for school children with asthma.

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To my family:

Matt for his strength, perseverance and belief that I could do it; and

Rebecca for making me realise what life is all about. Without them,

I would never have been able to complete a PhD.

ABSTRACT

Title: The role of peak flow in guided self-management protocols for school children with asthma.

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Self-management of asthma allows patients to fine tune treatment and is preferable to recurrent consultations. Peak flow measurement is commonly used as an objective measure of change in airway function associated with deteriorating asthma. Self-management plans offer information about levels of change in peak flow which require patients to respond by treatment changes or by seeking medical help. Self-management of asthma in adults appears more effective when accompanied by education and guidance about when and how to make such changes. Peak flow in children is less reliable and it's role in self-management is therefore unclear.

The aim of this study was to compare peak flow plus symptom based management with symptom-based management alone in school children with asthma. A randomised, controlled trial was performed.

One hundred and seventeen children were recruited via General Practitioners and hospital clinics and each studied for approximately 16 weeks. After a 4 week run up period, ninety children were randomised to receive either peak flow and symptom based management or symptom based management alone. All children performed twice daily spirometry at home, unsupervised and completed a symptom diary every morning. They were visited at approximately 4 weekly intervals. At each visit quality of life and use of health services were recorded.

There were no differences in mean daily symptom score, lung function, quality of life score or use of health services between the groups over time. During acute episodes children responded to changes in symptoms, irrespective of the randomisation group, so that peak flow did not contribute to self-management decisions.

In conclusion, knowledge of peak flow did not add significantly to the management of asthma in these children, even during acute exacerbations.

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<u>Abbreviations</u>

ANOVA	Analysis of variance	$HPEF_{PF}$	Highest peak flow from a peak flow manoeuvre
ATS	American Thoracic Society	IQR	Inter-quartile range
B	Baseline	κ	Cohen's kappa
BTPS	Body temperature & pressure, saturated with water vapour	κ_w	Cohen's kappa (weighted)
CAQ	Childhood Asthma Questionnaire	$MEF_{50}/$ FEF_{50}	Mid expiratory flow/ forced expiratory flow at 50% FVC
DSS	Data storage spirometer	MMEF	Mean mid expiratory flow
ER_{diary}	Extra reliever recorded in diary	PACQLQ	Paediatric asthma caregiver's quality of life questionnaire
ER_{dss}	Extra reliever recorded electronically in spirometer	PAQLQ	Paediatric asthma quality of life questionnaire
ERS	European respiratory society	PEF	Peak expiratory flow
FEF_{25-75}	Forced expiratory flow at between 25 & 75% FVC	PEF_{PF}	Peak expiratory flow from a peak flow manoeuvre
FER (%)	Forced expiratory ratio	PEF_{VC}	Peak expiratory flow from a vital capacity manoeuvre
FEV_1	Forced expiratory volume at one second	PF_0	Symptoms only randomisation group
FVC	Forced vital capacity	PF_1	Peak flow plus symptoms randomisation group
$HPEF_{VC}$	Highest peak flow from a vital capacity manoeuvre	QoL	Quality of life

RCT	Randomised controlled trial
RMANOVA	Repeated measures analysis of variance
r_s	Spearman rank correlation
r_z	Transformed Spearman rank correlation coefficients
SD	Standard deviation
SEM	Standard error of the mean
TLC	Total lung capacity
z	Transformed symptom score

SECTION I

BACKGROUND & INTRODUCTION

Chapter 1

1.1 Introduction

Asthma is the most common chronic disease in children in the industrialised world[1]. Co-ordinated international studies suggest that there is a wide variation in prevalence of asthma symptoms. The international study of asthma and allergy in children (ISAAC) involved 6-7 and 13-14 year old children and showed higher rates of symptoms such as wheeze in industrialised societies, in particular the United Kingdom (UK) and Australia [2]. Differences in language and comprehension could explain differences in recorded prevalence.

It has been suggested that 10-15% of children under the age of fifteen suffer from chronic wheezing [3]. In one UK study, incidence of wheezing illness was 18% by age seven rising to 24% by age sixteen[4]. Many of these will be in the pre-school age group which accounts for a high proportion of hospital admissions and demonstrated the highest increase in admission rate in the 1980's[3]. Around 15% of school children in the UK are in receipt of anti-asthma treatment [5]. Questionnaire data collected in Leicester (Kuehni, personal communication) suggested that in the 8-13 year age group, 20% reported having used reliever medication in the last twelve months and 11% preventer medication during that time. Mortality rates do not reflect this increase in morbidity, perhaps because asthma is milder, diagnosed earlier or as a result of the introduction of national guidelines [6] for management leading to improvement in acute and chronic management by families and the medical profession. In the decade up to 1995, asthma deaths in the 5-14year age group showed a downward trend [7] which Campbell *et al* attributed to the increased use of prophylactic treatment [8].

The financial burden of asthma to the National Health Service (NHS) is immense. The costs per patient per year in the U.K. have been estimated amongst the highest [9]. Direct costs such as medication and hospitalisation represent a great expense [3]. In addition, the indirect cost of lost work [10]and schooling [1]and social security payments represent approximately 50% of total costs [9]. Therefore the £100-£150 million of the health budget spent on asthma annually is an under-representation of true national costs [3].

In a disease such as asthma, where cure is not an option, measurement and management of disease are key to maintaining control. Educating patients and families about how and when to take medication, alter treatment and seek medical help may enhance this process, which would reduce treatment failures resulting in admission to hospital and may reduce costs[33].

Chapter 2

The management of asthma

2.1 Introduction

Management objectives may differ between patient and physician (table 2.1.1). For the child, symptom control is paramount and with it, a reduction in the impact of the disease on every day life. Physicians may aim to reduce inflammation, prevent airway wall remodeling, control bronchial hyper responsiveness and enhance lung function [11], often with a longer-term goal. More recently, Clark *et al* have suggested that physicians need to focus management strategies on patient needs in order to enhance compliance and thereby improve outcome [12].

Table 2.1.1 Schematic representation of Aims of Management

Management objectives	Child	Parent	Nurse	Doctor
↓ Impact	+ + +	+ +	+	+
↓ Symptoms	+ +	+ +	+ +	+ +
↑ Lung function tests	-	+	+	+ +
↓ Bronchial Hyper-responsiveness	-	-	±	+
Improve lung growth/ ↓ remodeling	-	±	±	+
↓ Health care costs	-	-	+	+ +

2.2 Standardised approach- guided self-management

Asthma has a variable clinical course. Management focuses on control by active intervention. Clinicians manipulate treatment to minimize symptoms, improve objective measures of disease state and enhance patients' quality of life. Frequent treatment changes mean that visits to the practice nurse, doctor and hospital are commonplace for children with asthma. Often these changes may be minor and the ability to "fine tune" prescribed treatment at home with guidance, to maintain health, is preferable to recurrent consultations. This is the essence of guided self-management. Guided self management is providing the patient (and family) with *"appropriate knowledge and training, so that when faced with a variety of circumstances they know when to seek medical attention and how and when to adjust treatments according to a plan worked out in advance with a health professional"* [13].

The components of self–management are:

- education & training in monitoring,
- written information,
- communication,
- regular review.

For the patient this process involves participation in management. This includes:

- avoiding situations which may act as triggers e.g. pets; pollen
- actively altering treatment when asthma deteriorates or improves
- seeking medical attention when asthma is poorly controlled or deteriorating
- increased knowledge of condition and when to alter treatment
- monitoring changes in condition in some way

Recent qualitative data from Jones *et al*[160] suggests that not all adult patients value the use of self-management.

Guidelines can be simple instructions or more complex written information with varying pathways giving people choices, dependent on changes in condition.

Self-management regimes imply that the patient too has responsibility for disease management. Health professionals remain responsible for prescribing. Compliance rests with the patient. Van der Palen [14]argues that compliance is the principal component of self-management both with medication and self-treatment guidelines. Cochrane [15,16] suggested reasons why people fail to comply, such as forgetfulness, lack of understanding, depression, fear of side effects and failure by health professionals to realise the goals of the individual patient when initiating guidelines. If patients are given appropriate information and training, they may feel more in control and more inclined to comply [17-19].

Greater overall burden of chronic disease and increased emphasis on community care embodied in the UK in the 1989 Government White Paper, have enhanced the use of self-management. Keeping patients at home and laying the responsibility for care with the patient/carers has become an important aspect of management and policy [20]. Both national and international guidelines in asthma management now stress the importance of patient education [21-24] in conjunction with guided self-management. In their survey, Hodges *et al* demonstrated that this had been accepted by health professionals[25].

2.2.1 Studies of asthma self-management in adults

Aspects of management on which treatment should be based are unclear. The value of self-management is recognised in terms of reduced morbidity but it is unclear which aspects of the self-management process are responsible for benefits.

A systematic review [26] of twenty two randomised controlled trials (RCT), of guided self-management and regular review for adults with asthma was carried out. Gibson *et al* showed that self-management education reduced hospitalisation, emergency hospital visits, unscheduled doctor visits, school and work absence and nocturnal asthma. Objective measures of lung function did not change significantly. To be included in the review the interventions contained the following components of self-management:

• written action plan,

• regular medical review,

• self-monitoring of PEF or symptoms and/ or asthma education.

The authors concluded that self-management training with education and regular medical review including a written plan, improved health outcomes in adults. Medication self-adjustment was more effective than other self-management. This review contained only randomised controlled trials and the guided self-management training included both education and regular medical review. Some of the component studies will be discussed further along with other self-management studies.

A number of studies have compared self-management with traditional treatment and demonstrated reductions in morbidity. Beasley *et al* [27] demonstrated the efficacy of self-management for adult patients with chronic asthma. Statistically significant reduction in morbidity and improvement in lung function were demonstrated in thirty patients who completed the six month study. This was not a randomised controlled trial and all patients were reviewed three times during the study period and had treatment changes as required. The study was open to the errors of bias and of spontaneous natural variation of asthma. D'Souza *et al* [28] used a symptom and peak flow-based credit card for self-management in a

sequential before and after design. In the short term (16weeks) statistically significant improvements were seen in asthma morbidity measured by peak flow, nights woken and days out of action. Reported inhaled corticosteroids prescribed for regular use (p<0.001) and the number of nebulisers used (p=0.02) increased. Other measures of outcome changed but did not reach statistical significance. When followed up at two years the same group demonstrated longer term benefits[29]. Improvements remained in night waking and in addition there were fewer emergency hospital visits and admissions for the previous twelve months. Peak flow was not reported. Outcome measures which showed a tendency to reduce over the short-term became significant at 1 & 2 years. This study was not controlled and some outcomes were subjective and recall -dependent: one year is a long time.

In a hospital outpatient department Lahdensuo[30] carried out a RCT to compare peak flow-based self-management and traditional treatment in adults patients followed up for one year. Significant improvements in morbidity were seen in terms of work days lost, need for rescue prednisolone and antibiotics and better quality of life in the peak flow group. Objective measures of lung function did not differ significantly. Ignacio-Garcia and Gonzalez-Santos recruited hospital clinic patients and compared peak flow-based self-management to management based on symptoms, spirometry and physician-based treatment[31]. Significant benefits were seen in subjective and objective measures of morbidity, including lung function test results. In a community population comparing peak flow-based self-management and regular nurse review, Jones et al[32] saw no difference in morbidity but the self-management group demonstrated quality of life improvement over time. However, patients in this study had input from a nurse, which was probably more than "usual care".

Taitel *et al* [33] performed a cost benefit analysis and demonstrated that their self-management programme was cost effective. The study this analysis was based on offered self-management training to all participants [34]. The control group had a longer waiting time for self-management training, providing an interval during which short-term outcomes were compared. The trained group had significantly fewer attacks in the morning and evening and recorded higher morning PEF. Significant improvements were demonstrated in cognitive measures after training. When both groups had received training, a before and after analysis demonstrated significant changes in morbidity, medication use, and cognitive and behavioural measures. Results were attributed to self-management training and were maintained for one year following the training package.

In a similar design, Yoon *et al* [35] recruited patients admitted for severe asthma and then offered training in peak flow-based self-management. At recruitment, significantly more controls reported having training in peak flow monitoring and asthma education. There was a seven times higher admission rate in the control group at ten months. Differences were also seen in numbers attending casualty and subject's ability to differentiate mild from severe attack. Asthma health beliefs and between group difference in knowledge of asthma drugs at ten months also reached significance. Wilson *et al* [36] compared four groups of patients. One group received nothing; the remaining three were given individual, group or workbook self-management education. All education reduced morbidity in adults but especially if given to groups. Improvements were demonstrated in subjective assessments but not lung function tests. Laird[37] reported results of a mailed survey of self-management and compliance practices. These data suggest that older patients and females were more likely to report compliance and adherence to self-management practices. However, these patients were highly motivated members of specialist asthma societies. This very specific group may be aware of what is expected of them in terms of

management of their asthma. These studies demonstrate improvements in several measures of morbidity by introducing self-management.

One study has demonstrated good compliance with self-management guidelines and inhaled treatment in a group of highly motivated patients[14]. However, patients in this study showed a reluctance to double inhaled corticosteroids during an episode. The majority of self-management studies do not report compliance data.

Other studies suggest that self-management implementation may not improve morbidity, despite enhancing knowledge [38]. Ayres and Campbell [39] recruited patients with chronic asthma into a therapeutic trial of budesonide. Patients who had sought professional help in the past six months for an exacerbation were randomised to a self or doctor managed regime. No between group differences were demonstrated in terms of clinic or diary recorded data. All outcomes improved for both groups but between group differences were not significant. The doctor-managed group received regular supervision, which may well have exceeded usual care.

In community patients the GRASSIC study concluded that peak flow management and self-management were unlikely to improve morbidity [40] and Charlton et al demonstrated before and after differences in outcomes but no between group differences [41] in outcomes. This study may have been testing the implementation of nurse-based management rather than self-management per se.

All of these studies recruited volunteers. Incorporated in table 2.2.1.1 are numbers of subjects who entered and completed each study. Completions vary from 30-99%. The authors do not state how many individuals were contacted or invited to participate, rather

those who started the studies. This demonstrates selection bias and makes generalisability of results difficult. Volunteers were motivated to participate in the studies and if a small proportion complete the studies these patients are a highly motivated, specific group.

In summary, several different methods have been applied to studies of guided self-management. Most of these studies suggest that self-management *per se* is good for patient care. Education without the other components of self-management appears to be of little use in improving health outcomes [26]. Which components of self- management are responsible for the benefits is unclear and further research is needed.

Table 2.2.1.1 Adult studies of self-management

Study and year	Design	Total subjects (and completions)	Intervention	Control	Outcomes improved for the following	Comment
Beasley 1989 [27]	Before & after	36 (30)	Peak flow-based self-management	None	Morbidity, lung function, treatment needs	• Improvements may be natural variation in condition with time
Yoon 1993 [35]	RCT	185 (56)	Self management	Waiting list for later self-management	Readmissions; accident & emergency attendance; morbidity	• Part of education programme comprising single education session
Wilson 1993 [36]	RCT	323 (310)	Self-management education in sub groups	Normal management	Symptoms, physical evaluation	• Claim group education best but better attendance than other groups • No difference in lung function, improvements in subjective measures.
D'Souza 1994 [28] and 1998 [29]	Before & after	69 (47)	Peak flow and symptom based management	None	Morbidity, treatment needs, PEF	• Advised that in this Maori population control group would fail because very close knit
Jones 1995 [32]	RCT	127 (72)	Self-management	Planned visits	Night waking, lung function, school/work absence	• Outcomes improved in both groups • Patients seen often and may assess implementation of nurse follow up not self-management

Study and year	Design	Total subjects (and completions)	Intervention	Control	Outcomes improved for the following	Comment
GRASSIC 1994 [40]	RCT	569 (485) sub-sample from larger study	Peak flow based self management	Usual care		• Mild group may be why no difference seen
Kotses 1995[34]	RCT	126 (76)	Self-management	Waiting list for later self-management	Symptoms, cognitive measures	• Well controlled at start of study therefore benefits from SM but some outcomes improved in both groups
Ignacio-Garcia & Gonzalez-Santos 1995 [31]	RCT	94 (70)	Peak flow-based self management	Physician managed	Lung function; Nocturnal wakening; work days lost; reliever use;	• Some improvements seen in both groups
Allen 1995 [38]	RCT	116 (113)	Self-managed with symptoms or peak flow	Normal management	Knowledge; reported compliance	• May be subject to recall bias • No objective compliance data
Ayres 1996 [39]	RCT	126 (125)	Self-managed inhaled steroids	Dr managed inhaled steroids	Number of disturbed nights, lung function, symptoms, activity limitation	• improvements in both groups, not between groups • control group frequent Dr visits

Study and year	Design	Total subjects (and completions)	Intervention	Control	Outcomes improved for the following	Comment
Lahdensuo 1996 30	RCT	122 (115)	Peak flow-based self management	Traditional treatment	Days off work; quality of life; rescue therapy; antibiotic courses; unscheduled Dr visits	• Relatively mild group
Cote 1997 [42]	RCT	188 (149)	Self-management by peak flow or symptom	Normal information and management	Knowledge, morbidity (in all groups)	• Severe patients • Morbidity improvements may be result of treatment optimisation or free medication for trial

2.2.2 Studies of asthma self-management in children

Where families are offered training in making treatment decisions at home within agreed guidelines, self-management is a commonly used phrase. The majority of studies, including a recent Cochrane review[159] use the term self-management, irrespective of whether children and/or parents received the education. However, many studies include education packages to parents and children and it is therefore unclear who is responsible for management decisions. Other terms such as "home-management"[51] have been suggested. The term self-management is used throughout this study to denote management carried out at home by participating families. Studies of self-management in children are few and outcomes vary. Comparisons between studies are difficult because of the wide variations in design, intervention and variables measured. Adult data cannot simply be extrapolated to children. Disease is often episodic with children remaining well between episodes. When managing disease in paediatric asthma, the family is actively involved and management is complicated by issues of joint responsibility [43]. Currently, there is no systematic review of the evidence.

Recruiting moderate to severe asthmatics, two studies demonstrated improvements in morbidity. Gillies *et al* found self-management plans were acceptable for use in children and successful in reducing some aspects of morbidity in a community population when introduced in a General Practice initiative [44]. Reduction in night disturbance, days out of action, General Practitioner (GP) visits, prescriptions for reliever medication and oral steroids all reached statistical significance. However, this study was not controlled and it is unclear which aspects of the study were responsible for the improvements. Sorrells *et al* [45] studied children attending camp between 6 and 12 years of age. They found reduced emergency visits and school absence when the education given emphasized self-management skills. The education was very intensive with daily sessions and the study was

uncontrolled. The authors highlight the potential for recall bias. Baseline data was based on questionnaire reporting of morbidity in the preceding twelve months. Outcomes were measured six months after the camp.

Fireman et al [46] educated parents and children over a period of weeks and demonstrated a reduction in acute attacks, school absence and hospital and emergency room visits. Taggart et al [19] provided shorter education and self-management training during a hospital clinic visit. This led to increased knowledge, reduced disruption by asthma and improved the sense of control over disease. These results are difficult to interpret as the study was small and not randomised.

Although improvements in some aspects of morbidity were demonstrated by these studies, they were not controlled trials and were carried out in different populations: community, hospital attenders and children at summer camp. Lewis et al [47] performed a randomised, controlled trial. Children in both groups received education with the parents of the experimental group also receiving information over five, one hour sessions about asthma treatment . In both groups knowledge increased and the experimental group reported changes in compliance. Morbidity, measured by reduced emergency visits and hospitalisations, was reduced in the experimental group. In another randomised study Ronchetti et al [48] showed that children receiving self-management education, even when the training time was reduced, demonstrated reduced use of emergency services and more appropriate medication use. This improvement was maintained for twelve months following the intervention. Charlton et al [49] have considered the role of self-management in children in a study of paediatric hospital patients seen by a practice nurse in a hospital setting. This randomised controlled trial attempted to enhance links between primary and secondary care. Statistically significant results were seen in only two morbidity variables.

The control group did not receive self-management guidance but were seen at three monthly intervals by study personnel. Outcomes were measured by questionnaire at twelve months.

Acute admissions to hospital have been used as an opportunity to offer education and self-management training. Two similar studies have given education to children prior to discharge from hospital and successfully reduced re-admissions [50,51]. Additional benefits were also seen in terms of A&E attendance, unscheduled GP visits, lost school days [50] and morbidity scores recorded by parents [51]. These results suggested that at this time parents and children are receptive to information.

Interpretation of data from paediatric studies is more difficult. Benefits can be seen in terms of knowledge gained [19] sometimes in both experimental and control groups [47] and morbidity [44-46]. Other studies demonstrate little benefit in terms of morbidity[47,49]. The method and timing of education and self-management advice may be the key factor [50,51]. The limited number of randomised controlled trials seem to suggest that the greatest benefit is in reduced need for emergency care [47,48,50,51] and response to attacks [49]. The proposed systematic review of the evidence of educational interventions should help to clarify this further and may provide information about which aspects of self-management training are responsible for any benefits [52].

Table 2.2.2.1 Self-management studies in children

Study and year	Design	Total subjects (and completions)	Intervention	Who[1]	Control	Outcomes improved for the following	Comment
Fireman 1981 [46]	Parallel controlled	26 (26)	Education plus management plan	B	Plan without training	Acute episodes; school absence; emergency room visits; costs	• Not randomised trial • Very intensive education
Lewis 1984 [47]	RCT	103 (76)	Small group education	B	Lecture based education	Hospitalisations; emergency room visits; reported compliance	• Knowledge outcomes improved for both groups • More children assigned to experimental group
Sorrells 1995 [45]	Before and after	90 (90)	Daily education sessions	C	None	Use of spacer devices and peak flow meters; morbidity	• Morbidity reported for 12 months pre-camp, recall may be difficult • Parents were questioned post camp
Taggart 1987 [19]	Before and after	12 (12)	Self management education programme in outpatient clinic	Not clear	None	Knowledge; sense of personal control increased; less disruption to family life (parents); self management behaviours (physicians)	• Small pilot study
Charlton 1994 [49]	RCT	91 (77)	Self-management education programme	B	Interview, peak flow meter and diary card	Activity restriction; response to attacks	• Intervention subgroups too small for analysis • Control group increased re-admissions

Study and year	Design	Total subjects (and completions)	Intervention	Who[1]	Control	Outcomes improved for the following	Comment
Gillies 1996 [44]	Before and after	110 (102)	Self management plan and	B	None	GP visits; morbidity; Rescue therapy	• No information of self-management advice for younger children
Ronchetti 1997 [48]	RCT	312 (209)	Educational programme	B *	No education	Emergency treatments	• Intervention subgroups too small for analysis • Benefits maintained for 12 months
Madg e 1997 [51]	RCT	201 (201)	Education programme of acute attack self-management	B	Usual care	Re-admissions; morbidity scores	• Variable follow-up times • No prednisolone data
Wesseldine 1999 [50]	RCT	160 (150)	Planned discharge package with education	B	Usual care	Re-admissions; A&E attendance; Emergency GP visits; school days lost	• No prednisolone data

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[1] Who column refers to who received self-management education: P= parents; C= children and B= both; * parents and children taught separately.

2.3 Peak flow monitoring and asthma self-management

Peak flow measurement offers objectivity in self-assessment of asthma status [53]. It is inexpensive, relatively simple, can be performed anywhere and is widely accepted as a means of monitoring condition by patients in the community [54].

2.3.1 Studies of peak flow monitoring for asthma self-management in adults

Early self-management studies routinely included peak flow monitoring as a means of managing asthma. When compared with traditional treatment peak flow-based self-management has been shown to be successful in reducing morbidity in hospital patients [30]. These benefits are both short and long term [34] and self-management intervention is cost effective when coupled with an education package [33]. Some studies suggest that benefits arise from self-management with symptoms or peak flow although greater improvements in morbidity were seen in the groups assigned to peak flow monitoring [31,35]. Some commentators found equivalent improvements in both groups, with no between-group differences [55]. In a before-and-after design using both symptoms and peak flow for self-management D'Souza et al showed improvements in morbidity [28,29]. Other studies have demonstrated that in mild asthma, peak flow-based self-management is equivalent to usual care [32,40,42] or doctor management [39] in terms of reducing morbidity. In two of these studies [32,42] patients in the "control group" received intense review appointments and were seen on a very regular basis. When attempting to assess acute episodes, Malo et al found symptoms to be as effective as peak flow measurement [56].

In one study a peak flow-based plan was found to be better than a symptom-based plan or no plan at protecting patients against acute severe attacks over a six-month period [57]. Participants were all recruited following attendance at casualty or clinic for urgent treatment. After receiving education as part of the protocol, asthma management in all

groups improved. The group measuring peak flow demonstrated a highly statistically significant reduction in emergency room attendance ($p<0.006$). Participants in this study had more severe asthma needing emergency help for asthma as an inclusion criterion. Other studies have suggested that for more severe patients peak flow monitoring may be beneficial [40].

Comparison between symptom and peak flow-based plans in a relatively stable adult population [55] demonstrated increased FEV_1, PEF, quality of life and PC_{20} and decreased symptoms in the short and longer term in both groups with no difference between groups. Cowie et al [57] studied self-management during exacerbations in adults with unstable asthma. Comparing a control group who received no plan and groups using peak flow-based and symptom based plans they found a lower rate of visits for emergency treatment in the peak flow group but all subjects demonstrated reduced morbidity with fewer disturbed nights and bronchodilator use irrespective of group. Since this included even the control group, it can be attributed to the education given to all participants, or may be a due to spontaneous improvement with time. Peak flow-based management reduced costs of emergency treatment and emergency visits over a six-month period when compared with symptom-based plans or no plan.

Cote et al [42] recruited patients during a hospitalisation or clinic visit. After a four week run up period incorporating four visits their treatment was optimised. These patients were randomised into education plus peak flow-based self-management, education plus symptom-based or control group, with no formal education. At one year morbidity had declined in all groups ($p<0.001$). Knowledge increased in both educated groups with time ($p=0.0001$) and compliance was similar in all groups at end. Improvement may arise from

participation in the trial and increased hospital visits, not education; hence no between-group differences.

In summary peak flow measurement appears to add little to self-management in adults. These studies add support to the earlier work and suggest that self-management *per se* is of benefit; teaching appears to be important [41,58] and peak flow cannot be affirmed as the factor responsible for these benefits [31].

Table 2.3.1.1 Studies of peak flow versus symptom self-management in adults

Study and year	Design	Total subjects (and completions)	Intervention	Control	Outcomes improved for the following	Comment
Malo *et al* 1993 [56]	RCT crossover	60 (31 experienced flare-ups)	Peak flow and symptom based self-management	Peak flow and symptom based self-management	Flare-ups detected	• Only considers efficacy of each at finding "flare-ups" • Carry over effect unknown
Charlton 1990 [41]	RCT	69 (69)	Peak flow-based self-management	Symptom self management	Improvements within both groups: Dr consultation; oral steroids	• Patients in both groups seen very often during study • May be testing introduction of a nurse run clinic rather that self-management • Improvements in outcomes seen in both groups- no between group differences
Cowie 1997 [57]	RCT	150 (139)	Peak flow-based self management	Symptom self management	Emergency treatment needs, morbidity	• Based on severe group who needed urgent treatment in last year • No improvement in conventional measures of morbidity • Both groups benefited from education
Turner [55]	RCT	92 (92)	Peak flow-based self-management	Symptom self management	Improvements in both groups: Lung function, quality of life, morbidity	• Improvements in outcomes within both groups- no between group differences

2.3.2 Studies of peak flow monitoring for asthma management in children

The role of peak flow monitoring in paediatric asthma management is unclear. In a small questionnaire based study, most parents could recall the danger level for peak flow for their child and valued PEF as a tool to aid recognition of deteriorating asthma [59]. However, participants were parents of children attending a clinic which routinely dispensed peak flow meters to children above five years, which may not represent "usual" practice. Some parents had the written management plan with them at the time. This may have aided recall but could be interpreted as a positive sign that parents routinely carried guidelines with them. In another study, parents were questioned following their child's attendance at asthma camp where education was given. Parents reported increased peak flow meter use three and six months later compared with pre camp data [45].

Other studies report that PEF is not the critical factor in self-management [41]. Symptom diaries have been shown to highlight deterioration during acute episodes before peak flow changes [60]. Changes in symptoms were more sensitive than twice daily PEF during acute exacerbations in the children in the study. Even in severe asthma, PEF adds little to symptom and bronchodilator use and is too insensitive in children with mild asthma [61].

Only one study has directly compared symptom-based and peak flow-based self-management in children [41]. Charlton *et al* included both adult and paediatric patients, with analysis being performed separately on the sub-groups. They found within-group improvements in consultations and oral prednisolone use over time and the use of nebulised salbutamol fell in the children using peak flow based management, but there were no statistically significant differences between groups, possibly due to a lack of statistical power.

The lack of data available directly comparing peak flow-based self-management with other types of self-management means that the validity of peak flow monitoring in paediatric asthma self-management remains questionable. Symptoms may be equally effective [41] particularly during exacerbations[60]. This question will become increasingly difficult to answer with the widespread use of guided self-management plans.

Table 2.3.2.1 Studies of peak flow versus symptom self-management in children

Study and year	Design	Total subjects (and completions)	Intervention	Control	Outcomes improved for the following	Comment
Charlton *et al* 1990 [41]	RCT	46 children	Peak flow-based self-management	Symptom-based self-management	Improvements within both groups: Numbers of Dr consultation; oral steroids	• Patients in both groups seen very often during study • May be testing introduction of a nurse run clinic rather that self-management • Improvements in outcomes seen in both groups- no between group differences • May be a type II error because analysis done on sub-sample.

2.4 Problems with peak flow

Peak flow has been shown to be more variable than FEV_1, even when measured using the same equipment [62,63]. Other flow rates, such as FEF_{25} and FEF_{75-85}, at the terminal part of the spirogram are even more variable [63]. The lack of portable, affordable equipment to monitor other parameters makes peak flow the only current practicable lung function parameter for widespread use.

The lack of controlled studies of the role of peak flow in self-management means data are inconclusive [53,64]. There are a number of problems associated with its use particularly in the paediatric population: accuracy of equipment, compliance with measurement, thresholds for management.

Equipment accuracy is critical for any clinical decisions which depend either on measures of PEF variability or on precise action thresholds. It has been suggested that error profiles found during repeated equipment testing may lead to errors in recording PEF variability [65]. This has implications for diagnosis and management. Correction factors have been applied to results which may improve estimates of severity [66] and which index of PEF is calculated will impact on interpretation of the results [67]. Issues of equipment may increase the variability of results obtained. With additional biological variability, results can be far from accurate. Diurnal peak flow variability of >15% is considered abnormal [23] and increased variability of peak flow is often used as an indication of poorly controlled asthma. Knowledge of medication use prior to recording peak flow is important. Including manoeuvres performed after bronchodilator use can significantly over-estimate daily PEF [68]. Some commentators have suggested that as children demonstrate greater variability, they should perform more peak flow manoeuvres within each session to achieve their maximum attainable PEF[69]. Others argue that increasing the numbers of sessions recorded

each day may provide more accurate assessment of diurnal variation [70]. This is not practical. Some studies have shown little or no relationship between peak flow from portable meters and those recorded during spirometry [71]. Others argue that home monitoring adds little to symptom and rescue medication reporting in management, even in quite severe disease [61].

Failure to comply with measurement is common [72], particularly in teenagers [73], even for a short time [4,58]. Where records are kept, these may be inaccurate [4,74]. Objective assessment of compliance is important in studies of accuracy of recording. Significantly greater compliance and accuracy has been shown in the group who were aware that details were being recorded [75].

Levels of peak flow (thresholds) at which patients should take specific action, are provided in peak flow-based self-management plans. They are calculated on an individual basis. Comparison between studies is made difficult because some clinicians use predicted PEF while others use personal best to calculate thresholds. Although the predicted value is a fixed value, it fails to account for the extreme range of normality and for patients with severe disease who may be unable to achieve more than 80% predicted [76]. Some studies use various levels of peak flow as thresholds for action without clear justification[76,77]. The optimum threshold for action is unknown. A variety of indices for peak flow can be calculated and difficulties arise in determining which to use for management or to predict episodes [67,78]. Chan-Yeung et al [60] argue that 70% of patients best is too stringent as the lower limit of adequate control. This is supported by Charlton et al [49] who claim 80% of normal should be used as the first level at which to change treatment. Choosing the wrong level for action has implications for the patient. Changing treatment at a higher level, may lead to over treatment and the problems of side effects associated with excessive

medication use [76]. Under-treatment may create additional problems of problematic symptoms for the patient or, more seriously, increase the risk of an acute episode and hospitalisation. A delicate balance needs to be reached to offer the optimum treatment, minimising potential side effects.

The role of peak flow in self-management therefore remains unclear. Within subject and within equipment variability of measurement suggest it is perhaps not a reliable measure on which to base treatment. The uncertainty regarding peak flow and its relationship with respiratory symptoms only adds to this difficulty. Further work is needed to determine whether correction factors, systematically applied with agreed levels for action can reduce the risks of side effects from over-treatment whilst optimising asthma control.

2.5 Hypothesis and aims of work

In summary, self-management of asthma is advocated in adults to allow improved control of asthma symptoms. This has been encompassed by national and international guidelines on asthma management although which aspect of the self-management is important is difficult to determine from available studies[22]. Whether self-management should be based on symptoms or peak flow monitoring to reduce morbidity is unclear [26]. Self-management studies in children have demonstrated varying degrees of success, and the role of peak flow remains uncertain. Interpretation is complex. Entry criteria, length of follow up and outcome measures are variable. My aim was to assess the effect of incorporation of peak flow measurement on self-management in school-children with asthma.

The primary hypothesis was that incorporation of peak flow into guided self-management for school children with asthma would improve the clinical and physiological outcome. The main outcome measure was mean change in symptom score. Other outcomes

included changes in lung function, quality of life and use of health services during the study.

Secondary questions

- What is the relationship between symptoms and lung function during an acute episode?

- What is the relationship between child own and parents assessment of the child's quality of life?

- What is the relationship between child's own and caregiver's own quality of life?

- What is the relationship between caregiver's own quality of life and parent's perception of child's quality of life?

- What is the relationship between quality of life assessment and other measures of morbidity?

- What is the relationship between symptoms and lung function tests?

- What is the relationship between various lung function parameters?

SECTION II

METHODOLOGY

Chapter 3

Measurement techniques: background and methods

3.1 Introduction

Measurement of disease severity to decide treatment step, response to therapy or impact of disease is a mainstay of asthma management [6]. Assessment may be subjective or objective. When combined, subjective measures like symptoms or activity limitation and objective information, such as spirometry or rescue therapy use, offer a more complete picture of disease impact. Measurement techniques vary. The invasive nature of some procedures and the amount of cooperation required by the patient makes them difficult or non-repeatable, particularly in young children.

3.1.1 Subjects
3.1.1.1 Selection and recruitment of subjects

Recruitment took place in Outpatient Clinics at the Children's Hospital and via local general practices. Hospital patients were approached in outpatient clinics in Leicester Royal Infirmary Children's Hospital and invited to participate. General Practitioners (GP) who agreed to help sent letters to their asthmatic patients, usually via the Practice Nurse and reply slips were returned to the research nurse involved in the study. Families fulfilling the inclusion criteria were contacted by letter from the surgery and asked to respond to the investigator if they were interested in taking part. Children aged 7-14 years were eligible if they had physician-diagnosed asthma and were in receipt of regular preventer therapy. At trial entry their asthma had to be relatively stable, with no changes to asthma treatment in the month prior to study entry. Children were excluded if they had any additional respiratory problems, were unable to perform full spirometric manoeuvres and were less than 50% compliant with lung function data collection during the run up. Any child who had difficulty understanding trial requirements was not invited to participate.

Any patient expressing an interest in the study was visited at home to discuss the study and supply further information. After recruitment and a run up period, self-management education was given to all children at the randomisation visit. Along with participating in self-management. randomised children were required to complete a number of tasks during the study (Figure 6.2.1.1). They were asked to complete daily diary recordings by hand and twice daily spirometric manoeuvres morning and evening. In addition, they were visited at home on five separate occasions.

3.1.1.2 Subjects studied

One hundred and seventeen children entered the run up period of the study. Of these ninety continued to be randomised and following randomisation only one child withdrew. The median age of the ninety children was 11 years with a range 7-14 years. The eighty nine children who were recruited and completed the study protocol were at various levels of asthma severity (Figure 3.4.2.1). The one child who withdrew following randomisation was a male adolescent (14 years) at Step 2 of the British Thoracic Society Guidelines for asthma management[6].

Figure 3.1.1.3 Disease severity of randomised children

BTS Step	Number of children	Percentage of sample (%)
2	67	75
3	17	19
4	4	5
5	1	1

3.2 Symptoms

3.2.1 Background

Symptoms offer a measure of illness severity which is highly subjective. Patients display definitive clinical features caused mainly by airway narrowing due to underlying inflammation and bronchial hyper-reactivity. For the patients, treatment is primarily aimed at abolition or control of symptoms (Table 2.1.1).

Symptom severity is highly variable within and between patients. Prevalence studies commonly list wheezing and coughing as determinants of disease presence [79]. For clinical purposes, in addition, symptoms include chest tightness and breathlessness. Details of intensity, timing and frequency of these symptoms are used to measure disease. Children with mild or poorly controlled disease may experience troublesome symptoms such as cough, particularly at night, wheeze or breathlessness on exertion as a result of poor control. Others, with more severe disease may have changes in respiratory function leading to increased symptoms and exacerbations which may be life threatening. Some children experience normal airway function except during an exacerbation when illness can be severe and have a huge impact (figure 3.2.1.1)

<u>Figure 3.2.1.1 Patterns of illness</u>

Chronic   Acute episodes   Acute and chronic
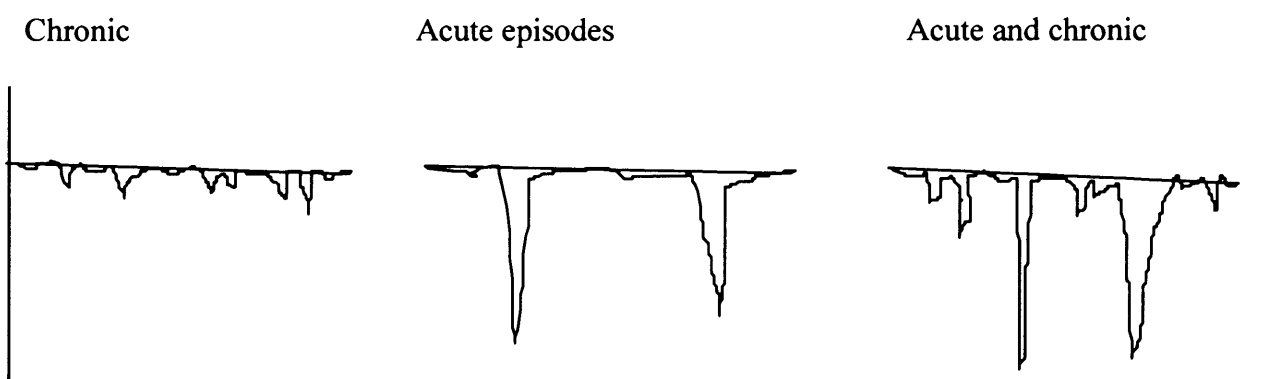
Adapted from [80]

Collecting information about wheeze and cough is commonplace in cross sectional population studies. This practice has been questioned recently. Closer examination of terms used suggests that comprehension may vary across cultures [79], between professionals and families [81], parents and children [82,83] and individuals. This highlights the importance of asking patients which symptoms are troublesome for them and monitoring changes with treatment. Asking the right questions is important to elicit detailed information [84]. Reported symptoms offer detailed information about the impact of the disease. Symptoms may be the only means of assessing condition without complex, difficult or invasive procedures.

Symptom diary completion can provide a fuller picture. Santanello *et al*[89] demonstrated that recording symptoms in a diary was comparable with other more objective measures. In addition data in adults from Malo et al[56] suggested that diary recorded symptoms were as reliable as peak flow in detecting "flare-ups" in asthmatic patients. However, there is increasing evidence that diary data may be unreliable [85]. Asking parents offers some measure of objectivity [86] although this may be inaccurate [83] or at odds with the child's report [82,87]. Compliance with diaries is often poor at best [75] and may be inaccurate [74]. Inaccuracy is impossible to assess with symptom diaries, except in the case of cough, when objective recordings can be made [85]. Retrospective completion has been demonstrated and recall bias will effect recordings made in this way [74]. Blocks of colour in written diaries suggest data recorded in blocks of days rather than on single days [74] and the most accurate data is collected during the first two weeks of recording (Brand, ERS Florence 2000, personal communication).

Despite these problems, symptom diaries are the only means currently available of collecting day-to-day information about the impact of disease.

3.2.2 Methods

Equipment for measurement.

Symptom monitoring was particularly important as both the basis for self-management and as an outcome. Day or night cough and wheeze and chest tightness or breathlessness, with or without exercise were symptoms recorded in the diary. Symptom and feeling scores were recorded every morning by hand written and electronic methods.

a) Hand-written methods

Symptom diaries were completed in the usual way (figure 3.2.2.1)[88]. This method of collection of symptom data has been validated [89]. The study diaries were based on those commonly used in clinical practice. Symptoms were scored (0-9) in three separate groups: nocturnal symptoms (0-3); daytime symptoms (0-3) and symptoms experienced on activity (0-3). Additional information was recorded about rescue medication and signs and symptoms of upper respiratory tract infection. Children were also asked to record any activities they took part in on a daily basis.

