1, 27</td>
</tr>
<tr>
<td>128</td>
<td>25</td>
<td>1, 23</td>
</tr>
<tr>
<td>129</td>
<td>0, 34</td>
<td>31</td>
</tr>
<tr>
<td>130</td>
<td>3, 23</td>
<td>1, 23</td>
</tr>
<tr>
<td>131</td>
<td>1</td>
<td>2, 42</td>
</tr>
<tr>
<td>132</td>
<td>0, 36</td>
<td>33</td>
</tr>
<tr>
<td>133</td>
<td>0</td>
<td>30</td>
</tr>
<tr>
<td>134</td>
<td>0, 27</td>
<td>29</td>
</tr>
<tr>
<td>135</td>
<td>4, 26</td>
<td>1, 29</td>
</tr>
<tr>
<td>136</td>
<td></td>
<td>0, 27</td>
</tr>
<tr>
<td>137</td>
<td>2, 32</td>
<td>0, 31</td>
</tr>
<tr>
<td>138</td>
<td>25</td>
<td>1, 27</td>
</tr>
<tr>
<td>139</td>
<td>34</td>
<td>0, 28</td>
</tr>
<tr>
<td>140</td>
<td>1, 29</td>
<td></td>
</tr>
<tr>
<td>Family</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>--------</td>
<td>----------</td>
<td>-----------</td>
</tr>
<tr>
<td>141</td>
<td>0, 28</td>
<td>5, 7, 9, 26</td>
</tr>
<tr>
<td>142</td>
<td>1, 27</td>
<td>24</td>
</tr>
<tr>
<td>143</td>
<td>0, 28</td>
<td>27</td>
</tr>
<tr>
<td>144</td>
<td>0, 29</td>
<td>27</td>
</tr>
<tr>
<td>145</td>
<td>25</td>
<td>0, 1, 26</td>
</tr>
<tr>
<td>146</td>
<td>1, 5, 28</td>
<td>4, 43</td>
</tr>
<tr>
<td>147</td>
<td>0</td>
<td>33</td>
</tr>
<tr>
<td>148</td>
<td>35</td>
<td>1, 31</td>
</tr>
<tr>
<td>149</td>
<td>0</td>
<td>23</td>
</tr>
<tr>
<td>150</td>
<td></td>
<td>1, 30</td>
</tr>
<tr>
<td>151</td>
<td></td>
<td>0, 21</td>
</tr>
<tr>
<td>152</td>
<td>1, 31</td>
<td>22</td>
</tr>
</tbody>
</table>
APPENDIX 17

COSTING DATA
The columns in the following table correspond to the items in the proforma in appendix 6

<table>
<thead>
<tr>
<th>Age</th>
<th>1a</th>
<th>1b</th>
<th>1c</th>
<th>2a</th>
<th>2b</th>
<th>3a</th>
<th>3b</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>TP</th>
<th>THS</th>
</tr>
</thead>
<tbody>
<tr>
<td>45</td>
<td>3.75</td>
<td>0</td>
<td>3.12</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3.75</td>
<td>3.12</td>
</tr>
<tr>
<td>10</td>
<td>0</td>
<td>6.20</td>
<td>30.95</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>6.20</td>
<td>30.95</td>
</tr>
<tr>
<td>28</td>
<td>0</td>
<td>0</td>
<td>13.72</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>13.72</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>0</td>
<td>0</td>
<td>3.68</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3.68</td>
<td>0</td>
</tr>
<tr>
<td>37</td>
<td>3.75</td>
<td>0</td>
<td>11.31</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3.75</td>
<td>11.31</td>
</tr>
<tr>
<td>17</td>
<td>0</td>
<td>0</td>
<td>59.91</td>
<td>0</td>
<td>0</td>
<td>7.23</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>67.14</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>0</td>
<td>5.49</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>5.49</td>
<td>0</td>
</tr>
<tr>
<td>20</td>
<td>21.25</td>
<td>0</td>
<td>28.88</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>21.25</td>
<td>28.88</td>
</tr>
<tr>
<td>9</td>
<td>0</td>
<td>0</td>
<td>6.39</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>6.39</td>
<td>0</td>
</tr>
<tr>
<td>23</td>
<td>8.00</td>
<td>0</td>
<td>7.46</td>
<td>0</td>
<td>9.05</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>8.00</td>
<td>16.51</td>
</tr>
<tr>
<td>9</td>
<td>0</td>
<td>0</td>
<td>21.32</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>21.32</td>
<td>0</td>
</tr>
<tr>
<td>45</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>5.04</td>
<td>10.86</td>
<td>0</td>
<td>0</td>
<td>5.00</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>10.04</td>
<td>10.86</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3.30</td>
<td>0</td>
<td>0</td>
<td>5.00</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>5.00</td>
<td>3.30</td>
</tr>
<tr>
<td>34</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>0</td>
<td>1.10</td>
<td>11.21</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1.10</td>
<td>11.21</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>9.62</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>9.62</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>0</td>
<td>13.17</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>13.17</td>
<td>0</td>
</tr>
<tr>
<td>29</td>
<td>17.00</td>
<td>7.30</td>
<td>18.70</td>
<td>0</td>
<td>18.10</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>24.30</td>
<td>36.80</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>11.40</td>
<td>2.47</td>
<td>0</td>
<td>18.10</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>11.40</td>
<td>20.57</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>0</td>
<td>8.22</td>
<td>0</td>
<td>9.05</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>17.27</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>0</td>
<td>4.13</td>
<td>0</td>
<td>18.10</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>22.23</td>
<td>0</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>16.98</td>
<td>0</td>
<td>18.78</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>16.89</td>
<td>16.89</td>
<td>35.76</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>2.25</td>
<td>8.16</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>15.40</td>
<td>17.65</td>
<td>8.16</td>
</tr>
<tr>
<td>13</td>
<td>0</td>
<td>0</td>
<td>6.11</td>
<td>0</td>
<td>9.05</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>15.16</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>0</td>
<td>0</td>
<td>2.00</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2.00</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>0</td>
<td>0</td>
<td>13.68</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>13.68</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>27.60</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>27.60</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>0</td>
<td>2.00</td>
<td>0</td>
<td>9.05</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>11.05</td>
<td>0</td>
</tr>
<tr>
<td>29</td>
<td>12.75</td>
<td>10.84</td>
<td>32.27</td>
<td>0</td>
<td>18.10</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>17.15</td>
<td>40.74</td>
<td>50.37</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>0</td>
<td>18.48</td>
<td>0</td>
<td>0</td>
<td>51.96</td>
<td>0</td>
<td>0</td>
<td>51.96</td>
<td>18.48</td>
<td></td>
<td></td>
</tr>
<tr>
<td>33</td>
<td>4.25</td>
<td>0</td>
<td>1.96</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4.25</td>
<td>1.96</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>2.19</td>
<td>6.61</td>
<td>0</td>
<td>9.05</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2.19</td>
<td>15.66</td>
</tr>
<tr>
<td>Age</td>
<td>1a</td>
<td>1b</td>
<td>1c</td>
<td>2a</td>
<td>2b</td>
<td>3a</td>
<td>3b</td>
<td>5</td>
<td>6</td>
<td>7</td>
<td>TP</td>
<td>THS</td>
</tr>
<tr>
<td>-----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>----</td>
<td>-----</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>5.52</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>5.52</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>0</td>
<td>0</td>
<td>2.00</td>
<td>0</td>
<td>0</td>
<td>9.05</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>11.05</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>25.83</td>
<td>12.11</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>25.83</td>
<td>12.11</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>4.23</td>
<td>16.39</td>
<td>0</td>
<td>18.10</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>100.00</td>
<td>104.23</td>
<td>34.49</td>
</tr>
<tr>
<td>18</td>
<td>12.75</td>
<td>10.34</td>
<td>22.04</td>
<td>0</td>
<td>18.10</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>23.09</td>
<td>40.14</td>
</tr>
<tr>
<td>9</td>
<td>0</td>
<td>0</td>
<td>109.49</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>120.80</td>
<td>0</td>
<td>120.80</td>
<td>109.49</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>0</td>
<td>34.08</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4.00</td>
<td>34.08</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>3.68</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3.68</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>0</td>
<td>7.60</td>
<td>.50</td>
<td>9.05</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>.50</td>
<td>16.65</td>
</tr>
<tr>
<td>16</td>
<td>0</td>
<td>.98</td>
<td>6.22</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>.98</td>
<td>6.22</td>
</tr>
<tr>
<td>22</td>
<td>0</td>
<td>10.38</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>10.38</td>
<td>0</td>
</tr>
<tr>
<td>41</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>0</td>
<td>5.97</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>5.97</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>15.98</td>
<td>31.52</td>
<td>0</td>
<td>18.10</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>24.32</td>
<td>0</td>
<td>40.30</td>
<td>49.62</td>
</tr>
<tr>
<td>30</td>
<td>4.25</td>
<td>0</td>
<td>4.66</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4.25</td>
<td>4.66</td>
</tr>
<tr>
<td>20</td>
<td>0</td>
<td>11.70</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>11.70</td>
<td>0</td>
</tr>
<tr>
<td>39</td>
<td>8.50</td>
<td>4.95</td>
<td>6.66</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>13.45</td>
<td>6.66</td>
</tr>
<tr>
<td>11</td>
<td>0</td>
<td>0</td>
<td>4.66</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4.66</td>
<td>0</td>
</tr>
<tr>
<td>36</td>
<td>0</td>
<td>0</td>
<td>6.66</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>6.66</td>
<td>0</td>
</tr>
<tr>
<td>16</td>
<td>0</td>
<td>.50</td>
<td>6.66</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>.50</td>
<td>6.66</td>
</tr>
<tr>
<td>32</td>
<td>8.50</td>
<td>4.75</td>
<td>6.21</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>40.00</td>
<td>53.25</td>
<td>6.21</td>
</tr>
<tr>
<td>11</td>
<td>0</td>
<td>0</td>
<td>4.00</td>
<td>.50</td>
<td>9.05</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>.50</td>
<td>13.05</td>
</tr>
<tr>
<td>22</td>
<td>0</td>
<td>3.49</td>
<td>17.70</td>
<td>0</td>
<td>18.10</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3.49</td>
<td>35.80</td>
</tr>
<tr>
<td>27</td>
<td>22.00</td>
<td>0</td>
<td>35.17</td>
<td>0</td>
<td>36.20</td>
<td>0</td>
<td>14.46</td>
<td>0</td>
<td>24.00</td>
<td>0</td>
<td>46.00</td>
<td>85.83</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>.40</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>15</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2.00</td>
</tr>
<tr>
<td>36</td>
<td>0</td>
<td>0</td>
<td>2.00</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>22</td>
<td>0</td>
<td>1.50</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1.50</td>
<td>0</td>
</tr>
<tr>
<td>28</td>
<td>4.25</td>
<td>21.10</td>
<td>4.66</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>25.35</td>
<td>4.66</td>
</tr>
<tr>
<td>9</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>18.10</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>23</td>
<td>48.00</td>
<td>71.00</td>
<td>18.10</td>
</tr>
<tr>
<td>6</td>
<td>0</td>
<td>0</td>
<td>7.64</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>7.64</td>
</tr>
<tr>
<td>31</td>
<td>0</td>
<td>0</td>
<td>12.42</td>
<td>0</td>
<td>9.05</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>21.47</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>0</td>
<td>18.74</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>18.74</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>0</td>
<td>0</td>
<td>3.36</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3.36</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>0</td>
<td>13.09</td>
<td>0</td>
<td>9.05</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>22.14</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>0</td>
<td>1.20</td>
<td>48.95</td>
<td>0</td>
<td>9.05</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>40.80</td>
<td>0</td>
<td>42.00</td>
<td>58.00</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>21.72</td>
<td>4.00</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>21.72</td>
<td>4.00</td>
</tr>
<tr>
<td>7</td>
<td>0</td>
<td>0</td>
<td>15.70</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>15.70</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>1.20</td>
<td>2.00</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1.20</td>
<td>2.00</td>
</tr>
<tr>
<td>24</td>
<td>8.50</td>
<td>6.99</td>
<td>7.60</td>
<td>0</td>
<td>18.10</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>15.49</td>
<td>25.70</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>9.45</td>
<td>36.40</td>
<td>0</td>
<td>9.05</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>20.48</td>
<td>0</td>
<td>29.93</td>
<td>45.45</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>.82</td>
<td>8.41</td>
<td>0</td>
<td>9.05</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4.40</td>
<td>0</td>
<td>5.22</td>
<td>17.46</td>
</tr>
<tr>
<td>36</td>
<td>4.25</td>
<td>26.50</td>
<td>2.00</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>60.00</td>
<td>0</td>
<td>90.75</td>
<td>2.00</td>
</tr>
<tr>
<td>11</td>
<td>0</td>
<td>24.10</td>
<td>33.60</td>
<td>0</td>
<td>0</td>
<td>270</td>
<td>0</td>
<td>0</td>
<td>60.00</td>
<td>0</td>
<td>354.10</td>
<td>33.60</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>0</td>
<td>5.60</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>5.60</td>
</tr>
<tr>
<td>21</td>
<td>12.75</td>
<td>0</td>
<td>9.60</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>12.75</td>
<td>9.60</td>
</tr>
<tr>
<td>13</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>5.60</td>
<td>2.00</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>50.00</td>
<td>0</td>
<td>55.60</td>
<td>2.00</td>
</tr>
<tr>
<td>19</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>158</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>1a</td>
<td>1b</td>
<td>1c</td>
<td>2a</td>
<td>2b</td>
<td>3a</td>
<td>3b</td>
<td>5</td>
<td>6</td>
<td>7</td>
<td>TP</td>
<td>THS</td>
</tr>
<tr>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
</tr>
<tr>
<td>10</td>
<td>0</td>
<td>8.50</td>
<td>6.76</td>
<td>0</td>
<td>18.10</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>8.50</td>
<td>24.86</td>
</tr>
<tr>
<td>32</td>
<td>0</td>
<td>22.77</td>
<td>2.00</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>10.00</td>
<td>0</td>
<td>32.77</td>
<td>2.00</td>
</tr>
<tr>
<td>10</td>
<td>0</td>
<td>0</td>
<td>5.28</td>
<td>0</td>
<td>9.05</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>14.33</td>
</tr>
<tr>
<td>40</td>
<td>34.00</td>
<td>10.34</td>
<td>33.62</td>
<td>0</td>
<td>27.15</td>
<td>13.75</td>
<td>116.3</td>
<td>440</td>
<td>30.00</td>
<td>18.00</td>
<td>546.09</td>
<td>177.07</td>
</tr>
<tr>
<td>14</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>0</td>
<td>0</td>
<td>41.41</td>
<td>0</td>
<td>18.10</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>59.51</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>52.87</td>
<td>18.32</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>74.80</td>
<td>0</td>
<td>127.67</td>
<td>18.32</td>
</tr>
<tr>
<td>47</td>
<td>8.50</td>
<td>1.75</td>
<td>17.95</td>
<td>.84</td>
<td>9.05</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>11.09</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>25</td>
<td>0</td>
<td>5.45</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>5.45</td>
</tr>
<tr>
<td>6</td>
<td>0</td>
<td>0</td>
<td>21.57</td>
<td>0</td>
<td>9.05</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>440.00</td>
<td>440.00</td>
<td>30.62</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>1.30</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1.30</td>
<td>9.05</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>23</td>
<td>0</td>
<td>54.25</td>
<td>10.00</td>
<td>0</td>
<td>18.10</td>
<td>0</td>
<td>0</td>
<td>65</td>
<td>0</td>
<td>0</td>
<td>119.25</td>
<td>28.10</td>
</tr>
<tr>
<td>28</td>
<td>0</td>
<td>2.50</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>15.96</td>
<td>0</td>
<td>18.46</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>20</td>
<td>4.25</td>
<td>7.75</td>
<td>3.16</td>
<td>0</td>
<td>9.05</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>12.00</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>0</td>
<td>6.22</td>
<td>0</td>
<td>18.10</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>24.32</td>
</tr>
<tr>
<td>27</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>30</td>
<td>29.75</td>
<td>0</td>
<td>35.40</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>30.80</td>
<td>20.00</td>
<td>80.55</td>
<td>35.40</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>1.00</td>
<td>47.72</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>7.23</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>54.95</td>
</tr>
<tr>
<td>21</td>
<td>0</td>
<td>48.00</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>64.00</td>
<td>6.00</td>
<td>118.00</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>15</td>
<td>0</td>
<td>.20</td>
<td>4.66</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>.20</td>
<td>4.66</td>
</tr>
<tr>
<td>13</td>
<td>0</td>
<td>.20</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>.20</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>0</td>
<td>0</td>
<td>5.60</td>
<td>0</td>
<td>9.05</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>14.65</td>
</tr>
<tr>
<td>7</td>
<td>0</td>
<td>0</td>
<td>21.85</td>
<td>0</td>
<td>9.05</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4.40</td>
<td>0</td>
<td>4.40</td>
<td>30.90</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>0</td>
<td>7.18</td>
<td>0</td>
<td>9.05</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>16.23</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>14.17</td>
<td>21.43</td>
<td>0</td>
<td>14.41</td>
<td>0</td>
<td>0</td>
<td>40.20</td>
<td>0</td>
<td>0</td>
<td>54.37</td>
<td>35.84</td>
</tr>
<tr>
<td>22</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>9.05</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>4.00</td>
<td>19.80</td>
<td>1.50</td>
<td>17.15</td>
<td>0</td>
<td>0</td>
<td>22.00</td>
<td>0</td>
<td>0</td>
<td>27.50</td>
<td>46.95</td>
</tr>
<tr>
<td>17</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>19</td>
<td>4.25</td>
<td>0</td>
<td>4.66</td>
<td>.50</td>
<td>9.05</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4.75</td>
</tr>
<tr>
<td>16</td>
<td>0</td>
<td>0</td>
<td>6.66</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>8.00</td>
<td>0</td>
<td>8.00</td>
<td>0</td>
<td>6.66</td>
</tr>
<tr>
<td>23</td>
<td>0</td>
<td>0</td>
<td>7.20</td>
<td>2.20</td>
<td>18.10</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>65.00</td>
<td>67.20</td>
<td>25.30</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>0</td>
<td>17.77</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>17.77</td>
</tr>
<tr>
<td>17</td>
<td>4.25</td>
<td>9.00</td>
<td>9.14</td>
<td>0</td>
<td>9.05</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>13.25</td>
</tr>
<tr>
<td>29</td>
<td>4.75</td>
<td>3.99</td>
<td>5.04</td>
<td>0</td>
<td>9.05</td>
<td>0</td>
<td>25</td>
<td>0</td>
<td>0</td>
<td>33.74</td>
<td>14.09</td>
<td>0</td>
</tr>
<tr>
<td>34</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>30</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>73.80</td>
<td>0</td>
<td>73.80</td>
</tr>
<tr>
<td>14</td>
<td>0</td>
<td>133.0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>133.0</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>0</td>
<td>20.50</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>20.50</td>
<td>0</td>
</tr>
<tr>
<td>54</td>
<td>4.75</td>
<td>0</td>
<td>6.36</td>
<td>0</td>
<td>9.05</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4.75</td>
</tr>
<tr>
<td>32</td>
<td>4.75</td>
<td>31.84</td>
<td>4.66</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>36.59</td>
</tr>
<tr>
<td>20</td>
<td>0</td>
<td>1.85</td>
<td>4.00</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1.85</td>
<td>4.00</td>
</tr>
<tr>
<td>23</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Age</td>
<td>1a</td>
<td>1b</td>
<td>1c</td>
<td>2a</td>
<td>2b</td>
<td>3a</td>
<td>3b</td>
<td>5</td>
<td>6</td>
<td>7</td>
<td>TP</td>
<td>THS</td>
</tr>
<tr>
<td>-----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>-----</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3.00</td>
<td>0</td>
</tr>
<tr>
<td>35</td>
<td>0</td>
<td>3.00</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3.00</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>0</td>
<td>3.00</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3.00</td>
<td>0</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>15.20</td>
<td>0</td>
<td>18.10</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>33.30</td>
</tr>
<tr>
<td>24</td>
<td>4.75</td>
<td>0</td>
<td>4.26</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4.75</td>
<td>4.26</td>
</tr>
<tr>
<td>20</td>
<td>4.75</td>
<td>0</td>
<td>4.53</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4.75</td>
<td>4.53</td>
</tr>
<tr>
<td>29</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
**APPENDIX 18**