Figure 3.2.2.1 Symptom diary questions used in study.

Date at start:																													
Were you woken by asthma last night? 0=none; 1=once; 2=twice; 3=lots 0-3																													
Did you have a DAYTIME wheeze or asthma cough today? 0-3 0=None; 1=Slight –no reliever , 2=Moderate-(symptoms relieved) 3=Severe, reliever did not lasting full time																													
Did you have wheeze or asthma cough brought on by activity today? 0-3 0=Able to do everything-no symptoms 1=wheezy on running -still do activity 2=wheezy when active had to slow up 3=Too wheezy had to stop.																													
Since yesterday have you had: (tick) cold or runny nose ?																													
Temperature?																													
Sore throat or earache?																													
Extra reliever: how many extra doses did you use since this time yesterday ?																													
Steroids (Prednisolone). How many tablets did you take since yesterday?																													
Have you done **anything** different which may have affected your chest e.g. parties/ animals/ extra activity ?																													
Extra preventer: How many extra doses used since this time yesterday?																													

b) Electronic methods

The Vitalograph Data Storage Spirometer (DSS) offered facilities in addition to spirometry to record responses to a series of questions (figure 3.2.2.2). Having completed spirometric manoeuvres in the morning, children answered six pre-defined questions which were programmed into the machine. The questions were repetitive to facilitate independent use by younger children. We expected children to answer independently of their parents. Questions about changes in condition, feelings in terms of asthma, medication use and treatment changes were asked to all children.

Questions	**Response options**
• Do you feel better since your last set of blows?	**Yes** / No
• Do you feel worse since your last set of blows?	**Yes** / No
• Since your last set of blows how well have you felt?	**0-** 10
• Since your last set of blows how well have you felt on activity?	**0-** 10
• Since your last set of blows how many different times have you used your reliever (no. of puffs)?	**0-20**
• Since your last set of blows have you changed treatment step?	**Yes** / No

The first two questions were combined for interpretation. The children were instructed to answer "No" to these two questions if they felt the same. Default responses were offered to every question (in **bold** above). Once they had chosen a response and pressed enter, they could not change their minds.

Figure 3.2.2.2 Vitalograph data storage spirometer
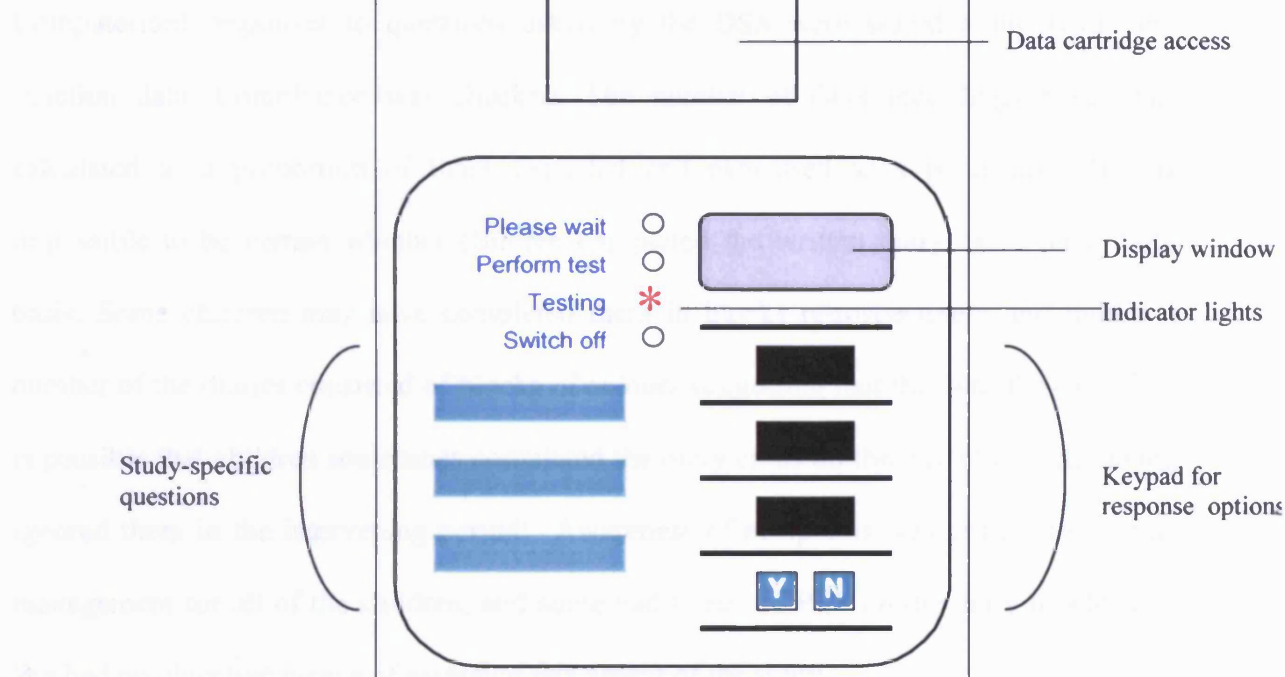
Procedure

Written diaries were collected during each visit and a blank one issued for the next four weeks. The diaries were completed by hand, by children alone or with parents, depending on the child. Children were asked to record the date at the time of diary completion so that any missing data could be accounted for. Children were asked to complete the diaries in the morning at the same time as they completed electronic responses. They were advised to consider each question carefully to provide an accurate picture of asthma status during the previous 24-hour period. Diary completion was important as for some children symptoms were the only means of asthma self-management. Each child was asked to consider the previous day and score their asthma symptoms for that time. The composite night, day and activity score was the daily symptom score used for analysis. Analysis of these data was important as the main outcome for the trial was mean change in symptom score during the trial period.

3.2.3 Validation of data collected

Compliance with symptom recording

Computerised responses to questions asked by the DSS were stored along with lung function data. Compliance was checked. The number of days recordings made was calculated as a proportion of those expected and expressed as a percentage. It was impossible to be certain whether children completed the written diary cards on a daily basis. Some children may have completed them in blocks retrospectively and indeed a number of the diaries consisted of blocks of colours suggesting that this was the case [74]. It is possible that children sometimes completed the diary cards on the day of a visit, having ignored them in the intervening period! Awareness of symptoms was critical to disease management for all of the children, and some had to record PEF on the diary in addition. We had no objective means of assessing this aspect of the study.

Compliance with diary completion was expressed as the proportion (%) of diary entries expected which were recorded legibly. All available written diary data were included in the analysis

Comparison of written and electronic methods

Comparison of electronic and hand written methods was possible by the repetition of one identical question in both methods. Children recorded bronchodilator use on a daily basis, in the morning and considered the last twenty-four hours. This information was recorded in the written diary and the DSS. The level of agreement between the two methods was assessed using Altman Bland analysis.

3.3 Lung function measurements

3.3.1. Peak flow measurement

PEF is the most widely used means to monitor levels of airway obstruction. It is defined as the 'maximum flow achieved during an expiration delivered at maximal force from the level of maximal lung inflation' [54]. In healthy individuals PEF is determined by a number of factors: lung size, lung elasticity, intrathoracic airway dimensions and respiratory muscle strength, the latter being dependent on coordination and effort and hence improved by training [90,91]. Lung size is determined by stature. Subjects with larger lungs tend to produce higher values of PEF [91]. This relates to the dimensions of the large airways which increase in calibre with growth.

Portable peak flow meters offer an inexpensive means of assessing airflow. Recommendations for PEF monitoring equipment are stringent [92]. Non- linear scales of so called 'mini-meters' have led to speculation about their accuracy [65], particularly in conditions of airway obstruction. Obstruction in the intrathoracic airways reduces PEF as a result of increased resistance.

PEF measurement should be done from a standing position as it is dependent on inhalation to total lung capacity and exhalation with maximal force [92]. In the absence of disease, the elastic recoil of the lungs is greatest at the point of maximal inspiration. The manoeuvre involves fast maximal inhalation, no pause at total lung capacity (TLC) and rapid expiration lasting approximately one second. Muscle strength and coordination are important in determining PEF, particularly expiratory (abdominal) muscles [91]. Inhalation time may be important in determining some of the force produced by expiration [90]. Highest values for PEF are obtained with minimal (or no) pause and rapid increase in expiratory pressure [93]. Pause at TLC, even for as little as 2 seconds reduces elastic recoil by stress

relaxation and reduces PEF. This has been documented in both healthy and asthmatic adults [91,94]. The neck should be held in the neutral position to avoid added resistance from extrathoracic airways [95,96] and coughing or spitting into the device produces falsely high values. Only three acceptable tests are needed and the highest of these is recorded.

There is debate about the accuracy of PEF and its relationship with other measures of disease, particularly in children [86]. The procedure requires considerable comprehension and co-ordination. In children a lack of clinical correlation between peak-flow measurements and symptoms has been repeatedly shown in clinical trials and borne out in clinical experience[98]. The most common observation is that the PEF remains within an acceptable "normal" range, while patients exhibit a wide range of symptoms and additional bronchodilator use. A number of possible explanations have been given for the poor correlation. Bronchodilator use itself may affect the recorded value of PEF. In particular, early-morning PEF may be increased by bronchodilators taken during the night. In children (as distinct from adults) asthma is often episodic, so that a discrepancy may emerge between apparently stable day-to-day values, despite quite severe acute episodes from time to time. Recording the best of 3 blows may result in a big-breath effect, leading to temporary amelioration of any airway obstruction, with a consequent increase in the recorded peak-flow. The opposite effect is occasionally seen. Finally, symptoms may be more closely related to reactivity of airways or small airway function (mid-expiratory flows) rather than to peak flow, suggesting a range of underlying pathology that cannot simply be represented by PEF.

3.3.2 Spirometry [92,99]

Spirometry is the measurement of volume as a function of time. This offers information about the amount of air which can be exhaled during a forced manoeuvre over a period of

time. Flow, the rate at which volume changes as a function of time[92] can also be measured. Flow-volume curves (figure 3.3.2.1b) are derived from volume-time curves (figure 3.3.2.1a). The tangent at a point on the volume-time curve represents a measure of flow at that point figure 3.3.2.2). Spirometry is non-invasive, effort dependent and relatively simple, technique improving with practice. It requires cooperation, comprehension and considerable co-ordination.

Figure 3.3.2.1 (a) Volume-time spirogram
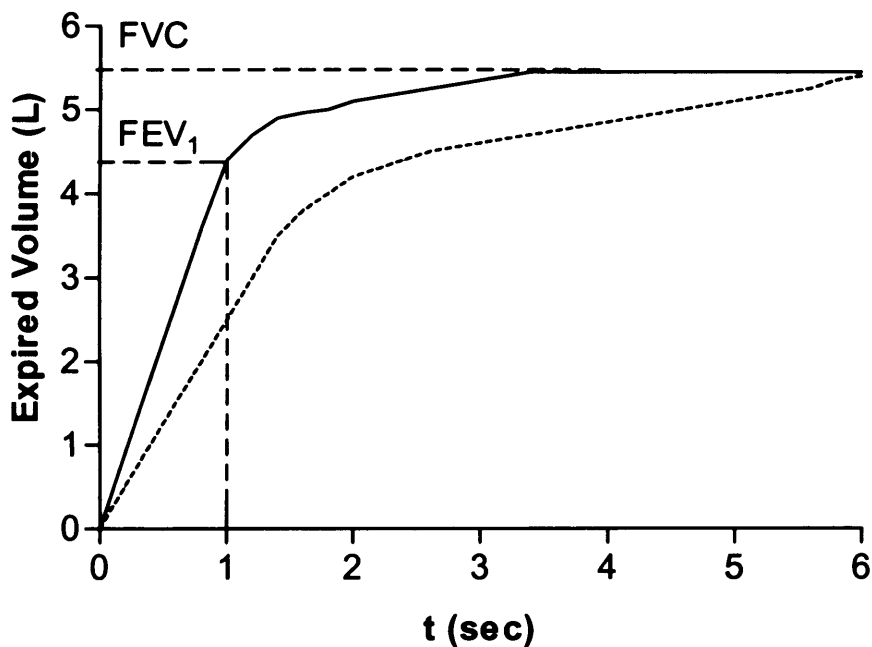
Figure 3.3.2.1 (b) Expiratory portion of flow versus time curve

Expired volume (L)
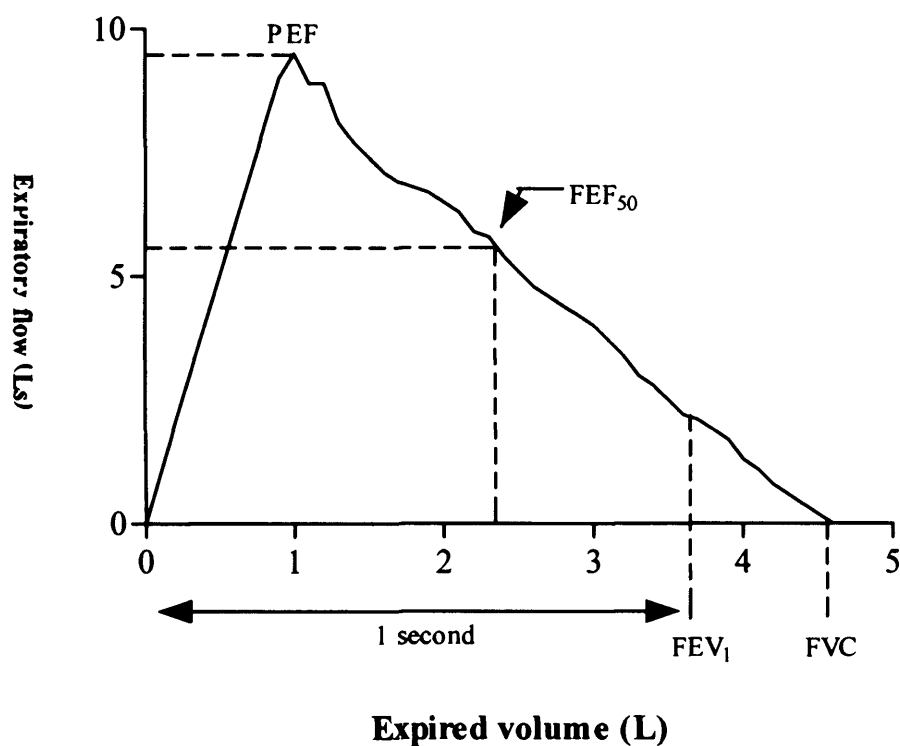
Figure 3.3.2.2 Derivation of flow-volume curve from volume time curve
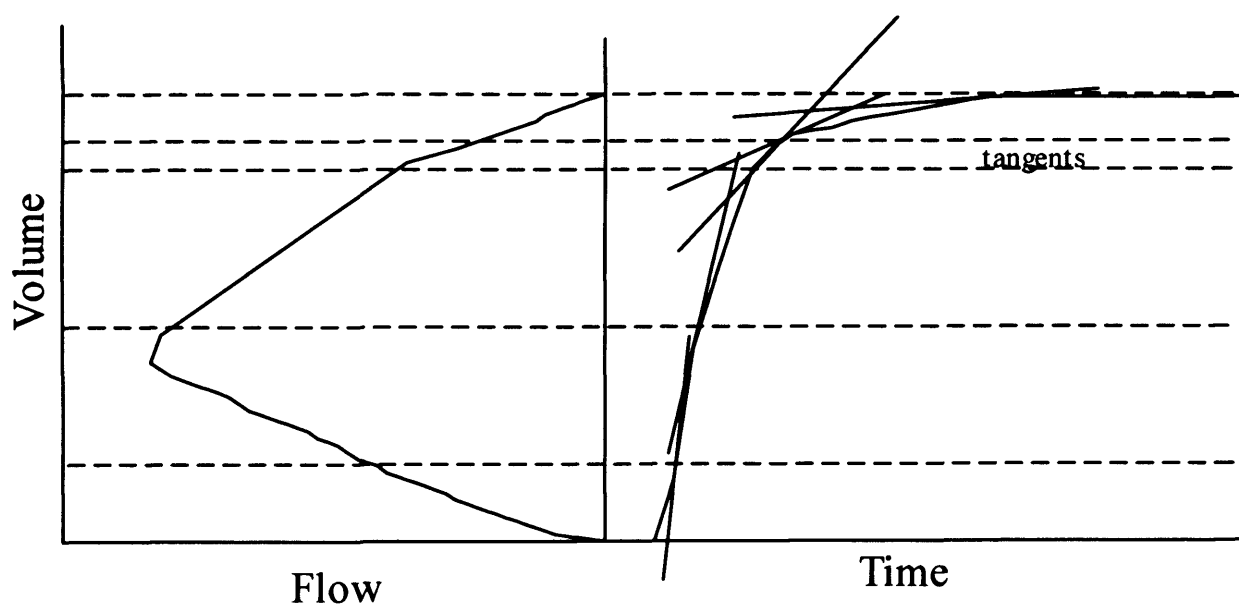
A number of parameters are available (Figure 3.3.2.1). Forced vital capacity (FVC) is the

maximal volume of air (litres) exhaled with maximal forced effort from total lung capacity

(TLC). Forced expiratory volume in 1 second FEV_1 (litres) is the amount of air that can be

expired in the first second of the FVC manoeuvre. In small children where FVC may be reached before one second, FEV_1 can be measured at 0.75 or 0.5 seconds. Forced expiratory flows (FEF) are measures of flow at different stages of FVC, (litres per second) e.g. FEF $_{25-75}$ is the forced expiratory flow at between 25 & 75% of FVC. Using the DSS, FEF is measured at 75% and 25% FVC and a mean of the two flows is reported. Other devices sometimes take a mean of intervening points between the two flows. Mid expiratory flow (MEF or FEF_{50}) is the flow at 50% FVC. Forced expiratory ratio (FER%) is the proportion of FVC which is exhaled in the first second (FEV_1). Inspiratory flows can also be recorded but this study involves only expiratory manoeuvres.

Bye *et al* performed spirometry with 65 children between 6 and 18 years. They were all well controlled asthmatics who had been symptom free for 6 weeks. Despite better than predicted values for PEF, mean mid expiratory flows (MMEF) were reduced. The authors concluded that in this stable group of asthmatic children failure to perform spirometry could have resulted in failure to recognise persistent peripheral airflow obstruction which could lead to a poorer prognosis [100]. Airflow obstruction in small airways may not be evident when measuring only PEF [86]. Measures of lung function other than PEF offer more detailed information and may be more appropriate for monitoring children with asthma[86,101].

Quality control and assessment of test performance are considered to be the most important issues [92]. Instructions and a demonstration should be given. This is particularly important in paediatric patients or those with asthma who may never have done this before or may be used to carrying out a peak flow manoeuvre. As with PEF, posture is important and maximal inhalation with fixed neck posture enhances results.

Technical factors in quality control

Problems arise at the start of exhalation, demonstrated by excessive hesitation at TLC before starting to blow. A false start can lead to loss of volume before a good seal is achieved. Excessive pause at TLC may lead to a reduction in FEV_1 as well as PEF (see above)[95]. Stress relaxation leads to reduced elastic recoil pressure and consequent reduction in maximal flow. Coughing during the manoeuvre will affect FEV1 and coughing at any other time may interfere with measurements or affect results. Volume should be stable for a reasonable time and (according to ATS criteria) manoeuvre should last at least six seconds. Most healthy children exhale completely within 2 seconds [102]. It has been suggested that end of test criteria be modified for the paediatric population [103] A leak or obstruction to the mouthpiece may be caused by the tongue or teeth in front of the mouthpiece. Such problems lead to greater difficulty in performance particularly by children because of the need for co-ordination and concentration. The FVC manoeuvre may itself induce cough.

3.3.3 Methods

Equipment recommendations. [92,99]

Minimal guidelines are supplied for equipment accuracy [92] and workshops have been dedicated to establishing equipment performance criteria [99].

The ATS guidelines state that at leasttwo acceptable manoeuvres are required recording forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1). The two best should not differ by more than 0.2L or 5% whichever is greater[92]. Acceptable tests should not necessarily be discarded or ignored because they are poorly reproducible but labelled as "non- reproducible" (according to ATS criteria). The interpreter of the results should decide whether the results are valid. The only criteria for unacceptable performance is fewer than two acceptable curves. The 'best test' is derived from the blow with the

highest FVC + FEV$_1$ value. The highest FVC, FEV$_1$ and PEF are stored and the other flows are taken from the manoeuvre with the highest FVC + FEV$_1$ sum.

The data storage spirometer (DSS)

Home spirometric measurements were made using a data storage spirometer (DSS., Vitalograph, Buckingham, UK) . Excepting equipment failure, each child was provided with one spirometer for the duration of the study. Designed for collecting longitudinal lung function data and storing it, it can be used anywhere. For ease of use it was mains operated or used with integral rechargeable batteries. It was portable and had a carrying case for practical purposes (Fig 3.3.3.1). This machine met and complied with ATS criteria for diagnostic/ monitoring equipment, according the manufacturer's literature. The following parameters were available: FVC; FEV$_1$; PEF; and FEF $_{25-75}$. Lung function parameters and date and time of session were stored numerically on a data cartridge and uploaded for analysis.

Figure 3.3.3.1 The DSS and carrying case
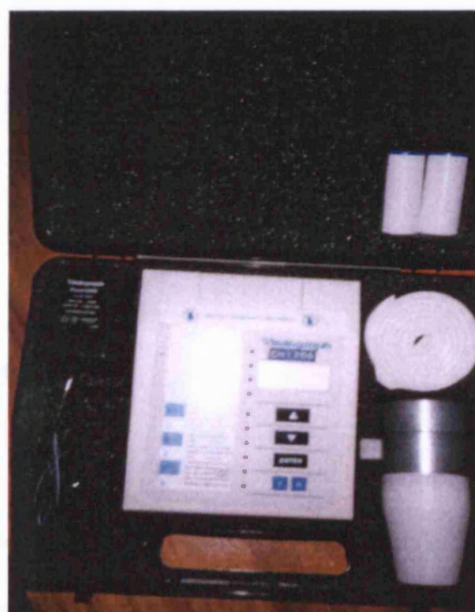
Equipment specification

The DSS measures flow using a Fleisch-type pneumotachograph, pressure transducer and microprocessor sampling at a rate of 100Hz. The linear range of the spirometer and flowhead in the DSS is shown in figure 3.3.3.2. Flow integration determines volume. According to the manufacturers, the maximum recordable FVC is 10 litres, with maximum recordable flow of 15 L/s (900l/min). Each test is recorded for no longer than 20 seconds duration. The machines operate optimally within the temperature range of 10-40 °C. Data from the manufacturers demonstrates that the equipment meets and complies with ATS [92] specification for accuracy, measured by deviation from target value, and precision measured by intradevice repeatability.

The manufacturers resistance data showed that the DSS was well within ATS specification, even at higher flows. The addition of safety mouthpieces increased resistance but it did not exceed ATS specification (figure 3.3.3.3). BTPS testing, injecting heated and humidified air demonstrated accuracy in FVC and FEV_1 measurement and therefore ATS criteria were met.

Figure 3.3.3.2 Linearity of flowhead
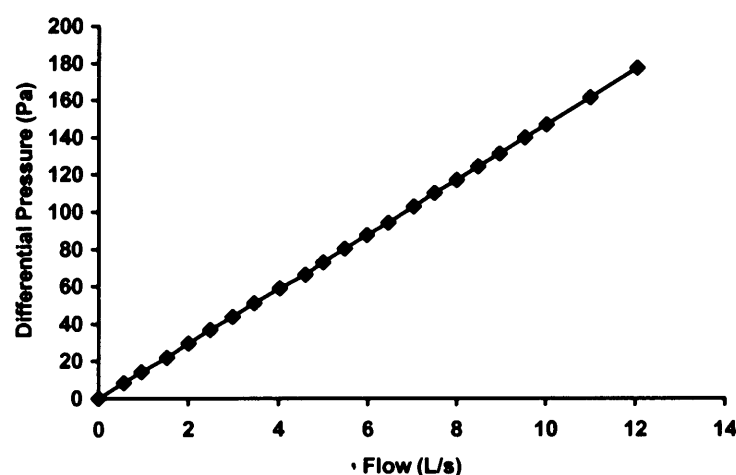
Reproduced by kind permission of Vitalograph, UK, Ltd.

Mouthpieces

One-way safety mouthpieces (Vitalograph, Buckingham,UK) were used by the children throughout the study. These are valved at one end to prevent inhalation through the mouthpiece.

Figure 3.3.3.3 Resistance data for valved mouthpiece[2]

Mouthpiece Back Pressure
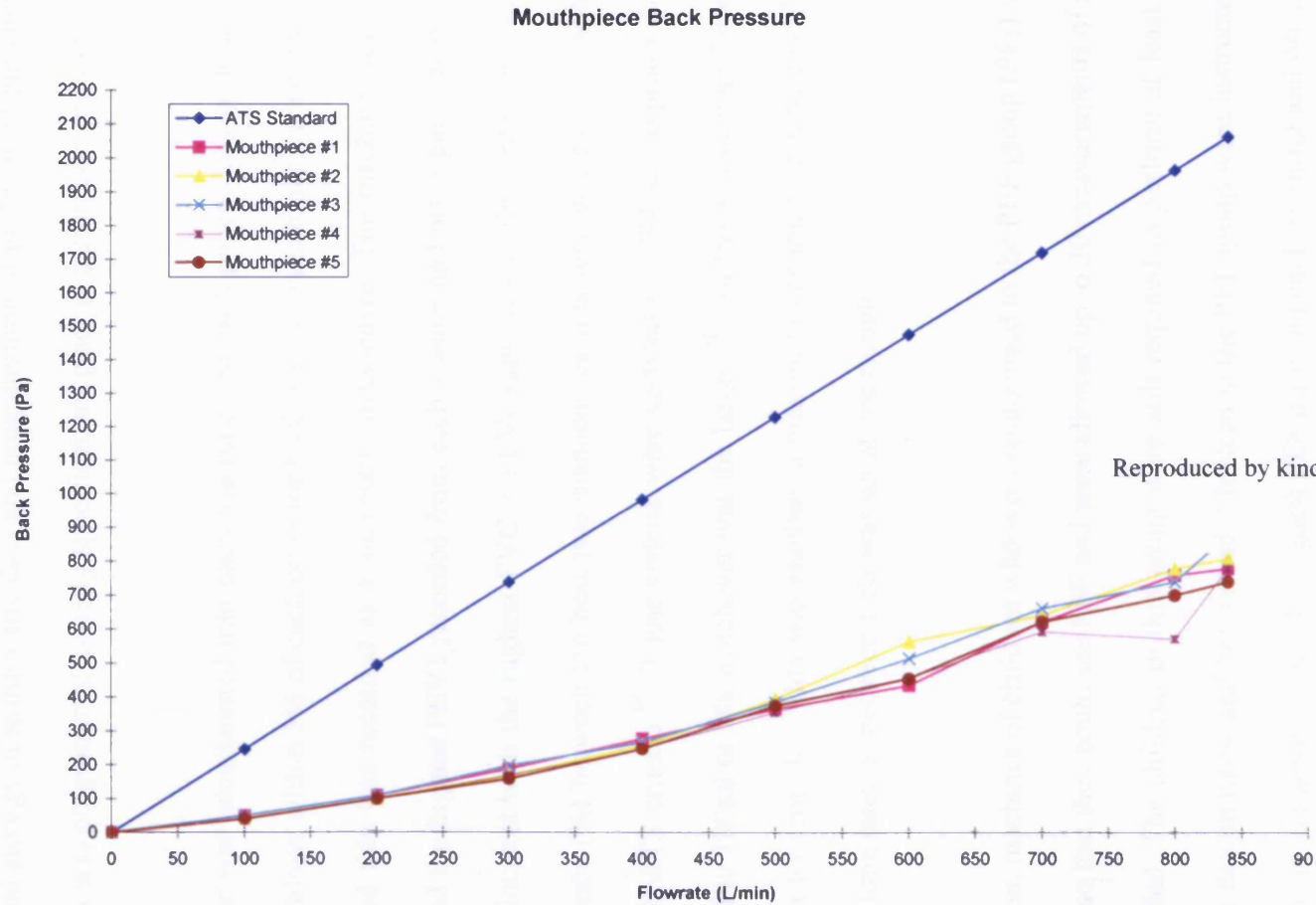
Reproduced by kind permission of Vitalograph,UK. Ltd.

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[2] The ATS maximum resistance (back pressure) recommended at different flows is shown by the blue line and complete squares. Using mouthpieces with valves does not increase the resistance (back pressure) sufficiently to exceed these requirements. Valved mouthpieces do not increase the resistance of the equipment to a level which exceeds the recommendations of the ATS.

Programming of the spirometers

Spirometers were supplied with software (Vitalograph, Buckingham, UK) which allowed interpretation and storage of spirometric data and programming of preferential parameters. Each spirometer was programmed to study specifications prior to calibration and use.

A trial identifier was programmed into each machine and each patient had an individual identifier. Two blows within 5% of each other for FVC + FEV_1 variability were considered reproducible and this was recorded as a successful manoeuvre. The machine stored the highest FVC and the highest FEV1 recorded from each session and other parameters from the within session test with the highest FVC + FEV_1 sum. Where this criterion was not met, the difference (%) between the best two manoeuvres was recorded by the machine. This meets with ATS criteria [99]. These criteria were updated in 1994 and reproducibility criteria changed to 200ml or 5% whichever was the larger [92]. For those sessions where the machine criteria for reproducibility was reached, a maximum variability can be calculated in ml. Minimal time interval between tests was set at one minute.

At randomisation, machines of children who were randomised to the PEF group (PF_1) were reprogrammed so that they could see PEF and were allowed up to 20 measurements of PEF per day as needed. The children in this group were still required to perform at least two manoeuvres per day on rising and before bed. Children in the PEF group were instructed to record manually, in the written diary the highest PEF achieved each morning and use it for management.

The data cartridge was cleared after each child had completed the study period, when the data had been uploaded into a statistical package for analysis. The internal battery of each

machine was fully charged prior to distribution, allowing subjects to choose mode of operation.

Calibration of spirometers

A calibration check was performed on each machine between subjects. Calibration maintenance was tested prior to commencement of recruitment when 5 machines were given out for regular use; 5 were kept unused at an ambient temperature of 23^0C and 5 were kept unused at room temperature. After 1week calibration was maintained in all cases within 3%.

At each calibration check, records were made of room temperature and drift from the previous calibration, using a 1litre syringe (Erich Jaeger GmbH, Hoechberg,Germany). Five litres was the reference volume, using a plastic adult mouthpiece. Each machine was calibrated using its own flow head and tubing and to maintain accuracy they were not moved between machines. Where the calibration check demonstrated that the calibration was not maintained within 3% a machine re-calibrated.

Cleaning & sterilisation of spirometers

Each machine was issued with a sterilised filter and new valved, safety mouthpieces. Cleaning and sterilisation took place between each patient use. Flow tubes and flowhead cone were cleaned externally with alcohol soaked wipes (Seton Prebbles Ltd., Oldham, UK) and cases were wiped clean with warm soapy water. Filters were semi disposable and could be sterilised before replacement. Between uses the filters were sterilised in solution made up from Presept tablets (Johnson and Johnson Medical Ltd. Ascot, Berks.) dissolved in water to a concentration of 140ppm available chlorine. This concentration is that recommended for baby bottles, teats and stainless steel equipment. After soaking for at

least 1 hour, the filters were rinsed thoroughly in distilled water and dried in a drying cabinet overnight before being replaced in the flow head. Replacement and cleansing of all parts of the equipment was carried out prior to programming and calibration.

Procedure

Each child was trained. Technical ability was assessed prior to study entry using a turbine spirometer (Microloop, Micro Medical, Kent, UK) which allows the expiratory portion of the flow-volume curve to be viewed and technically assessed (fig 3.3.3.4). Manoeuvres can be stored and printed out as a report at a later date (fig 3.3.3.5). Those able to carry out a full forced manoeuvre were allowed to enter the run up period. For the duration of the study, each child was asked to carry out two spirometry sessions daily on rising and before bed; requiring between two and five full forced manoeuvres per session, the machine indicating when two blows to ATS criteria had been achieved or five had been performed. After each morning session, the children were required to answer a series of questions by operating the spirometer and then complete a diary card with information about symptoms and rescue medication use during the previous day.

Figure 3.3.3.4 The Micro Medical Microloop

Figure 3.3.3.5 Print out available from Micro Medical Microloop

Patient Name: _____   _____
Test number: 109   Date: 06/10/97   Time: 10:25
Patient ID: 00003   Age: 28
Sex: Female   Height: 165 cm.

Spirometry Test and Flow Volume Loop

	Baseline	%Pred	PostBD	%Change	Normal Min	Max	Units
FEV1	3.42	107			2.59	3.83	L
PEF	487	114			338	516	L/M
FVC	4.05	110			2.98	4.40	L
FER	84.44	101			73	94	%
F50	3.97	88			2.69	6.31	L/S
F25	1.56	73			1.01	3.27	L/S
MEF	3.61	90			2.63	5.43	L/S
I50	6.63						L/S
R50	59.87						%
MVV(ind)	128.25						L

INTERPRETATION: Normal Spirometry
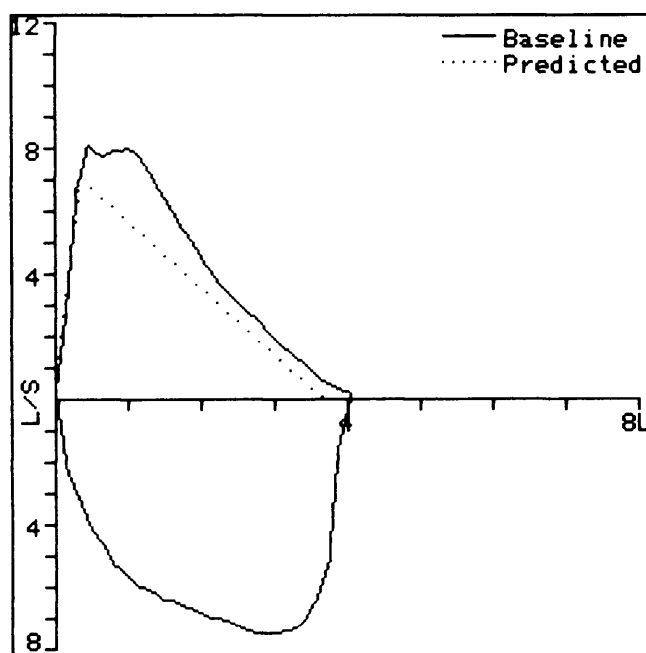
The DSS illuminates lights to instruct the patient (figure 3.2.2.2). Children were instructed to follow the lights. The best manoeuvre from each session was stored by the machine for later analysis. A successful session was recorded if the reproducibility of the two "best" manoeuvres was within 5%. A session was unsuccessful if fewer than two manoeuvres were performed. If a child performed five manoeuvres, but failed to reach reproducibility criteria of less than 5% variability in FVC + FEV_1 sum, the best test was stored. In these cases the machine stored the percentage variability reached. Each participant was informed that the date and time of each session was recorded by the machine in an effort to enhance compliance.

During the run up period, no information about spirometric results was available to the participants. This remained so for those patients randomised to receive a self-management plan based on symptoms alone. For those patients in the peak flow group, the DSS was reprogrammed. Following randomisation, at each manoeuvre, the patient was provided with a peak flow for that manoeuvre. Patients were instructed to record the highest PEF achieved at the morning session in their symptom diary and use this for management. Stored results were uploaded into DOS and then stored in EXCEL (Microsoft Corporation, Seattle, USA.) in windows before being transferred into SPSS (Version 3 SPSS Inc. Chicago, Illinois) for analysis.

Its durability and the simple instructions for the equipment made it acceptable for children to use! Electronic operation meant children were interested and quick to learn how to operate it. The one-way mouthpieces supplied for use with the spirometers were replaced as necessary during the study.

3.3.4 Assessing data collected

Any lung function data which failed to meet criteria [92] were excluded from the analysis. Default recordings of FVC or FEV_1 of 9999 were excluded from the analysis. These were considered to be equipment failure and were displayed where flows were not measured accurately.

Subject error was recorded for any manoeuvre where the machine recorded test failure. This meant that the test failed to meet all of the criteria or that insufficient manoeuvres had been recorded. Any stored value of FVC more than 3 standard deviations (SD) above the value for an individual child was excluded from the analysis. In these cases it was assumed that an adult had performed the manoeuvre, in the absence of any other obvious explanation. In summary any non erroneous results which met the machine criteria for reproducibility and which were less than 3 SD above the predicted value for that child were included in the analysis.

Compliance

Completed test sessions were recorded together with the date and time of the session. Compliance was defined as the proportion (%) of expected results which were recorded during the period between visits sessions which were carried out in the morning and evening. Compliance with recording was calculated using all manoeuvres recorded. Full compliance with the protocol required two sessions per day over 10 hours apart. This included weekend data where children may have carried out the morning session later than on week days, provided session two was subsequently carried out later in the evening.

Technical quality

Machine-defined technical quality or within-session reproducibility was assessed. Where two manoeuvres within a session reached less than 5% variability in FVC +FEV_1 sum, this

was considered a technically acceptable session. Technical quality is defined as the proportion (%) of sessions recorded which were coded as successful by the equipment. Machine errors were removed from the technical quality assessment as were non-repeatable manoeuvres. Blows where standard deviation score for FVC was more than 3 were also removed at this stage.

Valid data.

The amount of valid lung function data available from each patient when taking into account their ability to carry out the manoeuvre and their compliance with the protocol is composite of compliance and technical success. It is defined as the proportion (%) of results expected which were technically correct and carried out at the correct time.

In summary any result stored by the machine and coded as technically acceptable (included two manoeuvres which demonstrated less than 5% variablity in $FVC+FEV_1$ sum); performed in the morning or evening, at least ten hours apart and not showing any machine error was considered to be valid data and included in the analysis.

3.4 Health related quality of life

3.1 Background

Assessment of the impact of treatment on individual patients is especially important in chronic disease. Where cure is not a possibility, patients and their immediate families must come to terms with changes in lifestyle which may vary with time. Quality of life assessment is a formal measure of individual well-being, arguably a measure of health [104]. It can be defined as representing "the functional effect of an illness and its consequent therapy... as perceived by ...(the)... patient" [105]. Information about the physical, social, occupational and psychological effects of illness is sought, which may otherwise be overlooked by more traditional methods [106,107]. Quality of life measurement offers the ability to gain the patient's perspective of the impact of disease, encompassing a wide

range of health issues. Disease specific tools cannot be generalised or applied to any other situation e.g. Childhood Asthma Questionnaire [108], Juvenile Arthritis Questionnaire [109]. Paediatric assessment tools are limited in number and tend to consider all aspects of life in order to gain a more global picture. Patient perception is a critical aspect of disease course and much of the daily impact of the disease is subjective, as is decision to alter treatment as more patients are changing treatment with guidance at home. Discrepancies between quality of life assessment have been demonstrated between patients and doctors [98,107], and also parents and children [110], especially adolescents [111].

Until the development of questionnaires, all non-clinical data available e.g. school or work absences were considered to be useful in assessing health related quality of life. Availability of specific tools makes quality of life a realistic measure of outcome [107]. To ensure it is valid, a questionnaire inevitably requires some means of comparison with other measures of disease severity. Quality of life questionnaires include other measures of symptoms or activity limitation as part of their design. There is evidence that they measure some other aspects of the disease which are not wholly represented by other means of assessment [104]. Objective improvements in physical function are important but may not be relevant to the patient [112]. Improvements in functional status may be accompanied by similar improvements in quality of life in some patients but not others, whose overall health is not much better[104].

Quality of life assessment can be used to measure the impact of treatment. Most questionnaires have been designed for repeated assessment so that it is possible to measure it sequentially. Improvements in quality of life may enhance the patient's sense of well being. Negative feelings about disease impact, when symptomatic control is good, offer the

health professional the opportunity to elicit patient concerns and promote discussion to attempt to resolve the problems.

Attempting to measure quality of life may itself influence the clinician/ patient relationship [113]. Patients who feel their opinion is being sought may be more likely to listen to the health professional [113]. Knowledge about the emotional impact of illness and the way people feel about disease progression or treatment may enhance care. The patient's expectations from treatment are usually far from the clinician's aims or the medical therapeutic model [114]. It has been suggested that by paying attention to quality of life, patient satisfaction and hence adherence to therapy may be improved [113]. For instance, a simpler, less intrusive medication regime, may be more likely to be adhered to. The relationship between quality of life and compliance is complex and far from proven. Quality of life may improve without any significant changes in objective measures simply because the time involved in taking treatment is reduced.

Health professionals carry out quality of life assessment informally during clinical assessment: "How are you?" "How have you been since I last saw you?" This lacks focus, is highly subjective on the part of the clinician and is far from standardised between clinicians and patients. Clinicians may not "hear" the patients reply. Assessment is complex and dependent on time available, effectiveness of measurement tool, application of results and need for full assessment. Formal assessment is possible using quality of life measurement tools. Despite criticism of the subjective nature of these tools, there is a great similarity between these measures even though they have been developed in different ways [104].

A number of tools are available for use with children with asthma (Table 3.4.1).