Quality of life measures in adults.

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>DLQI1</th>
<th>DLQI2</th>
<th>PGI</th>
</tr>
</thead>
<tbody>
<tr>
<td>45</td>
<td>F</td>
<td>2</td>
<td>80</td>
<td></td>
</tr>
<tr>
<td>28</td>
<td>M</td>
<td>2</td>
<td>77</td>
<td></td>
</tr>
<tr>
<td>37</td>
<td>F</td>
<td>6</td>
<td>14</td>
<td>53</td>
</tr>
<tr>
<td>17</td>
<td>F</td>
<td>8</td>
<td>17</td>
<td>5</td>
</tr>
<tr>
<td>20</td>
<td>M</td>
<td>7</td>
<td>13</td>
<td>39</td>
</tr>
<tr>
<td>23</td>
<td>F</td>
<td>9</td>
<td>11</td>
<td>45</td>
</tr>
<tr>
<td>45</td>
<td>F</td>
<td>1</td>
<td>4</td>
<td>30</td>
</tr>
<tr>
<td>29</td>
<td>F</td>
<td>2</td>
<td>8</td>
<td>53</td>
</tr>
<tr>
<td>29</td>
<td>F</td>
<td>2</td>
<td>11</td>
<td>12</td>
</tr>
<tr>
<td>33</td>
<td>F</td>
<td>2</td>
<td>10</td>
<td>33</td>
</tr>
<tr>
<td>18</td>
<td>M</td>
<td>10</td>
<td>10</td>
<td>50</td>
</tr>
<tr>
<td>16</td>
<td>F</td>
<td>3</td>
<td>7</td>
<td>55</td>
</tr>
<tr>
<td>22</td>
<td>F</td>
<td>0</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>41</td>
<td>F</td>
<td>1</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>30</td>
<td>F</td>
<td>1</td>
<td>10</td>
<td>100</td>
</tr>
<tr>
<td>20</td>
<td>F</td>
<td>3</td>
<td>5</td>
<td>90</td>
</tr>
<tr>
<td>39</td>
<td>M</td>
<td>3</td>
<td>1</td>
<td>37</td>
</tr>
<tr>
<td>36</td>
<td>F</td>
<td>5</td>
<td>6</td>
<td>100</td>
</tr>
<tr>
<td>16</td>
<td>F</td>
<td>3</td>
<td>4</td>
<td>40</td>
</tr>
<tr>
<td>32</td>
<td>F</td>
<td>5</td>
<td>6</td>
<td>100</td>
</tr>
<tr>
<td>22</td>
<td>F</td>
<td>9</td>
<td>11</td>
<td>18</td>
</tr>
<tr>
<td>27</td>
<td>F</td>
<td>9</td>
<td>11</td>
<td>18</td>
</tr>
<tr>
<td>22</td>
<td>F</td>
<td>1</td>
<td>5</td>
<td>100</td>
</tr>
<tr>
<td>28</td>
<td>F</td>
<td>24</td>
<td>25</td>
<td>20</td>
</tr>
<tr>
<td>31</td>
<td>F</td>
<td>11</td>
<td>10</td>
<td>27</td>
</tr>
<tr>
<td>24</td>
<td>F</td>
<td>8</td>
<td>10</td>
<td>40</td>
</tr>
<tr>
<td>36</td>
<td>F</td>
<td>4</td>
<td>5</td>
<td>100</td>
</tr>
<tr>
<td>21</td>
<td>F</td>
<td>2</td>
<td>4</td>
<td>45</td>
</tr>
<tr>
<td>19</td>
<td>M</td>
<td>1</td>
<td>5</td>
<td>100</td>
</tr>
<tr>
<td>32</td>
<td>F</td>
<td>10</td>
<td>13</td>
<td>32</td>
</tr>
<tr>
<td>40</td>
<td>M</td>
<td>12</td>
<td>18</td>
<td>18</td>
</tr>
<tr>
<td>47</td>
<td>F</td>
<td>5</td>
<td>12</td>
<td>15</td>
</tr>
<tr>
<td>25</td>
<td>F</td>
<td>2</td>
<td>3</td>
<td>38</td>
</tr>
<tr>
<td>23</td>
<td>F</td>
<td>9</td>
<td>10</td>
<td>32</td>
</tr>
<tr>
<td>28</td>
<td>F</td>
<td>4</td>
<td>7</td>
<td>100</td>
</tr>
<tr>
<td>20</td>
<td>F</td>
<td>3</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>27</td>
<td>F</td>
<td>4</td>
<td>3</td>
<td>100</td>
</tr>
<tr>
<td>28</td>
<td>F</td>
<td>4</td>
<td>13</td>
<td>30</td>
</tr>
<tr>
<td>30</td>
<td>F</td>
<td>8</td>
<td>10</td>
<td>28</td>
</tr>
<tr>
<td>21</td>
<td>F</td>
<td>9</td>
<td>11</td>
<td>47</td>
</tr>
<tr>
<td>22</td>
<td>F</td>
<td>10</td>
<td>16</td>
<td>0</td>
</tr>
<tr>
<td>17</td>
<td>F</td>
<td>7</td>
<td>6</td>
<td>35</td>
</tr>
<tr>
<td>Age</td>
<td>Sex</td>
<td>DLQ11</td>
<td>DLQ12</td>
<td>PG1</td>
</tr>
<tr>
<td>-----</td>
<td>-----</td>
<td>-------</td>
<td>-------</td>
<td>-----</td>
</tr>
<tr>
<td>19</td>
<td>M</td>
<td>2</td>
<td>2</td>
<td>70</td>
</tr>
<tr>
<td>23</td>
<td>F</td>
<td>15</td>
<td>24</td>
<td>18</td>
</tr>
<tr>
<td>17</td>
<td>M</td>
<td>10</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>29</td>
<td>F</td>
<td>2</td>
<td>5</td>
<td>22</td>
</tr>
<tr>
<td>34</td>
<td>M</td>
<td>5</td>
<td>10</td>
<td>32</td>
</tr>
<tr>
<td>30</td>
<td>M</td>
<td>6</td>
<td>4</td>
<td>20</td>
</tr>
<tr>
<td>54</td>
<td>F</td>
<td>5</td>
<td>7</td>
<td>14</td>
</tr>
<tr>
<td>32</td>
<td>F</td>
<td>9</td>
<td>19</td>
<td>18</td>
</tr>
<tr>
<td>20</td>
<td>M</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>23</td>
<td>F</td>
<td>3</td>
<td>3</td>
<td>60</td>
</tr>
<tr>
<td>35</td>
<td>F</td>
<td>7</td>
<td>7</td>
<td>50</td>
</tr>
<tr>
<td>24</td>
<td>F</td>
<td>7</td>
<td>11</td>
<td>31</td>
</tr>
<tr>
<td>20</td>
<td>M</td>
<td>6</td>
<td>8</td>
<td>30</td>
</tr>
<tr>
<td>29</td>
<td>M</td>
<td>2</td>
<td>2</td>
<td>70</td>
</tr>
</tbody>
</table>
# Appendix 19

Children's quality of life data.

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Section 1</th>
<th>Section 2</th>
<th>Section 3</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>F</td>
<td>7</td>
<td>10</td>
<td>10</td>
<td>27</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>8</td>
<td>20</td>
<td>3</td>
<td>31</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>4</td>
<td>7</td>
<td>1</td>
<td>12</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>12</td>
<td></td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>F</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>3</td>
<td>6</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>3</td>
<td>9</td>
<td>15</td>
<td>27</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>5</td>
<td>4</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>3</td>
<td>5</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>15</td>
<td>M</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>0</td>
<td>8</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>1</td>
<td>3</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>11</td>
<td></td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>2</td>
<td>5</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>7</td>
<td>14</td>
<td>2</td>
<td>23</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>1</td>
<td>5</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>2</td>
<td>4</td>
<td>8</td>
<td>14</td>
</tr>
<tr>
<td>11</td>
<td>F</td>
<td>5</td>
<td>5</td>
<td>13</td>
<td>23</td>
</tr>
<tr>
<td>13</td>
<td>M</td>
<td>5</td>
<td>5</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>3</td>
<td>5</td>
<td>5</td>
<td>13</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>9</td>
<td>7</td>
<td>0</td>
<td>16</td>
</tr>
<tr>
<td>14</td>
<td>F</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>5</td>
<td></td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>F</td>
<td>9</td>
<td>14</td>
<td>7</td>
<td>30</td>
</tr>
<tr>
<td>15</td>
<td>F</td>
<td>12</td>
<td>11</td>
<td>12</td>
<td>35</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>13</td>
<td>M</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>15</td>
<td>M</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>1</td>
<td>5</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>8</td>
<td>11</td>
<td>1</td>
<td>20</td>
</tr>
<tr>
<td>16</td>
<td>F</td>
<td>5</td>
<td>13</td>
<td>6</td>
<td>24</td>
</tr>
<tr>
<td>14</td>
<td>M</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>3</td>
<td>5</td>
<td>2</td>
<td>10</td>
</tr>
</tbody>
</table>
ADDENDUM

The following problems with the sampling scheme outlined in chapter 2 and estimates of prevalence in chapter 3 have been identified.

1(a) The sampling procedure selected families with probability proportional to size. This attribute was true for families but not for age groups within families. It follows that in the random cluster sample in group 3 the sampling within age groups was not with probability proportional to size. Furthermore, non-responder did not follow any probability proportional to size rule. The estimated numbers with atopic dermatitis within age strata cannot be assumed to be unbiased.

1(b) The formulae used for the estimates in sampling groups 1 and 2 assume sampling with replacement. This assumption is not crucial when the sampling fraction is low as in group 3 but is important when the sampling fraction is high as in groups 1 and 2.

1(c) The prevalence estimates were calculated on the basis of sampling with probability proportional to size. In groups 1 and 2 this may have been important.

1(d) The estimate of variance relies on the assumption that the proportion of family members within age strata in group 1 is homogeneous. This is not true. However any one family member having atopic eczema increases the probability of any other family member of any age having atopic eczema and this reduces this problem.

2. Bounds - ages 2-11

Cochran WG, Sampling Techniques, Third edition, p259, 9A.7. This section the Horvitz-Thompson Estimator for sampling with unequal probabilities without replacement. \( \pi_i \) is the probability of the \( i \)th unit being in the sample. \( \pi_{ij} \) is the probability that both units \( i \) and \( j \) are in the sample.
\[ Y = \sum y_i / \pi_i \]

where \( y_i \) = number in \( i \)th unit
and \( \pi_i \) = the probability of \( i \)th cluster being in sample.

Then in group 1, the probability of being in the sample is related to all ages

\[ \pi_i = 0.93 \text{ (approximated as the sampling fraction)} \]
\[ Y = 35/0.93 = 37.6 \]
\[ \text{Var} \ (Y) = \sum (0.07/0.93)y_i^2 \]
\[ = (0.07/0.93) \times 36 \]
\[ = 2.71 \]

In group 2
\[ \pi_i = 0.89 \]
\[ Y = 13/0.89 = 14.6 \]
\[ \text{Var} \ (Y) = 1.61 \]

In group 3
\[ \pi_i = 0.08936 \text{ for a family size 3} \]
\[ \pi_i = 0.11734 \text{ for a family size 4} \]
\[ \pi_i = 0.17077 \text{ for a family size 6} \]
\[ \pi_i = 0.19626 \text{ for a family size 7} \]

and for two families size 4
\[ \pi_{ij} = 0.01383 \text{ etc} \]

\[ Y = \sum y_i / \pi_i = (2/0.17077) + (2/0.11734) + (2/0.11734) \ldots \]
\[ = 79.1 \]
\[ \text{Var} \ (Y) = \sum ((1-\pi_i)/\pi_i)y_i^2 + 2\sum \sum ((\pi_{ij} - \pi_{ij})/\pi_{ij}) y_{ij} \]
\[ = 108.9 + 0.825 \]
\[ = 109.7 \]
\[ \sum Y = 131.3 \]
\[ \text{Var} \ (\sum Y) = 114.02 \]

Prevalence estimate = \((37.6 + 14.4 + 79.1) / 1397\) * 100%
\[ = 7.7\% \]

SE = \((\sqrt{114.02})/1397\) * 100%
\[ = 0.8\% \]
Bounds - ages 12-15

Groups 2 and 3 yielded no cases of AD. Instead of calculating the SE it is better to quote confidence limits, with the lower limit being the frequency of AD in group 1. The upper limit is calculated with an estimate of variance assuming a frequency of 0.5 in groups 2 and 3.

95% confidence limits for Y are [10, 13.6]
This gives 95% confidence limits for the prevalence of [1.6, 2.2]

Bounds - ages 16-24

Similar to ages 12-15
95% confidence limits for Y are [29, 34.8]
This gives 95% confidence limits for the prevalence of [1.8, 2.2]

Bounds - ages 25-40

Calculations for this group are similar to 2-11 range.
Prevalence estimate = 2.3%
SE = 0.24

Bounds - ages 41+

Similar to ages 12-15
95% confidence limits for Y are [5, 7.9]
This gives 95% confidence limits for the prevalence of [0.15, 0.24]
Clinical review

Recent advances in atopic dermatitis

J.A.A. HUNTER and R.M. HERD

From the University Department of Dermatology, The Royal Infirmary, Edinburgh

Introduction

Atopic dermatitis remains, in many respects, as strange a condition now as when Coca and Cooke classified it in 1923.1 Its inheritance and pathogenesis still fuel much research and controversy; its treatment may test patients, their families and their doctors to the limit. But real progress in understanding different aspects of the disease has been made during the last ten years.

Diagnosis

Sound and simple diagnostic criteria are fundamental to all studies on the condition, especially those which are based in the community and conducted by those without clinical experience of atopic dermatitis. Williams convened a working group which has suggested some 'gold-standard' clinical features.2 To qualify as a case of atopic dermatitis, an individual must have an itchy skin condition (or parental report of scratching or rubbing in a child) plus three or more of the following: history of involvement of the skin creases such as folds of elbows, behind the knees, fronts of ankles or around the neck (including cheeks of children under 10 years); a personal history of asthma or hay fever (or history of atopic disease in a first-degree relative in children under 4 years); a history of general dry skin in the last year; visible flexural eczema (or eczema involving the cheeks/forehead and outer limbs in children under 4 years); onset under the age of 2 years (not used if child is under 4 years). The beauty of these criteria is that they are simple, take under two minutes to determine and do not require the subject to undress. They have been carefully validated, there is good agreement between doctors about the presence or absence of these features, and individual doctors are consistent in their assessment of them. Discrimination of atopic dermatitis was impressive, with a sensitivity of 85% and specificity of 96%. We no longer need to depend on signs such as keratosis pilaris and fine hair, on which dermatologists too often disagree. The criteria do not include total IgE concentrations in the blood, positive IgE titres to specific antigens, positive responses to prick tests, or combinations of these,3 although there is undoubtedly a need to validate such tests in a similar way to the clinical diagnostic criteria proposed by Williams' working group.