Table 3.4.1 Quality of life measurement tools for children with asthma

Measure type	Name of assessment tool	Who completes	Age	Comments
Asthma (disease specific)	Childhood Asthma Questionnaire [115] form A Form B Form C	child & parent child alone child alone	4-7 8-11 12-16	• uses smiley faces • difficult concepts for youngest group
Asthma (disease specific)	Paediatric Asthma Quality of Life Questionnaire [116] Caregivers Quality of Life Questionnaire [117]	child parent	6-17 parent	• interview or self administered • children seem to find some questions ambiguous • caregivers complete questionnaire relating to the impact of asthma from a carers perspective
Asthma	Usherwood [118]	Parent	Children	• primary care tool • proxy measure

The choice of questionnaire depends on a number of factors. Quality of life questionnaires should meet minimum criteria before being applied to a population. Validity and repeatability checks should be carried out and available in the public domain [106,107,119]. A tool is valid if it measures characteristics it purports to. Scientific tests have standardisation of procedure and are therefore valid [120].

It is important to choose a questionnaire which has been validated appropriately. Where all appropriate tools have undergone necessary development and testing, practical issues become important. Ease of application and number of questions are important considerations if quality of life is to be measured in a busy outpatient department, for example. If a disease specific measure is used, individuals are unlikely to have a problem understanding the relevance of the questions. A questionnaire with a large number of questions may be intimidating. Questions should be easy to comprehend, brief and to the point and unbiased. The accessibility of the results is important. Parent alone may provide responses, by proxy [118], parent and child may complete the questionnaire together [115] or the child may answer alone e.g. CAQ form B & C [115] Paediatric Asthma Quality of Life Questionnaire [116]. There is usually a choice of responses. These should be clear and straightforward. During completion, individuals should not require clarification as this may result in the introduction of bias. For use in the clinical situation, answers should be available and accessible immediately to allow patient and clinician to discuss any issues raised at the time of completion.

Problems with measurement

Administration may be aided by comprehensive background information. There is a great potential for introduction of bias, particularly when working with children, especially if active interviews are needed. Comprehension problems may arise. Language differences

can cause obvious problems but even in English speaking countries word choice means parents and children may not understand a questionnaire which has been developed elsewhere (chapter 5). Cultural differences may cause problems of comprehension or applicability of some questions. Literacy becomes an issue if the questionnaires are to be self-completed. Parents or children may be reluctant to admit to reading difficulties. If an interview is possible, it may be wise to offer the choice. Some developers have assessed their questionnaire in populations to determine the reading level needed e.g. PAQLQ [121]; whereas others have designed age specific forms of their questionnaires e.g. CAQ [115].

Quality of life questionnaires usually report the situation over a specific time period e.g. the previous week. Poor memory may make recall difficult, while young children may have difficulty with the concept of elapsed time [97]. One commentator suggests it useful to consider some activity or event to act as a focus and aid memory [122]. Some questionnaires are designed to be answered by the parent [118], which avoids this problem but relies on parental assessment which may itself be inaccurate [111,123]. The older the child, the less likely are the parents to be able to report accurately, the impact of disease.

Some measures for use with whole populations have reference values to act as a guide. Disease specific measures cannot by definition use reference values from healthy populations but within-subject changes over time can be used to assess effects or interventions.

Where children are to be asked directly this should be done in the absence of parents [122]. Some parents may be suspicious but only in this way are the child's views properly represented. Children need to be reassured that whatever answer they give is acceptable! They may be looking for reinforcement but neither prompts nor clues to the desirability of particular answers should be offered. Juniper recommends merely repeating the question if

a child is hesitant or voices concern [122]. This takes time and patience. Hurried children may sense disapproval which may be reflected in their responses. All measures offer some range of responses. Adults and children may interpret these differently [123]. This should be considered if using proxy measures or those which parent and child complete together or if a comparison is to be drawn between parent's and child's answers.

Whilst it is relatively easy to carry out quality of life measurement as a means of assessing outcome, dealing with the results is another matter. Some measures have had such widespread use that they have normal values to which patient results can be compared and the result is a norm-referenced measure. Unfortunately in paediatric medicine, many of the current tools do not have reference values, either because thus far experience is limited or because, by definition, disease specific questions cannot be answered by healthy people. For clinical care the main application of these tools is to assess change following an intervention such as a management change. The main impetus is to assess within-patient changes in quality of life following an intervention, irrespective of clinical outcome. Scores should be used to give a qualitative guide, and not interpreted as precisely as, for example FEV_1 or PEF. Most questionnaires incorporate symptomatic outcome as one of the areas within the assessment tool so there is likely to be some degree of correlation between overall quality of life change and the clinical assessment. As questionnaires develop, some provide a guide to the size of change in score which is clinically significant to provide guidance for clinicians who wish to include it in their management strategy [124,125].

In summary it is possible to measure quality of life in children with asthma using validated, well developed questionnaires. Although a number of studies have used quality of life assessment as a measure of outcome, use in clinical practice is limited to date. Quality of

life assessment offers additional information to enhance management and improve communication between physicians, parents and children.

3.4.2 Methods

Equipment for measurement (appendix 1)

Two asthma-specific quality of life tools were available for children at the start of the study; the Childhood Asthma Questionnaires (CAQ) [108,126] and the Paediatric Asthma Quality of Life Questionnaire [116]. The latter was chosen for use with this study because it was designed for use with 7-16 year olds which encompassed our age group. This meant one questionnaire could be used for all the children in the study. It was the most widely used questionnaire to measure asthma-specific quality of life in children and the same group had produced a questionnaire for completion by parents of children with asthma [117]. The paediatric quality of life questionnaire (PAQLQ) and caregivers questionnaire (PACQLQ) were used to assess quality of life of children and parents who took part in the study. These are disease specific questionnaires designed for completion by asthmatic children and their parents. The development of these questionnaires is well documented [116,117].

PAQLQ [116]

The PAQLQ was developed using a population of asthmatic children aged 6-17 years. The questionnaire comprises 23 items in 3 domains (activity n=5; emotion n=8 and symptoms n=10). The 23 individual items each carry equal weighting therefore overall quality of life score and individual domain scores range from 1-7. Each child was asked to complete the questionnaire by choosing, either verbally or by marking a box, a number from 1-7 on an interval scale. The lower the "score", the greater the impairment. The respondent was asked to consider one week prior to questionnaire completion. It is individualised at first administration and this was completed at baseline. The child chose three regularly

performed activities which were problematic because of their asthma. These activities remained for the duration of the study. If they had difficulty there was a list of activities that served as a prompt (table 5.4.2). It can be self or interviewer-administered and guidelines for completion are available from the authors [122].

PACQLQ

This questionnaire consists of 13 questions relating to caregivers feelings about their asthmatic child's condition. The PACQLQ was completed by the main caregiver of the child from the parents perspective.

Procedure

The child-parent pairs were visited at home on five separate occasions; an initial recruitment visit to obtain baseline measurements and four follow up visits at four weekly intervals. Following recommendations of the developers, the PAQLQ was the first task completed at each visit before any discussion about the child's asthma [122]. Children were asked to complete the PAQLQ in the absence of parents. Age determined the mode of administration of the PAQLQ to the children. Those children of 7-10 years were interviewed and 11-14 years completed the self-administered version.

Parents were asked to complete both the PAQLQ and the PACQLQ in a separate room, at the same time. They were asked to choose three activities, without consultation, which they felt bothered the child most in terms of their asthma. After choosing activities, parents were told to put themselves in the child's position and "complete the PAQLQ as you think they would for the previous week". This provided an opportunity to assess parental perception of child's asthma related quality of life. Parents and children could not confer about questionnaire completion. Completed questionnaires were immediately returned to the researcher.

3.4.3 Validity of quality of life data

Questionnaires were completed during a visit and taken away. The data were recorded by the child in my presence with the parent completing their copy in another room at the same time. Imputation, the process of calculating missing answers based on all available scores, was used to complete missing data for any questions after the first visit [122]. Children who missed an activity may have done so as a result of worsening asthma, an important factor in this study. Missing data may have impacted on the resulting quality of life score and led to bias in the results for the activity domain. Imputing the score for missed activity allowed this to be taken into account, by using scores for other items in the same domain to calculate the missing value (section 6.4.3). The relationship between symptom domain (quality of life) score and diary symptom score was assessed. The mean daily symptom score recorded for the week prior to each visit was compared with the mean quality of life score for the symptom domain. Separating out the symptom domain ensured that the same constructs were being measured by both methods.

3.5 Self-management plans (appendix 2)

3.5.1 Background

Self-management under the guidance of health professionals is now recognised as almost routine in asthma management. Decisions about treatment changes can be made by patients once education and training has been given and the family are confident about manipulating treatment. Written guidelines are important to avoid confusion. There is evidence to suggest that individualisation of plans makes understanding easier and may enhance compliance.

The self-management plans developed for use during the study provided guidelines for all participants regarding alteration in treatment in response to changes in asthma severity to

optimise asthma control (appendix 2). For ease of use the plans used a traffic light system

of colour coding, based upon plans in use in the local hospital and current guidelines.

Double preventer?

"Doubling" of preventer therapy at the onset of an acute episode, was included in the plans

as a step up from normal treatment. This has become common practice in clinical care

although there is no evidence to support its' efficacy in young children [6]. Charlton et al[49]

argue that their sub-group of patients in the intervention group who doubled inhaled

corticosteroids had a tendency to do better. Garrett et al in a more recent study [127] disputed

this. They carried out a randomised, double blind; placebo controlled crossover study to

investigate doubling of inhaled steroids for exacerbation of asthma. They found no

significant difference in any morbidity or spirometric outcome between steroid and

placebo groups and concluded that increasing inhaled steroid was ineffective. Further

research is needed. The small numbers of children in the sub- group of patients in the

Charlton study mean results are inconclusive [41]. Although the latter study had power, the

children were treated for only three days before intervention with definitive treatment and

this may have been insufficient for an effect to be seen. Other studies have demonstrated

an effect with high dose inhaled steroids. In pre-school children receiving 2.25mg

beclomethasone diproprionate daily for five days, reduced severity but not duration of

illness was seen [128]. Older children treated for seven days or until asymptomatic had

reduced day and night time wheeze during the week following attack onset[129]. In both

these studies parents reported a preference for the active treatment. Garrett et al report that

patients prefer to make decisions based on symptoms [131].

3.5.2 Methods

Equipment for self-management (appendix 2)

In all plans, symptom changes were used as a guide for patients and/ or parents. Increased symptomatology was described and individualised treatment changes advised to maintain control and prevent or deal with exacerbations. Danger signs and instructions to seek medical help were also highlighted. At randomisation, all children received a self-management plan. Those entering the peak flow arm of the trial were provided with a plan which, in addition to the symptom information, also provided, individualised peak flows at which to take action. These were 70%; 50% and 33% of personal best PEF recorded during the 4 week run up period of the study. The best value was chosen from the highest PEF obtained during the run up, from a machine-defined technically acceptable manoeuvre.

All of the plans were specific to individual patients and any changes made to treatment during the course of the study were incorporated into the plans.

Procedure

Following randomisation, families were taught self-management. Both the child and the main caregiver were present at the teaching session, irrespective of the age of the child. The visits for education and randomization took between 90 and 180 minutes. The education session lasted between approximately 30 and 90 minutes. This was not a prescriptive teaching package. It involved a step-wise approach and was led by the child and parent. The plan was shown to the child and parent, and the child's current medication was recorded on it. The plan was systematically explained to the child incorporating their own medication regime. Each of the colour coded sections was explained. Changes in condition were explained in terms of traffic light changes (appendix 2ii). In the green section the child could carry on as usual. If their asthma deteriorated and they entered the

yellow/amber section they had to make changes. Increased symptoms such that they entered the red zone, they had to stop and take action. In the peak flow group (PF_1) additional information was supplied. Values of peak flow were 70%, 50% and 33% of personal best (appendix 2i).

All children were included in the education, irrespective of age. All of the children included in the study were school children, spending substantial periods of time every day, away from parents. At the simplest level, these children made decisions re: when to take bronchodilators, potentially on a daily basis. It was therefore important to offer some level of education, even at this young age.

At each stage both parents and children were asked if they had any questions. Spontaneous questions were answered and the parent and child determined the length and content of the teaching package. Information given was highly individualised. To ensure the child understood the principles of self-management, once the parent and child were happy with the self-management plan, two scenarios were described to the child and they were asked what they would do.

Any problems encountered with the self-management plan were answered by telephone or at subsequent visits. After the initial teaching session, no further formal self-management training was given. Questions at subsequent visits were answered and any treatment changes were incorporated into the plan.

In summary, the education was led by the parent and child, who were taught together. It varied in length between families and was responsive to their needs. When the self-management plan was discussed, peak flow levels were calculated for and discussed with only those children who were randomised to the PF_1 group.

Chapter 4

Measuring peak flow: comparison of forced vital capacity and peak flow manoeuvres.

4.1 Introduction

PEF values can be obtained using peak flow meters and so called PEF manoeuvres, or during forced vital capacity manoeuvres using spirometers. Peak flow meters are widely available, inexpensive and highly portable. Home monitoring of PEF is advocated for asthma self-management. It allows fine-tuning of asthma control by patients and has been shown in adults to improve well-being and reduce the need for hospital admission [30]. However the validity of this measurement has been questioned recently, particularly in relation to the use of the Wright peak flow mini meter [71] and in comparison with other lung function tests [101].

4.1.1 Measuring PEF

In place of PEF meters, spirometry has been advocated for monitoring adults and children with asthma at home [132,133]. Electronic spirometry provides much more information about airway function while still providing a value for PEF. Discrepancies have been demonstrated between PEF measured by portable PEF meters and during spirometry [61] but little work has been done to determine whether the difference is physical, related to recording equipment itself, or biological, dependent on the type of forced expiratory manoeuvre required. Nevertheless, electronic recording spirometers are increasingly being used in primary care and domicilliary settings to record PEF and spirometric indices, as in the RCT reported here.

4.2 Aims

The main aim of this study was to investigate whether, in children, using a turbine spirometer the value of PEF from peak flow manoeuvres (PEF_{PF}) was equal to that obtained during forced vital capacity manoeuvres (PEF_{VC}). The effect of using the highest PEF obtained during a forced vital capacity manoeuvre ($HPEF_{VC}$) was also considered. The PEF results obtained by each method were then compared to assess the difference between them.

4.3 Methods

4.3.1 Subjects

Eighty children aged 7-16 years (median age 10.5 years) attending outpatient clinics in secondary or community settings were invited to participate in the study.

Non- asthmatic subjects (n= 42) were recruited if they had no current respiratory illness and no upper respiratory symptoms within the last two weeks. This group comprised children with orthopaedic problems and healthy siblings of asthma clinic attenders.

Asthmatic subjects (n=38) had physician-diagnosed asthma and were in receipt of regular anti-inflammatory treatment, at least at Step 2 of the British Thoracic Society Guidelines [6]. Any child currently taking oral corticosteroid medication for any reason or receiving nasal therapy, and any asthmatic child with unstable or acute asthma or who had taken β_2 agonists in the last 4 hours was excluded.

Verbal consent was obtained from parents and children and the manoeuvres were carried out in the clinic area while children were waiting for their appointment. Eligible children were asked after instruction, to stand and give *up to* five blows each of the FVC and PEF manoeuvres. Any child who, after 5 attempts was unable to produce 2 blows within 5% of maximum sum of FVC + FEV_1 [99] and a total of 3 peak flow manoeuvres was excluded.

Nose clips were not used. The children were all volunteers and the study was approved by the Leicestershire Research Ethics Committee. As is usual practice, any abnormal or potentially clinically significant results would be discussed with the child's parents before taking further action.

4.3.2 Procedure

Children carried out the series of PEF or FVC manoeuvres, in random order to prevent bias. PEF was performed first by 44 and FVC first by 36 children. The randomisation was computer generated (SPSS 6.0. SPSS Inc., Chicago, Illinois, USA). After instruction, each child was asked to perform up to five blows using the first assigned set of manoeuvres with a short break between each blow. The procedure was then repeated for the second set of manoeuvres. For the peak flow manoeuvre (PEF_{PF}), children performed at least three manoeuvres until the two best were within 5%, or five blows had been recorded, whichever was sooner. For the vital capacity manoeuvre (PEF_{VC}) children performed at least three manoeuvres until the $FVC + FEV_1$ was within 5% for the two best blows, or five blows had been recorded, whichever came first. All measurements were carried out on a turbine mini-spirometer (Microloop, Micro Medical, Kent, UK) which met American Thoracic Society (ATS) 1994 criteria for equipment [9]. Each recording can be viewed in order to permit immediate technical assessment. The value of PEF from each blow was recorded by hand. Each FVC manoeuvre was saved electronically and printed out at the end of the session. The manoeuvre with the greatest $FVC + FEV_1$ sum was selected and the PEF derived from that manoeuvre was used for analysis. A maximum of 25 minutes was needed to complete the whole process.

4.3.3 Analysis

The mean difference between the two PEF manoeuvres and the limits of agreement were determined by an Altman Bland analysis [134]. Although it is known that age, sex, and height affect PEF the crossover study design ensured that these factors were all controlled. Data from healthy and asthmatic children were analysed separately. A sample size of 40 in each group was calculated to have 90% power at the 0.01 level to detect a 10% difference in PEF between the two manoeuvres. Analysis of variance (ANOVA) was used to determine the difference between the three values of PEF obtained. An alternative means of selection of PEF from spirometry, is simply to record the highest value from a series. Selection of one peak flow from a series for monitoring purposes is simplified for patient use in this way.

4.4 Results

Eighty eligible children agreed to participate in the study. Seven children (4 with asthma) refused to complete all manoeuvres following randomisation and were therefore withdrawn from the study. Data are presented for 73 children. More boys than girls were recruited into both groups and although the asthmatic group were slightly older and taller this did not reach statistical significance.

Table 4.4.1 Anthropometric data of children on whom adequate data was collected

	Asthma (n=34)	Healthy (n=39)
Age (yr): median (range)	11 (7-15)	10 (7-16)
Height (cm): mean (SD)	150 (14.8)	142.2 (14.7)
Boys: no (%)	25 (73.5)	25 (64.1)
PEF$_{PF}$: (% pred) mean (SD)	103.1 (18.5)	108.9 (18.2)

Reference values calculated from [135]

Sixty-three children (86%) provided reproducible vital capacity manoeuvres (2 blows within 5% of maximum FVC + FEV_1 sum)[99]. Fifty-four children (74%) provided reproducible FVC manoeuvres together with less than 5% variability between the best 2 values for peak flow. Data for these children were analysed separately from those children whose technique was non-reproducible. There were no differences in age, height, sex or asthma status between reproducible and non-reproducible groups of children.

The differences in peak flow from different manoeuvres were highly significant. The difference occurred in both asthmatic and non-asthmatic children (Table 4.4.2) and in both the reproducible and non-reproducible groups. There was no order effect (p <0.50) and no period effect (p= 0.17). The overall mean difference between PEF_{PF} and PEF_{VC} was 9.7 L/min (Fig.4.4.4a), about 5%, and for the asthmatic group slightly less (3%). However, the limits of agreement were very wide, -57.7 to + 38.3 L/min, a range of 96 L/min.

Using the highest peak flow achieved during a series of manoeuvres, we found that the mean maximum PEF, was 8 L/min (2.7%) higher than the value obtained for the "best" FVC measurement, for both asthmatic and healthy volunteers.

Table 4.4.2. Mean peak flow (SD) from three different manoeuvres

	Peak flow Manoeuvre	Vital capacity manoeuvre	Highest PEF from any Vital capacity manoeuvre	significance of difference[3]
All children – difference*	306.9 (87.2)	292.0 (89.0) 5%	300.3 (90.4) 2%	p < 0.001
Asthmatic children – difference *	326.1. (100.1)	317.4 (103.7) 3%	325.2 (106.2) 0.3%	p = 0.001
Non- asthmatic children – difference *	290.1 (71.3)	269.9 (67.9) 7%	278.6 (68.0) 4%	p < 0.001

* from PEF manoeuvre

---

[3] Each column represents the mean of the means for each child. The p value relates to the difference between the peak flow manoeuvre and the vital capacity manoeuvre results.

Figure 4.4.3 Values of PEF (L/min) obtained by different methods[4]
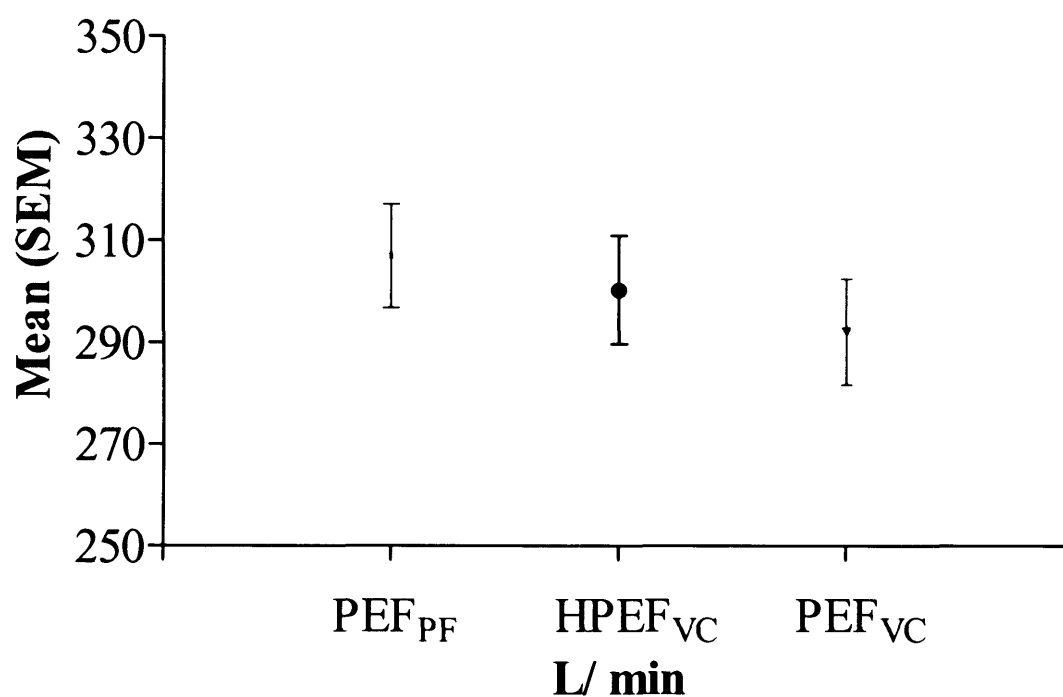
[4] Mean and standard error bars show the difference in value of PEF obtained from different manoeuvres: PEF_{PF}- PEF from a peak flow type manoeuvre; $HPEF_{VC}$- Highest peak flow from a vital capacity manoeuvre and PEF_{VC}- Peak flow from a vital capacity manoeuvre.

Figure 4.4.4 Comparison of different manoeuvres by Altman Bland plot

(a)
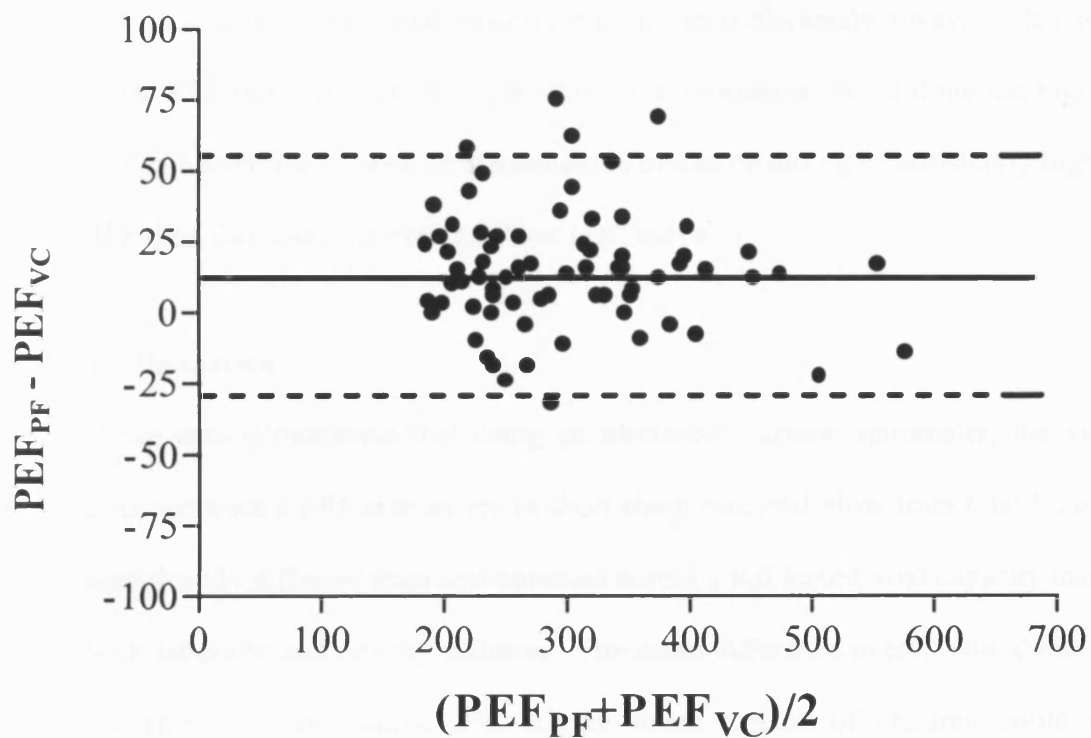
(b)
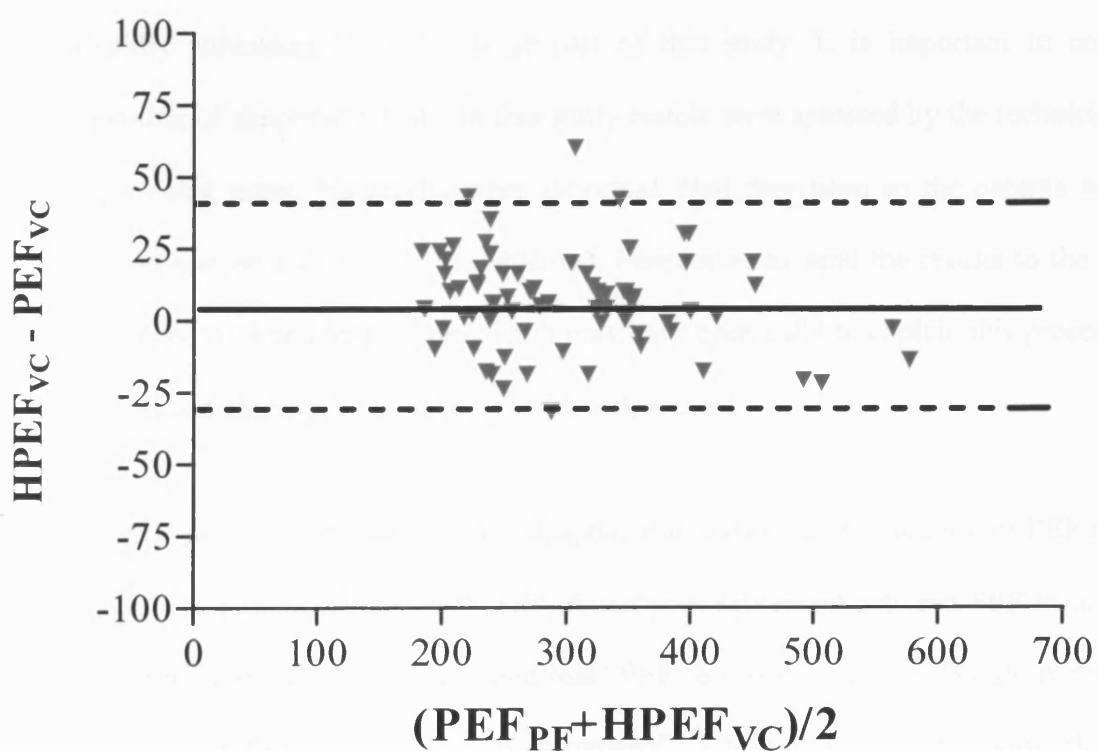
Generally observed differences between PEF obtained from each manoeuvre are not consistently higher or lower. By definition, in the case of PEF$_{VC}$ and HPEF$_{VC}$, the highest PEF recorded during a vital capacity manoeuvre is obviously always higher or equivalent to the PEF recorded from the best vital capacity manoeuvre. Taking the highest value of PEF obtained from a peak flow manoeuvre means recording a consistently higher value for PEF than that obtained from the "best test" curve.

4.5 Discussion

These data demonstrate that using an electronic, turbine spirometer, the value of PEF obtained from a PEF manoeuvre (a short sharp maximal blow from total lung capacity) is significantly different from that obtained during a full forced vital capacity manoeuvre, for both asthmatic and healthy children. The mean difference overall was about 5 % and for the children with asthma, 3%. Eighty seven percent of children could carry out a reproducible full forced manoeuvre successfully, fulfilling ATS criteria [99]. Seventy four percent fulfilled the criteria set for both manoeuvres.

Healthy volunteers formed a large part of this study. It is important to consider the reporting of abnormal results. In this study results were assessed by the technician and the supervising nurse. No results were abnormal. Had they been so the parents would have been contacted and the results explained. Permission to send the results to the GP would have been obtained before doing so. It may have been valid to explain this procedure to the parents and children when gaining informed consent.

Uwyedd *et al* [61] studied children with asthma to assess the contribution of PEF monitoring at home to asthma management. They found poor agreement between PEF from meter and PEF from spirometer and concluded that "PEF recorded by a mini Wright meter does not necessarily reflect that recorded by spirometer". Using mechanical methods, Hankinson *et*

al postulated that PEF meters overestimate PEF at lower flow rates [136] and the variable error of measurements obtained using mini-Wright meters is well recognised [65]. Accepting that the non-linearity of portable peak flow meters increases error, if the expiratory manoeuvre is also important, the error may be exaggerated by the technique employed.

PEF measurement and spirometry are effort dependent manoeuvres requiring training [137]. The training effect may be quite prolonged, if increased respiratory muscle strength contributes to this [90]. Even with prior experience, young children can achieve higher flows with succeeding blows [69], so that up to 5 attempts may be insufficient to achieve the maximum PEF. We recruited healthy children who were unused to performing lung function tests along with children with asthma, most of whom were. The children in our study were randomised to complete either the PEF or the FVC manoeuvre first so that learning did not explain the difference.

Posture might have played a part. All subjects stood to complete the manoeuvres because PEF was the result of interest [92] with no attempt to fix the head and neck posture. D'Angelo *et al* suggested that changes in neck posture can impact on the FVC manoeuvre, particularly affecting the FEV_1 & PEF [95]. Kano *et al* also found significant changes in PEFR with changing neck posture [96].

Guidelines should be followed in performance of spirometry [92]. It has been suggested that there should also be standardisation of the inspiratory component of the FVC manoeuvres. Inspiratory speed has been demonstrated to affect PEF. A number of studies have demonstrated that with faster inspiration a larger PEF is produced [91,94], although this is not necessarily true for all subjects [90]. Inspiratory speed has not been differentiated from breath hold at total lung capacity (TLC) in most studies. A breath hold, by reducing elastic recoil and increasing airway wall compliance, impacts on all spirometric indices, the greatest

reduction being seen in the initial portion of the curve and therefore affecting PEF & FEV_1 [94,95]. Data from Wanger *et al* suggest that breath hold of as little as 2 seconds significantly reduces PEF, both in healthy and asthmatic adults [91,94]. In our study, breath-holding was not encouraged as part of the manoeuvre. We saw no obvious pause at TLC, but the length of any breath hold was not measured. Although there are no studies assessing incidental breath hold at TLC, we suspect that this phenomenon is more common during a full forced manoeuvre than during a short sharp (peak flow) manoeuvre, particularly in children who may have some difficulty with instructions and co-ordination.

An alternative means of selection of PEF from spirometry, is simply to record the highest value from a series of blows. We found that the mean maximum PEF selected this way, was 8 L/min (2.7%) higher than the value obtained for the "best" FVC measurement. This was true for both asthmatic and healthy volunteers.

Although these results reach statistical significance, they are not clinically significant. The mean difference was 9.7 L/min. However, the limits of agreement (- 57.7 to + 38.3 L/min) had a wide range of 96 L/min which could be clinically important particularly in young children. The difference is greater than the estimated limits of agreement of PEF_{PF} for repeated observations on a single occasion (- 26 to +26L/min) [63]. It is not surprising that our study demonstrated wider limits than this. However, it would be important in the future to show that individual differences between the two techniques were consistent.

4.6 Summary & conclusions

In summary, PEF derived from a PEF manoeuvre was statistically significantly greater than that derived for a FVC manoeuvre using a turbine spirometer, for both healthy and stable asthmatic children. However the difference was very small and of no clinical

significance. These conclusions may not apply during acute severe episodes of airway obstruction. PEF derived for spirometric measurements appears to be adequate for clinical monitoring. The highest value achieved by the children during a test session is easily recognisable. $HPEF_{VC}$ can thus be recorded by hand in a diary card and used for management. Although a turbine spirometer was used for this study and a pneumotachograph spirometer was used for the main study, both spirometers met ATS criteria for monitoring and therefore the results should be interchangeable.

This work has justified the use of $HPEF_{VC}$ in monitoring children with asthma at home to investigate the role of PEF in self-management protocols for school children with asthma.

Chapter 5

Quality of life measurement: UK version of the paediatric asthma quality of life questionnaire (PAQLQ)

5.1 Introduction

Quality of life measurement is now accepted as contributing to clinical management and research protocols to assess the impacts of treatments [138] and interventions on patients and families [104]. Measures have been specifically designed to evaluate the quality of life of children with asthma. Measurement tools designed for children are either completed by a parent acting as proxy [118]; by parent and child together [108] or by children alone [108,116]. These tools can be used in conjunction with currently widely used objective measurements to provide an added dimension to overall patient assessment. The most widely used questionnaire is the PAQLQ. Despite its widespread use, the PAQLQ had not been developed for use in the UK. Although it was developed in an English speaking country, language use differences meant it may be difficult for British children to understand.

5.2 Aims

The aim of this study was to (a) pre-test the questionnaire amongst a sample population of children in this country and (b) make any changes necessary to enhance its comprehension amongst children who may be asked to complete it. The UK version of the PAQLQ underwent development at Leicester Royal Infirmary in the presence of Professor Juniper who kindly agreed to its use for the study and was involved in piloting the questionnaire in Leicester.

5.3 Methods

5.3.1 Subjects

A convenience sample of children aged seven to sixteen years attending an asthma clinic at Leicester Royal Infirmary Children's Hospital on a specific date were invited to participate by letter. The letter included an invitation to help us along with a slip and freepost envelope to return denoting interest. All children were attending the asthma clinic and were at least step two of the British Guidelines on Asthma management [6]. In addition they were English speaking and the final group included only Caucasian children.

5.3.2 Procedure

Activity list (table 5.3.2.1)

Many of the activities listed in the Canadian version of the PAQLQ were inappropriate for children living in the UK (table 5.3.2.1). A second list was prepared prior to interviewing British children. The activities chosen were based on information from a sample of children attending Children's outpatient department or participating in other clinical trials with asthma who were asked "What activities do you do, in which you are bothered by your asthma?". The most often stated activities were included in the UK version of the questionnaire.

Interviewing the children

Children between 11 & 14 years completed the self-administered version of the questionnaire; younger children were interviewed. Each questionnaire completion took 10-15 minutes. Following completion, children were asked about their comprehension of specific words used in the questionnaire itself. The questionnaire was discussed with each child for a maximum of thirty minutes.

5.4 Results

Ten children agreed to help in the development of the UK version of the questionnaire. As a result of time constraints, only eight were included in this development phase. All were prescribed regular preventer therapy.

Table 5.4.1 Anthropometric data of children

SEX	male: female	3:5
AGE	Median (range)	10 (7-13)
Atopic Family History	% yes	75

The major changes were to the activity list and were carried out prior to this session. None of the children added or wished to remove any activities from the list, or chose activities which were not listed.

Table 5.4.2 Activity lists for Canadian and UK version of PAQLQ

List of activities from Canadian PAQLQ [116]			List of activities from UK version of PAQLQ		
1. Ball hockey	13. Sleeping	24. Doing Crafts or	1. Hockey	13. Sleeping	24. Doing Crafts or
2. Baseball	14. Soccer	hobbies	2. Netball	14. Rugby	hobbies
3. Basketball	15. Swimming	25. Shouting	3. Basketball	15. Swimming	25. Shouting out
4. Dancing	16. Volleyball	26. Gymnastics	4. Dancing	16. Volleyball	26. PE
5. Football	17. Walking	27. Rollerblading	5. Football	17. Walking	27. Rollerblading/
6. Playing at Recess	18. Walking Uphill	28. Skateboarding	6. Playing at	18. Walking Uphill	roller-skating
7. Playing with pets	19. Walking	29. Track and field	Playtime	19. Walking	28. Skateboarding
8. Playing with	Upstairs	30. Tobogganing	7. Playing with pets	Upstairs	29. Athletics
friends	20. Laughing	31. Skiing	8. Playing with	20. Laughing	30. Scouts/cubs/
9. Riding a bicycle	21. Studying	32. Ice Skating	friends	21. Schoolwork	guides/ brownies/
10. Running	22. Doing	33. Climbing	9. Riding a bicycle	22. Helping with	beavers etc
11. Skipping Rope	Household Chores	34. Getting up in	10. Running	housework	31. Rounders
12. Shopping	23. Singing	the morning	11. Skipping	23. Singing	32. Ice Skating
		35. Talking	12. Shopping		33. Climbing
					34. Getting up in the
					morning
					35. Talking

The mean quality of life score for each child is shown in figure 5.4.3. This can be separated and a score for each of the three domains. One child produced highly statistically significantly different results from the others in all domains with very little scatter in the results. This child demonstrated a much lower quality of life than the rest of the group. This was true for all domains.

Figure 5.4.3 Mean quality of life score for each subject

PAQLQ score
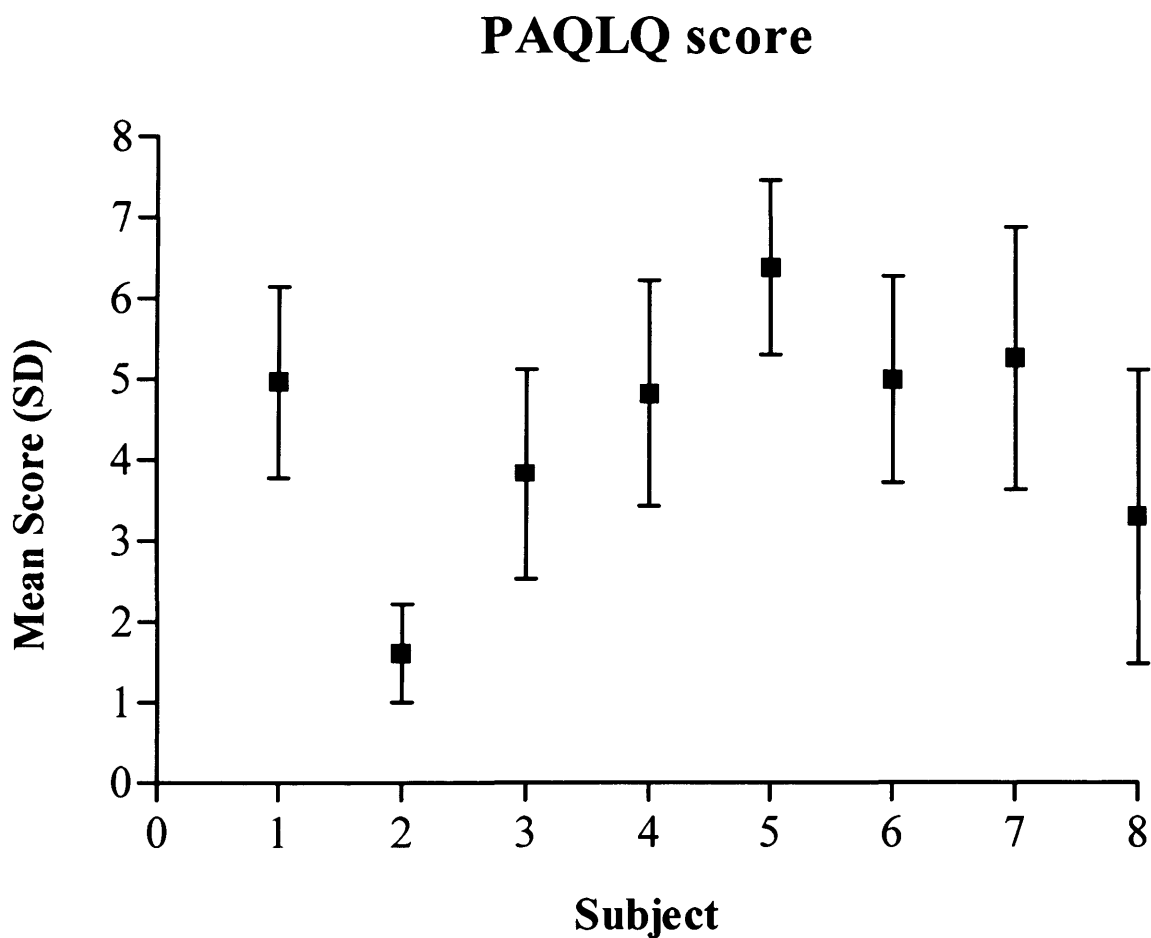
The children answered the questions quickly and easily without prompting. One of the questions caused some difficulty for the respondents. "How often did your asthma make you feel irritable during the past week?". Children in our sample experienced difficulty with the word "IRRITABLE". Although irritable remained as a part of the questionnaire, apparent difficulties seen during the development phase led to the addition of grumpy in the UK version, to be used if required. For English children, question 11 was changed to "How often during the last week did you feel irritable (grumpy) because of your asthma". Other changes were in word order to aid clarity.

5.5 Discussion

Few changes were needed to make the PAQLQ acceptable to a UK paediatric asthmatic population. The scores are of limited value when taken alone. Since these were all one off measurements, it is difficult to assess the value of the score per se. The questionnaire was designed for repeated use, although for this development work, a one off application was considered adequate. For each question, optimum quality of life score is 7, the worst is 1. However, the rather surprising results from one child highlighted the importance of reviewing this type of measure with the child following completion to identify specific problems and focus management [43].

Language difficulties did not arise in using the questionnaire in our English speaking, Caucasian population. Some problems of vocabulary were evident. Words commonly used in Canada (e.g. irritable) were often new to British children, particularly in the younger age group. The body of the questionnaire remained the same with the exception of two word changes. Only the activity list was changed to a great extent (Table 5.4.2).

5.6 Summary and conclusions

In summary, the PAQLQ required minimal changes to be made acceptable to a paediatric population in the United Kingdom. Many of the activities listed in the Canadian version of the questionnaire were inappropriate for children in this country and this was changed substantially. This work has made the PAQLQ acceptable to UK children.

SECTION III

RANDOMISED CONTROLLED TRIAL OF GUIDED SELF-MANAGEMENT FOR SCHOOL CHILDREN WITH ASTHMA

METHODS & PRIMARY OUTCOMES

Chapter 6

6.1 Introduction (summary of Chapter 2).

National and international guidelines on the management of asthma advocate guided self-management as the optimum means of controlling disease[22]. Introducing self-management involves communication, co-operation and education [17]. Studies have demonstrated the benefits of self-management, although it is difficult to know which parts of the process are responsible for these benefits [22]. A recent systematic review of available data suggests that education and self-management training, providing written information about medication adjustment in response to peak flow or symptom changes may improve health outcomes for adults with asthma [26]. Patient's understanding of changes in condition and knowledge of when and how to react to such changes are an important aspect of the process disease management[13,17].

Changes to treatment may be based subjectively on symptoms or objectively on PEF. Peak flow measurement is the most widely available objective means of assessing airway obstruction [139], although the role of peak flow in the self-management process is unclear [64]. There are few controlled studies of the use of peak flow meters in management. Patients with mild disease or limited experience may benefit from simple instructions about when to seek help. Patients with more experience and those with more severe disease perhaps require more information about when to make treatment changes. This could include levels of peak flow at which to take action [140].

Only one study has directly compared peak flow versus symptom management in children. This included both adults and children but the results for children were analysed separately (Table 2.3.2.1)[41]. In a community-based population, Charlton et al [41] studied 115 patients (46 children) who were randomly assigned to receive a self-management plan based on

symptoms (27 children) or peak flow monitoring (19 children). Morbidity was measured in terms of doctor consultations and oral steroid and nebulised salbutamol use. Adults and children in both groups demonstrated improved outcomes, although there were no between group differences. When the total population was considered, the outcomes all reached statistical significance for pre and post intervention in both groups with the exception of nebulised salbutamol use which was not used in the symptoms only group. All subjects in this study received improved care. The Charlton study[41] may have measured the implementation of a nurse-run clinic to all patients rather than aspects of self-management.

The primary aim of this study was to assess the added benefit of peak flow measurement together with a symptom-based plan in guided self-management for school children with asthma, compared with a symptom-based plan alone.

Secondary aims included consideration of what happens during an acute episode. What prompts children to change treatment as their asthma deteriorates? Also, for those children in the symptoms only group, at what peak flow threshold would they alter treatment, in accordance with the self-management plan. The various measures of lung function and the relative sensitivity of each of these measures along with symptoms was investigated.

The relationships between various quality of life measurements were considered: between child's own and parents assessment of the child's quality of life, child's own and parents own quality of life and between parent own quality of life and parents perception of child's quality of life. The role of quality of life assessment in relation to other measures of morbidity was also considered.

6.2 Outline of study and study design (Figure 6.2.1.1)

This was a randomised, un-blinded controlled trial. Children attending children's outpatients were approached by a research nurse (DW) whilst waiting for their appointment in asthma clinic. A brief description of the study was given along with an information sheet to take away. Further contact was made inviting them to participate and offering a home visit to supply further information. Patients of general practitioners (GP) in the locality were contacted by letter via the practice nurse. This included an information sheet for the main caregiver and the child and a response slip and freepost envelope addressed to the research nurse involved in the study. Interested families were contacted to determine eligibility.

At the home visit the child and main caregiver were seen and details of the study were explained (see appendix). For those who were happy to take part, both parent and child participants gave written informed consent and were recruited into the run up period of the study. At this stage characteristics of the child were recorded, including details of treatment and baseline quality of life measurements. Ability to perform a forced vital capacity manoeuvre was assessed and training in the use of the equipment was given, along with a contact number should any problems arise. During this run up period, all lung function data was collected and stored by the machine but it was inaccessible to the children and was not visible to them.

Four weeks later the family were revisited and data collection was assessed. Those children who were happy to continue, had successfully collected data and whose compliance was above 50% were randomised into one of the two groups: to manage asthma using peak flow and symptoms or using symptoms alone. Once randomised, each child was issued with a self-management plan based on symptoms and/ or peak flow and taught the

principles of self-management. Following randomisation, each child was visited a further three times, at four weekly intervals. At each visit, questionnaires were completed about morbidity and quality of life, data was uploaded, forced vital capacity manoeuvre technique was assessed and a symptom diary collected.

Ethical Approval for this study was given by the Leicestershire Health Authority Ethics Committee.

Figure 6.2.1.1 Trial structure

Primary care

General practices contacted
Letters via practice nurses
Respond to research nurse

Secondary care

Approached in children's outpatients
Given information sheet & summary

Telephone ——
contact

Home visit
& recruitment

Baseline
characteristics
Quality of life
questionnaire
Given spirometer

Telephone   4 weeks
contact

Randomisation

Self-management
plan provided
Quality of life
questionnaire
Download data
Collect diary &
issue next
Check technical
ability

4 weeks

Home visit 3

Quality of life
questionnaire
Download data
Collect diary &
issue next
Check technical
ability

4 weeks

Home visit 4

Quality of life
questionnaire
Download data
Collect diary &
issue next
Check technical
ability

4 weeks

Completion

Quality of life
questionnaire
Download data
Collect diary &
issue next
Collect equipment

6.2.1 Power calculations

Symptom diary data from previous studies carried out on children with mild/ moderate asthma by Glaxo Wellcome (personal communication) were used to determine the variability of the data. On a once daily symptom score (scale 0-3), the within subject SD was 0.9. The scale for our symptom score diary was 0-9 therefore a SD of 2.7 was assumed. Power calculations based on these data suggested that 53 children in each group were needed to have 80% power to detect a between group difference in mean symptom score of 1.5. Recruiting children to take part in this complex and demanding study was recognised as potentially difficult. The aim was to recruit 120 children (60 in each group) to allow for withdrawals.

6.2.2 The randomised controlled trial

The length of the study was 16 weeks in total: 4 week run up period, followed by a 12 week trial period after randomisation. This was considered long enough to provide self-management data, yet short enough to promote compliance.

The 90 children who successfully completed the run up period were randomly assigned to one of two self-management groups:

(a) self-management based on symptoms alone (PF_0).

(b) self-management based on symptoms plus peak flow (PF_1).

The randomisation was computer-generated (Minitab, Minitab Inc., USA.) in blocks of ten without stratification and placed into individual, sequentially numbered, sealed envelopes by non-study personnel. The next envelope in sequence was opened once a patient had completed the run up period and agreed to enter the randomised controlled trial. The investigator was blinded up to the point of randomisation. Blinding was not possible after

randomisation as the investigator was involved in teaching the children self-management, although any treatment decisions were made by the clinicians usually responsible for the child's asthma care and not study personnel.

6.2.3 Subject recruitment

Patients were recruited from Outpatient Clinics at the Children's Hospital and local general practices. Hospital patients were approached in outpatient clinics in Leicester Royal Infirmary Children's Hospital and invited to participate. General Practitioners (GP) who agreed to help sent letters to their asthmatic patients, usually via the Practice Nurse and reply slips were returned to the research nurse involved in the study. The practices involved in the study included 2 local market town practices; 2 busy city centre practices and 1 small village practice. Families fulfilling the inclusion criteria were contacted by letter from the surgery (see appendix) and asked to respond to the investigator if they were interested in taking part. An information sheet was given to all families who expressed an interest and discussed in full (see appendix)

Inclusion criteria for the study were (i) age 7-14 years at entry, (ii) physician diagnosed asthma, at least step 2 of the British Thoracic Society guidelines for asthma management [6], (iii) no changes to asthma treatment in the month prior to study entry, (iv) no respiratory problems other than asthma, (v) able to perform full spirometric manoeuvres and (v) able to understand trial requirements (vi) more than 50% compliant with lung function data collection during the run up.

Children remained eligible to participate in the trial if they had completed the run up period and were willing to participate.

6.2.4 Trial profile (Figure 6.2.4.1)

Over a period of 2 years 3 months 511 children were highlighted as potential recruits for the study. The hospital recruits were highlighted during routine clinic visits. Lists of patients in general practice were generated by practice nurses in the locality, either by computer (n= 3 practices) or by hand (n=2). Some of the children were found to be ineligible prior to letters being sent out (n= 54). The remainder received a letter offering information.

Information about the study was given or sent to 457 families. A large proportion were ineligible or chose not to respond. The main reason for non-recruitment was failure to respond to the letter sent out (57%). Some parents and/or children declined to participate (8%). The remainder expressed an interest and were contacted and visited at home to discuss trial entry. At this visit a further 9% were excluded either by the researcher (5%), or the child or family (4%). The main reasons for exclusion were the use of seasonal treatment and no current use of preventer therapy. These children no longer fulfilled the entry criteria.

One hundred and seventeen children were recruited into the run up period of the study. Following the run up period, 27 children were not randomised and did not enter the main study. The main reason for non-randomisation was poor commitment or compliance during the run up period. This left ninety children (20%) who entered the randomised trial, 46 in the peak flow and symptom group (PF_1) and 44 in the symptom-based management group (PF_0). Only one child withdrew following randomisation and despite repeated efforts, data are incomplete on this child. The reason given was poor compliance "I keep forgetting to do it".

All children studied fulfilled the eligibility criteria. Incomplete quality of life data was

available for 2 of the remaining 89 children. Full data for analysis were available on 87

children.

Figure 6.2.4.1 Recruitment profile


```
┌─────────────────────────────────────┐
│ Population considered-children       │
│ available at least step 2 BTS        │
│               511                    │
└─────────────────────────────────────┘
```

Ineligible ∴ no contact   54   **457**
(no preventer: 47; seasonal treatment: 1;
additional Resp. Prob: 4; (CF:1, PCD:2,
Bronchiectasis:1); GP advice: 2)
Did not reply to contact letter   262   **195**
No thanks   37   **158**

```
┌─────────────────────────────────────┐
│          Number visited             │
│               158                   │
└─────────────────────────────────────┘
```

Self excluded   21   **137**
     (out for visit: 3; stopped Rx:12; ill family
     member: 2; calls not returned: 4)
Researcher excluded   20   **117**
     (seasonal Rx: 7; too old: 2; problems- manoeuvre
     n= 3; comprehension difficulties: 5; moved away: 3)

```
┌─────────────────────────────────────┐
│          Number recruited           │
│               117                   │
└─────────────────────────────────────┘
```

Withdrawals following run up   27   **90**
     (don't want to, poor compliance: 19; manoeuvre
     problems: 4; comprehension difficulties: 2;
     eqpmt problems:1; GP advice: 1)

```
┌─────────────────────────────────────┐
│          Number randomised          │
│                90                   │
└─────────────────────────────────────┘
```

```
┌──────────────────┐        ┌──────────────────┐
│  PEF + symptoms  │        │     Symptoms     │
│      (PF₁)       │        │      (PF₀)       │
│       44         │        │       46         │
└──────────────────┘        └──────────────────┘
```

$PEF + symptoms\ (PF_1)\ 44$

$Symptoms\ (PF_0)\ 46$

6.4. Methods

6.4.1 Symptom diaries (section 3.2)

Written methods (section 3.2.2a)

Diaries were issued for each four week period and collected during the subsequent visit. Written diaries were completed by children alone or with parents. Analysis of these data was important, as the main outcome for the trial was mean change in symptom score during the trial period. Children were asked to record the date at the time of diary completion so that any missing data could be accounted for. All available diary data were included in the analysis. Compliance with written diary entry was assessed, as was

agreement between written and electronic methods of data collection using one question identical to both modes of recording. Children recorded the previous 24 hours bronchodilator use each morning.

Electronic methods (section 3.2.2b)

The electronic diary was completed every morning after performing spirometric manoeuvres. Children provided "feeling scores" in this diary and a comparison with the written symptom scores was not possible.

6.4.2 Lung function (section 3.3)

Children were instructed to measure their lung function morning and evening for the duration of the study. Once recorded, data were recorded in a spreadsheet format with date, time and lung function parameters from the "best test" within each session stored. Once transported into an analysis package, compliance, technical quality based on machine criteria and the amount of valid data available was assessed. Mean FVC, FEV_1, PEF and FEF_{25-75} (%best value) were calculated for each manoeuvre, for each child during each study period. For FVC, FEV_1 and PEF, the highest value achieved during the run up period was used to calculate % best value. In the case of FEF_{25-75}, the value from the "best test" i.e that with the highest $FVC+FEV_1$ was used to calculate % best, in accordance with ATS criteria [92]. Those children who were randomised into the peak flow group (PF_1) were instructed to manually record the highest peak flow achieved within each morning session in the written diary card.

6.4.3 Quality of life (section 3.4)

Questionnaires were completed during a home visit and taken away. The data were recorded by the child in my presence while the parent completed their questionnaires (PAQLQ and PACQLQ) in another room at the same time. Occasionally parents and

children did not record answers to particular questions or had not performed a recorded activity during the week prior to the visit. Since the reason for not participating in the activity may have been related to deterioration in asthma and therefore study related, it was felt that missing values may create bias in the results. In these cases, imputation was used to complete missing data for any questions after the first visit [122], thereby reducing (but not eliminating) potential bias. This involved "pro-rating" the patients score where data were missing. This allowed the score reported at baseline to be used in the approximation of subsequent missing scores.

For example:

(i) baseline scores (A): 4+2+(2)+5+3 = 16

(ii) subsequent scores with a missing value (B): 2+2+ (?)+2+1= 7

To calculate the missing value only values recorded on both occasions are used

Thus: Baseline (A): 4+2+5+3=14

Subsequent visit (B): 2+2+2+1=7

Missing value = (Total B/Total A)* Value A of item missing at B

(B) = (B/A).2

= (7/14).2

= 1

Therefore imputed score = 1

Baseline score = 4+2+(2)+5+3= 16 (mean value 16/ 5= 3.2)

Subsequent score = 2+2+ (1)+2+1=8 (mean value 8/5 = 1.6)

In the case of parents completing the PAQLQ, 53% of parents missed at least one item. This led to 7.3% of the results from parents being imputed. For children this was slightly

higher: 66% of children missed at least one answer leading to imputation of 9% of answers.

The relationship between the mean symptom domain quality of life score and the mean diary symptom score was assessed over the corresponding period (one week prior to the interview date) thus ensuring that the same constructs were being measured by both methods.

6.4.4 Measurement of morbidity

At each visit, parents and children were asked a series of questions concerning morbidity as a result of asthma since the previous visit. Questions were asked about emergency GP attendance, hospital visits or admissions, treatment changes and asthma-related school absence. Reported morbidity was recorded and data were not verified objectively.

6.4.5 Self-management plans (section 2.5)

Compliance with self-management guidelines was assessed by response to behaviourally defined episodes. When the children increased their preventer therapy for 2 consecutive days, or commenced oral prednisolone, data were analysed for the ten days before and ten days following the onset of increased medication. Mean daily symptom score, mean daily extra reliever used and daily FEV_1 and PEF (expressed as a percent of best obtained during the run up period) were calculated for each group.

6.4.6 Statistical analysis

Statistical analysis was carried out using SPSS (version 6, SPSS Inc. Chicago, Illinois, USA) Unpaired t-tests were performed for between-group comparisons at particular time points. Repeated measures analysis of variance was performed on longitudinal data to

assess within- and between-group effects, with sex as a factor in the analysis. Simple chi-squared test were used for proportional data.

Repeated measures analysis of variance was applied using baseline data as a covariate. This allows baseline data to be accounted for in the analysis to see whether data recorded during the run up period influenced data recorded later. For symptom score and lung function data this meant all the data collected during the run up period was used as a covariate. The quality of life data analysis used the randomisation visit as the covariate. Using this period as the covariate in the model allows the way children behave in the run up to be taken into account during the trial period. The fact that children were collecting diary data and carrying out daily lung function at this time meant that this was most appropriate. The use of run up and baseline data as a covariate in analysis added precision to the analysis by taking account of variation at trial entry. In all cases the run up period was the covariate within the model.

Where possible, non-parametric data were transformed to allow parametric analysis. Where this was not possible, unpaired data were analysed using Mann-Whitney U tests and Wilcoxon Rank Sum tests were applied to paired data.

The non-parametric symptom score data were log transformed using the following transformation :

$$z = \log \left(\frac{X + 0.5}{9.5 - X} \right)$$

Where X = diary recorded symptom score

Bland and Altman analysis for agreement between methods was used to assess agreement between electronic and written recording of extra reliever use.

Agreement between parent's and child's responses to PAQLQ questions was measured using kappa for inter-rater agreement (κ). Kappa does not take account of the size of any difference, measuring only exact agreement. In order to compensate for this a quadratic weighting was applied (κ_w)[141]. Parents whose recorded results were closer to those of their child were attributed a higher weighting than those whose results were more discrepant. The calculation was 1- (diff)^2 /36. The resulting weighting scores ranged from 0 if the parent and child scores differed by 6 (the maximum possible difference) to 1 if the scores were identical. Spearman Rank Correlation Coefficients were used to assess the association between quality of life scores for each domain at each visit.

Non-parametric Spearman rank correlation coefficients were transformed using Fisher's Transformation. This produced results which could be analysed using repeated measures analysis of variance[142].

$$z = \tfrac{1}{2} \log \left(\frac{(1+r)}{(1-r)} \right)$$

Where r= Spearman rank correlation

Correlation was calculated to assess the relationship between measures of disease and quality of life scores.

6.5 Results

6.5.1 Subject characteristics

Baseline data for the run up period were available for one hundred and seventeen children. Of these, ninety children were randomised into one of the study groups. One child withdrew following randomisation and as a result of investigator illness, quality of life data are incomplete for 2 of the remaining 89 children. Complete baseline, diary, lung function

and diary data are available for 87 children. Data are presented for 89 children except quality of life data which are presented for 87.

Figure 6.5.1.1. Data available for analysis

```
                        ┌──────────────────────┐
                        │  Number randomised   │
                        │      n= 90           │
                        └──────────────────────┘
                    ┌──────────────┴──────────────┐
        ┌───────────────────┐         ┌───────────────────────┐
        │ No. Recruited     │         │ No. Recruited         │
        │ CONTROL (PF₀)     │         │ INTERVENTION (PF₁)    │
        │ n= 46             │         │ n=44                  │
        └───────────────────┘         └───────────────────────┘
                 │                              │
        ┌───────────────────┐         ┌───────────────────────┐
        │ No. completing    │         │ No. completing trial  │         Withdrawal following
        │ trial period      │         │ period                │─────── randomisation  n= 1
        │ n= 45             │         │ n= 44                 │
        └───────────────────┘         └───────────────────────┘
                 │                              │
        ┌───────────────────┐         ┌───────────────────────┐       ┌──────────────────────────┐
        │ No. With full set │         │ No. With full set of  │       │ quality of life data     │
        │ of data available │         │ data available        │───────│ unavailable for last     │
        │ n= 44             │         │ n= 43                 │       │ visit  n= 2              │
        └───────────────────┘         └───────────────────────┘       └──────────────────────────┘
```

Figure: Data available for analysis. Number randomised n= 90; No. Recruited CONTROL (PF_0) n= 46; No. Recruited INTERVENTION (PF_1) n=44; No. completing trial period n= 45 (control) and n= 44 (intervention); Withdrawal following randomisation n= 1; No. With full set of data available n= 44 (control) and n= 43 (intervention); quality of life data unavailable for last visit n= 2.

The 27 children recruited but not randomised (figure 6.3.1.1) differed only in age (table 6.5.1.2) from those who were randomised. The children who withdrew prior to randomisation were younger than those who continued. Differences were also evident in spirometric data collected during the run up period. Although the mean compliance was maintained above 60% in both groups, many children in the non-randomised group stopped performing manoeuvres within the first two weeks of entering the run up period. Diary completion was also poor amongst this group. According to machine criteria, the lung function data from the non-randomised children were significantly technically superior in terms of reproducibility. On all other parameters measured during the run up period there were no significant differences between the groups.

Anthropometric data for the 90 randomised children are shown in table 6.5.1.3. In all baseline parameters except sex distribution there was no difference between groups. The random difference in the distribution of boys and girls between the groups was adjusted for in the analysis.

Table 6.5.1.2 Characteristics of children recruited (n= 117)

		Randomised	Rejected	Significance
Age in years	Median (range)	11 (7-14)	10 (7-14)	p=0.02
Sex	% male	53	48	NS
Family History (report)	% yes	42	56	NS
Height (cm)	mean (SEM)	146.0 (1.5)	145.9 (4.68)	NS
Age at diagnosis (years)	median (range)	4 (4/12-12)	3 ($^3/_{12}$-12)	NS

Morbidity data of children recruited

	Randomised	Rejected	Significance
Severity (%>BTS 2)	24	22	NS
Ever admitted (report % yes)	39	30	NS

Data from run up

			Randomised	Rejected	Significance
Lung Function	Compliance	%	81.39 (1.34)	62.31 (7.88)	P=0.03
	Technical ability	%	81.86 (1.5)	91.02 (1.96)	P<0.05
	Valid data	%	73.64 (1.5)	56.02 (7.06)	P<0.05
Written Diary	Compliance	%	89.7 (1.4)	51.54 (8.19)	P<0.05
	Daily symptom score	mean (SEM)	1.44 (0.15)	1.35 (0.35)	NS

Quality of life data (baseline)

		Randomised	Rejected	Sig.
Caregiver	mean (SEM)	5.79 (0.12)	6.03 (0.20)	NS
Child	mean (SEM)	4.99 (0.14)	4.98 (0.23)	NS
Parental perception	mean (SEM)	5.36 (0.11)	5.20 (0.21)	NS

Table 6.5.1.3 Characteristics of children randomised (n=90)

		NPF (46)	PF (44)	Significance
Age in years	median (range)	12 (7-14)	11 (7-14)	NS
Sex	% male	39	68	p= 0.005
Family History(report)	% yes	46	39	NS
Height (cm)	mean (SEM)	147.0 (2.11)	144.9 (2.3)	NS
Age at diagnosis (years)	median (range)	5 ($^6/_{12}$-12)	3 ($^4/_{12}$-12)	NS

Morbidity data of children recruited

	NPF (46)	PF (44)	Significance
Severity (%>BTS 2)	20	30	NS
Ever admitted (report % yes)	40	43	NS

Data from run up

			NPF (46)	PF (44)	Significance
Lung Function	Compliance	%	81.50 (2.05)	81.27 (1.73)	NS
	Technical ability	%	82.86 (2.12)	80.82 (2.20)	NS
	Valid data	%	74.26 (2.20)	73.25 (2.04)	NS
Written Diary	Compliance with diary	%	90.51 (1.48)	88.91 (2.37)	NS
	Daily symptom score	mean (SEM)	1.52 (0.22)	1.35 (0.20)	NS

Quality of life data- (baseline)

		NPF (46)	PF (44)	Significance
Caregiver	mean (SEM)	5.62 (0.17)	5.96 (0.15)	NS
Child	mean (SEM)	5.09 (0.19)	4.89 (0.2)	NS
Parental perception	mean (SEM)	5.18 (0.16)	5.55 (0.14)	NS

6.5.2 Quality and completeness of data collected

6.5.2.1 Compliance

Written diary

Compliance with diary data was highly variable between subjects and over time. Compliance with written diary data deteriorated over time in both groups. This deterioration occurred much sooner in the peak flow group and as a result there was a statistically significant difference in compliance for the second period of the study (p=0.01). This did not occur at any other time and by the end of the trial, between group compliance was very similar. Despite this deterioration, mean compliance with the written diary was maintained above 74% for the duration of the study. The PF_1 group demonstrated poorer compliance than the PF_0 group. Although there were more boys in the PF_1 group, incorporating sex as a factor in the analysis did not demonstrate that gender was an independent variable. These two facts are therefore unrelated.

Figure 6.5.2.1.1 Compliance with written diary completion over time in peak flow and symptom only groups

Period of study

⎯⎯*⎯ symptoms only group (PF$_0$)

⎯⎯■⎯ peak flow plus symptoms group (PF$_1$)
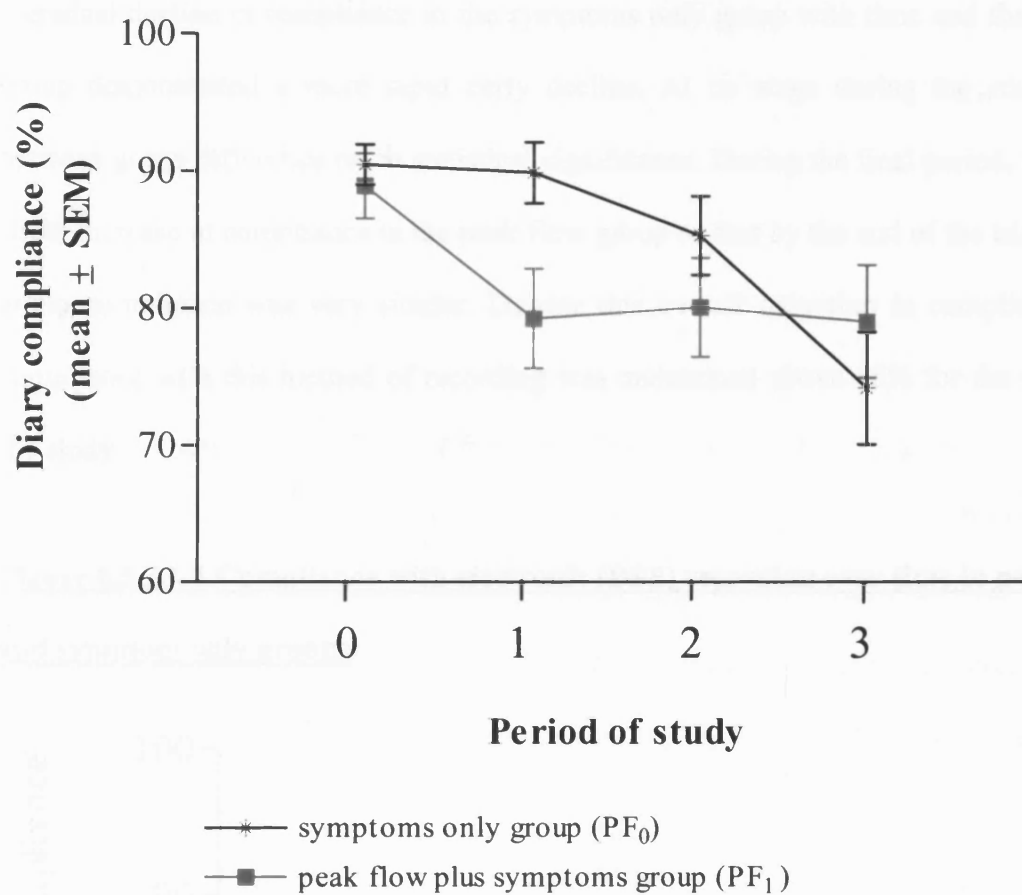
Electronic diary

Compliance with electronic recording of diary data declined similarly with time. There was a gradual decline in compliance in the symptoms only group with time and the peak flow group demonstrated a more rapid early decline. At no stage during the study did the between group difference reach statistical significance. During the final period, there was a slight increase in compliance in the peak flow group so that by the end of the trial, between group compliance was very similar. Despite this overall reduction in compliance, mean compliance with this method of recording was maintained above 68% for the duration of the study.

Figure 6.5.2.1.2 <u>Compliance with electronic (DSS) recording over time in peak flow and symptom only groups</u>

— *— symptoms only group (PF_0)

—■— peak flow plus symptoms group (PF_1)
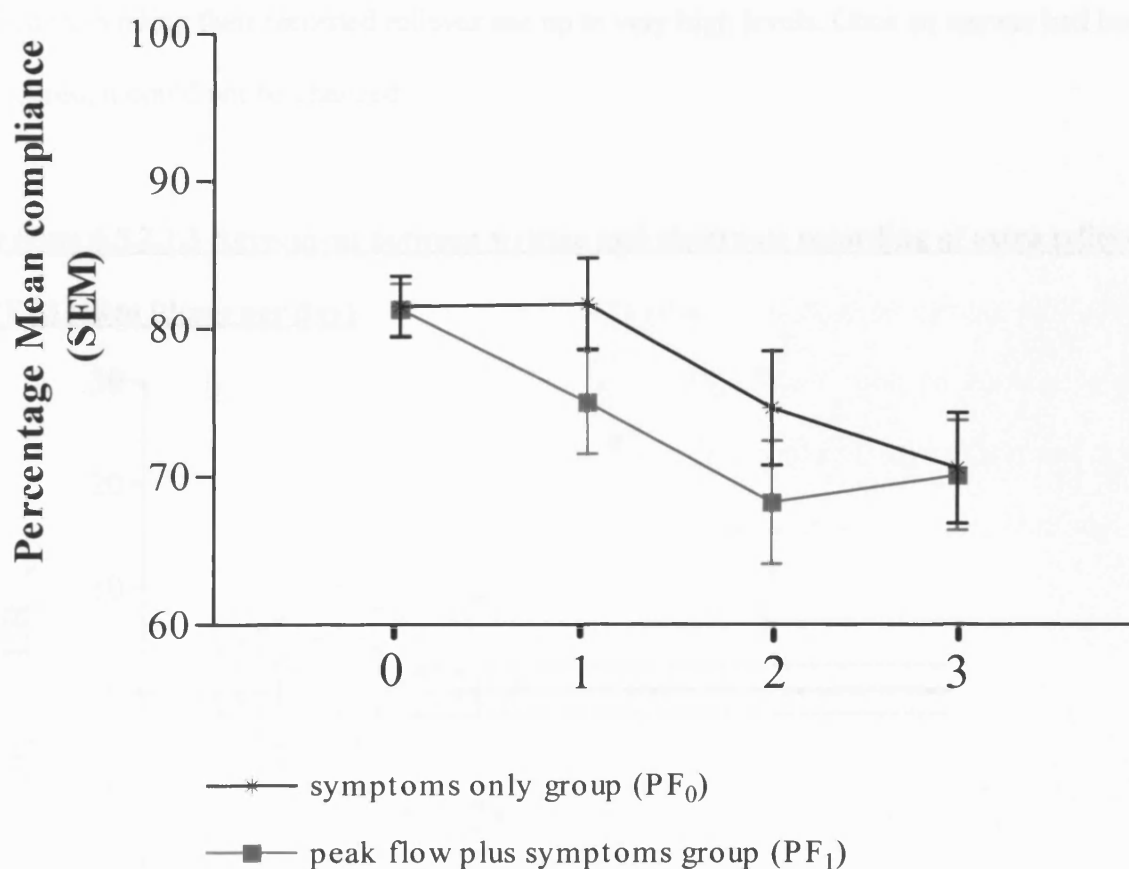
Agreement between electronic and written methods

The agreement between written (diary card) and electronic (DSS) methods of recording was assessed using Altman Bland analysis (figure 6.5.2.1.3). Reliever use was recorded by both methods. In the written diary children were asked "How many different times have you used your reliever since this time yesterday?". For electronic recording the question read "Since your last set of blows how many different times have you used your reliever?". Children were thus instructed to always consider the previous 24 hours and record reliever use during that time. There was no systematic difference, but the limits of agreement widened with greater reporting of reliever medication. A couple of children reported reliever use of 24 and 25 puffs. The default range of values possible by the DSS was 0-25. Pressing the down arrow (figure 3.2.2.2) took the score down through zero to 25, the top of the range. It was reasonable to assume that those children mistakenly pressed the wrong button, sending their recorded reliever use up to very high levels. Once an answer had been entered, it could not be changed.

Figure 6.5.2.1.3 Agreement between written and electronic recording of extra reliever (ER) taken (doses per day)

$ER_{DSS} - ER_{diary}$

$\dfrac{ER_{DSS} + ER_{diary}}{2}$ (puffs/day)
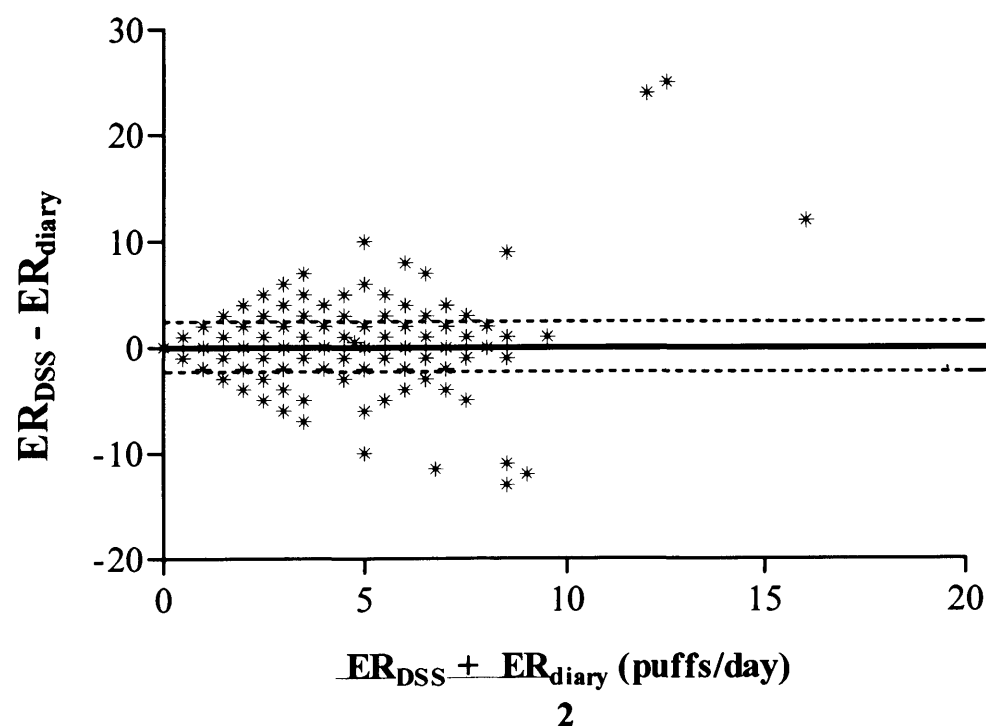
6.5.2.2 Lung function

A number of recorded results were problematic (table 6.5.2.2.1). Twenty-eight children (31%) were found to have recorded at least one unsuccessful session when the machine recorded within-session test failure. This meant that insufficient manoeuvres had been performed during the session and these were considered to be subject error. All other errors were defined as machine error. Some results seemed to far exceed the childrens usual results yet were considered by the machine to reach the reproducibility criteria. In these cases it was assumed that another person had carried out the manoeuvre or that a machine error had occurred. When 9999 (the error message) was recorded for any lung function parameter, this value was excluded from analysis. Machine error was recorded if a default result was stored (9999) or if the value stored was more than 3SD above the predicted value. This was chosen because 99.7% of the population will be within 3SDs of the predicted values. Since these children were asthmatic and more likely to record lower than predicted, these manoeuvres were excluded from analysis. The percent predicted values were calculated using the best results obtained during the run up for each of FVC, FEV_1, and PEF (table 6.5.2.2.2). All best values obtained during the run up were above 90% of predicted values [135] and for PEF above 100%. There were no between group differences. Only manoeuvres which met the machine reproducibility criteria and were considered to be technically acceptable were considered to be valid and hence included in the analysis.

Table 6.5.2.2.1 Problems with lung function data collected

	Subjects with problems	Blows with problems
Unsuccessful sessions (Test failure)	28 (31%)	52 (0.3%)
Another/ machine error (High values stored)	61 (68%)	603 (3.5 %)
Sessions coded as 9999 (Default error)	72 (80%)	400 (2.3%)
Machine error (Default error recorded as good)	30 (33%)	71 (0.41%)

Table 6.5.2.2.5 Best value obtained during run up as a percent of predicted value by group (mean ± SEM)

Best as a percent of predicted	PF_0	PF_1	significance
FVC	96.6 (1.77)	97.8 (1.75)	ns
FEV_1	94.8 (1.81)	95.8 (2.08)	ns
PEF	105 (1.77)	106 (3.23)	ns

Any stored manoeuvres completed at the correct time were considered compliant, irrespective of their technical quality. Technical quality was achieved if a successful manoeuvre was recorded and machine error (9999) was not recorded. Valid data required both compliance and adequate technical quality. Compliance deteriorated over time. The technical quality of the data was maintained. The resulting deterioration in the amount of valid data was influenced mainly by changes in compliance with time (table 6.5.2.2.3).

Table 6.5.2.2.3 Compliance with and quality of lung function data collected (mean ±

SEM)

Period of study	0		1		2		3	
Compliance %	81.4	(1.34)	78.4	(2.34)	71.5	(2.83)	70.4	(2.68)
Technical Ability %	81.7	(1.54)	80.2	(1.88)	80.8	(1.93)	80.2	(1.96)
Valid data %	73.6	(1.75)	64.3	(2.51)	59.7	(2.81)	57.6	(2.66)

Figure 6.5.2.2.4 Changes in compliance, technical quality and valid data over time

—✳— Compliance

—□— Technical Ability

—■— Valid data
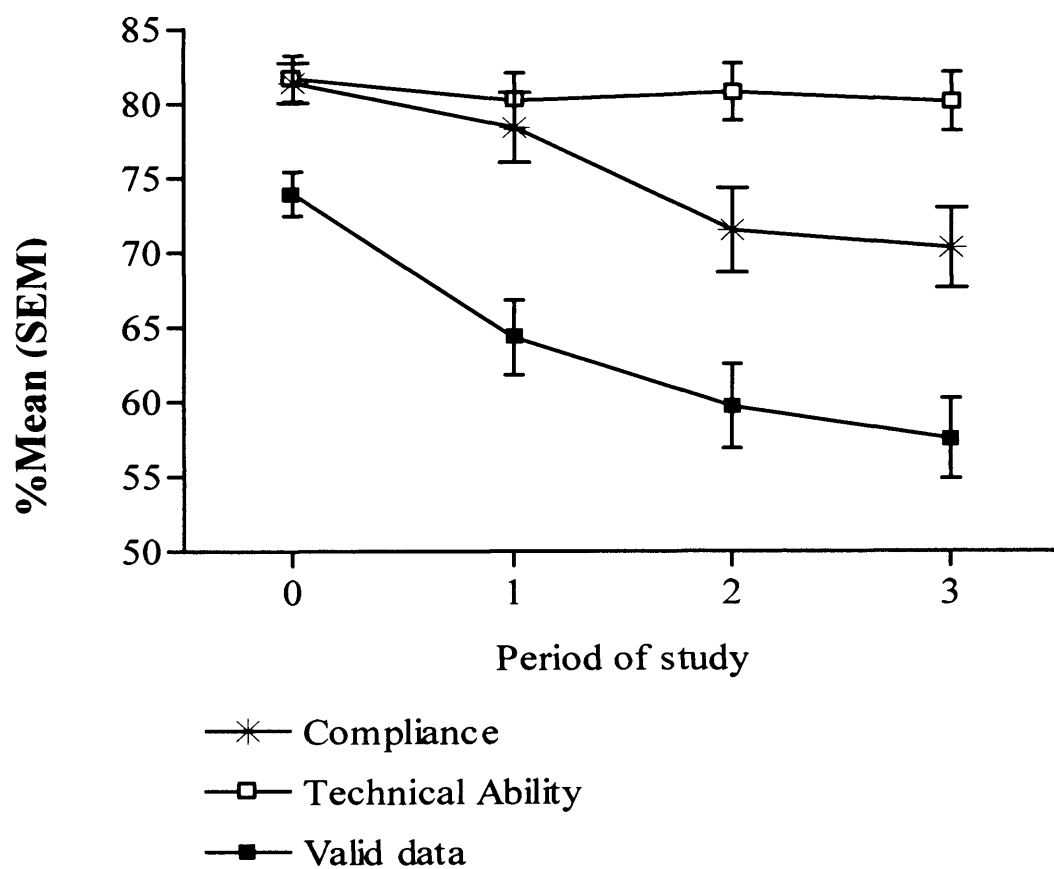
In summary, there were problems with some of the lung function data. Any problematic results were excluded from the analysis. Data analysed included only manoeuvres which met reproducibility criteria set by the machine.