Prevalence and epidemiology

Good population-based studies are necessary to obtain an accurate estimate of the frequency of the condition. Atopic dermatitis is subject to many influences such as race and climatic conditions.4 Early reports relied on a variety of sources of data, such as questionnaires sent to parents, health visitor observations and government health census statistics.5-7 Comparisons between studies is difficult because of the different measures of frequency which were used, such as point prevalence, period prevalence or cumulative incidence, and the diversity of populations examined. Understanding is further hampered by the retrospective approach of most studies.

One of the first published estimates of prevalence was by Walker and Warin in 1956 using health visitor cards.8 Their quoted prevalence of 3.1% for infantile eczema was probably an underestimate, because they included only cases where there was no doubt about the diagnosis. In 1955, Eriksson-Lihr
mentioned two large Finnish studies on the occurrence of allergy in school children.\(^8\) The first, from Turku, based on information from questionnaires to parents, school health cards and local health centre records revealed that 3% of 4832 children had eczema. The second, from Helsinki involving 27,999 children aged 7–14 years, took advantage of school health cards and medical examinations and showed that 2% had eczema.

Since these early studies, many reports have revealed a steady increase in the reported prevalence of atopic dermatitis. Despite the pitfalls of making comparisons, the evidence strongly suggests that this increase is genuine and parallels the rising incidence of other atopic diseases.\(^9\)\-\(^14\)

Why has there been such an increase in the incidence of atopic dermatitis in recent years? Several plausible explanations are examined by Williams.\(^9\) A change in chronicity, possibly as a result of the widespread use of topical steroids, may result in more frequent or prolonged periods of exacerbation, causing an apparent but false increase in prevalence. New household cleaning materials may be acting as disease modulators for atopic dermatitis allowing sensitization through damaged skin. Changes of lifestyle and increasing environmental pollution are frequently cited causes.\(^14\) Polychlorinated biphenyl levels in human breast milk have been reported as rising in recent years, and agricultural chemicals in cows milk provide a further source of exposure to these chemicals in infants.\(^15\) The issue is far from resolved, and the subject of environmental pollutants is bound to throw many other hypotheses to explain the increasing prevalence of atopy.

The most recent, reliable figures are cumulative incidence rates of 12% for 5-year-olds, and between 9% and 12% for 7-year-olds.\(^10\)\(^,\)\(^11\)\(^,\)\(^16\)\(^,\)\(^17\) In children aged 12–16 the point prevalence has been estimated at 3.0%, declining rapidly with age.\(^18\) Our unpublished data, generated from a community study of a large general practice, yielded one-year period prevalence figures of 6% for the under 2s and 13% for the 2–12-year age group.

The epidemiology of adult atopic dermatitis has been largely neglected. Published figures indicate a prevalence of 'eczema' of 2–7% without atopic dermatitis being quoted separately.\(^19\) The results of our recent community study using the UK Working Party criteria suggest a prevalence of 1% in the over-25 age group, with a steep decline with age.

Atopic dermatitis begins in early childhood in the majority of patients, with a M:F sex ratio of between 1:1 and 1:1.7.\(^25\) Queille-Roussel et al.\(^20\) in a study of 500 children, published figures on the age of onset in children attending a paediatric dermatology unit. The results are biased downwards because it was not a cohort study, but it is of interest that 91% of their patients developed atopic dermatitis before the age of two, and 65% before they were 6 months old.\(^20\) Rajka's figure of 80–90% of patients having developed the condition before the age of seven may be more accurate.\(^21\)

### Genetic aspects

Recent studies on the inheritance of atopy have been well summarized by Savin.\(^22\) It seems clear that atopic dermatitis, asthma and hay fever tend to run true to type in families,\(^23\)\(^,\)\(^24\) although some unfortunate individuals have the full house of atopic manifestations. Two studies\(^25\)\(^,\)\(^26\) indicate that atopy is inherited more often from the mother than the father, a suggestion made earlier by Cookson et al. from Oxford when they linked atopy, based on an IgE definition, to markers on chromosome 11q13 in about 60% of cases.\(^27\) Linkage of atopy to 11q13 has since been replicated by two other teams, a Dutch group,\(^28\) using sibling pairs, and a Japanese group,\(^29\) using Lod score methods. Sandford et al.\(^30\) have gone on to propose a theoretically attractive candidate gene, coding for the β subunit of the high affinity receptor for IgE, which lies on chromosome 11q13. All would be well if it were not for the dissenting voices of some other groups who have failed to detect linkage between atopy and chromosome 11q.\(^31\)\(^,\)\(^32\) Genetic heterogeneity and methodological differences may well explain the dilemma.

### Immunological aspects

A fundamental defect which is specific for atopic dermatitis, rather than common to all types of atopy, has been difficult to establish. The many abnormalities found in atopy, reviewed by Chapman and Parish,\(^33\) include decreased delayed hypersensitivity responses, decreased numbers of mature T lymphocytes in the blood (particularly those with suppressor activity), defective metabolism of essential fatty acids which are the precursors of eicosanoid mediators of inflammation, increased permeability of intestinal mucosa to food allergens, abnormal signal transduction from a and b adrenergic receptors due to increased amounts of cAMP phosphodiesterase, and abnormal vascular responses to histamine, nicotinic acid and acetylcholine.

However, it is hard to believe that IgE antibody, serum levels of which are raised in 80–85% of patients with atopic dermatitis, does not play a critical role in triggering the rash.\(^36\) Recent studies have demonstrated a high-affinity IgE receptor on human epidermal Langerhans' cells\(^37\)\(^,\)\(^38\) and have shown that these cells, which are increased in number in atopic dermatitis,\(^39\) are capable of presenting house dust mite antigen to CD4\(^+\) (helper) T lymphocytes.\(^40\) Hauser et al. have also found that T
helper lymphocytes, repeatedly stimulated with hapten-modified cultured Langerhans cells, produce interleukin-4 and stimulate IgE production by B cells.41 Although the situation in the human is not so clear, it has been shown convincingly in mice that there are two helper T-cell populations which can be distinguished by the cytokines which they produce. Th1 cells produce IL-2 and IFNγ, whereas Th2 cells produce IL-4 and IL-5.42 Interestingly, IL-4 inhibits the synthesis of IFNγ and induces the synthesis of IgE in human mixed lymphocyte cultures.43 There is growing evidence that T cells from atopic dermatitis patients are predominantly Th2 in type.44,45 It is no longer difficult to envisage that important antigens, such as those of the house dust mite,46 are trapped in the epidermis by specific IgE antibody bound by the high-affinity IgE receptors on the surface of Langerhans cells, and then processed for antigen presentation. This encourages the local accumulation of Th2-type cells and, by the above mechanisms, induces further production of IgE by B cells. However, this sequence of events cannot explain the pathogenesis of the rash in those atopics with no detectable or normal levels of IgE.35 Recently, an alternative pathway leading to the accumulation of inflammatory cells in the skin, independent of IgE, has been suggested. Bacterial toxins released by Staphylococcus aureus, which colonizes over 90% of atopic dermatitis lesions, may not only elicit production of IgE antibody,57 but also exacerbate atopic dermatitis by a different mechanism. These toxins are prototypic superantigens.48 Sensitization to such superantigens is not necessary to prime the immune response. Superantigens align with a variety of class II MHC molecules outside their antigen presentation groove and, without any cellular processing, may directly signal different classes of T cells within the large family carrying a Vb type of T-cell receptor. By these means, superantigens are capable of inducing massive T-cell proliferation.

Assessing disability

Although atopic dermatitis is not a life-threatening condition, it can result in considerable disability, both physical and psychological.49 The skin is the most visible organ in the body, and any abnormality or blemish is immediately apparent and can lead to stigmatization. This has been addressed principally with regard to psoriasis and leprosy, but in recent years there has been an increasing interest in the impact of atopic dermatitis on quality of life.50-52 Assessment of disability is necessary for routine management of patients, and in research for the comparison of groups of patients receiving new treatments.53 The UK Sickness Impact Profile (UK SIP) has been used to assess the impact of hyperten-

sion, angina and the side-effects of new drugs, and has been used in the validation of the Psoriasis Disability Index (PDI).54,55 This comparison has shown that the PDI is an appropriate and rapid method of assessing quality of life impairment in psoriasis. The use of an Eczema Disability Index derived from the PDI, although initially promising, has failed to show a clear link with the UK Sickness Impact Profile.56,57 A new compact questionnaire called the Dermatology Life Quality Index has yielded promising results in the assessment of atopic dermatitis patients.58 The reproducibility of this measure is reassuring judging from a one-week test-retest study, but formal comparison with the UK SIP and PDI has yet to be completed. Our own work suggests that loss of sleep, skin irritation when swimming, and embarrassment about appearance rank as the three aspects of the disease which cause most distress to patients.

These questionnaires may be useful tools in adults but the majority of patients with atopic dermatitis are children. The problems of assessing quality of life impairment in children are enormous, and this may explain why so little work has been done in this area and why, as yet, no measure of disability exists for children.