6.5.2.3 Quality of life data (section 3.5)

Quality of life data were collected during each home visit. No child or parent refused to complete the questionnaire. Occasionally children had not performed a particular activity and therefore blanks were recorded in the questionnaires. Imputation was used to score the missing answers. The quality of life data were complete with the exception of four questionnaires. These were not completed as a result of investigator illness. All other data from these children were included in the analysis.

To assess validity of the quality of life results the mean symptom domain quality of life score was compared with the symptom score recorded in the diary for the week prior to each visit (figure 6.5.2.3.1).

Figure 6.5.2.3.1 Relationship between diary symptom score and symptom domain of quality of life questionnaire for visits 1-4, for each individual

Visit 1
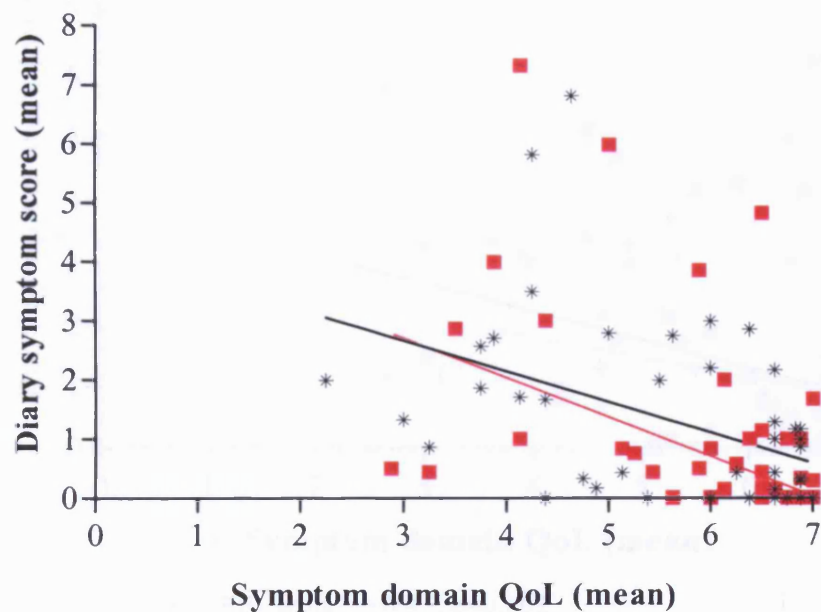
PF$_0$ group r= 0.45, p= 0.001

PF$_1$ group r=0.45, p= 0.003

Visit 2
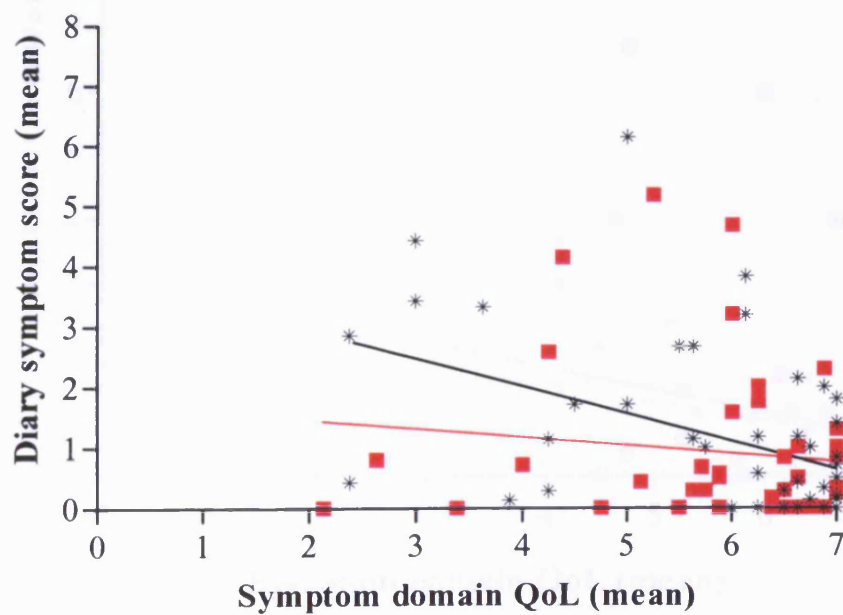
PF$_0$ group r= 0.44, p=0.003

PF$_1$ group r= 0.12, NS

Visit 3

Diary symptom score (mean)

*   PF$_0$ group r= 0.45, p=0.002
■   PF$_1$ group r= 0.22, p=NS

Symptom domain QoL (mean)

Visit 4

Diary symptom score (mean)

*   PF$_0$ group r= 0.49, p=0.02
■   PF$_1$ group r= 0.14, NS

Symptom domain QoL (mean)
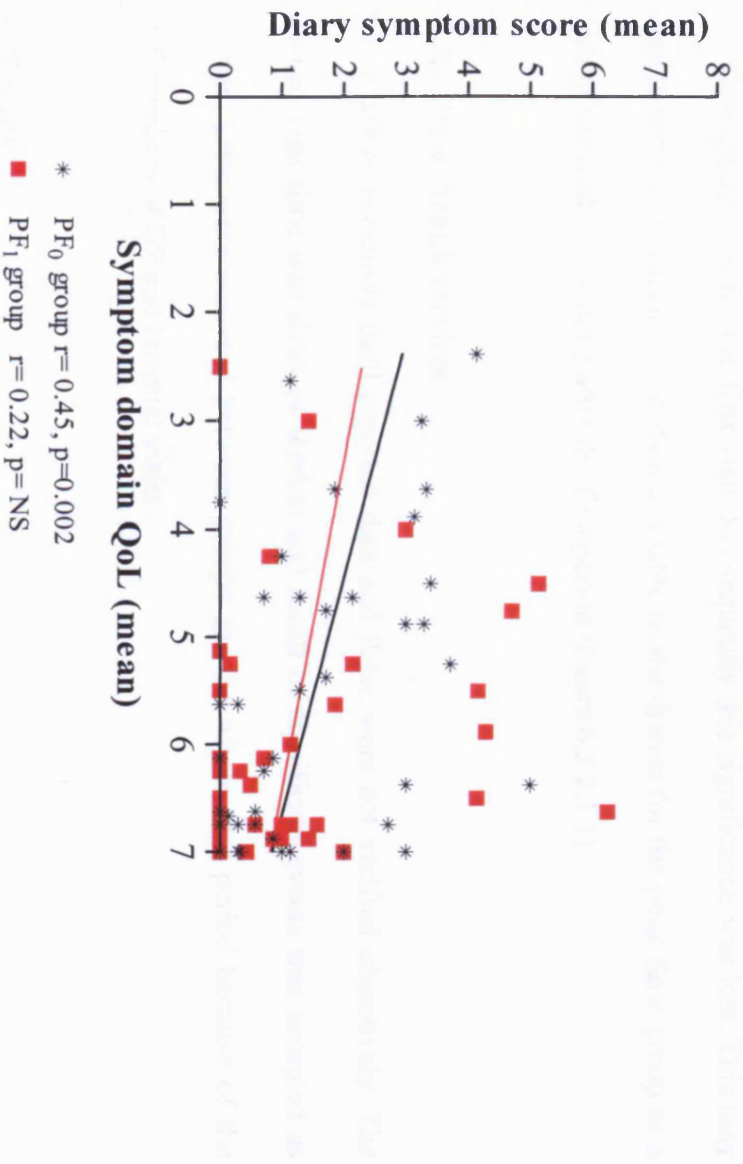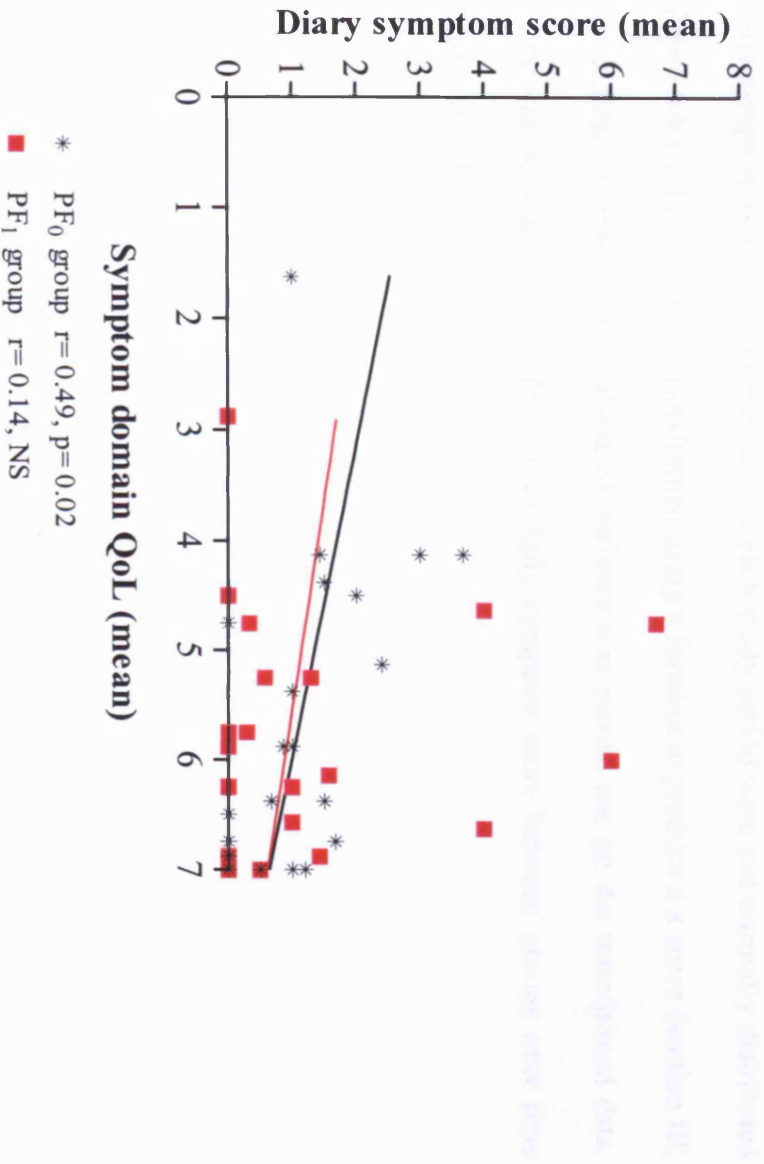
Statistical significance was reached for correlation between diary and symptom domain of quality of life score in the symptoms only (PF$_0$) group for each visit. This was true for the peak flow group only for the first visit. Subsequently this significance was lost. This may relate to the reduced quantity of data available in the diaries for the peak flow group as a result of reduced compliance after the first period (figure 6.5.2.1.1)

6.5.2.4 Use of health services

Questionnaire responses used reported data and these were not verified objectively. The between visit time was short (4 weeks) and recall of significant events was accepted as accurate. Data were analysed between groups for the whole trial period because of the small numbers of GP and hospital visits.

6.6. Results

6.6.1 Symptom scores

6.6.1.1 Mean symptom score

Daily symptom scores for each child, for each study period were not normally distributed (figure 6.6.1.1.1). Data were transformed using a formula to produce a z score (section III, 6.4.6). Repeated measures analysis of variance was carried out on the transformed data. There was no significant difference in daily symptom score between groups over time (figure 6.6.1.1.2).

Figure 6.6.1.1.1 Box and whisker plot showing median, inter-quartile range (IQR)

and range of symptom scores
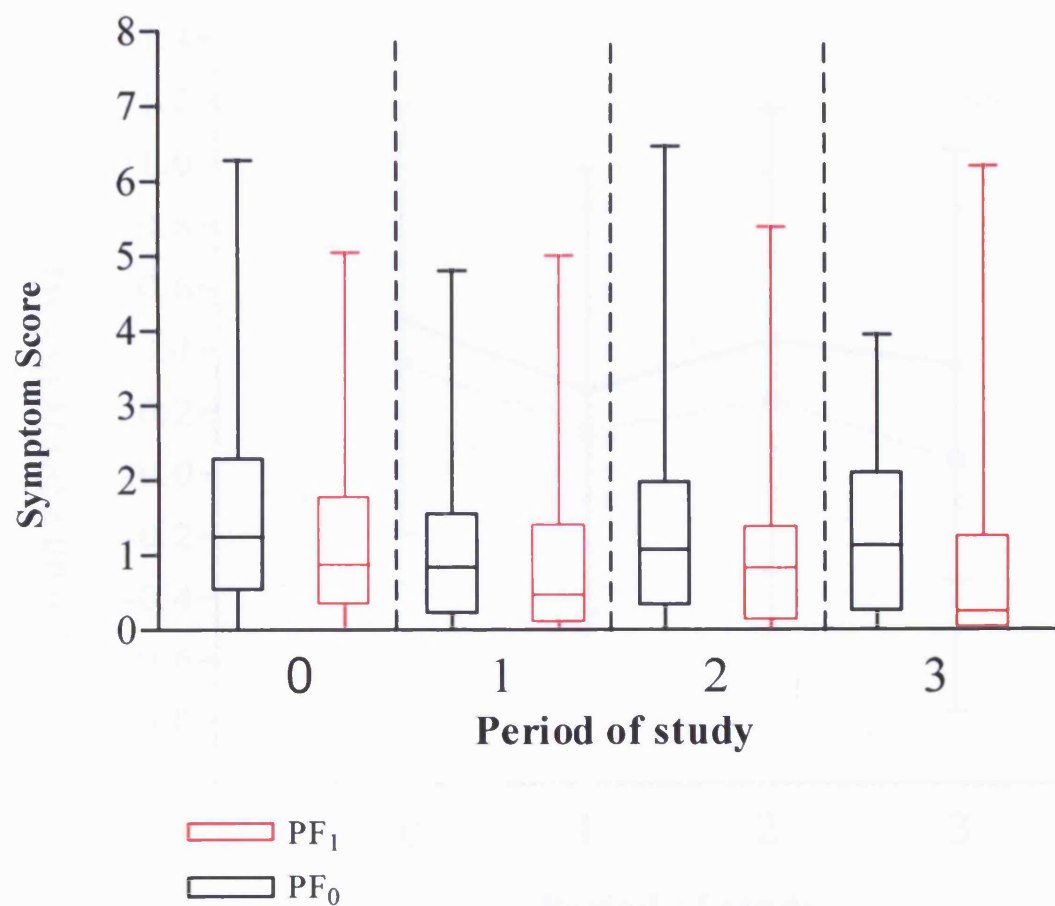
Figure 6.6.1.1.2 Transformed symptom scores over time in peak flow and symptoms only group
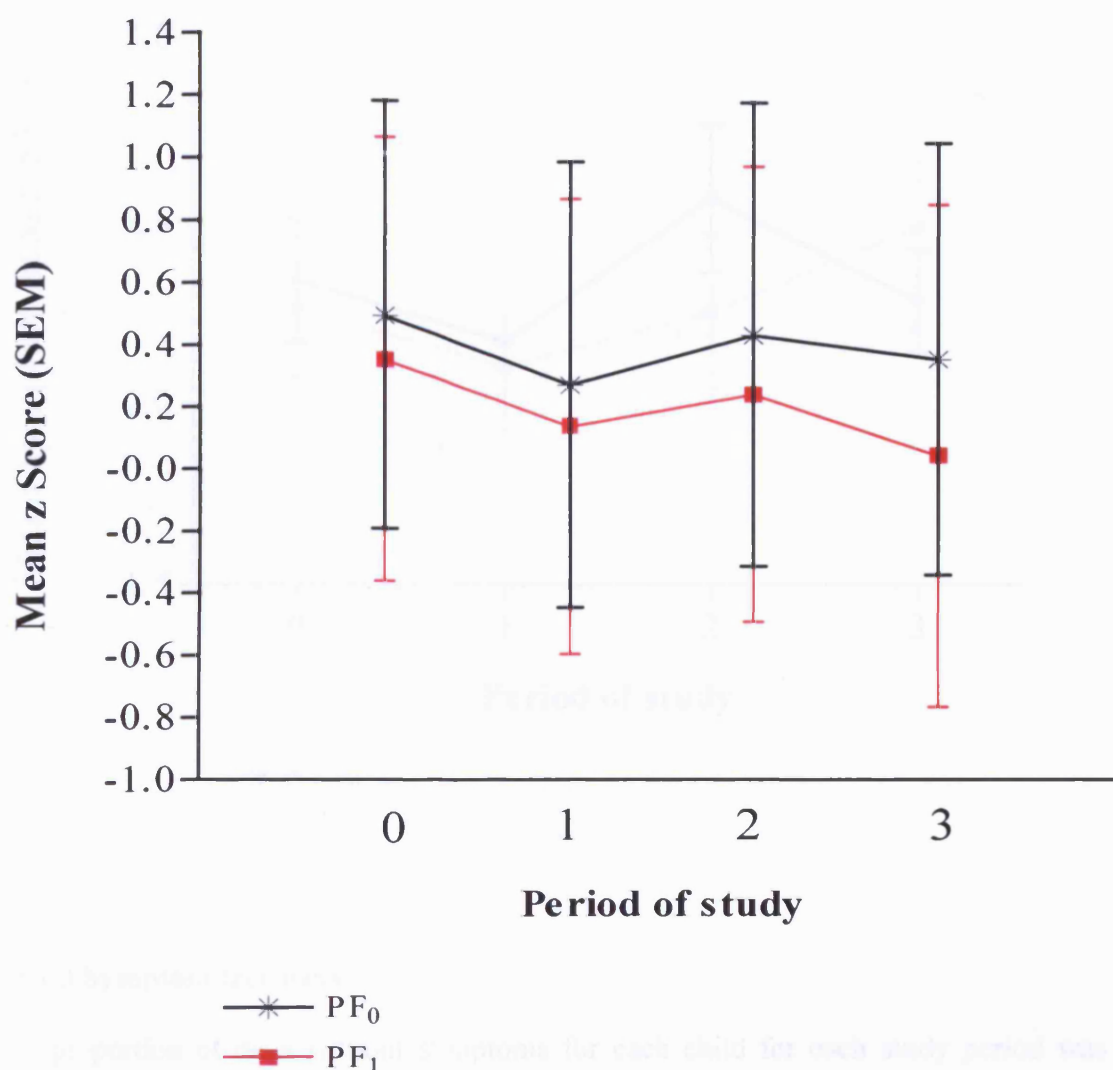
6.6.1.2 Symptom score on symptomatic days

Selecting only those days when children reported symptoms in the diary, the analysis was repeated. There were no significant differences within or between groups in mean symptom scores for symptomatic days (figure 6.6.1.2.1). Acute episodes will be dealt with elsewhere (chapter 7).

Figure 6.6.1.2.1 Symptom scores on symptomatic days over time in peak flow and

symptoms only group
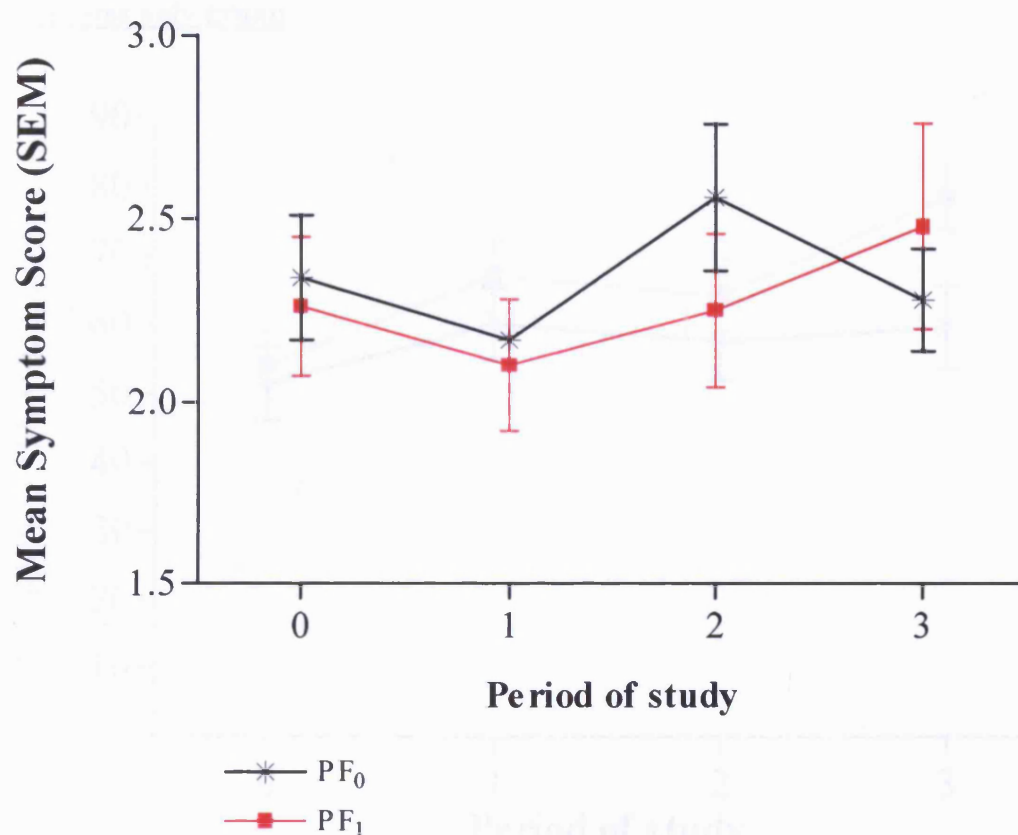
6.6.1.3 Symptom free days

The proportion of days without symptoms for each child for each study period was no different between groups until the final 4 week period of the trial when the peak flow group report a greater proportion of symptom free days (figure 6.6.1.3.2).

Figure 6.6.1.3.1 Symptom free days during study over time in peak flow and

symptoms only group
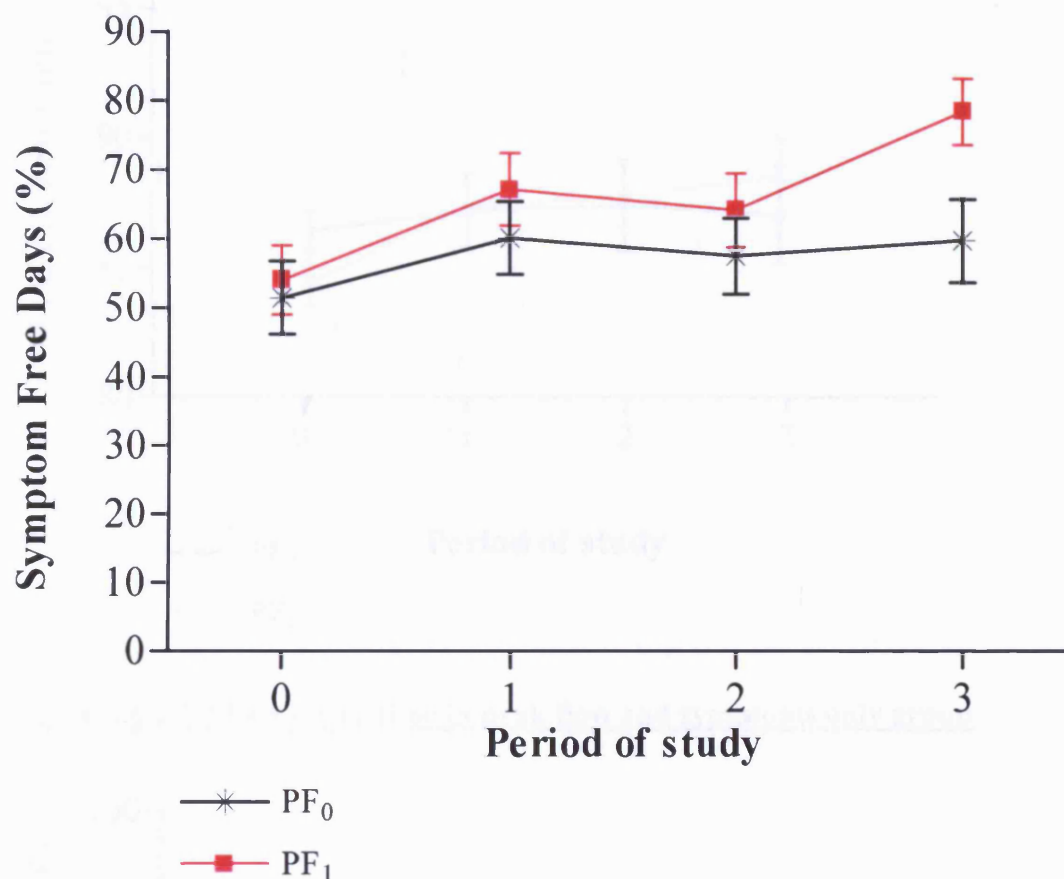
6.6.2 Lung function

6.6.2.1 Comparison of lung function data over time between groups

No significant differences were found between the groups in any lung function parameter for any study period. Applying repeated measures analysis of variance to the data demonstrated differences in PEF when sex was a factor. There was a significant ($p<0.05$) complex interaction between sex, group and time for peak flow results. This was due to an unsustained trivial (2%) fall in group mean PEF for the girls in the PF_0 group during period 2 (table 6.6.2.1.5).

Figure 6.6.2.1.1 FVC over time in peak flow and symptoms only group
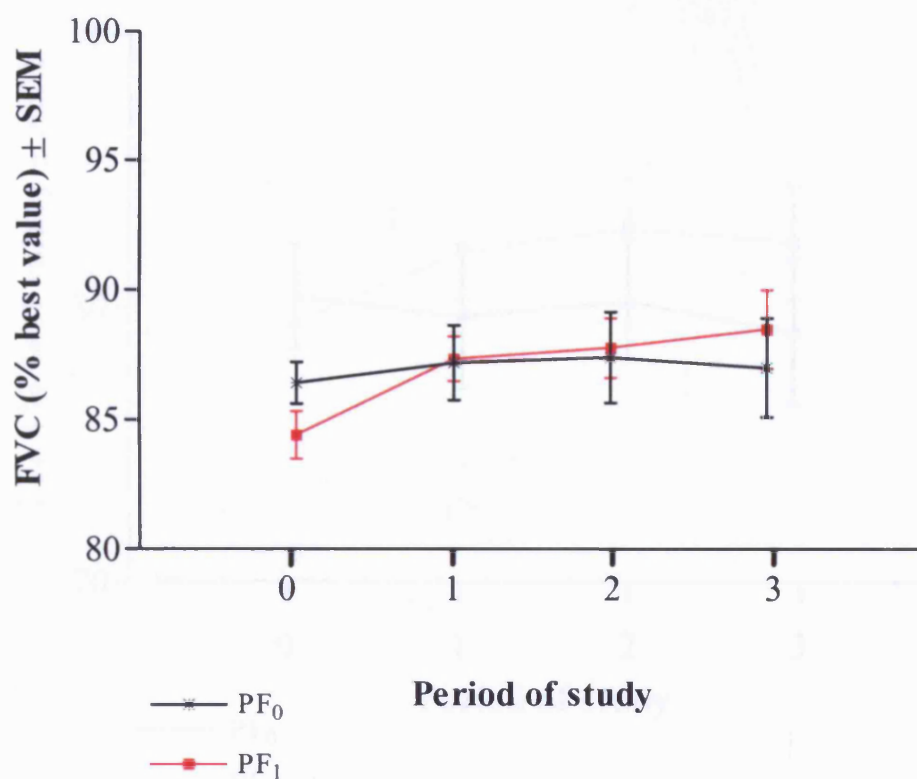
Figure 6.6.2.1.2 FEV₁ over time in peak flow and symptoms only group
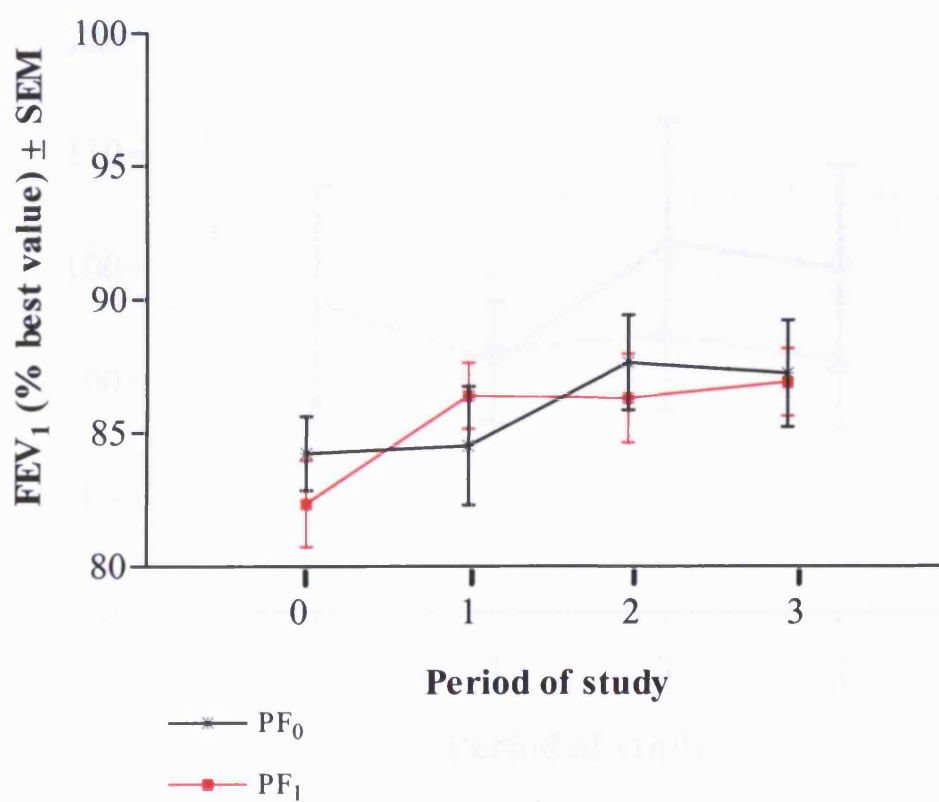
Figure 6.6.2.1.3 PEF over time in peak flow and symptoms only group
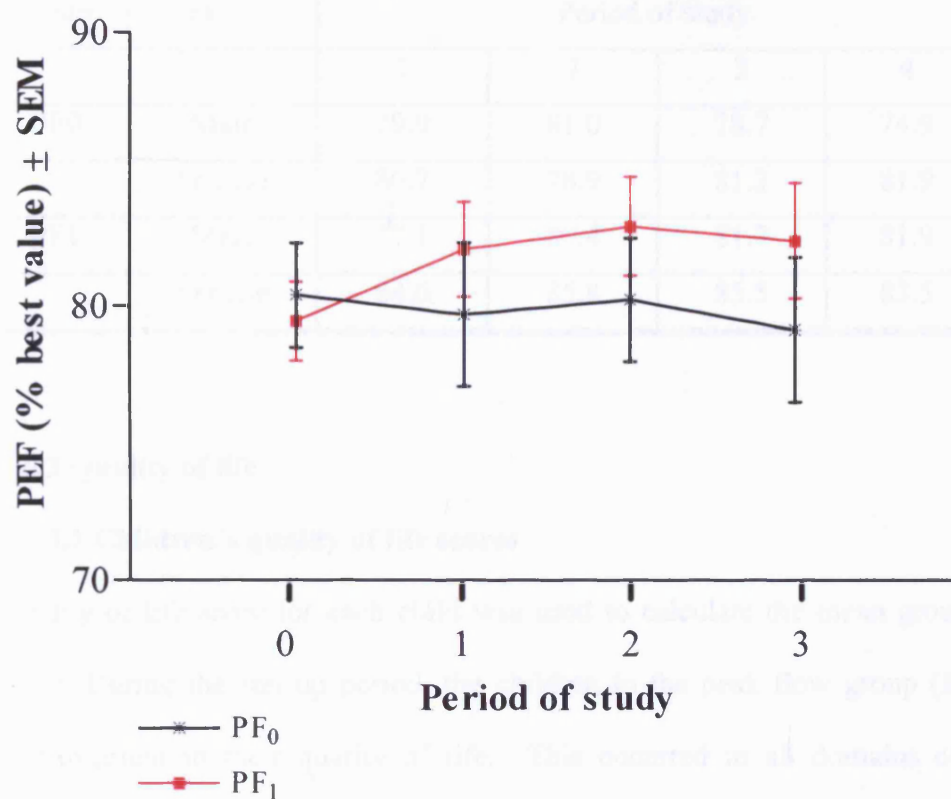
Figure 6.6.2.1.4 FEF$_{25-75}$ over time in peak flow and symptoms only group
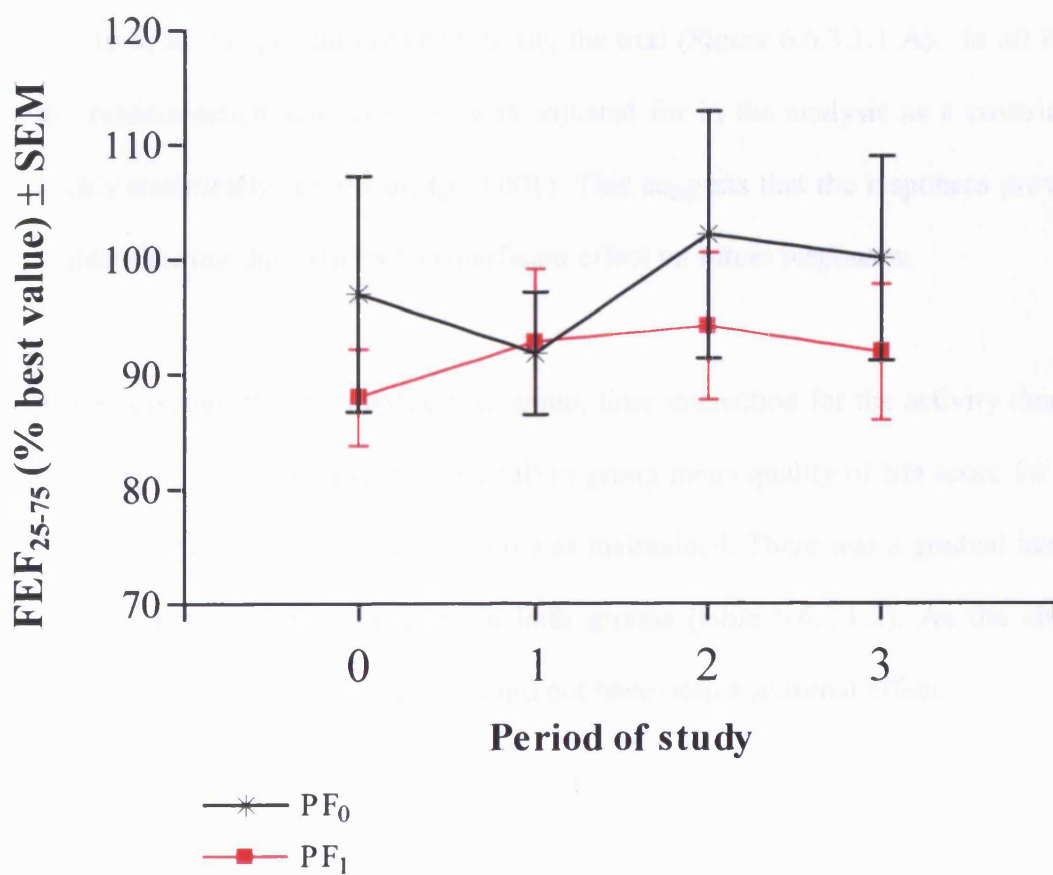
Table 6.6.2.1.5 Mean peak flow (% best) by group, sex and time

Group	Sex	Period of study			
		1	2	3	4
PF0	Male	79.9	81.0	78.7	74.9
	Female	80.7	78.9	81.2	81.9
PF1	Male	77.1	80.4	81.7	81.9
	Female	84.6	85.8	85.5	83.5

6.6.3 Quality of life

6.6.3.1 Children's quality of life scores

Quality of life score for each child was used to calculate the mean group quality of life score. During the run up period, the children in the peak flow group (PF_1) recorded an improvement in their quality of life. This occurred in all domains of quality of life measured separately (Figure 6.6.3.1.1B-D). Repeated measures analysis of variance (RMANOVA) demonstrated no between group differences in overall quality of life score or any of its component domains during the trial (Figure 6.6.3.1.1 A). In all RMANOVA the randomisation visit (visit 0) was adjusted for in the analysis as a covariate and was highly statistically significant ($p<0.001$). This suggests that the responses provided by the children during this visit had a significant effect on future responses.

There was significant complex sex, group, time interaction for the activity domain quality of life ($p<0.05$). This was due to a fall in group mean quality of life score for the boys in the PF1 group during period 2 which was maintained. There was a gradual increase in the activity domain scores for girls in both groups (table 6.6.3.1.2). As the children were recruited at all times of year, this could not have been a seasonal effect.

Figure 6.6.3.1.1 Childs quality of life scores

A. Childs overall QoL score

B. Childs activity domain QoL score

C. Childs emotional domain QoL score

D. Childs symptom domain QoL score

PF_0
PF_1
B baseline
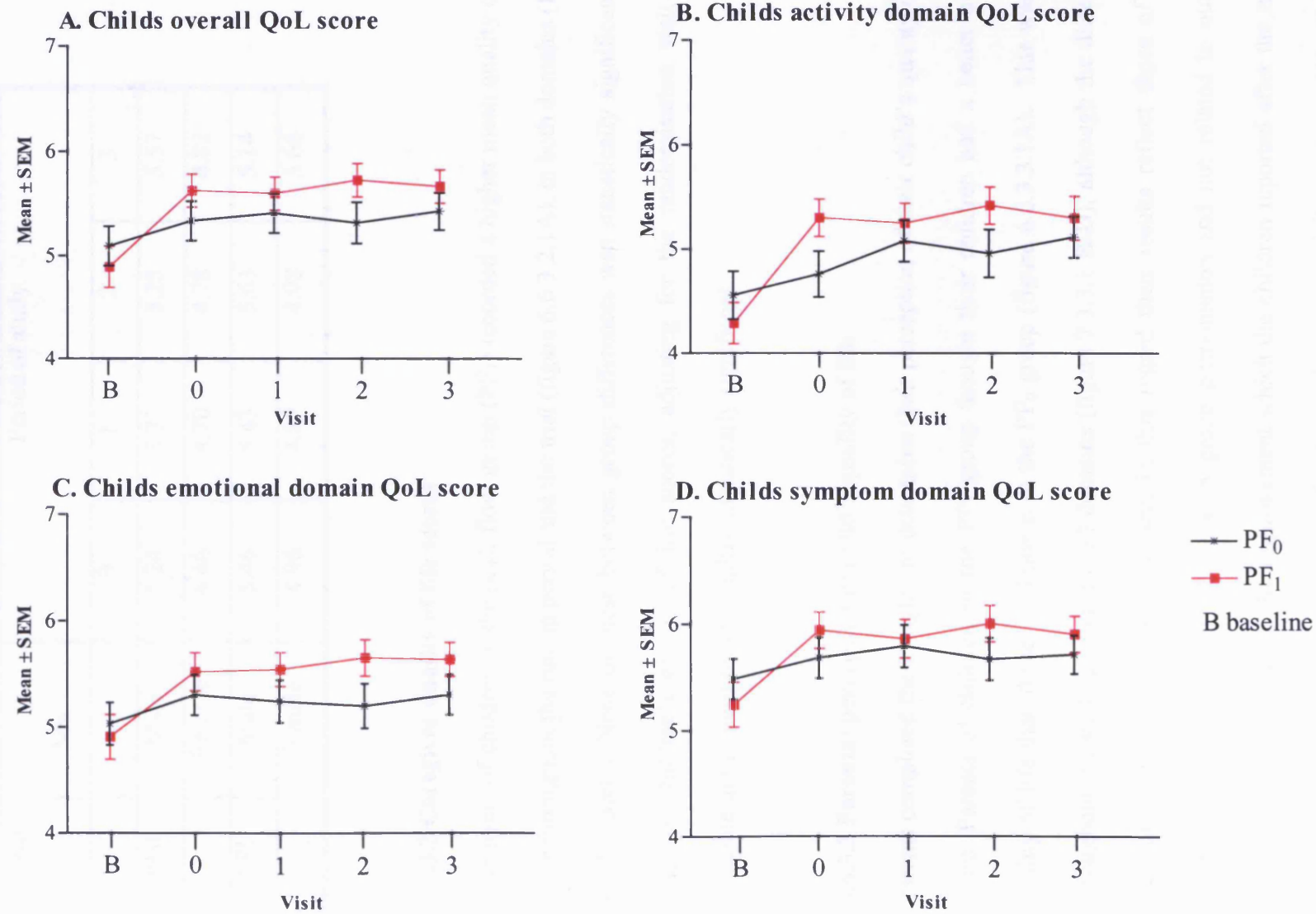
Table 6.6.3.1.2 Mean quality of life scores (activity domain) by group, sex and time

Group	Sex	Period of study			
		0	1	2	3
PF0	Male	5.24	5.71	5.25	5.57
	Female	4.46	4.70	4.78	4.82
PF1	Male	5.46	5.43	5.63	5.14
	Female	4.96	4.87	4.98	5.68

6.6.3.2 Caregiver quality of life scores

Caregivers of children in the peak flow group (PF_1) recorded a higher mean quality of life score throughout the run up period and the trial (figure 6.6.3.2.1A), in both domains (figure 7.3.2.1 B&C). None of these between group differences was statistically significant. As with the children's quality of life scores, adjusting for the randomisation visit as a covariate in the analysis was highly statistically significant.

6.6.3.3 Parental perception of child's quality of life

Parents completed the PAQLQ to determine their perception of their child's quality of life score. Parents of children in the PF_1 group thought their children had a better overall quality of life than those of children in the PF_0 group (figure 6.6.3.3.1A). This was true throughout the study period, for all domains (figure 7.3.3.1 B-D), although the difference did not reach statistical significance; in this regard their results reflect those of their children (figure 6.6.3.1.1). This was a group phenomenon and not related to outliers. Parents failed to recognise the improvement which the children reported after the run up period (figure 6.6.3.1.1). Adjustment for the randomisation visit as a covariate produced similarly significant results as the other quality of life assessments.