Economics

The importance of atopic dermatitis lies in its high prevalence in children, and the dramatic impact on the lives of those who are most severely affected. It is therefore surprising that the economics of atopic dermatitis have been largely ignored, and that there have been only two publications on this subject in recent years compared with 181 dealing with the economics of HIV infection. A conservative estimate of the annual cost of treating atopic dermatitis in children in the USA is $364m.59 A direct comparison with the UK is not possible, owing to the differences in the delivery of health care. In the UK much of the economic burden is shouldered by the state, but loss of employment, frequent purchase of over-the-counter preparations, prescription charges and damaged clothing and bedding can lead to considerable personal costs. In our own recent unpublished work, the monthly cost to the patient can be up to £390 and the cost to the Health Service up to £650. However, the monthly cost for the majority of patients is very much less than this, the median being about £3. A final analysis of this data has yet to be completed.

Treatment

Judicious local corticosteroid treatment and emollients remain the cornerstone of treatment for atopic
dermatitis. Useful adjunctive therapies, which have attracted attention recently, include ultraviolet-B radiation and psoralen phototherapy (PUVA). Short courses rather than prolonged maintenance courses are preferable. There has been much debate about the value of gamolenic acid in evening primrose oil. Different groups have used the same data, obtained from placebo-controlled double-blind trials, to support opposing views on its efficacy. Many doctors, with their therapeutic backs to the wall, will try gamolenic acid as an adjuvant to conventional treatment, believing that it may have a modest beneficial effect in about a third of patients and knowing that it has almost no side-effects. For years clinicians have found prolonged courses of anti-staphylococcal antibiotics helpful; some might feel reassured that the discovery of bacterial superantigens has given theoretical respectability to this practice. Intermittent courses of cyclosporin A (a drug which reduces T-cell activation), should give hope to those atopic patients whose lives have been made miserable with widespread and recalcitrant dermatitis. The avoidance of food allergens, either prophylactically or when food allergy is diagnosed, remains as controversial as the place of food allergy in the pathogenesis of atopic dermatitis. Zeiger et al. showed that the gains when expectant mothers practised food allergen prophylaxis were relatively short-lived. If there is no doubt, on historical grounds, that certain foods either lead to an exacerbation of the dermatitis or cause urticaria, then they should be excluded from the diet, possibly after RAST testing. Avoidance of contact with dust mite allergen appears more promising. Genuine advances are being made in unravelling the complexities of this strange disease.

References
28. Collee JM, ten Kate LP, de Vree HJ, Kliphuis JW, Bouman


341:1121–2.


40. Muder G, van Reijesen FC, Boland GF, de Gast GC, Bruinzeel PLB, Briuinzeeel-Kromen C. Allergen presentation by epidermal Langerhans’ cells from patients with atopic dermatitis is mediated by IgE. Immunol 1990; 69:335–41.


Prevalence of atopic eczema in the community: the Lothian atopic dermatitis study

R.M. HERD, M.J. TIDMAN, R.J. PRESCOTT* AND J.A.A. HUNTER
University Department of Dermatology, Level 4, Lauriston Building, Royal Infirmary of Edinburgh NHS Trust, EH3 9YW and *Department of Public Health Sciences, University of Edinburgh, U.K.
Accepted for publication 19 October 1995

Summary An epidemiological study of atopic eczema (AE), based on a semirural community in Scotland, using sound diagnostic criteria, has yielded prevalence data for all age groups including infants and adults. The overall 1-year period prevalence, age-standardized to the Scottish population, was 2-3%. The 1-year period prevalence was highest in the under 2s (9-8%), and showed a continuous reduction with increasing age. Over the age of 40, AE was found to be relatively rare, with a 1-year period prevalence of 0-2%. Adults over 16 years made up 38% of all patients with AE.

Atopic eczema (AE) has major socio-economic implications. 1 Although the cellular mechanisms behind the atopic phenotype have become clearer, and powerful new treatments have been introduced, 2,3 reliable epidemiological data are sparse. The few studies of prevalence have not always defined their diagnostic criteria, and some have based on health visitor records or questionnaires that have relied on a parental diagnosis. A variety of measures of frequency have been used, e.g. cumulative incidence or point prevalence. AE in infants, and adults, largely has been ignored. The aim of our study was to estimate, accurately, from a representative population, the prevalence of AE at all ages.

Methods The study population comprised a semirural general practice, of 9786 patients, situated in Livingston, a new town in central Scotland. The age distribution differs from that in the rest of Scotland, with a larger proportion of young adults, and a correspondingly smaller proportion of adults over 65. The social class distribution is biased slightly towards social class III, and away from the higher and lower social classes. 4

Howden Health Centre is a well-organized practice, served by eight general practitioners (GPs). Access to medical records was facilitated by a computerized records system. One of us (RMH) examined all available patients with a coding of eczema on the practice computer, together with the other members of the family, to identify those with AE. As infants were poorly represented in this sample, every family with a child aged less than 2 was contacted. To estimate the number of patients with AE in the remaining practice population not identified on the computer, a one-stage random cluster sample of 10% was taken, each cluster being a family. 5

The diagnosis of AE was established using the U.K. Working Party’s diagnostic criteria. 5 These require a history of an itchy skin condition, and three other criteria, only one of which relies on examination. This protocol was adhered to strictly. The possible effects of seasonal variation were eliminated by recruiting patients over a 1-year period, and by measuring the 1-year period prevalence. Prevalence and standard errors were calculated by stratified cluster sampling techniques, with a finite population correction. 5

Results The contact rate was 93% for patients with GP-diagnosed eczema and their families, 89% for the under 2s, and 87% for the random cluster sample. Altogether, 2365 patients were sampled in these groups, 24% of the practice population.

The U.K. Working Party’s diagnostic criteria proved ideal for use in a community setting. No cases of AE were thought to be missed. Conversely, two adults who fulfilled the criteria did not have AE: one had nickel dermatitis causing eczema on her neck, the other had pityriasis versicolor. Both were excluded.

The 1-year period prevalences of AE, for the different age groups, are shown in Table 1, and demonstrate a steady decline with increasing age. The male:female
ratio, of 1.5:1, among infants under 2 (1-year period prevalence for males, 11.9%, and for females, 7.2%), was reversed in older age groups (1-year period prevalences aged 2-11, 12-24 and 25+ for males, 7.7, 1.4 and 1.1% respectively, and for females, 11.4, 2.4 and 1.3%). Sixty-five per cent of patients diagnosed as having AE had active eczema at the time the diagnosis was made. The overall 1 year period prevalence, age-standardized to the Scottish population for all age groups, was 2.3%. Only 52% of patients with AE were aged between 2 and 15, leaving almost half of AE patients in the poorly studied groups below the age of 2 and over the age of 16. Thirty-eight per cent of all patients with AE were over 16. The 1-year period prevalence in the 16-40 group was 2.0% dropping to 0.2% in the over-forties.

The prevalences of active eczema are also displayed. While 66% of individuals, aged below 16, were in remission at the time they were examined, only 47% of adults over 16 were in remission.

**Discussion**

The 1-year period prevalence for infants under 2 was 9.8%. The possible reason for the neglect of the epidemiology of AE in infants is that, until now, there have been no reliable diagnostic criteria. Recent reports have glossed over the issue of robust inclusion criteria, which may have contributed to a high lifetime incidence of 20-4%, in the under 3s, in one study.7 The U.K. Working Party's criteria contribute a framework for comparison between this and future studies, provided that the format is adhered to closely.

Information on the prevalence of AE in adults is very sparse. The figures presented in the Lambeth study, in 1976, of a prevalence of 12.5% for ages 35-54, suggest, as acknowledged by the authors, that many conditions other than AE must have been included under the banner of ‘eczema’.8 There appears to be a rising prevalence of AE in children9 and, if this shows a cohort effect, it will be reflected in the adult population, resulting in a commensurate increase in the proportion of affected adults. We have shown that the decline in AE, known to occur with increasing age during childhood and due possibly to age, period or cohort effects, continues in adult life, until over the age of 40, when AE becomes relatively uncommon. In one sense this justifies the almost exclusive attention given to school children but, when one considers that 38% of all AE patients are over 16 years of age, the size of the problem in the adult population becomes apparent. It is clear from the prevalence figures of active eczema, in Table 1, that an adult with AE is more likely to have active disease than a child.

This study is unique in three respects: it uses firm diagnostic criteria in a community setting, standard errors are quoted for prevalences, and accurate prevalence figures for adults are given. As AE is a seasonally influenced disorder, we recommend that the 1-year period prevalence is the best measure of its frequency, and should be used in comparative studies.

**Acknowledgments**

We wish to express our gratitude to all staff at Howden Health Centre, who were always courteous and helpful, and to the Edinburgh Dermatological Research Fund for funding.

**References**

The cost of atopic eczema

R.M.Herd, M.J.Tidman, R.J.Prescott* and J.A.A.Hunter

Departments of Dermatology and *Public Health Sciences, University of Edinburgh, Edinburgh, EH3 9YW, U.K.

Accepted for publication 18 December 1995

Summary

Atopic eczema affects 2·3% of the U.K. population. We have carried out a community study in a semi-rural area to assess its economic impact. One hundred and fifty-five patients with atopic eczema were identified and expenditure was assessed over a 2-month period. The mean personal cost to the patient was £25·90, while the mean cost to the health service was £16·20. There were 58 lost working days and 17 lost school days. A cohort of 10 severely affected patients attending the Royal Infirmary of Edinburgh were studied; each patient spent, on average, £325 in 2 months, and lead to a mean health service expenditure per patient of £415, in 2 months. If these results were extrapolated to the U.K. population, the annual personal cost to patients with atopic eczema would be £297 m, the cost to the health service would be £125 m, and the annual cost to society of lost working days would be £43 m, making the total expenditure on atopic eczema £465 m.

Medical practice in the U.K. is becoming increasingly shackled by economic constraints, necessitating a firm understanding of the financial implications of different diseases, both to the patient and to the health service. This is particularly important for the most prevalent disorders, such as atopic eczema (AE), which affects 1·4 million people in the U.K.¹

The economic considerations of AE have received scant attention, with only one relevant publication in recent years.² These authors conservatively estimated the annual cost of treating children in the U.S.A. to be $36·4 m.² One objective of the Lothian Atopic Dermatitis Study was to estimate the costs associated with treating AE in patients of all ages in the U.K.

Methods

The target population was a semi-rural general practice of 9786 patients in Livingston, West Lothian. This is served by eight general practitioners, all of whom use computerized records that contain diagnostic coding for various forms of eczema, allowing easy identification of eczema sufferers known to the practice. The effect of seasonal variation on the cost of treatment was eliminated by conducting the study over a 1 year period: each of the eight GP lists, selected in random order, was studied over a 6-week period. The sample was chosen in four stages to identify as many individuals with AE as possible:

1 Patients with a coding of any type of eczema on the practice computer were selected and subsequently examined, together with their families, to confirm the precise classification.
2 It was apparent that relatively few infants with AE were registered on the diagnostic index. Therefore, all families in the practice with a child aged under 2 years were questioned and examined.
3 It was assumed that the diagnostic index on the practice computer was not comprehensive. To estimate the number of cases in that section of the population not included in stages 1 or 2, a random cluster sample was chosen. Each cluster was a single family sampled with probability proportional to size.⁴ Families were contacted by telephone and each adult family member was interviewed. Adults were questioned about their children, and anyone with a history of an itchy skin was examined.
4 All members of one family in six which had denied the presence of an itchy member at stage 3 were also examined, to reduce the chance of cases of AE being omitted.

Confirmation of the diagnosis of AE was made using the diagnostic criteria of a U.K. working party.⁴ Adults and parents of children who fulfilled these criteria were asked to record on a proforma, over a 2-month period, all costs relating to their skin condition (Table 1). These costs could be attributed either to the patient (e.g. prescription charges and over-the-counter preparations), to the health service (e.g. drugs and doctor or nurse time), or to society (e.g. lost working days). The cost of
doctor and nurse time included their salaries and the general running costs of the hospital or health centre, and were calculated by standard methods, as was the cost to society of lost working days.

This was primarily a study of AE in the community, and only a few patients in the practice had severe disease. To evaluate the costs of the latter, a cohort of 10 patients, randomly selected over a 1-year period, with AE severe enough to require attendance at the Royal Infirmary of Edinburgh (RIE) for dressings or for in-patient treatment, was assessed in a way similar to that used in the community study. Patients were recruited at the time of commencement of dressings or admittance at the ward, when expenditure was likely to be at its highest.

The distribution of the data is highly skewed and, therefore, does not lend itself to parametric statistical analysis. The aim of this community survey was to estimate the cost of AE to the whole community and, as a measure of average, means are an appropriate guide to community expenditure. In contrast, medians are a more representative measure of average than means when outlining the distribution of expenditure in the target population, and are used where appropriate.

Patients were grouped into three age ranges: 0–2 years, 2–15 years, and over 16 years, and each age group considered separately. The results were extrapolated to the whole practice population with the assumption that the costs of those not identified by the sampling scheme would be similar to those identified in the random cluster sample in stage 3.

The chi-squared test with Yates' correction and the Mann–Whitney U-test were used in the analysis.

Results

One hundred and fifty-five of the 2365 individuals sampled in the community fulfilled the diagnostic criteria for AE and were studied in detail: 103 from sampling stage 1; 38 from stage 2; and 14 from stage 3. Sampling stage 4 produced no further cases. One hundred and forty-six questionnaires were completed for the costing assessment; 19 concerned patients less than 2 years, 58 patients aged 2–16 years, and 69 patients aged 16 years and over. Fifty-eight lost working days and 17 lost school days were attributable to AE over a 2-month period. A summary of these figures, expressed per annum, is given in Table 2, and the distribution of costs to the patient and health service are shown in Figure 1.

**Personal costs**

Over 2 months the mean personal expenditure by patients was £25.90 and the maximum spent by an individual was £546, 81% of which was due to salary loss. Ten patients spent over £100 and three spent over £300. Some patients in remission, and some who were only mildly affected, had no expenditure attributable to AE, and this included 45% of those aged less than 16, compared with 26% of those over 16; i.e. significantly more of the younger group had no expenditure \( (\chi^2 = 7.47, P < 0.01) \). Expenditure at 2–15 years
was significantly lower than that in the over 16 group (medians £0.50 and £6.73, \(P < 0.05\)), while that in the under 2 group was significantly lower than the older age groups, with a ceiling of £40 (median £0.00, \(P < 0.05\)). The median was £0.00 because over 50% of parents of the under 2s had no expenditure.

Patients below the age of 16 do not pay for prescriptions and, of the 69 over 16 years, only 28 spent money on prescriptions, which accounted for 7% of personal costs.

Treatments bought over the counter by patients accounted for 21% of the total cost. These mainly consisted of emollients, bath additives, shampoos and evening primrose oil. Very little was spent by adults on bath additives compared with the younger groups, while relatively more was spent on shampoos.

There was substantial salary loss but the largest part of expenditure by patients was on clothing and laundry. Other expenses consisted of visits to a homeopath by two children, herbalist advice to one adult, and a visit to London for Chinese herbal medicine by one child and his parent.

**Health service costs**

The mean 2-month cost to the health service was £16.20 and the maximum attributable to one patient was £177.07. Ten patients cost the health service over £50 but only two cost over £100. The median cost in the 2–15 age group was significantly higher than that in the over 16 age group (£10.86 and £6.22, \(P < 0.05\)) while that in the under 2 group had a median of £18.72, significantly higher than the older groups (\(P < 0.05\)).

The majority of health service costs were on treatments: 38% was on emollients or bath additives, 32% was on topical steroids, 10% on bandages, while the remaining 20% was for antihistamines, shampoos, antibiotics and evening primrose oil.

Eighty-nine percent of prescribed steroids were moderately potent and mildly potent; 68% of those prescribed to adults were moderately potent and 69% prescribed to the younger group were mild.

GP consultations comprised almost 30% of costs while hospital consultations comprised only 6% of costs.

**Hospital cohort**

The 2-monthly cost to the health service of the more severely affected cohort attending hospital was up to £1500 per patient (mean £415), 63% of which was incurred by the hospital and 34% by the GPs. The maximum personal cost was £1225 (mean £325) over 2 months, 75% of which was due to loss of salary.

**Extrapolation to the wider population**

The information provided by the sampling scheme detailed above can be extrapolated to the whole practice population of approximately 225 patients with AE. The estimated total annual cost to the health service, and to the patients in this practice of 9786, would have been £50,005; 58% would have been incurred by the patients and 42% by the health service. An estimated 427 working days and 170 school days would have been lost annually.

Any projection to a wider population is subject to error but, if these results were representative of the whole country, they would add up to a total annual expenditure of the U.K. of £297 m by patients. The estimated annual cost to the health service would be £125 m. The cost to society of lost working days would be £43 m, resulting in a total cost in the U.K. of £465 m, or a per capita cost of £7.38 per annum.

**Discussion**

Appraisal of therapeutic cost-effectiveness must become an essential part of the national allocation of limited resources, and may be used to identify areas where savings can be made.\(^6\)–\(^8\) Furthermore, this knowledge should demonstrate the value of certain treatments which might appear to be expensive and inefficient. Any assessment of costs should include those borne by the health service, by the sufferers and their families, and any other costs borne by the rest of society.\(^6\)

Sufferers from AE, and perhaps other dermatological disorders, appear to pay a high price for their disease and, according to our results, a total of £297 m is spent in the U.K. as a result of AE.