Figure 6.6.3.2.1 Caregiver quality of life scores

A. Caregiver overall QoL score

B. Caregiver activity domain QoL score

C. Caregiver emotional domain QoL score
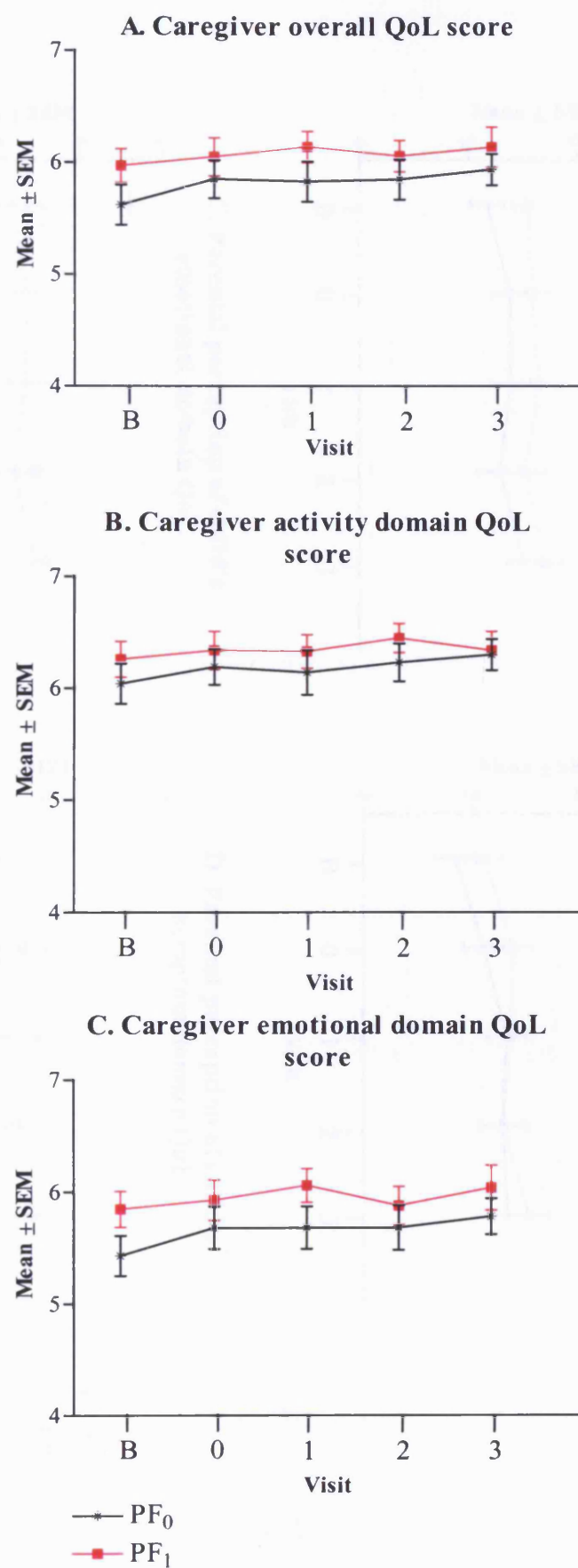
Figure 6.6.3.3.1 Parental perception of childs quality of life

A. Parental perception of child's overall QoL

B. Parental perception of childs activity domain QoL

C. Parental perception of child's emotional domain QoL

D. Parental perception of child's symptom domain QoL

PF_0
PF_1
B baseline
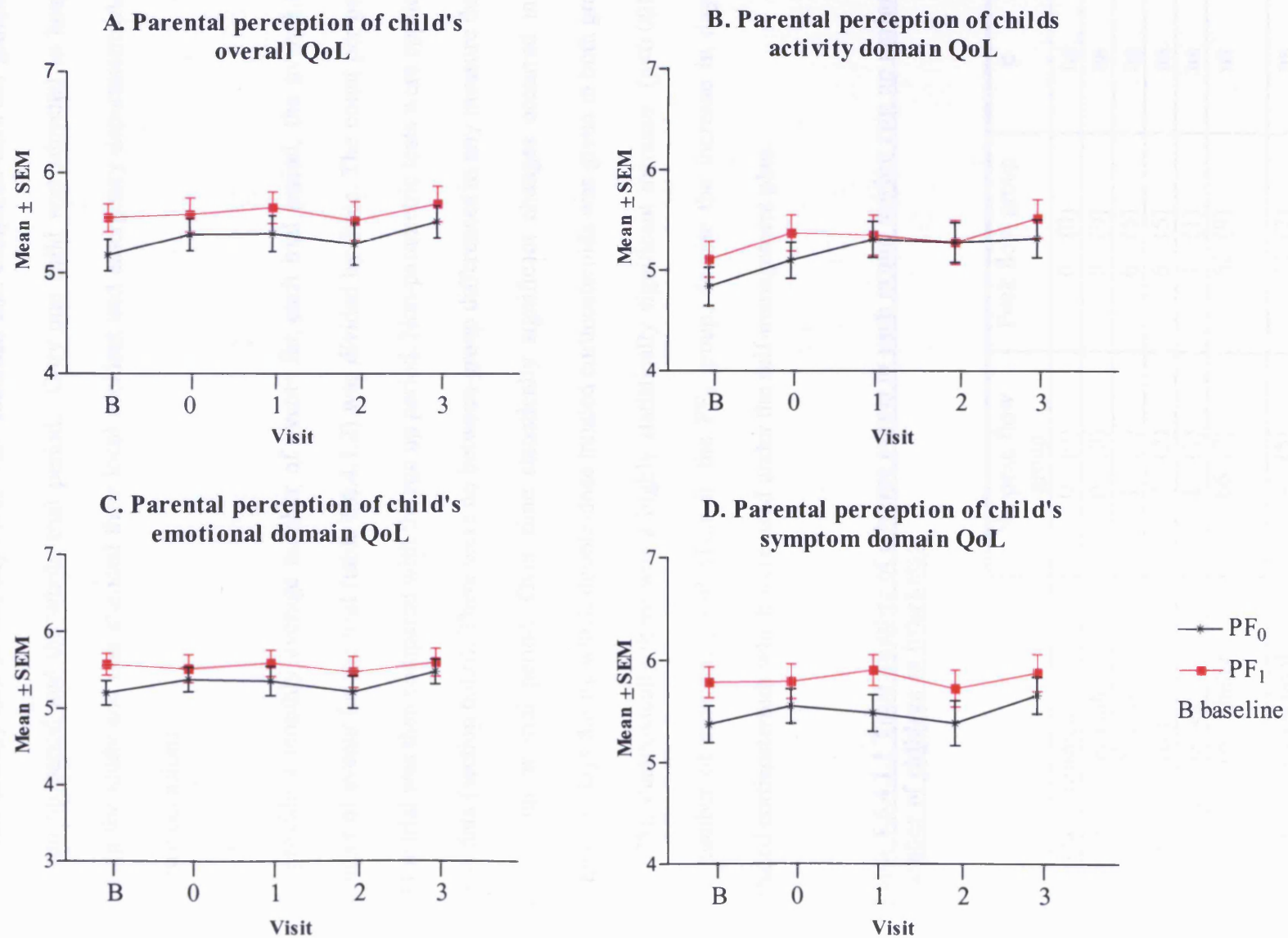
6.6.4 Use of services between groups

The total number of hospital or GP visits, emergency treatments prescribed, doubling of preventer therapy and school days lost were recorded and compared between groups for the run up period and the whole trial period. Only one child was admitted to hospital during the study and one attended their local accident and emergency department (A&E) on two occasions.

To provide a monthly average number of events for each trial period, the overall total number of events for the trial (table 6.6.4.1.2) was divided by three. The count per period of the trial was then compared with the run up period. Non-parametric tests were applied to these data (section 6.4.6). There were no between-group differences in any measure during the run up or trial period. Over time statistically significant changes occurred in the number of days during which double-dose inhaled corticosteroids was given in both groups ($p < 0.05$). Paradoxically there was a highly statistically significant increase ($p < 0.001$) in the number of emergency GP visits in the PF_0 group, despite the increase in days of inhaled corticosteroids which were used under the self-management plan.

Table 6.6.4.1.1 Total number of adverse events in each group during run up period (number of children in brackets)

	No peak flow group	Peak flow group	p
Hospital admissions	0 (0)	0 (0)	ns
Attendance at casualty	0 (0)	0 (0)	ns
Emergency GP visits	1 (1)	6 (5)	ns
Antibiotic courses	3 (2)	6 (5)	ns
Oral steroid courses	1 (1)	1 (1)	ns
Days of doubled inhaled corticosteroids	66 (7)	62 (9)	ns
Days absent from school	9 (5)	21 (7)	ns
Cold/ runny nose	24 (24)	18 (18)	ns

Table 6.6.4.1.2 Overall total number of adverse events in each group during trial period (number of children in brackets)

	No peak flow group	Peak flow group	p
Hospital admissions	0 (0)	1 (1)	ns
Attendance at casualty	0 (0)	2 (1)	ns
Emergency GP visit	22 (11)	18 (10)	ns
Antibiotic courses	7 (5)	7 (5)	ns
Steroid courses	5 (5)	9 (5)	ns
Days of doubled inhaled corticosteroids	621 (27)	526 (22)	ns
Days absent from school	47 (13)	44 (15)	ns
Cold/ runny nose	64 (35)	70 (38)	ns

SECTION IV
SECONDARY QUESTIONS

Chapter 7

Response to acute episodes

7.1 Introduction

Some children experienced acute episodes during the study which led to increases in treatment, guided by the self-management plan. Previous data in adults suggested that PEF based management provided effective protection against serious exacerbations in severe asthma [57]. In patients with milder disease it has been argued that symptoms are as effective as PEF in highlighting exacerbations[56].

The aim of this analysis was to determine the relationship between lung function and symptoms during behaviourally defined acute episodes, in order to determine their relative sensitivity in children's responses to episodes.

7.2 Methods

7.2.1 Subjects

Children participating in the trial who responded to an episode by recording an increase in treatment in the diary card, were included in this analysis. Each episode was analysed and contributed to the results.

7.2.2 Episodes

Increased preventer episodes

Acute episodes were behaviourally defined using diary data. Any child who temporarily increased inhaled preventer therapy for more than 2 consecutive days was considered to have had an episode. When describing episodes, all valid lung function data, symptom score data and recordings of extra reliever were analysed. Data from 10 days prior to increasing treatment and 10 days following the increase were included in the analysis to

provide as much information as possible about the onset of the episode and the period of increased therapy. An interval of at least seven days at the usual dose of preventer was necessary before a second episode could be defined. Where the interval between two periods of increased preventer therapy (for acute episodes) was less than seven days, only a single episode was considered to have occurred.

Oral steroid episodes

Any child who recorded taking oral steroids in the written diary was considered to have had episode. As above data were taken from 10 days before and 10 days after the day oral steroids were commenced.

7.3 Results

7.3.1 Comparison of episodes requiring doubling of preventer therapy between the groups

Diary data suggested that 42 children increased inhaled preventer therapy in response to 59 episodes. This was lower than the 49 children suggested by the questionnaire data (table 6.6.4.1.2). Data are presented for 42 children (table 7.3.1.1). There were a small number of children who increased their inhaled corticosteroids for substantial periods of time. This may explain the tenfold increase in days of inhaled corticosteroids demonstrated by the questionnaire data (Table 6.6.4.1.2). Compliance, technical quality and the amount of valid data did not differ significantly within groups during the period around an episode compared with other periods (table 7.3.1.2). Comparisons between the groups showed that there was a tendency for the PF_1 group to provide less valid data, although this did not reach statistical significance.

Table 7.3.1.1 Baseline characteristics of children who recorded an episode requiring increased preventer therapy and those who did not

		Episode recorded n=42	No episode recorded n=47	significance of difference
Group [1]	(# (%) PF$_1$)	16 (38%)	28 (58%)	ns
Sex[2]	(#(%) male)	22 (52%)	26 (54%)	ns
Family history asthma[2]	(# (%) yes)	18 (54%)	20 (42%)	ns
Severity [3]	(BTS>2 #(%) [2])	14 (33%)	8 (17%)	ns
Ever admitted[2]	(# (%) yes)	18 (43%)	17 (35%)	ns
Age at diagnosis yrs[2]	median (range)	4 ($^4/_{12}$-12)	4 ($^6/_{12}$-12)	ns
Age at recruitment yrs[2]	median (range)	11 (7-14)	11.5 (7-14)	ns
Caregiver QoL score[2]	mean (SEM)	5.44 (0.2)	6.09 (0.12)	p=0.02
Child QoL score[2]	mean (SEM)	4.65 (0.2)	5.29 (0.18)	p=0.007

[1] Chi-squared test
[2] Non- parametric Mann Whitney U test
[3] Unpaired t-test scores at baseline
ns   p>0.05

Table 7.3.1.2 Compliance with and quality of lung function data during the time around an episode with increased preventer therapy (%) compared with that during other times

	Episode			Non-episode		
	All children	**PF_0**	**PF_1**	**All children**	**PF_0**	**PF_1**
Compliance	76.09	80.12	69.54	75.70	77.00	73.52
Technical quality	73.56	76.96	68.03	74.70	77.19	70.66
Valid data	55.88	61.61	46.55	56.53	59.59	51.55

Children who experienced an episode requiring increased preventer therapy were not different demographically from those who did not (table 7.3.1.1). The children recording an episode were not necessarily more severe. There were 28 (67%) at BTS step 2; 12 (28%) at BTS step 3 and 2 (5%) at BTS step 3. The distribution of children with episodes between the two groups was as follows: PF_0 26/ 46 (56%) and PF_1 16/44 (36%). A higher percentage of children in the PF_0 group recorded an episode, but the difference was not statistically significant (p=0.06). Baseline quality of life scores recorded by the children and caregivers were worse for those children who went on to experience an episode during the trial. These differences reached statistical significance (table 7.3.1.1) and were all greater than the 0.5 minimal important difference highlighted by the developers of the questionnaires as being clinically significant [124].

Recorded mean daily symptom score and beta-agonist use, along with percent best PEF and FEV_1 were noted for this period. There was a marked decline in PEF in both groups around 1 day prior to increasing treatment (figure 7.3.1.3). Mean group symptom score was around 1 from ten days prior to the start of the episode and symptoms increased mainly the day before treatment was increased. Children began taking reliever medication

on average one day prior to increasing preventer, although there was sporadic extra reliever use 4-6 days earlier.

The PF_1 group doubled inhaled steroids before their mean peak flow reached a level for action (70%). After commencing treatment there was an improvement in lung function and group mean symptom score declined rapidly with the former taking five days to recover and the latter, two days. The symptoms only (PF_0) group seems to have responded at a slightly (but not significantly) lower symptom score. They used less additional bronchodilator, and their response in terms of lung function and symptoms was slower, taking nine and seven days respectively. At the onset of an episode (day −1 or 0), group mean PEF was again higher than the threshold of 70%. No children reached the threshold of 70% on day −1 or 0.

The PF_0 group showed very little change in FEV_1 even when PEF fell. In the PF_1 group the FEV_1 followed the pattern of PEF more closely but on day −1 when PEF fell, FEV_1 did not fall to the same level. Forced expiratory volume at one second (FEV_1) was less sensitive than PEF during the period around an episode with increased inhaled preventer therapy (figure 7.3.1.4).

Figure 7.3.1.3 Comparison of lung function, symptoms and reliever use during episodes in which increased inhaled corticosteroids were commenced on day 0 (Mean ± SEM).

A. PF_0

B. PF_1
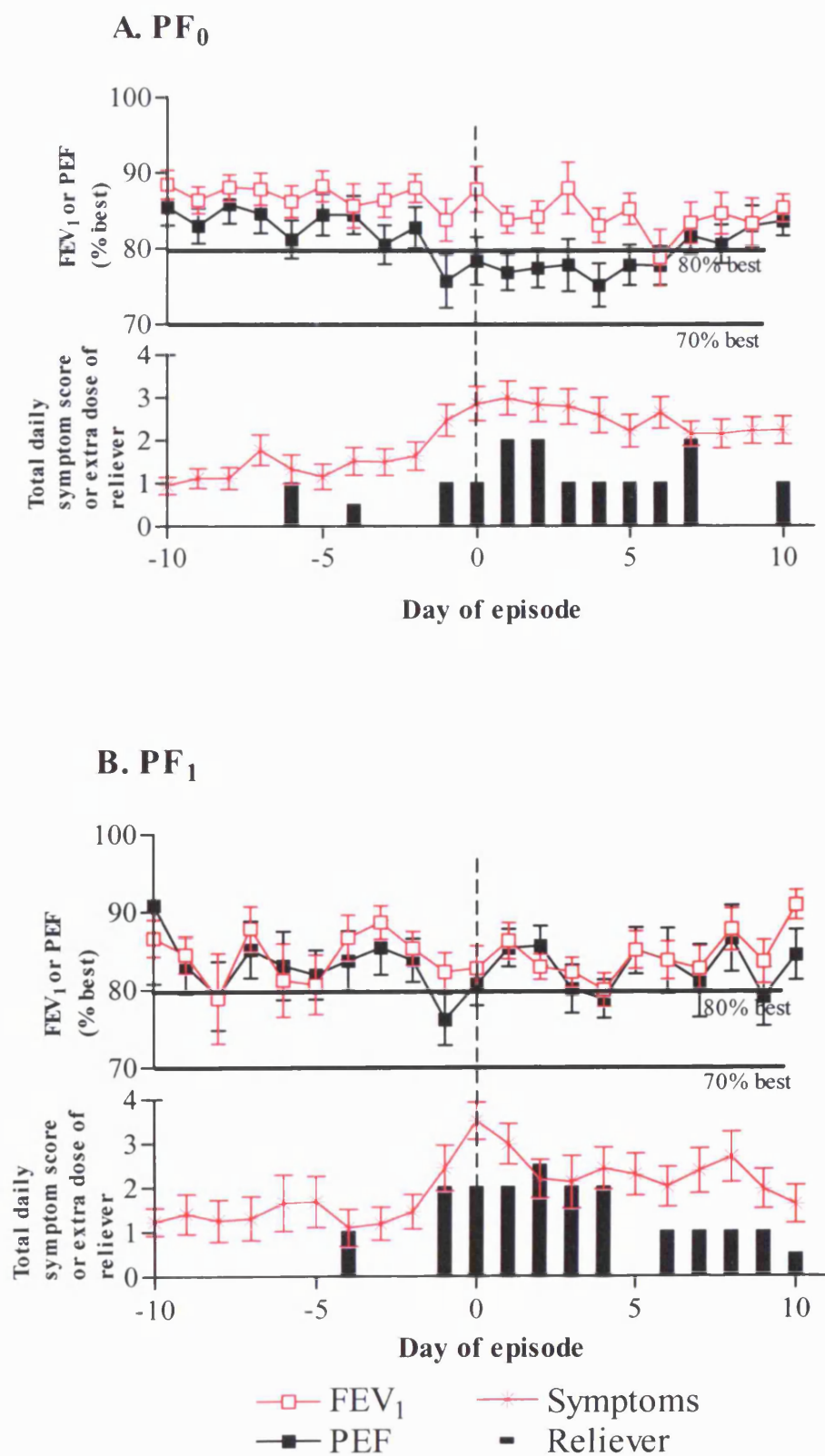
Figure 7.3.1.4 Relationship between PEF (% best) and FEV1 (% best) during the period around an episode in which increased preventer therapy was used
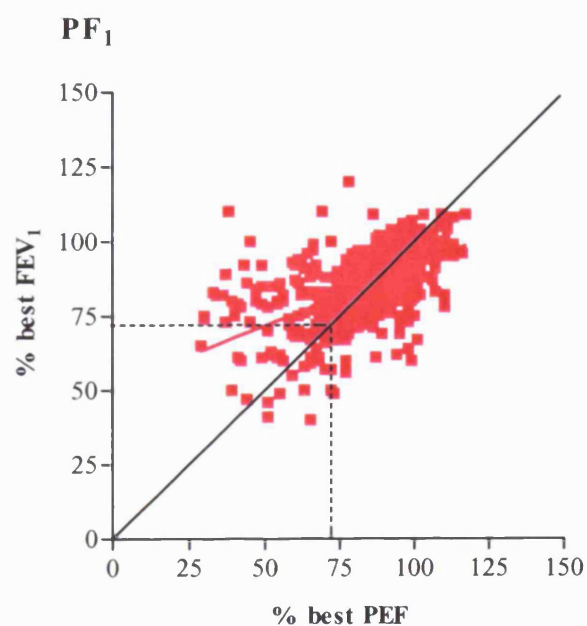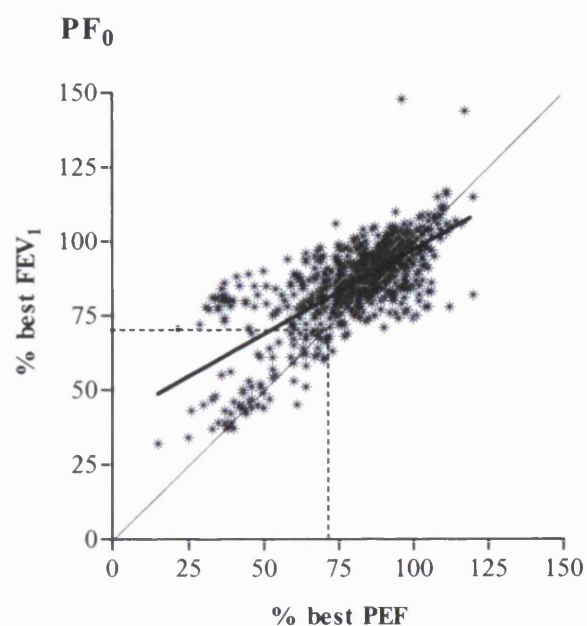
7.3.2 Comparison of episodes requiring oral steroids

Some children took oral steroids on more than one occasion. Ten children took oral steroids during the trial period for fourteen episodes (table 7.3.2.1). Two children in the PF_1 group recorded taking 3 courses on oral prednisolone each.

Children who took oral steroids during the trial were significantly more severe than those who did not. A greater proportion of these children were above step 2 of the BTS guidelines. They were more likely to have been admitted to hospital and were younger when they received a diagnosis of asthma (table 7.3.2.1). In addition, the caregivers of the children who went on to take oral steroids during the trial recorded a statistically significantly lower quality of life at baseline than the parents of those who did not.

The only between group difference in those children who recorded using oral steroids during the trial was in caregiver quality of life. The caregivers of children in the PF_0 group who took oral steroids during the trial recorded a statistically significantly lower quality of life than caregivers of children in the PF_1 group.

Table 7.3.2.1 Characteristics of children who recorded an episode requiring oral steroids and those who did not

		Took oral steroids 10	Did not take oral steroids 79	significance
Group [1]	(# (%) PF$_1$)	5 (50%)	39 (49%)	ns
Sex [1]	(#(%) male)	5 (50%)	43 (54%)	ns
Family history asthma [1]	(#(%) yes)	5 (50%)	33 (41%)	ns
Severity [1]	(BTS>2 # (%) [2])	6 (60%)	16 (20%)	p<0.001
Ever admitted [1]	(# (%) yes)	8 (80%)	27 (34%)	p<0.001
Age at diagnosis [2]	median (range)	1 ($^4/_{12}$-9)	4.5 ($^8/_{12}$- 12)	p=0.01
Age at recruitment [2]	median (range)	11 (7-14)	11 (7-14)	ns
Caregiver QoL score [3]	mean (SEM)	4.66 (0.47)	5.93 (0.11)	p=0.02
Child QoL score [3]	mean (SEM)	5.04 (0.35)	4.99 (0.15)	ns

[1] Chi-squared test
[2] Non- parametric Mann Whitney U test
[3] Unpaired t-test
ns   p>0.05

The results suggest differences in lung function and reliever use between groups. In the PF$_0$ group symptoms started to increase at the same time as changes in lung function were seen, a couple of days before commencing oral steroids. When symptoms began to increase children commenced prednisolone. In both groups the mean symptom score was between 5 and 7 in the 2-3 days prior to the children commencing oral prednisolone. Median daily reported reliever use on each of the ten days prior to oral prednisolone was between 1 and 7 for the peak flow group and 1 and 4 for the symptoms only group (figure 7.3.2.2).

After commencing treatment there was a steady decline in mean daily symptom score in both groups although the lung function and extra reliever use varied independently of oral steroid use.

Lung function was more variable during the period around an episode, particularly in the symptoms only group. In this group PEF fell 5-7 days before oral prednisolone was commenced, to a level of less than 70% of best. In the PF_1 group there was an underlying reduction in lung function present. This group usually functioned at a level between 70% and 50% of best PEF (figure 8.1.3.1B). In the PF_0 group peak flow, FEV_1 and symptoms took approximately 3, 3 and 10 days respectively to recover. In the PF_1 group the group mean peak flow reached level above 70% on day 4 but fell again until day 9 after which it did not fall below 70% again. In this group mean symptom score continued around 2-3 up until day 10. During an episode requiring prednisolone, PEF was more sensitive than FEV_1 in both groups (figure 7.3.2.3).

Episodes requiring an increase in inhaled preventer therapy seemed to arise acutely. Increased symptoms and reduced lung function in the days immediately prior to increasing treatment were characteristic of this type of episode in both groups. Episodes requiring prednisolone were more difficult to define, particularly in the PF_1 group which included two children who had 3 episodes each, all requiring oral prednisolone. One child had relatively mild asthma (Step 2). The other child was very severe (Step 5) and suffered chronic symptoms. These episodes were set against a background of more chronic symptoms and daily reliever use with variable lung function, suggesting poor control.

Figure 7.3.2.2 Comparison of lung function, symptom scores and reliever use during episodes in which oral prednisolone was commenced on day 0 (Mean ± SEM)

A. PF_0

B. PF_1
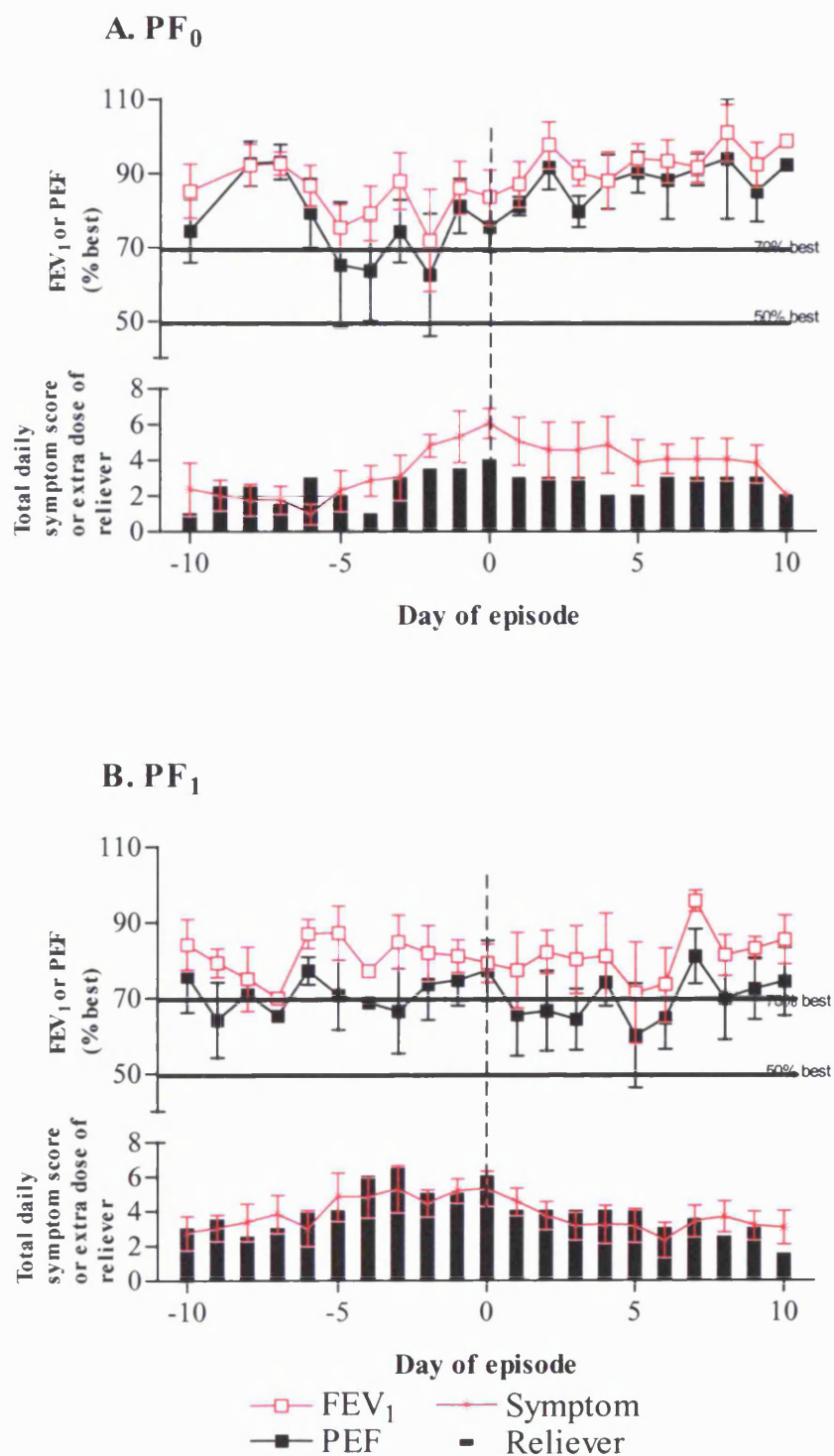
Figure 7.3.2.3 Relationship between PEF (% best) and FEV1 (% best) during the period around an episode in which oral prednisolone therapy was used

PF$_0$

PF$_1$
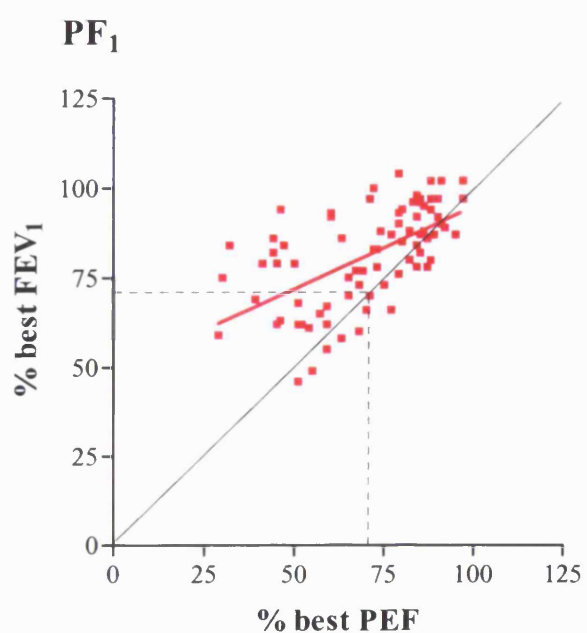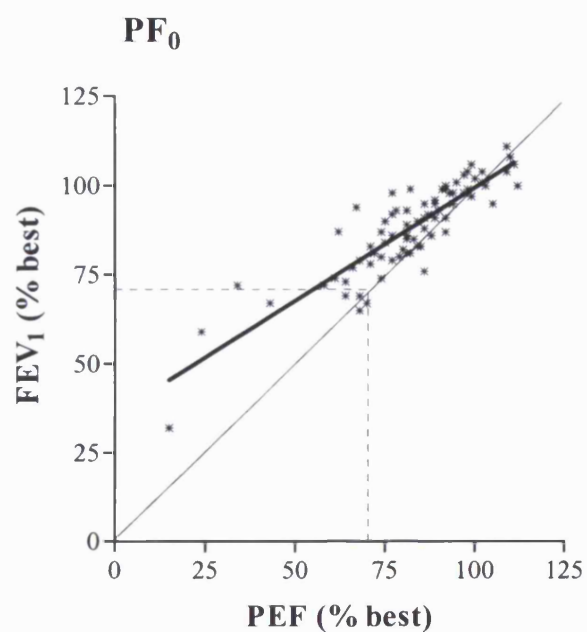
Chapter 8

Quality of life assessments: agreement between parents and children

8.1 Introduction

Parents of children with chronic illness are often asked about disease impact. The discrepancy in symptom reporting between parents and children has been highlighted, particularly in relation to cough[83,85] In terms of quality of life, poor agreement between parents and child's responses has been demonstrated by some studies[111], but not all [109], albeit in children with arthritis rather than asthma. In the present study, although we found no difference between groups, in any quality of life score during the trial (section 6.6.3), we wished to determine whether parents and children agreed in their assessment of the impact of asthma on the child's quality of life.

8.2 Methods

8.2.1 Subjects

All children and caregivers who took part in the study completed quality of life questionnaires simultaneously but independently. Parents completed two forms in any order, the PAQLQ and the PACQLQ. As a result of investigator illness, quality of life data were unavailable for 2 children for the last visit. Data are presented for 87 children.

8.2.2 Quality of life questionnaires (appendix 1)

Children completed the PAQLQ at the start of every visit. A quality of life score was calculated. Parents were asked to put themselves in their child's position and also completed the PAQLQ. In addition, parents completed the PACQLQ to provide a quality of life score as caregivers of children with asthma.

Mean overall quality of life score was calculated for each child and each parent for each visit. The level of agreement between parents' and children's responses for each domain for each visit was calculated using Cohen's kappa (κ). The relationships between parental perception and children's quality of life scores using the PAQLQ, child and caregivers quality of life scores from the PAQLQ and PACQLQ respectively and the parental perception and caregiver quality of life from the PAQLQ and PACQLQ respectively were assessed using Spearman rank correlation coefficients. This was done by group for each visit. Where the correlation coefficients were not normally distributed, the data were transformed using Fisher's transformation (section 6.4.6) to allow repeated measures analysis of variance to be carried out to assess the correlation coefficients over time.

Mean daily diary symptom score recorded for one week before the visit was calculated. The correlation between the mean symptom score and the symptom domain quality of life score recorded by the child was calculated.

8.3 Results

The only between-group difference in those children included in this analysis was in the sex distribution (table 8.3.1) which reflected the make up of the groups as a whole (table 6.5.1.2).

Table 8.3.1 Characteristics of children on whom quality of life data were available

		PF$_0$ n=44	PF$_1$ n=43	significance
Sex[1]	(# (%) PF$_1$)	17 (39%)	29 (67%)	p=0.07
Family history asthma (report) [2]	(#(%) male)	20 (45%)	16 (37%)	ns
Severity [2]	(BTS>2 # (%) [6])	9 (20%)	13 (30%)	ns
Ever admitted[1]	(# (%) yes)	16 (36%)	18 (42%)	ns
Age at diagnosis [2]	(# (%) yes)	5 ($^6/_{12}$-12)	3 ($^4/_{12}$-12)	ns
Age at recruitment[2]	median (range)	12 (7-14)	11 (7-14)	ns

[1] Chi-squared test
[2] Non- parametric Mann Whitney U test

8.3.2 Relationship between parent's and child's own assessment of child's quality of life

There were no systematic differences in mean scores recorded by parents and children. The level of agreement between the two raters was poor as measured by κ even after weighting (section 6.4.6), to add proportionality to the level of agreement (table 8.3.2.1).

Spearman rank correlation was calculated for each parent child pair of quality of life scores for each visit. The resulting correlations were not normally distributed and there was wide variation between subjects (figure 8.3.2.2) therefore the data were transformed to allow repeated measures analysis of variance (section 6.4.6). After transformation (Fisher z scores), repeated measures analysis of variance showed no difference in this correlation between the groups or change within groups over time, p= 0.513 (figure 8.3.2.3), although a baseline and in period 3 the degree of correlation was better in the symptoms only group.

The correlation between parent and child quality of life scores did not change between groups over time.

Table 8.3.2.1 Inter-rater agreement between parent's and children's responses to the PAQLQ

Visit	Domain	Weighted * Kappa (κ)	Level of agreement [143]
1	Activity	0.08407	Poor
	Symptom	0.09986	Poor
	Emotion	0.17381	Poor
2	Activity	0.08175	Poor
	Symptom	0.18562	Poor
	Emotion	0.16282	Poor
3	Activity	0.09266	Poor
	Symptom	0.15179	Poor
	Emotion	0.11172	Poor
4	Activity	0.14555	Poor
	Symptom	0.18632	Poor
	Emotion	0.14075	Poor
5	Activity	0.13225	Poor
	Symptom	0.15518	Poor
	Emotion	0.15083	Poor

* section 6.4.6

Figure 8.3.2.2 Variance in Spearman rank correlation between parent's perception and child's own quality of life scores for each period of study, by group (median, interquartile range and range)[5]
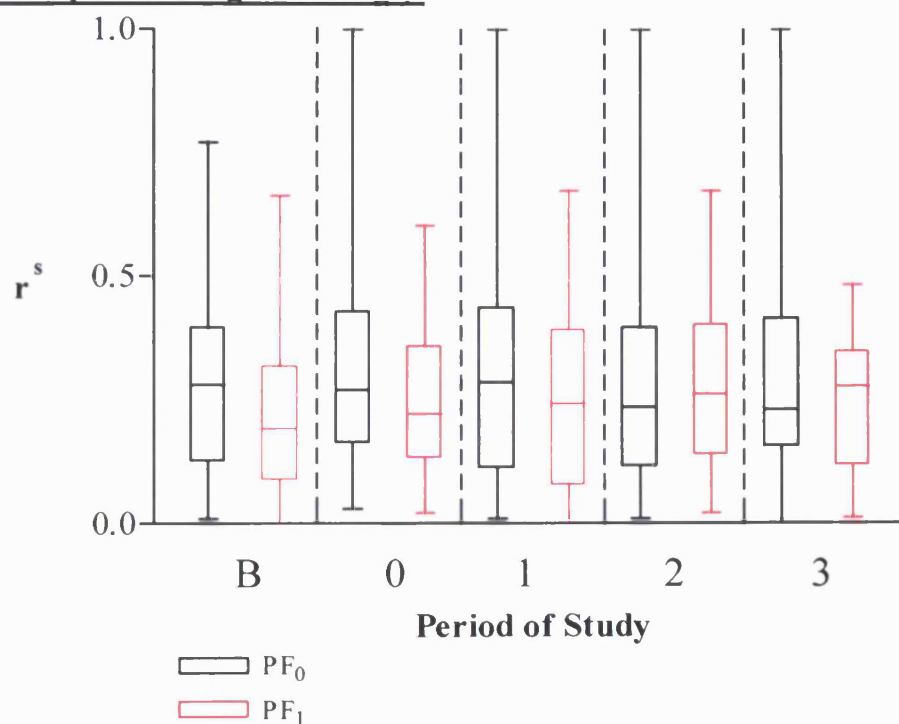
Figure 8.3.2.3 Transformed r_s coefficients (r_z) over time, by group[6]

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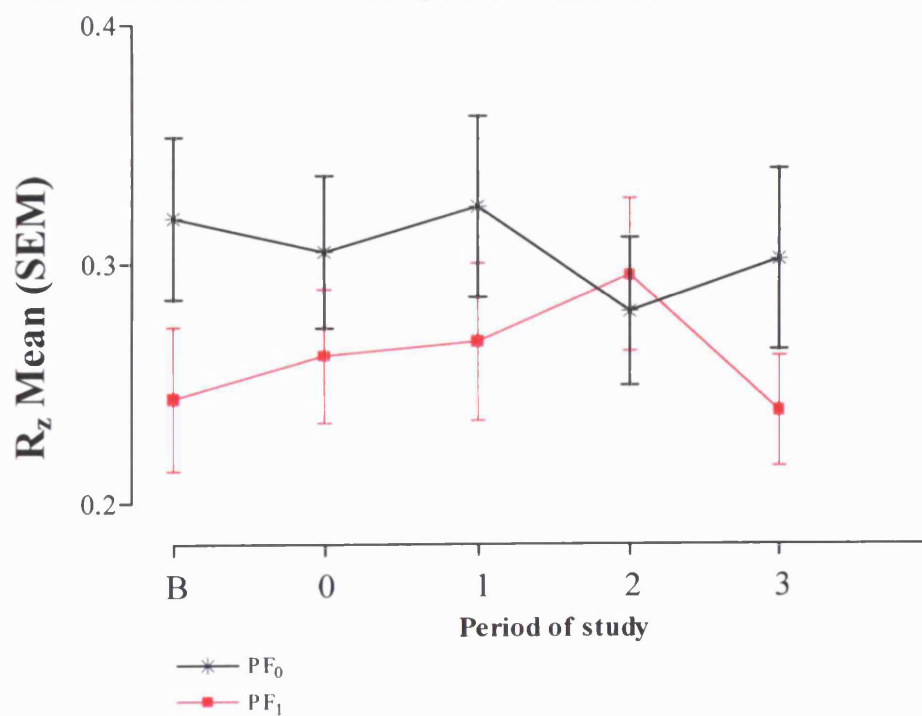
[5] Box and whisker plot of variance in Spearman rank scores demonstrates the non-parametric nature of the results

[6] Transforming the data allow parametric analysis and shows the lack of difference between groups over time. No difference in the level of correlation over time was seen : p=0.513

Figure 8.3.2.4 Correlation between parental perception of child's quality of life and child's own quality of life scored using PAQLQ by parents and children during each visit : individual data and r_s, by group

Visit B

* PF$_0$ r_s =0.26 p= ns
■ PF$_1$ r_s =0.28 p= ns

Visit 0

* PF$_0$:r_s= 0.42, p= <0.005
■ PF$_1$:r_s= 0.11, p= ns

Visit 1

* PF$_0$: r_s 0.47, p<0.005
■ PF$_1$: r_s 0.21, p=ns

Visit 2

* PF$_0$:r_s 0.44, p<0.005
■ PF$_1$:r_s 0.16, p=ns

Visit 3

* PF$_0$:r_s = 0.32, p<0.05
■ PF$_1$:r_s= 0. 15, p=ns
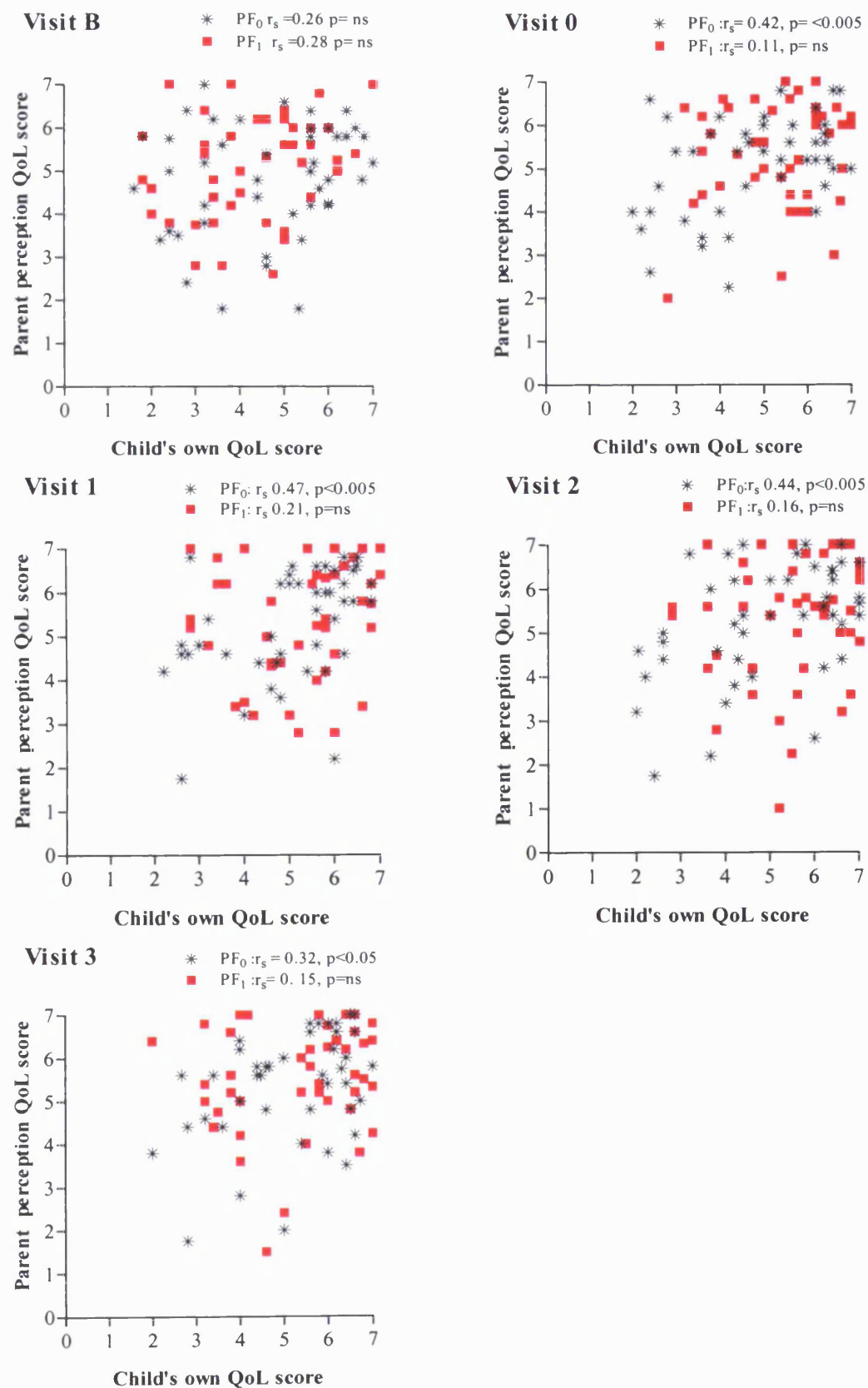
Correlations were performed between the overall PAQLQ scores of parents and children for each visit (figure 8.3.2.4). The correlations were greater in the PF_0 group: on no visit was there a significant correlation between parents' and children's overall scores for the PAQLQ in the peak flow group. This was true when the results for each domain were analysed separately (table 8.3.2.5). Statistical significance was reached in both groups for all visits for the emotional domain. On one occasion the correlation between parents' and childrens scores was significant in the symptom domain in PF_1 group. The PF_0 group demonstrated much better correlations and significance throughout. The emotion domain reached significance throughout the study for both groups.

Table 8.3.2.5 Relationship between parent's perception of child's quality of life score and child's own quality of life score for each domain for each visit, by group

		PF_0		PF_1	
Visit	Domain	r_s	P	r_s	P
B	Activity	0.2592	0.082	0.2844	0.061
	Symptom	0.5943	< 0.001	0.3819	0.011
	Emotion	0.5673	< 0.001	0.3606	0.016
0	Activity	0.4231	0.003	0.1070	0.495
	Symptom	0.5688	< 0.001	0.2364	0.127
	Emotion	0.5328	< 0.001	0.4415	0.003
1	Activity	0.4726	0.001	0.2063	0.179
	Symptom	0.6424	< 0.001	0.1852	0.229
	Emotion	0.5630	< 0.001	0.3797	0.011
2	Activity	0.4394	0.003	0.1572	0.308
	Symptom	0.6981	< 0.001	0.1432	0.354
	Emotion	0.6886	< 0.001	0.3313	0.028
3	Activity	0.3221	0.035	0.1544	0.329
	Symptom	0.5497	< 0.001	0.2622	0.093
	Emotion	0.5089	< 0.001	0.4635	0.002

8.3.3 Relationship between child's quality of life score and caregiver's quality of life score

Children's own assessment of their quality of life (PAQLQ) was compared with caregiver's assessment of their own quality of life (PACQLQ) at each visit (figure 8.3.3.1). The correlations between caregiver's quality of life score and child's quality of life score were stronger in the PF_0 group. Statistical significance was reached for each visit. The PF_1 group reached significance only at visit two. The r_s did not change with time between the groups (figure 8.3.3.2).

Figure 8.3.3.1 Correlation between quality of life scores recorded by caregivers and children during each visit, by group

Visit B — PF$_0$ r$_s$ = 0.32 p<0.05; PF$_1$ r$_s$ = 0.25 NS

Visit 0 — PF$_0$: r$_s$ = 0.40, p< 0.01; PF$_1$: r$_s$ = 0.31, p< 0.05

Visit 1 — PF$_0$: r$_s$= 0.50, p< 0.001; PF$_1$: r$_s$= 0.27, p= NS

Visit 2 — PF$_0$: r$_s$ = 0.51, p <0.001; PF$_1$: r$_s$= 0.17, p=NS

Visit 3 — PF$_0$: r$_s$ = 0.42, p<0.001; PF$_1$: r$_s$ = 0.25, p= ns
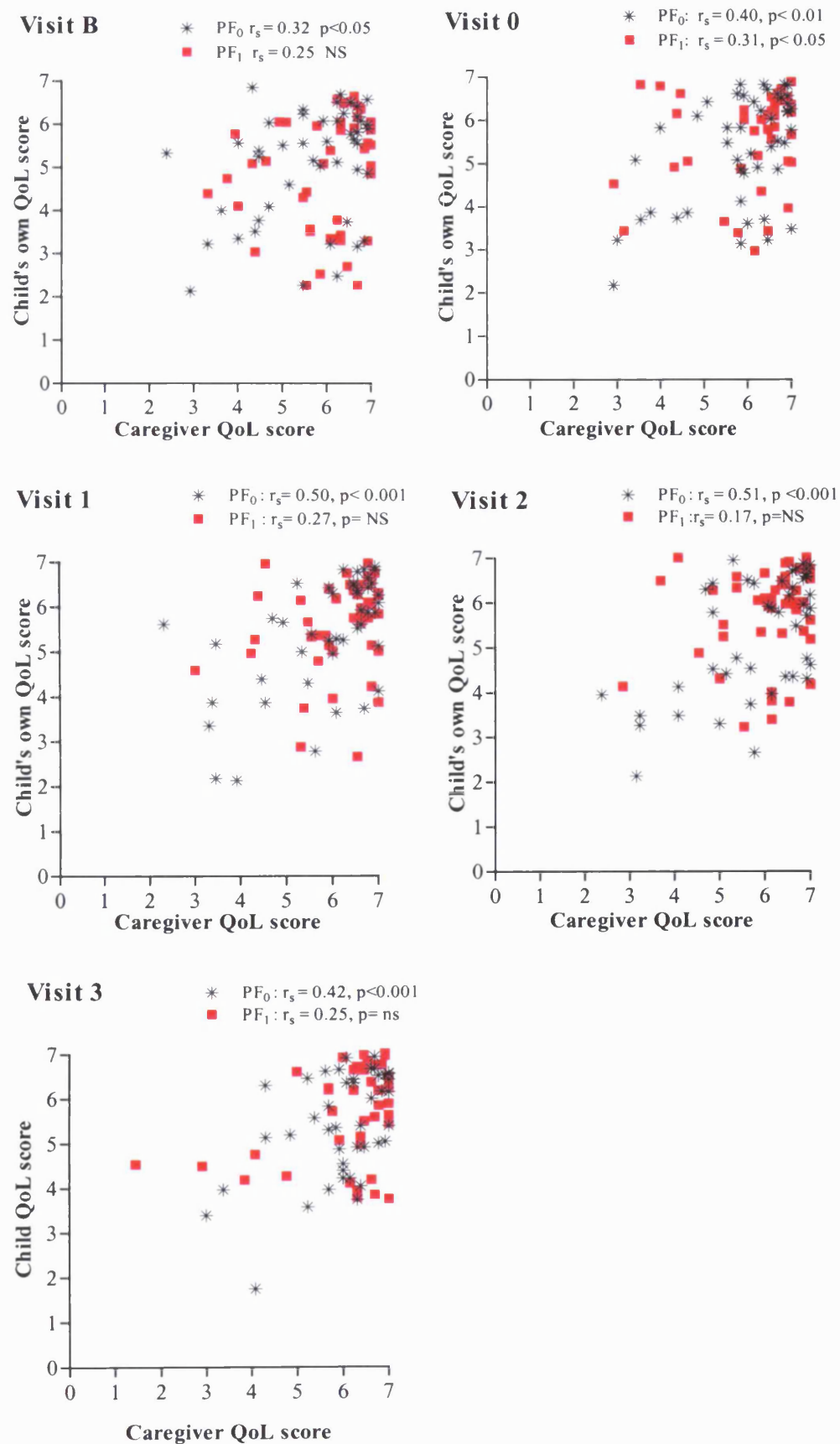
Figure 8.3.3.2 Spearman rank correlation coefficients between caregiver's own (PACQLQ) and child's own (PAQLQ) quality of life scores, by group and period
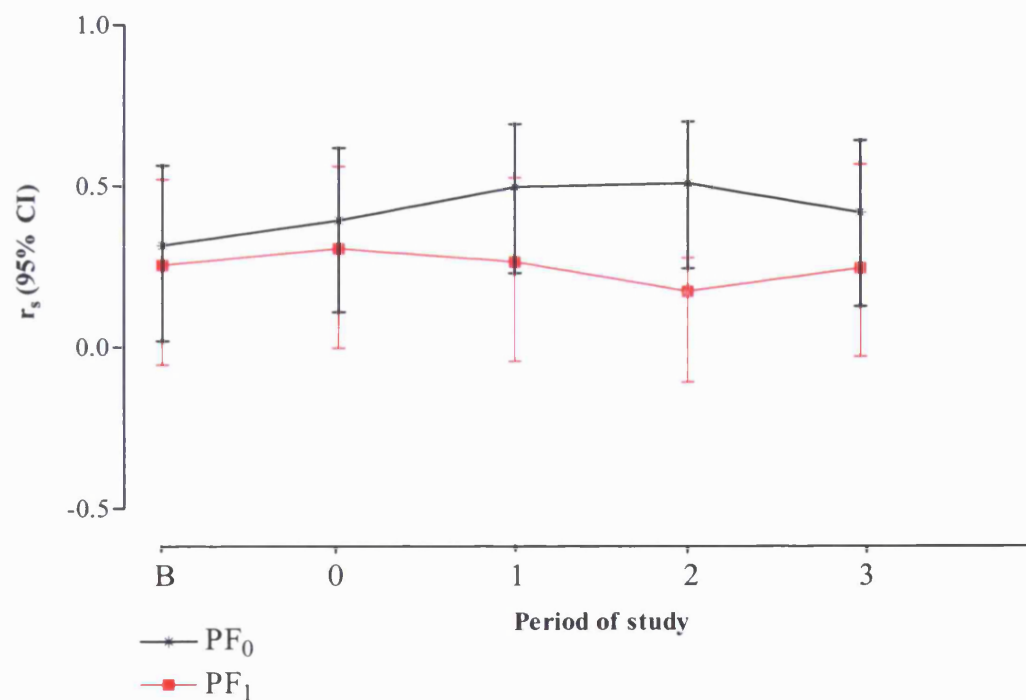
8.3.4 Relationship between caregiver's own quality of life score and their perception of their child's quality of life score

The correlations between caregiver's own quality of life score and their perception of their child's quality of life score were highly significant for both groups at each visit (figure 8.1.3.1 and 2), in striking contrast to the poor correlation between the parent's perception of the child's quality of life and the child's own quality of life (section 8.3.2).

Figure 8.3.4.1 Correlation between caregiver's own quality of life score (PACQLQ) and their perception of their child's quality of life and score (PAQLQ) recorded during each visit: individual data and r_s, by group

Visit B
※ PF_0 : $r_s = 0.69$, p<0.0001
■ PF_1 : $r_s = 0.66$, p<0.0001

Visit 0
※ PF_0 : $r_s = 0.74$, p<0.0001
■ PF_1 : $r_s = 0.70$, p< 0.0001

Visit 1
※ PF_0 : $r_s = 0.80$, p<0.0001
■ PF_1 : $r_s = 0.66$, p<0.0001

Visit 2
※ PF_0 : $r_s = 0.76$, p< 0.0001
■ PF_1 : $r_s = 0.76$, p< 0.0001

Visit 3
※ PF_0 : $r_s = 0.86$, p<0.0001
■ PF_1 : $r_s = 0.85$, p< 0.0001
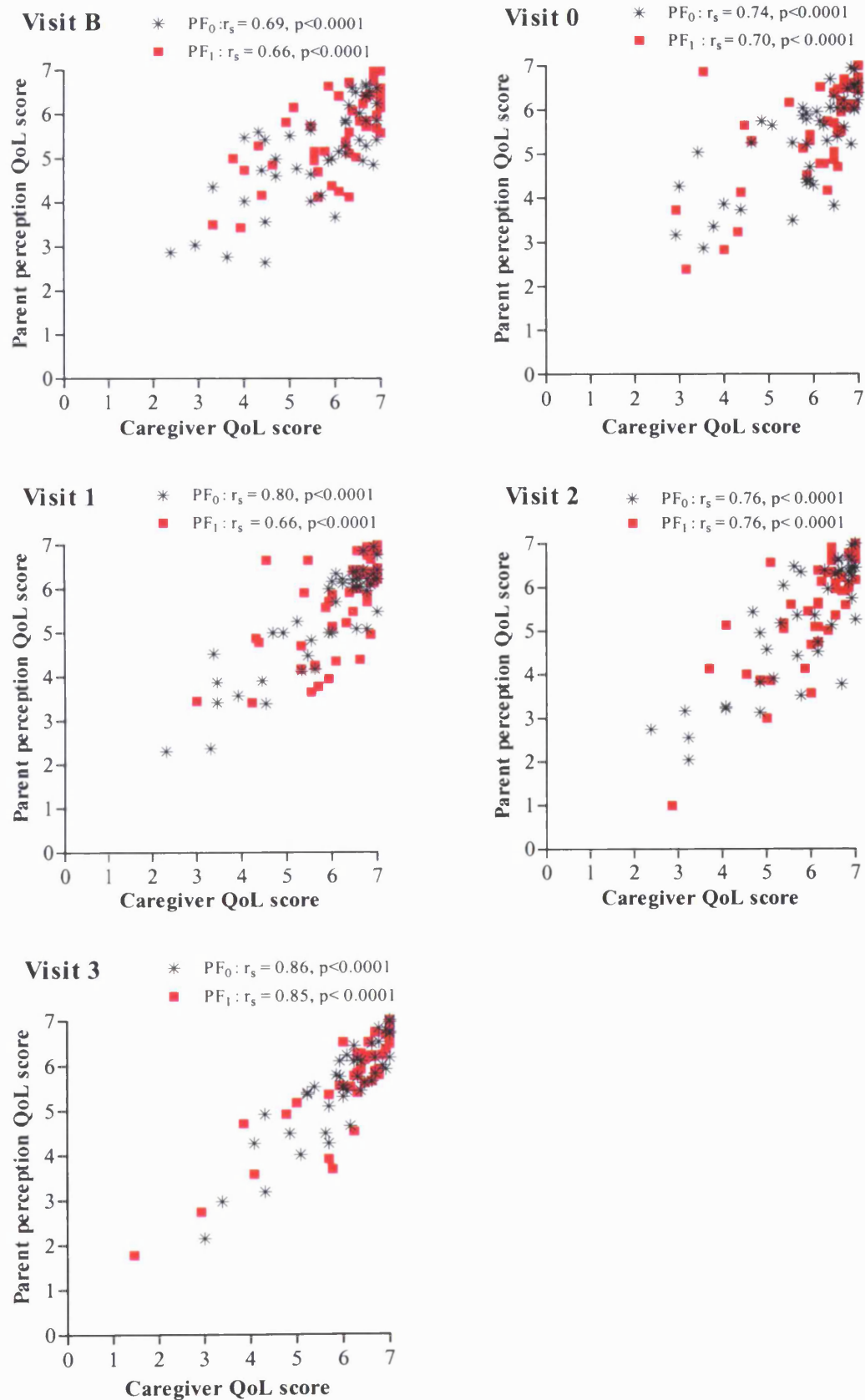
Figure 8.3.4.2 Spearman rank correlation coefficients between caregiver's own quality of life (PACQLQ) and parent's perception of child's quality of life (PAQLQ), by group and period
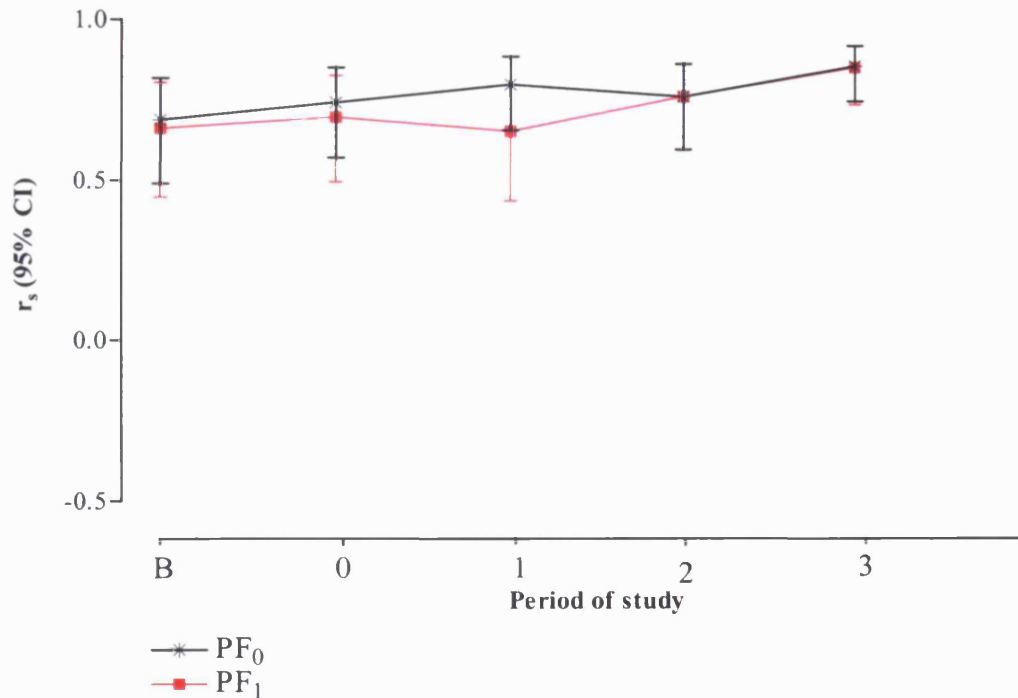
8.3.5 Relationship between quality of life score and written diary symptom score

Because of missing diary data for the week prior to a visit (when quality of life questionnaires were completed), numbers of comparisons for each period or the study were small (table 8.3.5.1). The correlation was modest at best (figure 6.5.2.3.1) with the PF_0 group demonstrating significance and no significance in the PF_1 group beyond visit 2. Repeated measures analysis of variance showed no difference between groups over time (fig 8.3.5.3).

Table 8.3.5.1 Numbers of subjects in each group included in correlation between symptom domain of quality of life score (PAQLQ) and diary symptom score for the previous week

Visit	Period	Group	
		PF_0	PF_1
2	0	23	24
3	1	26	23
4	2	24	23
5	3	20	23

Figure 8.3.5.2 Spearman rank correlation coefficients between child's own quality of life score (PAQLQ) and diary symptom score, by group and period
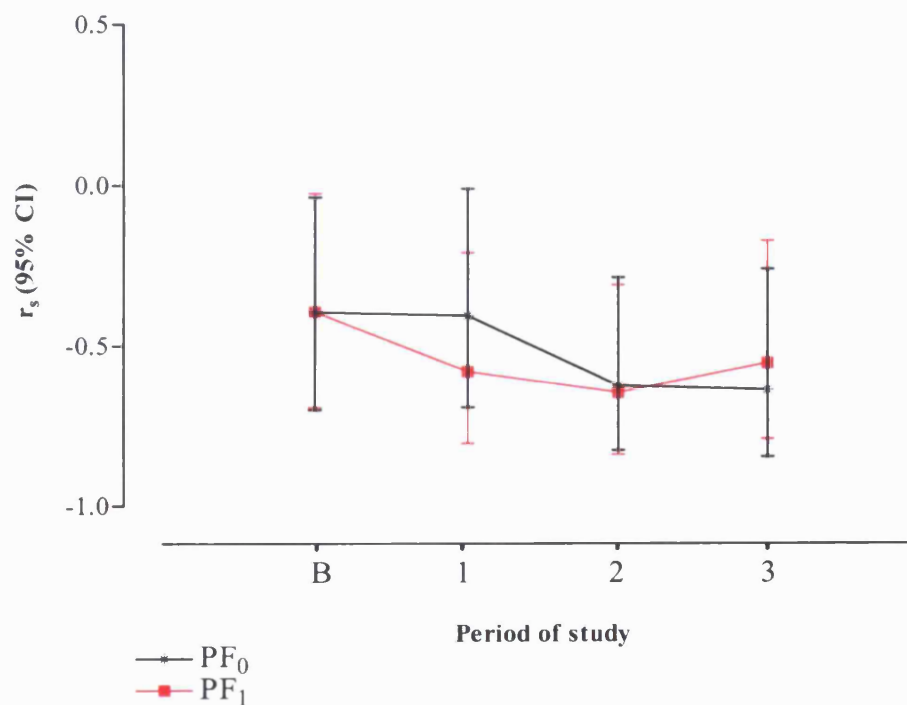
Chapter 9

Relative sensitivity of lung function parameters

9.1 Introduction

Peak flow has been the parameter of choice for monitoring asthma. Its role in self-management is unclear, particularly in paediatric asthma (chapter 2). In stable asthma, peak flow recorded on a meter is comparable with that recorded using spirometry (chapter 4) and spirometry has been advocated for monitoring adults and children with asthma [132,133]. Spirometry provides a number of other parameters in addition to peak flow which offer more detailed information about changes in lung function. In children with asthma, it is possible for PEF to be within normal limits despite reduced lower flow rates (FEF_{25-75}) [86]. This is true when they are asymptomatic [86,101] and show no clinical signs [100]. In addition FEF_{25-75} has been shown to be more sensitive than FEV_1 during a wheezing episode [144].

During episodes, our data demonstrated that PEF was more sensitive than FEV_1 (chapter 7). The aim of this analysis was to determine the relative sensitivity of PEF and other lung function parameters, during the trial as a whole.

9.2 Methods

9.2.1 Subjects

Lung function data were available for all 89 children who completed the study. The high numbers of lung function performed meant that for sixteen weeks, twice daily recorded results were stored. A sub-sample of nineteen representative children from each group was chosen for this analysis because the format of the data rendered this analysis very laborious. To prevent selection bias, the first nineteen children randomised into each of the two randomisation groups were included in this analysis.

9.2.2 Lung function data

All valid lung function data (section 3.3.4) from the thirty eight children were included in the analysis. All data were normalised to the best value for that child recorded during the run up period (section 6.4.2). Linear regression was used to determine relationships between the lung function parameters: FEV_1, MMEF and PEF.

9.3 Results

Data are presented for 38 children, 19 in each group (table 9.3.1). There were no differences between the groups in this sub-sample of children. The mean best value of FVC, FEV_1 and PEF during the run up period was above 95% of predicted value in both groups (table 9.3.1).

Table 9.3.1 Characteristics of children who were included in this analysis

		PF$_0$ n=19	PF$_1$ n=19	significance
Sex[1]	(% male)	8 (42)	13 (68)	ns
Family history asthma (report) [1]	(% yes)	8 (42)	9 (47)	ns
Severity [1]	(% BTS>2 [6])	2 (11)	6 (32)	ns
Ever admitted[1]	% yes	8 (42)	9 (47)	ns
Age at diagnosis [2]	Median (range)	2.5 ($^6/_{12}$- 12)	2 ($^4/_{12}$-9)	ns
Age at recruitment[2]	Median (range)	9 (7-14)	9 (7-14)	ns
Best FVC as % of reference[2]	Mean (SEM)	98.4 (2.58)	100.61 (2.8)	ns
Best FEV$_1$ as % of reference[2]	Mean (SEM)	95.5 (2.6)	99.4 (3.72)	ns
Best PEF as % of reference[2]	Mean (SEM)	103.9 (2.82)	114.0 (6.15)	ns

[1] Chi-squared test
[2] Non- parametric Mann Whitney U test
[3] Unpaired t-test using best from run up data

These data suggested that PEF measured during a forced vital capacity manoeuvre, was more sensitive than the corresponding FEV$_1$. In other words, for a given change in PEF the change in FEV$_1$ was smaller (both expressed as percent best). In the majority of cases PEF (% best) was lower than the corresponding FEV$_1$ (% best) for both groups (figure 9.1.1). The slopes were variable but in general for a given change in FEV$_1$ change in PEF was greater. The variability in the slopes meant it was not possible to calculate a mean regression line. MMEF was more sensitive than FEV1 (figure 9.1.3) but the increased variability of MMEF makes it unreliable (figure 9.1.2, 9.1.3).

Reference to figure 7.3.1.3 suggests that these observations also apply to data collected around acute episodes.

These data suggest that when PEF and FEV_1 were measured during the same manoeuvre, using a pneumotachograph, PEF was more sensitive.

Figure 9.1.1 Relative sensitivity of PEF and FEV$_1$ by group: regression for individual subjects

PF$_0$

PF$_1$
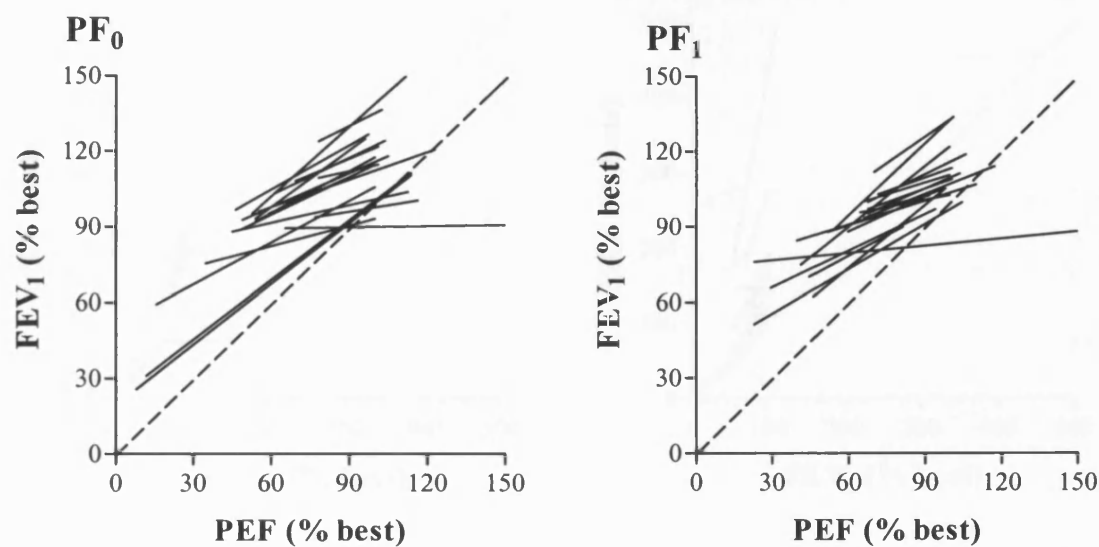
Figure 9.1.2 Relative sensitivity of PEF and MMEF by group

PF$_0$

PF$_1$
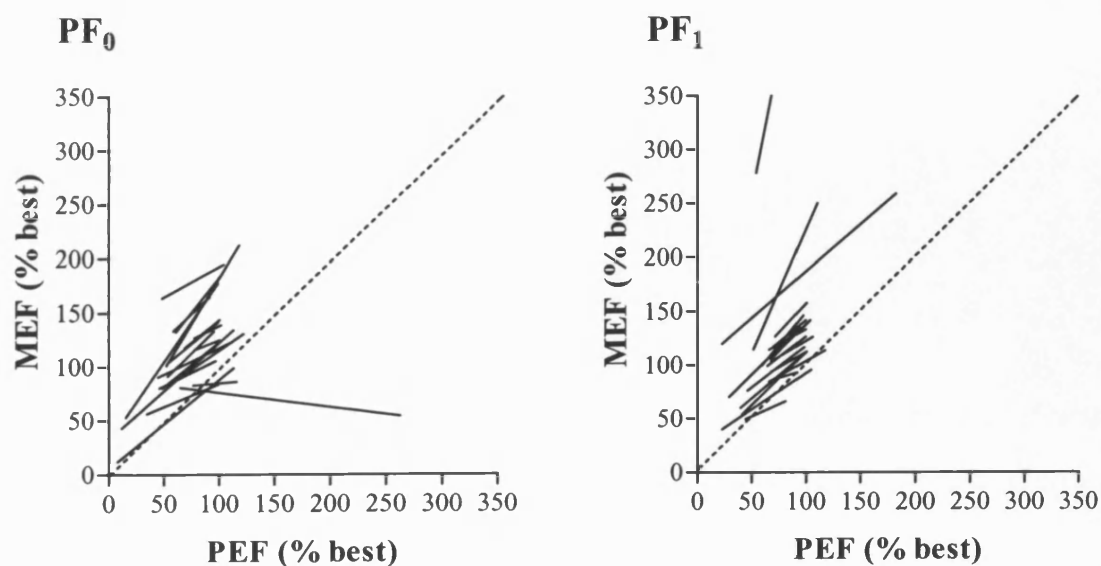
Figure 9.1.3 Relative sensitivity of PEF and MMEF by group
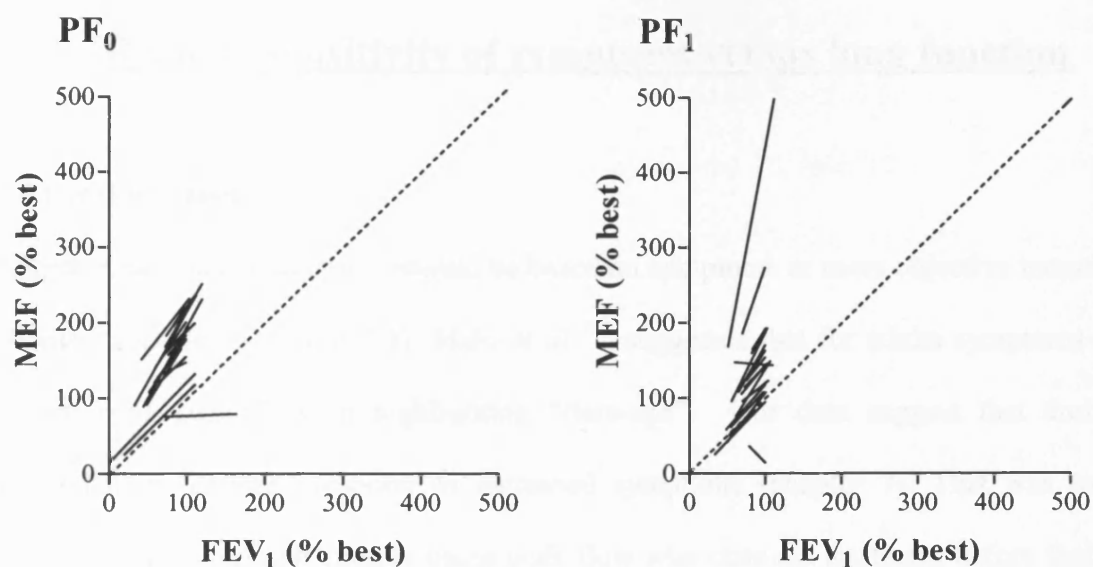
Chapter 10

Relative sensitivity of symptoms versus lung function

10.1 Introduction

Whether asthma management should be based on symptoms or more objective measures of disease is unclear (section 2.3). Malo *et al* [145] suggested that for adults symptoms are as effective as peak flow in highlighting "flare-ups". Our data suggest that during an exacerbation, children respond to increased symptoms (chapter 7). This was true for children managing their asthma using peak flow who changed treatment before their peak flow reached the thresholds for action displayed on their self- management plan (figure 7.3.1).

The aim of this analysis was to determine the relative sensitivity of symptoms versus lung function, in children with asthma.

10.2 Methods

10.2.1 Subjects

All 89 children recorded both symptoms and lung function during the trial. Seventeen children never scored more than 2 in their symptom diary. Seventy-two children recorded a score of 3 on at least one occasion and thirty children a score of 6 at least once.

The range of possible symptom scores was 0-9. This was a composite score of three groups of 0-3, representing nocturnal symptoms, daytime symptoms and symptoms experienced during activity. Only those children who had recorded a symptom score of 3 at some time during the study were included in this analysis.

Lung function data and the written diary data for the corresponding day were stored in a database. Percent best value for each measure of lung function was plotted against symptom score and a regression line calculated. Assuming that the symptom score was the independent variable (a), the intercept was calculated to determine the level of lung function (y) at which the child experienced symptoms which should have resulted in a change in self-management. The calculation $y = (a)x + (b)$ was applied to the data where y= resulting percent best lung function; a = symptom score; x= slope angle and b= intercept. Based on the response to episode data (chapter 7, figures 7.3.1.3 and 7.3.2.2), symptom scores of 3 and 6 were incorporated into the equation as the levels at which children might have increased preventer therapy and commenced oral steroids respectively.

10.3 Results

Characteristics of children included in this analysis are shown in table 10.3.1. Between group analysis showed that the children in the PF_1 group were significantly younger when they were given a diagnosis of asthma. The difference in sex distribution between the groups merely reflects the mal-distribution in the make up of the groups as a whole (table 6.5.1.2).

Generally as symptom score increased, lung function declined (figures 10.3.2 & 10.3.3). In the majority of cases lung function declined as symptoms increased. However, symptoms appeared to be more sensitive as they often had to increase dramatically before an appreciable change in lung function was detected. In some cases, symptom score increased greatly without any change in lung function. Symptoms were much more sensitive than any lung function parameter. Additionally, PEF was more sensitive than FEV_1 and FVC.

Table 10.3.1 Baseline characteristics of children who were included in this analysis

		PF$_0$ n=39	PF$_1$ n=33	significance
Sex[1]	(% male)	15 (39%)	24 (73%)	p= 0.05
Family history asthma [1]	(% yes)	17 (44%)	14 (42%)	ns
Severity [1]	(% BTS>2 [6])	9 (23%)	8 (24%)	ns
Ever admitted[1]	% yes	13 (34%)	13 (39%)	ns
Age at diagnosis [2]	Median (range)	6 ($^{6}/_{12}$-12)	3 ($^{4}/_{12}$-12)	P=0.03
Age at recruitment[2]	Median (range)	12 (7-14)	11 (7-14)	ns
Best FVC as % of reference[3]	Mean (SEM)	96.8 (1.96)	97.3 (1.96)	ns
Best FEV$_1$ as % of reference[3]	Mean (SEM)	94.9 (2.01)	94.6 (2.33)	ns
Best PEF as % of reference[3]	Mean (SEM)	104.6 (1.89)	103.1 (3.65)	ns

[1] Chi-squared test
[2] Non- parametric Mann Whitney U test
[3] Unpaired t-test using best from run up data

Figure 10.3.2 Symptoms only group (PF_0) relative sensitivity of lung function parameters and symptoms.