Extrapolation of these data to the wider population of the U.K. should be interpreted cautiously, but the final estimate of the cost is likely to be an underestimate for the following reasons:

1. The prevalence of AE in Scotland is less than in the rest of the U.K., according to the 1958 National Child Development Study.\(^9\)
2. The GPs in the study practice are low prescribers.\(^10\)
3. None of the patients in the study population had required hospital treatment during the course of the study.
Table 3. Annual per capita cost of treating AE compared with other medical conditions

<table>
<thead>
<tr>
<th>Condition</th>
<th>Cost (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.K.</td>
<td></td>
</tr>
<tr>
<td>Atopic eczema (this study)</td>
<td>£7.38</td>
</tr>
<tr>
<td>Venous ulceration</td>
<td>£6.73</td>
</tr>
<tr>
<td>Stroke in Scotland</td>
<td>£18.78</td>
</tr>
<tr>
<td>Benign prostatic hypertrophy</td>
<td>£1.04–£1.53</td>
</tr>
</tbody>
</table>

4 All patients lived within walking distance of the health centre, and this minimized travel costs.

5 The cost to society of time spent by carers looking after dependants is not included.

The data do, however, give some indication of the magnitude of the problem, with a national cost of £465m.

Chronic skin diseases differ from most other medical conditions when their costs are being assessed. A plethora of over-the-counter preparations is available for problems ranging from acne to warts. Remedies for treating dry skin conditions like AE are particularly numerous, and vary greatly in price. A further drain on patients’ resources comes from the need for new clothing or bedding, and from the laundry costs which accounted for 45% of expense to patients in the whole study, and 63% of the costs to families with children aged less than 16. One 10-year-old boy, for example, needed new cotton sheets every 2 months, partly because of repeated washing, but also because nocturnal scratching led to extra wear and tear on the sheets. Patients’ readiness to spend large sums of money for relief from their skin disease is demonstrated by 10 patients in the community paying over £100 in 2 months.

An analysis of the economics of AE in the U.S.A. was limited for three reasons: it dealt only with children; treatment in the community was not included; and costs to the patient were omitted. It would, therefore, be incorrect to make direct comparisons with our data.

Only a few attempts have been made to quantify the cost to the health service of medical treatments in the U.K., and direct comparisons are impossible due to differences in methodology and in spectrum of disease (Table 3). The cost of treating venous ulceration which, in contrast to AE, requires considerable hospital outpatient and in-patient time, has been estimated to be £400m, or £6.73 per head of population, a figure close to that for AE. The total annual per capita cost of treating benign prostatic hypertrophy has been estimated at £1.04–£1.53. The per capita cost of treating strokes, which usually require prolonged in-patient therapy, was recently estimated to be £18.78 annually in Scotland. Few would have expected the economic burden of these conditions so closely to resemble that of AE.

The financial impact of severe AE has considerable repercussions on sufferers. Adults with AE have to pay for prescriptions and are further punished by loss of salary and high clothing and laundry expenses. We have shown that an individual attending hospital can spend as much as £1225 (mean £325) over a 2-month period which is 12 times that of the average patient in the community. The financial burden is heavy and the ceiling of expenditure high.

Acknowledgments

We would like to thank Howden Health Centre staff for allowing access to their practice and the Edinburgh Dermatological Research Fund for its financial assistance.

References

Prevalence of atopic eczema in the community: the Lothian atopic dermatitis study

R.M. HERD, M.J. TIDMAN, R. J. PRESCOTT* AND J. A. A. HUNTER
University Department of Dermatology, Level 4, Lauriston Building, Royal Infirmary of Edinburgh NHS Trust, EH3 9YW and
*Department of Public Health Sciences, University of Edinburgh, U.K.
Accepted for publication 19 October 1995

Summary
An epidemiological study of atopic eczema (AE), based on a semirural community in Scotland, using sound diagnostic criteria, has yielded prevalence data for all age groups including infants and adults. The overall 1-year period prevalence, age-standardized to the Scottish population, was 2.3%. The 1-year period prevalence was highest in the under 2s (9.8%), and showed a continuous reduction with increasing age. Over the age of 40, AE was found to be relatively rare, with a 1-year period prevalence of 0.2%. Adults over 16 years made up 38% of all patients with AE.

Atopic eczema (AE) has major socio-economic implications.1 Although the cellular mechanisms behind the atopic phenotype have become clearer, and powerful new treatments have been introduced,2,3 reliable epidemiological data are sparse. The few studies of prevalence have not always defined their diagnostic criteria, and some have been based on health visitor records or questionnaires that have relied on a parental diagnosis. A variety of measures of frequency have been used, e.g. cumulative incidence or point prevalence. AE in infants, and adults, largely has been ignored. The aim of our study was to estimate, accurately, from a representative population, the prevalence of AE at all ages.

Methods
The study population comprised a semirural general practice, of 9786 patients, situated in Livingston, a new town in central Scotland. The age distribution differs from that in the rest of Scotland, with a larger proportion of young adults, and a correspondingly smaller proportion of adults over 65. The social class distribution is biased slightly towards social class III, and away from the higher and lower social classes.4 Howden Health Centre is a well-organized practice, served by eight general practitioners (GPs). Access to medical records was facilitated by a computerized records system. One of us (RMH) examined all available patients with a coding of eczema on the practice computer, together with the other members of the family, to identify those with AE. As infants were poorly represented in this sample, every family with a child aged less than 2 was contacted. To estimate the number of patients with AE in the remaining practice population not identified on the computer, a one-stage random cluster sample of 10% was taken, each cluster being a family.5

The diagnosis of AE was established using the U.K. Working Party’s diagnostic criteria.6 These require a history of an itchy skin condition, and three other criteria, only one of which relies on examination. This protocol was adhered to strictly. The possible effects of seasonal variation were eliminated by recruiting patients over a 1-year period, and by measuring the 1-year period prevalence. Prevalence and standard errors were calculated by stratified cluster sampling techniques, with a finite population correction.5

Results
The contact rate was 93% for patients with GP-diagnosed eczema and their families. 89% for the under 2s, and 87% for the random cluster sample. Altogether, 2365 patients were sampled in these groups, 24% of the practice population.

The U.K. Working Party’s diagnostic criteria proved ideal for use in a community setting. No cases of AE were thought to be missed. Conversely, two adults who fulfilled the criteria did not have AE: one had nickel dermatitis causing eczema on her neck, the other had pityriasis versicolor. Both were excluded.

The 1-year period prevalences of AE, for the different age groups, are shown in Table 1, and demonstrate a steady decline with increasing age. The male:female
ratio, of 1:5:1, among infants under 2 (1-year period prevalence for males, 11-9%, and for females, 7-2%), was reversed in older age groups (1-year period prevalences aged 2–11, 12–24 and 25+ for males, 7-7, 1-4 and 1-1% respectively, and for females, 11-4, 2-4 and 1-3%). Sixty-five per cent of patients diagnosed as having AE had active eczema at the time the diagnosis was made. The overall 1 year period prevalence, age-standardized to the Scottish population for all age groups, was 2-3%. Only 52% of patients with AE were aged between 2 and 15, leaving almost half of AE patients in the poorly studied groups below the age of 2 and over the age of 16. Thirty-eight per cent of all patients with AE were over 16. The 1-year period prevalence in the 16–40 group was 2-0% dropping to 0-2% in the over-forties.

The prevalences of active eczema are also displayed. While 66% of individuals, aged below 16, were in remission at the time they were examined, only 47% of adults over 16 were in remission.

Discussion

The 1-year period prevalence for infants under 2 was 9-8%. The possible reason for the neglect of the epidemiology of AE in infants is that, until now, there has been no reliable diagnostic criteria. Recent reports have glossed over the issue of robust inclusion criteria, which may have contributed to a high lifetime incidence of 20-4%, in the under 3s, in one study.7 The U.K. Working Party’s criteria contribute a framework for comparison between this and future studies, provided that the format is adhered to closely.

Information on the prevalence of AE in adults is very sparse. The figures presented in the Lambeth study, in 1976, of a prevalence of 12-5% for ages 35–54, suggest, as acknowledged by the authors, that many conditions other than AE must have been included under the banner of ‘eczema’.8 There appears to be a rising prevalence of AE in children9 and, if this shows a cohort effect, it will be reflected in the adult population, resulting in a commensurate increase in the proportion of affected adults. We have shown that the decline in AE, known to occur with increasing age during childhood and due possibly to age, period or cohort effects, continues in adult life, until over the age of 40, when AE becomes relatively uncommon. In one sense this justifies the almost exclusive attention given to school children but, when one considers that 38% of all AE patients are over 16 years of age, the size of the problem in the adult population becomes apparent. It is clear from the prevalence figures of active eczema, in Table 1, that an adult with AE is more likely to have active disease than a child.

This study is unique in three respects: it uses firm diagnostic criteria in a community setting, standard errors are quoted for prevalences, and accurate prevalence figures for adults are given. As AE is a seasonally influenced disorder, we recommend that the 1-year period prevalence is the best measure of its frequency, and should be used in comparative studies.

Acknowledgments

We wish to express our gratitude to all staff at Howden Health Centre, who were always courteous and helpful, and to the Edinburgh Dermatological Research Fund for funding.

References