PF_0

PF_0

PF_0

PF_0
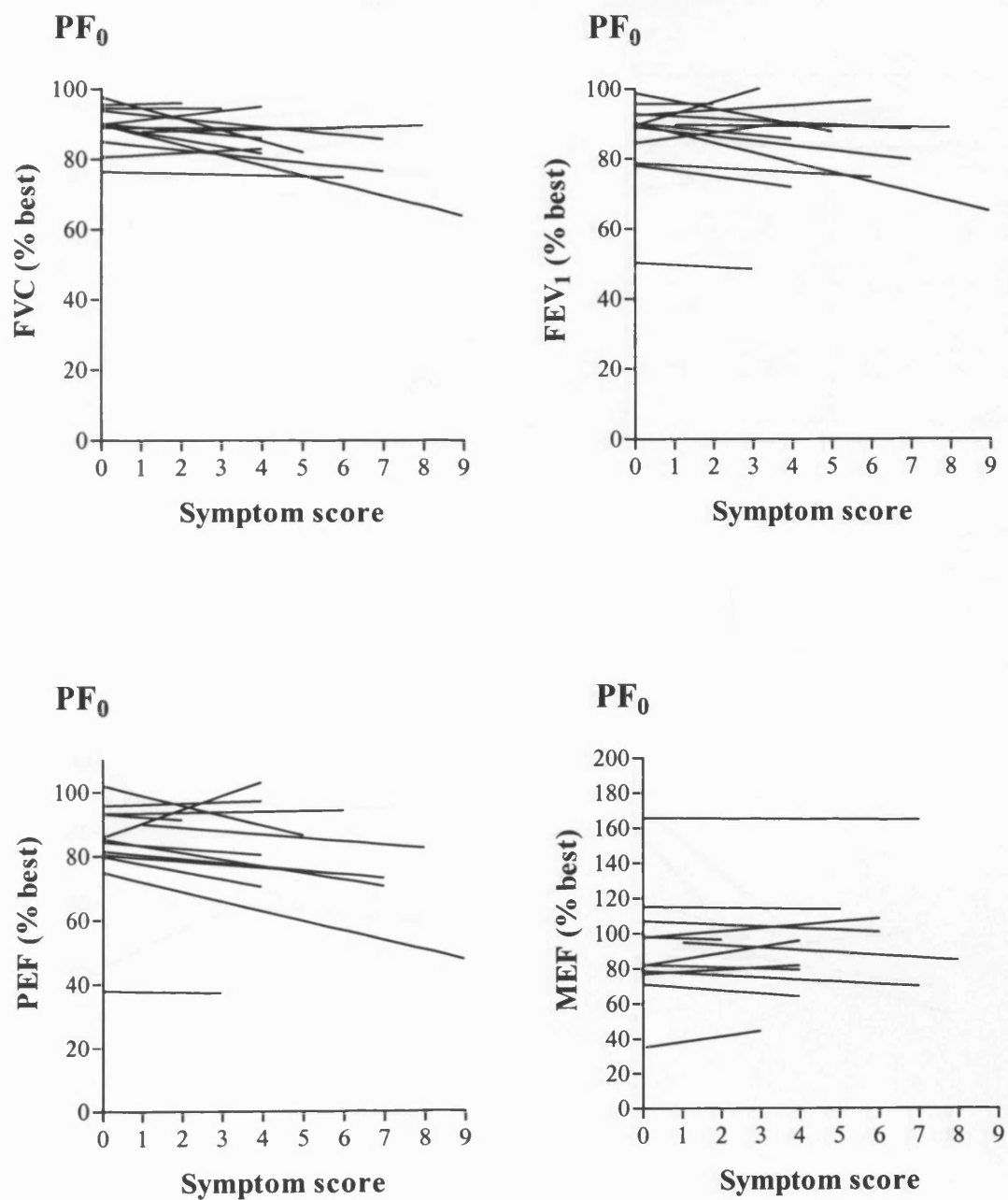
Figure 10.3.3 Peak flow plus symptoms only group (PF₁) relative sensitivity of lung function parameters and symptoms.
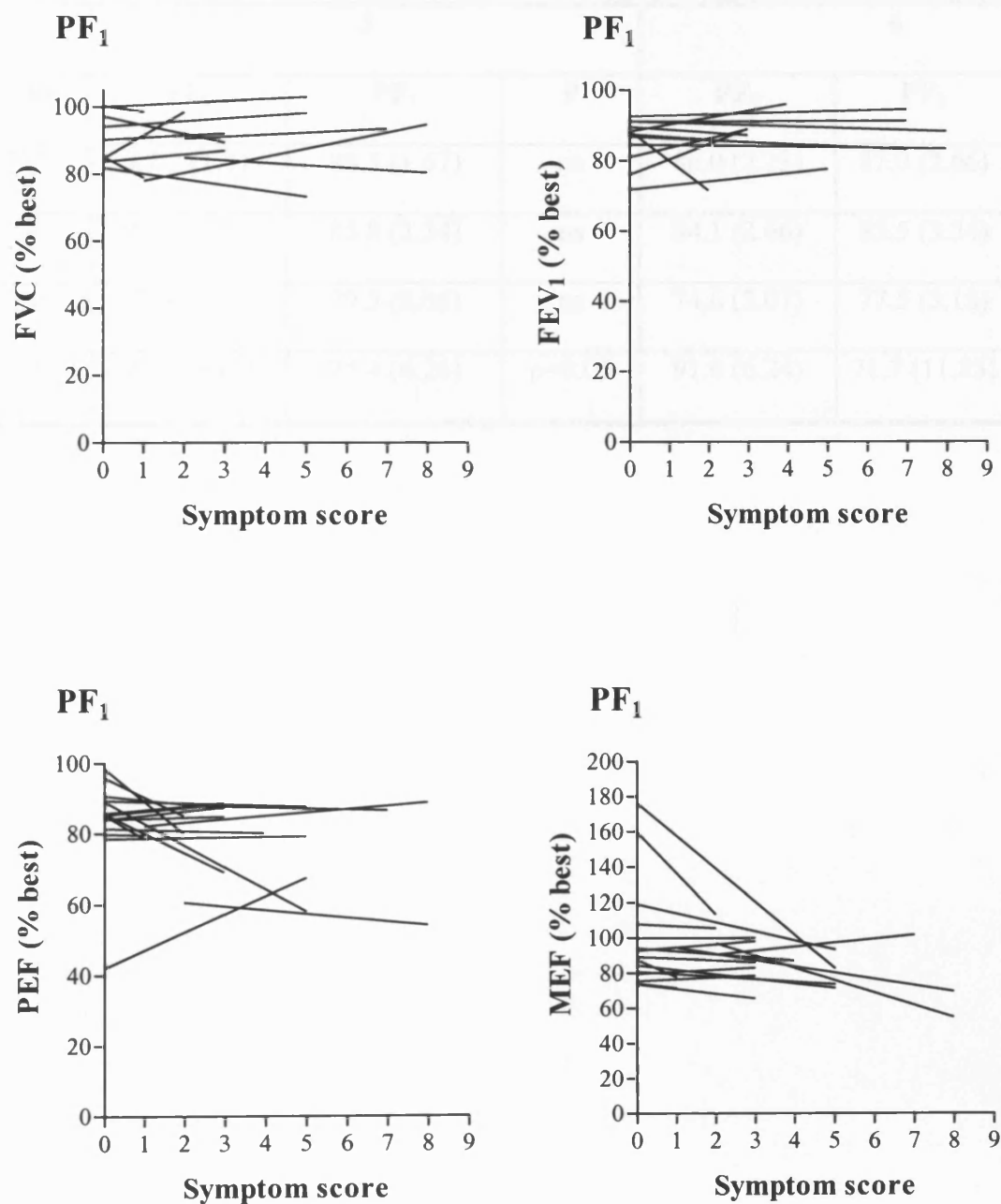
Table 10.3.2 Predicted mean levels of lung function (% best) calculated from symptom scores of 3 & 6 when children might have altered treatment

Group	3			6		
	PF_0	PF_1	P	PF_0	PF_1	p
FVC	87.2 (1.9)	88.5 (1.67)	ns	86.0 (2.23)	87.0 (2.66)	ns
FEV_1	85.7 (1.78)	85.8 (2.34)	ns	84.1 (2.66)	85.5 (3.34)	ns
PEF	77.9 (2.73)	79.5 (2.08)	ns	74.6 (3.07)	77.5 (3.18)	ns
MEF	93.5 (6.12)	75.4 (6.26)	p=0.05	91.0 (6.24)	71.7 (11.85)	ns

SECTION V

DISCUSSION AND FUTURE DIRECTIONS

Chapter 11

Discussion and future directions

The concept of self-management is familiar to any patient with asthma. They make treatment decisions on a daily basis, for instance by taking reliever medication when they feel unwell. This is true even for young school children. Self-management has been shown to be useful [26]. Difficulties arise in determining which aspects of self-management are responsible for the benefits (chapter 2). The term self-management has been used throughout the present study, despite the fact that parents and children were involved in the education and the younger children may not have made decisions alone to alter treatment. This is the conventional term for management of asthma at home. It is widely used and recognised by asthmatic patients. Studies involving children and adults use this terminology although other terms such as home management have been suggested[51]. Whilst this may be more appropriate for children, particularly in the younger age groups, it is important to consider the impact this may have on the families concerned. Phrases such as "self-management" and words such as "reliever" and "preventer" are well recognised, changes without discussions with bodies such as the National Asthma Campaign may generate confusion for patients who are "self-managing". This is particularly relevant for those children whose parents may suffer from asthma and be extremely familiar with the terms in use.

Peak flow measurement is widely accepted as a means of monitoring asthma but in terms of self-management, benefits seem to be limited to highlighting deteriorations in patients with severe disease [42,57]. In children, self-management studies have demonstrated varying degrees of success and only one study directly compared symptom and peak-flow based management, the results of which were inconclusive [41]. The question of the role of peak

flow is an important one, since currently it is the only relatively cheap, widely available means of gaining lung function information.

The aim of this study was to assess the additional impact of peak flow monitoring on symptom-based guided self-management for schoolchildren with asthma. The hypothesis was that incorporating peak flow measurement into guided self-management protocols for this group would improve the outcome. The main outcome measure was mean change in symptom score. Secondary outcomes included use of health services, quality of life measurement and lung function.

Figure 11.1.1 Conceptual model of asthma management

Disease pathology (lung function)

+ therapeutic efficacy

+ training/ experience

Impact QOL

Response to disease level (behaviour)

Awareness = perception (Symptom Score)

+ ability to respond (knowledge)
+ motivation (compliance) +
+ memory (some children never remember!)
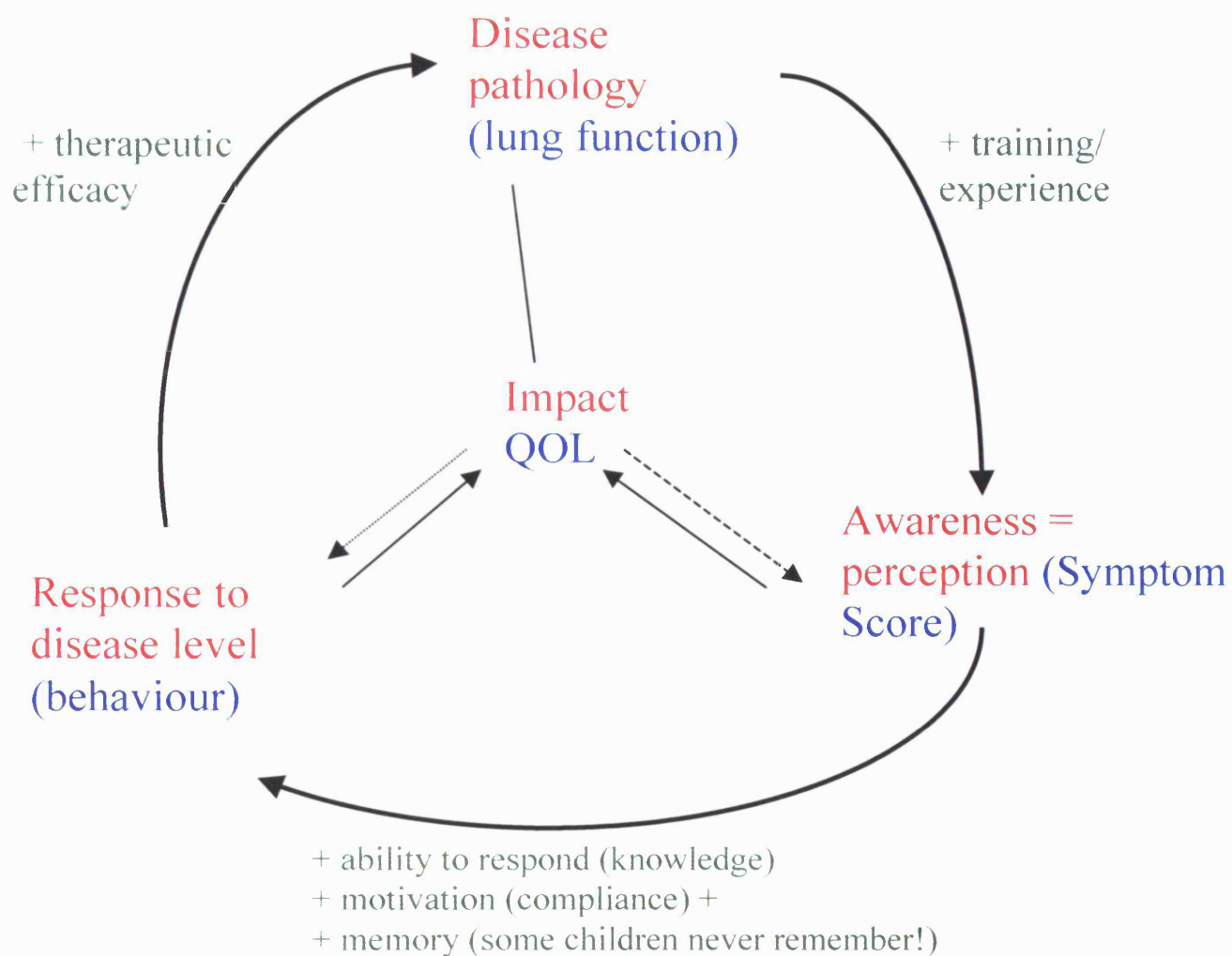
Conceptual model of asthma

There is a complex interplay between objective and subjective measures of disease severity involved in asthma management (figure 11.1.1). In the present study, each aspect of self-management (red text) was represented by a surrogate (blue text) which signified data collected. In addition, consideration was given to the processes (green text) involved in self-management. The most commonly used objective assessment of condition is peak flow. It is used as a marker for disease severity and offers information about maximal flow of air through a peak flow meter. Lung size [54], equipment [65,66] and technique [95,96,137] all effect peak flow although training can improve the latter [90,146]. More detailed information can be obtained using spirometric tests which proffer greater information about air flow (section 3.3.2). Subjective information about impact can be gained from symptom diaries. This information is valuable where recording is conscientious, although this is difficult to ascertain and poor compliance is commonplace [74,147], particularly in adolescence [73].

There are problems with the relationship between these measures. Asthma is highly variable between-subjects and within-subjects over time. Some patients may experience small changes in lung function, to which they are highly perceptive and sense the need for treatment. Other patients may be extremely insensitive to large changes in lung function and be unlikely to take rescue therapy, even when their respiratory function is compromised [138,148].

The contribution of objective measures of lung function was found to be questionable in this group of school children with mild asthma. However, the children demonstrated a willingness to participate in self-management and alter treatment. They were motivated to comply for a substantial period of time and could remember to do so.

This study found no between-group differences in symptom score, lung function parameters, quality of life or use of services over time when asthma was managed by symptoms alone or peak flow plus symptoms.

This discussion will focus on the methodological issues arising from the study and then consider the collection, validation and analysis of the data collected in turn. The intervention itself will be discussed and finally the secondary issues arising from the study will be discussed. At each point, consideration will be given to further possible research arising from this study.

11.2 Methodological issues

11.2.1 Study Design

A randomised controlled trial is considered the "gold standard" of trial design [149,150]. The randomised controlled trial eliminates the risk of bias by providing the best chance that the groups are identical in their make up. The investigator was blind to randomisation group up to the point of randomisation to prevent bias. Following randomisation, the trial was not blinded because assignment determined management, therefore the investigator and clinicians (GPs and hospital consultants) responsible for patient care were aware of group assignment. An open design was employed because the plan had to be available to all professionals involved in the care of the child. This is a key component of self-management which enhances communication between health professionals and families involved in asthma management [17]. The investigator prepared the self-management plan but was not responsible for clinical management. Clinicians responsible for patient care were aware of the instructions and thresholds incorporated into the plan. By chance, significantly more boys were randomised to the peak flow group. Stratification by sex would have prevented this. Since both groups received management plans this study did

not have a "control" group. This study did not answer the question "is guided self-management effective?", as this had already been demonstrated by a number of studies (chapter 2)[26,30,42,44,48,159].

11.2.2 Recruitment and subjects studied

One potential problem was that the study may not have had sufficient power to detect a difference in symptom scores between the groups. One hundred and seventeen children were recruited into the study and a total of 90 were randomised. The sample size calculation of 106, based on data from Glaxo Wellcome (personal communication) suggested that 53 children in each group would be needed to have 80% power of detecting a difference in symptom score of 1.5 at the 5% level. A symptom score difference of 1.5 was thought to be clinically relevant, on a scale of 0-9. Withdrawals prior to randomisation and lack of objective information concerning the validity of the written diary data meant that this was an unrealistic goal and should not be used as a main outcome measure in clinical trials. The mean symptom scores during the final study period for each group were 1.27 for the PF_0 group and 1.02 for the PF_1 group. With a possible range of 0-9 this small difference was not clinically significant. A priori predictions suggest that the trial is underpowered. In retrospect the groups were so similar that for this difference to reach statistical significance, approximately 800 children would have to be studied.

In retrospect an alternative method may have been to consider the proportion of acute episodes in each group. The number of acute episodes was not a primary outcome measure. There was a small difference in favour of the PF_1 group. For this difference to be statistically significant as an outcome, 95 children in each group would have to be studied to have 80% power at the 5% level.

Recruitment may have been enhanced if patients had been recruited during hospitalisation but children would not have been stable at this time. In a study of self-management Charlton et al [49] recruited 91 children over a two year period, 59 of whom were in-patients at the time of enrollment. Seventy-seven of these children completed the study and fulfilled requirements (85%). In a community based study, the same group recruited 115 patients after inviting them to make an appointment with the practice nurse but they do not provide information about numbers who failed to respond or withdrew after recruitment[41]. Eighty-nine (75%) of our sample completed the study.

Sixteen weeks was the length of study period. This length of time was considered long enough for children to experience an episode but short enough to promote compliance. Trial demands were high and far in excess of any current expectations on patients in the clinical setting. The expectations were that children would perform lung function and complete diaries daily, along with making time for visits every four weeks. It was anticipated that following the run up period a small number of children would withdraw. Predicted withdrawals at this stage were not as high as the twenty-seven children who voluntarily withdrew prior to randomisation. The biggest single reason for non-randomisation was voluntary withdrawal (n= 23). Some children reported problems with the spirometry manoeuvre, but the majority simply did not want to continue (figure 6.3.2.1). This highlights the risk of potential bias. The results are based on data from children who were committed. This may affect the outcome and reduces the generalisability of the results. Extrapolation of this factor to the general population suggests that for every 117 children asked to perform intensive monitoring for a four week period (equivalent to the run up period), 77% will provide adequate information. This is high, particularly considering that in clinical practice, poor control is often a reason for requesting this type of monitoring. These 117 children were 26% of the 457 children

invited to participate and therefore only 20% of the original eligible children (figure 6.3.1.1). Compliance with peak flow recording in children is high but declines rapidly over a period of 4 weeks [151]. Group mean compliance with diary recording during the 4 week run up period in the non-randomised group was just above 50% (table 6.5.1.2).

The baseline characteristics of the non-randomised and randomised children were compared, along with their run up data (table 6.5.1.2). The children who voluntarily withdrew were slightly younger than those who completed the study and were significantly less compliant with spirometry and diary completion. They were significantly more technically competent but the reduced compliance led to much less valid data being available (table 6.5.1.2). This non-randomised group may have become more rapidly bored by the demands of twice daily spirometry and once daily diary completion. Only one (male adolescent) child withdrew following randomisation, citing non-compliance as the reason for withdrawal. Despite repeated attempts to contact this boy, no further data were obtained following withdrawal. Children were told at recruitment that they would be participating for four months. Any child who felt unable to commit to this time scale was not recruited.

Most of the children (94%) were managed in primary care. The children had not received oral corticosteroids or changed treatment for one month prior to randomisation and were thus defined as stable. Studies comparing self-management with doctor-management have shown improvements in morbidity with time[39]. Often in these studies, patients in the control group were monitored more regularly as part of the study protocol [32] or a before an after design showed changes in morbidity [27]. This was not seen in the present study, perhaps because the investigator was not involved in management and any health problems were dealt with by the GP. Other studies of self-management have recruited patients during

or immediately following a hospitalisation [57] or have optimised treatment at the start [42].

Participants had to have physician-diagnosed asthma and be in receipt of regular preventer

therapy. Any child who reported not taking or needing preventer therapy was not recruited

(figure 3.4.1). Children volunteered after being approached and the study therefore had

selective entry. Children who participated may have done so for philanthropic reasons or

because they had poorer asthma control. However, if the latter had been the case an overall

improvement as seen in other studies [31,32,39,41,55] would have been expected. In patients with

severe asthma, Cowie *et al* [57] demonstrated improvements in all participants over time.

After the run up period, the children in the present study did not show a preferential change

over time.

Further studies

These children were stable asthmatics and in this group who experienced a limited number

of attacks, PEF may not be the best measure. However, for those children who experience

more attacks and are unstable, this kind of in-depth study requiring large numbers of

measurements may be inappropriate[130]. A simpler design with fewer, more specific

outcomes including the need for emergency treatments would be more appropriate.

This study was not designed to consider the effect of psychological factors or cognitive

development in either the compliance with or the outcome of guided self-management.

There may be certain personal factors which render some children more able to cope with

self-management than others. These could be physical, relating to length of time with

disease or previous experience; or psychological, relating to such issues as self-confidence

or intelligence. An exploration of these issues would be helpful to target existing

programmes and in new methods to cope with those who find self-management difficult.

11.3 Data collection, validation and analysis

11.3.1 Diary scores

Quality of data

Written diary compliance was over 74% for the duration of the study in both groups. Studies attempting to measure compliance with diary completion have demonstrated discrepancies between written and electronic methods [74,147]. Hyland *et al* [74] showed that there can be a large discrepancy between reported compliance and actual compliance with peak flow diary recording. Verschelden *et al* [147] demonstrated that not only does compliance vary between written and electronic recordings when carried out covertly but that a small number (10%) of the written values may be inaccurate. In the present study some diaries contained gaps. Others contained complete pages of symptom scores of zeros which suggested that they may have been completed retrospectively and may thus be inaccurate [75]. At times, blocks of colour were seen which suggested retrospective completion [74]. The accuracy of written diary data was assessed by recording responses to the single question in written and electronic form, the numbers of additional doses of bronchodilator taken (figure 6.5.2.2.3). Written values were discrepant by as much as 2.5 puffs (mean) higher or lower than machine recorded values. The date and time of the machine data entry was stored, which is an advance on written diaries, but doesn't rule out cheating. The fact that this information was unavailable for the written diary data meant that discrepancies were likely to have occurred if the written diary was not completed at same time as the electronic diary. This added to speculation about accuracy of diary data resulting from retrospective diary completion or fabricated data [4,147, 151]. In view of this, additional outcome measures were used in this study.

Results of clinical trials in asthma often use outcome measures recorded in written diaries [32,56]. These include diary recorded PEF [30] and symptom score [49]. Information recorded in

diaries is important[152] and the discriminatory properties of diaries have been demonstrated in children[89]. However, information obtained is valuable only if it is reliable. The reliability of peak flow recording has been called into question [151]. Some studies mention problems with diary cards and the resulting data. Turner *et al* [55] reported that some of their data could not be evaluated because of non-compliance with diaries, visits or medications. Ignacio-Garcia and Gonzalez-Santos [31] reported difficulties in diary cards on symptom free days and Allen *et al* [38] reported taking measures to enhance diary cards. Malo *et al* [56] directly compared PEF and symptoms recorded in a diary. They confronted the problem of non-compliance by asking subjects not to invent values if they forgot and highlighted the problem of being unable to objectively assess compliance. Other studies do not mention assessing compliance with diary completion even when subjects were expected to complete diary cards for as long as six months [34] or the main outcome was diary recorded symptom score [49].

Additional measures were taken to validate the diary data in the present study. The finding of the negative primary outcome was confirmed by separating the symptom score data into symptomatic and symptom free days and repeating the analysis (section 6.6.1). In addition, the relationship between the symptom domain of the quality of life questionnaire was assessed using correlation (figure 6.5.2.3.1). Correlations were weak but reached significance for the PF_0 group throughout the study. This was not true for the PF_1 group. It may be that symptoms became a focus for those children who were not recording peak flow and as a result they were more able to recall them when completing the questionnaire.

We found no difference in symptom score between groups over time. The PF_0 group showed a fall in compliance with diary completion during the trial period with a greater fall during the last study period. Changing compliance altered the amount of available data

and may have influenced these results, increasing the risk of a type II error because of the reduced amount of data in the analysis. The peak flow group were perhaps more fastidious when they were well and produced higher scores for those days. The authors of one study [31] reportedly detected problems with diary data on symptom free days although they did not discuss this fully. Children in the PF_0 group were more compliant with the diary completion. Additionally, these children were less likely to complete the lung function tests when they were unwell, although the opposite was true for the PF_1 group (table 7.3.1.2). Children thus seemed more likely to comply with the method of monitoring to which they were assigned. However, the peak flow group did not use PEF for management (chapter 7). Towards the end of the study, when compliance deteriorated, diary completion may have become more discriminating, with children completing the diary only when they had symptoms worth reporting. Despite these compliance issues, the lack of difference in the primary outcome (symptoms) was supported by the symptom data from the QoL questionnaire. The consistency of the results irrespective of outcome measure suggests that the negative result of the trial is valid.

Further studies

Further work using symptom score as an outcome measure would involve recording a score electronically, together with the date and time of recording stored alongside. This would allow for compliance with the diary to be more objectively assessed. In addition, a shorter period of recording may enhance compliance and although there would be perhaps be less data, it may be more reliable[151]. Compliance with diary completion will be poor if patients do not consider it to be worthwhile. A more pragmatic approach would lead to higher quality data.

11.3.2 Spirometric data

Quality of data

Since spirometry recorded at home is unsupervised, an accompanying paper diary to record problems has been recommended [132]. Children completed a paper diary alongside the electronic spirometry but this was to record symptoms and not problems with equipment performance. The fact that compliance deteriorated with time was not surprising [58,147]. The children were fully aware that the date and time of each session was recorded which may have enhanced compliance [75]. Children rarely reported problems with equipment. Where machine error or non-repeatability was recorded by the DSS, the manoeuvre had been performed and therefore children had complied. Twice daily spirometry was demanding, particularly during exacerbations.

The fact that participants performed the tests at home, meant that the manoeuvres could not be assessed to see if they were acceptable according to full ATS criteria [92] although the DSS recorded within-session reproducibility. Within-session reproducibility of two blows where the sum of $FVC+FEV_1$ was within 5%, provided the only objective assessment of manoeuvre performance. The amount of valid data available for analysis was calculated as the multiple of compliance (any attempt to record lung function at the correct time) and technical quality (within- session reproducibility of less than 5% $FVC+FEV_1$). Reduced compliance towards the end of the study reduced the amount of data available for analysis (table 5.2.2.2). Pelkonen et al[133] demonstrated higher compliance. However, the children in that study were newly diagnosed asthmatics who were probably enthusiastic and performed home spirometry for shorter periods of time. The best PEF obtained during the run up was used to calculate PEF thresholds for self-management. Therefore percent best FVC, FEV_1 and FEF_{25-75} were used in the analysis. Standard deviation scores were not used because they could not be used as self-management thresholds. The analysis showed

no differences between the groups over time in any of the lung function parameters. The chance randomisation of more boys into the peak flow group meant that a sex, group, time interaction analysis was important. A sex, group, time interaction was demonstrated for PEF as a result of a small drop in group mean PEF amongst the girls in the PF_0 group. However, it was not maintained (6.6.2.1.5).

The highest PEF from a technically acceptable manoeuvre, performed unsupervised during the run up was used to calculate thresholds for management for the duration of the study. Group mean best results were lower for FVC and FEV_1 and higher for PEF (table 6.6.2.2.3). The best values for PEF were higher (%) than those in the general population [135]. Conversely, the group mean values for FVC, PEF, FEV_1 during the trial were around 80% of best value obtained during the run up period (section 6.6.2). A number of explanations exist for these observations:

- Children may have used their reliever medication prior to performing manoeuvres leading to an elevation of lung function.

- There was a machine error. However, machine errors were removed from the analysis.

- PEF may be artificially elevated as a result of coughing or spitting into the machine or children may have performed PEF rather than an FVC manoeuvre (see chapter 4) which could also explain the elevated best MEF values (figure 9.1.2, 9.1.3). However, the machine test for reproducibility should have rejected any manoeuvre where this occurred.

- The majority of subjects were managed in primary care (94%) so that these relatively good values may be genuine;

- Spuriously high values for PEF may have been chosen for some children, despite the criteria applied, elevating the group mean.

Three best values of PEF recorded during the run up were outliers. Two of these children reported a symptom score of 0 over 98% of the time, the third recording a score of $\geq$ 3 100% of the time. In addition, for the same manoeuvre, these children all recorded values above their predicted values for FVC and FEV_1 suggesting that these were genuinely high values and these children had better-than-predicted lung function. The implications for the choice of PEF in individuals, in which to base their management are discussed in more detail in section 11.4. Other studies of self-management have found no difference in lung function, even where differences were found in more subjective measures of assessment [36].

Further studies

Evaluation of available data and the amount of information available is important when carrying out spirometry. It would be valuable for future studies to have more information about individual recordings within a session. This would allow within-session reproducibility to be considered. Additionally, the DSS produces values for each lung function parameter. It would be useful to be able to retrospectively assess the curves for validity.

11.3.3 Quality of life data

Quality of data

The QoL questionnaire was completed at each visit so that its reliable recording was assured. The PAQLQ has been extensively validated [116] and used in research protocols [138]. Children completed the questionnaire in the presence of myself, a trained interviewer. The fact that I was the person involved with recruitment, training and collecting data from these

children was a potential source of bias. The responses given by the children may have been influenced by the fact that I was carrying out the study and over time developed a relationship with the children. The developers of the PAQLQ highlight the potential for bias, particularly when using the interviewer administered version of the questionnaire and suggest ways in which this can be reduced [122]. Since results obtained as a result of the interview were numeric, analysis was unlikely to be influenced by this factor.

There was a weak but significant correlation between the symptom domain of the questionnaire and the symptom diary results for the week prior to each visit (figure 6.5.2.3.1) in the peak flow group. The fact that the correlations were poor was surprising when all the children used symptoms for management. There is no gold standard. The quality of life data is perhaps more credible because it was collected at each visit, subjects were given a set time frame to think about and the responses were considered carefully during its completion (section 11.3.1).

A paired t-test of baseline visit and randomisation visit demonstrated that improvement in quality of life in the PF_1 prior to randomisation reached statistical significance and increased by an amount considered to be clinically significant by the questionnaires designers [124]. The questionnaire was administered at the start of every visit and therefore at the time of completion of these two questionnaires, the children, parents and investigator were unaware of randomisation group and this cannot have influenced the results. This improvement could be attributed to the Hawthorne effect [153] where participants in trials exhibit changes in behaviour merely by taking part. Bouchet *et al* [154] have suggested that QoL results are particularly susceptible to this effect. The PF_1 group were diagnosed earlier and had suffered from asthma for longer, were more severe and were more likely to have been admitted to hospital although none of these trends reached statistical significance.

During the run up period the group mean diary symptom score was lower than that for the PF_0 group.

11.3.4 Use of health services

Quality of data

Use of health services and school absence were recorded retrospectively at each visit, for the period since the previous visit. It was not verified. The four week period was relatively short to recall significant occurrences (table 6.6.4.1.1, 6.6.4.1.2). It was therefore likely to be accurate. One apparent discrepancy arose with the number of children requiring an increase in preventer therapy. The diary data suggested that slightly fewer children increased preventer therapy than in the questionnaire data. This could have arisen as a result of differences between parent and child reports. The parents often responded to the questionnaire data whereas the children were asked to complete the diaries. In light of the differences arising in QoL scores (Chapter 8, section 11.5.2), it is not surprising that small differences arose here.

The very small number of events reported made analysis by period inappropriate for these data. Direct comparison of adverse events between group for the run up period and mean monthly events during the trial showed no difference.

The statistically significant increase in days of doubled inhaled steroids in both groups is striking. There are several possible explanations. In most clinical trials patients improve with time, possibly because recently symptomatic subjects tend to be over-represented. In the present study, stable asthmatics were selected. The inherent variability of asthma means that on average, a deterioration in not unexpected. A more likely explanation is that families were "given permission" to vary treatment during self-management training, and hence were more liberal in the use of their training. The relative size of these effects is

impossible to predict. However, the significantly greater GP visits in the PF_0 group could suggest that in the PF_0 group the GP was consulted before any change was made. It is possible that having increased their inhaled steroids children made unplanned visits to the GP for review or to see whether further treatment was required. The timing of the GP visits was not recorded in the diary. The most important outcome of the trial should not be overlooked: there were no differences between the groups.

Self-management took place during the run up period suggesting that a number of children were already actively involved in this process.

Further studies

Health service utilisation data of this kind should be verified from other sources [50] and may be especially relevant in more severe asthma. Children with more severe disease may be unable to record large numbers of outcomes and fewer more specific measures are more appropriate for this group.

11.4 The intervention

The plan (appendix 2)

The self-management plans were based on plans used in clinical practice and data from other studies. The traffic-light system of colour coding was used for simplicity and parents and children were instructed together in its use. A separate pathway was provided if the child had a cold linked with an exacerbation. These two pathways were not separated for the analysis because the pathway the child followed was not recorded. Although children recorded cold or runny nose in the diary, it was unclear whether this related to allergic symptoms or a cold and therefore the two could not be differentiated. Any increase in

inhaled preventer therapy for more than two days or any oral corticosteroid use was considered to indicate an acute asthma episode.

Controversial use of doubling of preventer therapy was included as a standard recommendation at the time, although there is no evidence of efficacy [6]. This enabled us to assess the behavioural response of the children. The practice is widely used as an intermediate step for deteriorating asthma although it is not proven. Garrett *et al* [127] argue that doubling inhaled steroids has no effect and should be removed from self-management plans. Some children had used self-management prior to enrollment into the study. During the run up period sixteen children increased their inhaled steroids at some point, suggesting that this was common practice when they felt unwell.

Educational issues

There was no formal education package, or protocol to follow. The benefits of general education are limited. In their recent systematic review, Gibson *et al* reported that for adults, education alone without some self-management training, demonstrated little benefit in improving health outcomes [155], although increased knowledge could be demonstrated[34]. There is no comparable review in children although the review of educational interventions by Wolf *et al* [52] provides further information about education and improved outcomes. Group education [36] or a set package of advice[50] may have improved response. Because the educational package was not set, different children and their caregivers received different information depending on their level of interest, experience with the disease and the questions they asked. Self-management training was only given during the randomisation visit. Thereafter, the plan was discussed only to answer questions or to make changes if the child's treatment had been changed since the previous visit. It may have been valuable to discuss the plan at other times during the study, to act as a revision

session. A set package of information with planned updates and reminders would have ensured all participants received the same information and the self-management aspect of the study was uppermost in the minds of the children throughout. Other studies have demonstrated dramatic changes in outcome with set education packages. Madge *et al* [51] and Wesseldine *et al* [50] supplied fixed education packages including self-management to parents and children at discharge from hospital and demonstrated dramatic reductions in re-admissions.

It is possible to develop different education packages for different ages of children, in line with cognitive development. This may have been valuable in this study as the ages ranged from 7-14 years. Future work should consider the types of education for each age group and the optimum ages to teach with parents present or absent. Another person present during education may support learning and provide a reference point for forgotten information at a later date.

In summary, it may have been more valuable to provide a set package of education with regular revision sessions at each visit. This would have allowed the opportunity to reinforce not only previous information, but also self-management behaviours to encourage future use. Without revision, it is possible that the children and their parents simply forgot much of the training. However, since the researcher was also the educator, to avoid bias, another educator, blinded to randomisation group and education package would probably have been more appropriate. It may have been more valid to include other individuals to perform the education to prevent such bias.

PEF thresholds (& symptom thresholds)

Levels of peak flow at which to change treatment are controversial and choosing a level of peak flow at which to take action is inherently difficult. The three chosen levels of action in this study were based on those of Charlton et al [41]. Subsequent studies have suggested that this may be too low and higher thresholds may be more appropriate, such as 80% [49]. Levels for action were 70%, 50% and 30% of best value achieved during the run up period from a technically acceptable manoeuvre according to the machine criteria. This was pragmatic. Scrutiny of figure 7.3.1.3 suggests that the threshold of 80% would lead to overtreatment of many children whose clinical condition was stable and relatively symptom free. Defining child-specific targets may be useful, especially for those with wide discrepancies between symptom (perception) and physiological measures of severity. This demanding approach warrants further investigation (section 11.6). Until it is made clear whether the target for therapy is symptoms, lung function, bronchial responsiveness or long term airway remodeling (Table 2.1.1); it will not be possible to provide clear advice on guided self-management to families.

The question of what target PEF value to use to calculate the thresholds is problematic: the best recent value or the value predicted from reference data?

The present study used percentage of patients best PEF recorded during the run up period of the study, using the same equipment which was used during the study. Reddel et al [67] tested a series of calculations to assess which index of peak flow is most useful but this was done when patients were stable. The best value being taken as the highest single PEF value achieved during a two week recording period. Choosing the best result from a period of consistent recording is commonplace but poor technique can increase (e.g. coughing) or and decrease (e.g. poor effort) the best PEF. Only PEF values from technically acceptable

manoeuvres were used to counteract this problem but the unsupervised nature of this study meant that this was a possible factor. The group mean best values of PEF from the run up were higher than the predicted values in both groups (table 6.5.2.2.5). The median values were similar for the PF_0 group (107) and the PF_1 group (102) therefore this factor did not introduce any bias into the study but the presence of outliers reduced the power, increasing the scatter of the data.

Choosing the best value from a period of recording is difficult (section 11.3.2). What is the best value? Any spuriously high best values during the run up would produce a lower mean day to day value for peak flow (% best). Children in the PEF group would hit the threshold for change in treatment at a lower level of symptomatology and higher absolute values of PEF would determine changes in treatment. In addition, any absolute change in PEF represents a smaller proportion of a falsely high value. This would reduce the sensitivity of PEF and reduce the change in PEF in relation to FEV_1. Simply choosing the highest single value may be problematic in clinical practice. Brand et al [156] pointed out that the reference range for PEF is too wide to use as the basis for calculating PEF thresholds for self-management. Douma et al [76] highlight the risk of over-treatment if guidelines for level at which to change treatment are strictly adhered to. This is also true if the best value from which thresholds are calculated is inaccurate or unreliable.

There are a number of ways to select a reference value for self-management:

- Pre-treatment with beta-agonists or oral prednisolone to achieve optimum;

- The mean value from a period of monitoring after treatment optimisation is a possibility;

- Selecting the optimum from a series of supervised blows.

PEF does not equal pathology but if PEF was not relevant one would expect FEV_1 to be more sensitive because it is representative of larger and smaller airways. If PEF represents only large airways it misses significant pathology and one would expect FEV_1 to be more sensitive.

Further studies

Further studies need to take account of the widespread use of self-management for asthma and designs should allow children to use plans already in place. This aids understanding but requires guidelines for developing individualised plans.

11.5 Secondary questions

11.5.1 Response to episodes

During an exacerbation leading to a doubling of inhaled steroids, children in both groups responded to symptoms. Malo *et al* [56] studied adult asthmatics and concluded that symptoms and PEF were equally good at detecting "flare-ups" (figure 7.2.2). It was standard practice at the time, to advise children to double the dose of inhaled steroids at the onset of an episode. While this advice has recently been questioned[127], the scientifically valid data are limited. The present trial cannot resolve this issue.

As noted (page 148) the duration of the inhaled steroid episodes seemed to be less in the PF_1 than the PF_0 group in spite of the fact that lung function and symptom score were very similar in the days immediately preceding an increase in therapy. Knowledge of PEF did not seem to impact on the decision to increase inhaled corticosteroids but it may explain the differences following the increase. More reliever was used in the PF_1 group during the episode after an increase was instigated (Fig 7.3.1.3), this may have led to improved lung

function. Alternatively, despite instructions, it is possible that some children measured their lung function after using bronchodilator, knowing that it would give a "better" recording. It is impossible to determine the relative contributions of each of these factors. However, the similarity in the graphs prior to the increase in therapy demonstrates that PEF knowledge did not provide a more sensitive clue to the early detection of an episode.

The requirement for oral steroids was more difficult to assess. Only 10 children required oral prednisolone for 14 episodes and demonstrated increased symptoms scores and reliever use, and declining lung function in the few days prior to commencing oral steroids (figure 8.1.3.1). The small numbers made conclusions difficult and two children required prednisolone on more than one occasion therefore there is some repetition of subjects in these data. Cowie *et al* [57] in their study of peak flow versus symptom-based management in adults, found that PEF usefully highlighted a deterioration for patients with severe asthma. This must depend on the chosen PEF threshold. The present study involved children and there are no data available about who made decisions to increase treatment. In some cases, if parents instructed children to increase treatment, this could have been at a time when parents were disturbed at night by children coughing. The discrepancy between parent's reports, child's reports and objective cough recordings is recognised [83,85].

Episodes were behaviourally defined. This provided a means to identify principal factors which determined change in therapy. An alternative approach could have been to define episodes arbitrarily, based on change in symptoms or PEF, and to analyse patient behavior around such episodes. Although the data is available, this analysis is complex and it was not feasible within the timescale to develop and test the methodology to perform this far from standard analysis. This is an important topic for future research.

11.5.2 Relationship between parent's and children's perception of the impact of asthma

Juniper *et al* [111] suggested that caregivers were poor perceivers of change in their child's health status, based on poor levels of agreement between parents and child assessment of child's quality of life measured by kappa (κ). Agreement using κ measures the amount of exact agreement. Weighting κ provides proportional evaluation of agreement (section 6.4.6). The poor level of agreement reached despite this weighting, with a high level of association as measured by Spearman rank correlation suggests that although there is some correlation between scores, overall agreement is poor. Duffy *et al* [109] used weighted κ to show a high level of agreement between parents and children in a dysfunction score for juvenile chronic arthritis. It is not surprising that the levels of agreement were higher because children with arthritis may need more direct help from parents. However, the authors did not describe the amount of weighting applied to the data, a higher weighting will increase the value of κ.

The fact that there were between -group differences in the relationship between caregiver's and child's quality of life scores (figure 8.3.3.1) suggested that in the PF_0 group when asthma impacted on the quality of life of the child their caregiver was affected. Symptoms are visible, particularly when asthma deteriorates and for this group, symptoms were the only means of management. The greater correlation suggests heightened awareness of symptoms by parents. One suggestion could be that the addition of peak flow reduces sensitivity to symptoms as a result of monitoring fatigue. Perhaps parents who are aware of a threshold value of peak flow simply consider that if the value of PEF exceeds this, all must be well.

The highest correlations were seen between the parent's perception of their child's quality of life and their own quality of life recorded by PACQLQ (figure 9.1.3.1). It was not possible to calculate a value of κ because different questionnaires were used. Spearman rank correlations were highly statistically significant throughout the study for both groups (figure 9.1.3.2). Parents appeared to measure their own quality of life twice, unable to put themselves in their child's position, perceiving their child's quality of life in light of their own. This supports evidence about the disparity between parental and child reporting of respiratory symptoms [82,110]. Children should be asked directly about the impact of asthma, although additional information from parents may be valuable [83].

An alternative explanation could be that parents quality of life change in response to that of their children. However, if this were the case one might expect the agreement between the child and caregiver quality of life to be somewhat better (fig 8.3.2.4)

11.5.3 Relative sensitivity of different lung function parameters

The present study suggested that PEF was more sensitive than FEV₁, during episodes (figure 8.1.2.1, figure 8.1.3.1). This was also true at other times (figure 10.1.1; 10.1.2). Lebecque et al [144] studied 100 asthmatic children and suggested that over one third of the children in their sample had abnormal spirometry, despite exhibiting no clinical signs. Ten percent of the sample demonstrated only a reduction in FEF 25-75 leading the authors to conclude that this was more sensitive than FEV₁. All children with clinical wheezing demonstrated significant reduction in FEF 25-75 with only a small number having reduced FEV₁. PEF was not reported. The lung function tests from Lebecque's study were performed in a laboratory, with trained technicians able to assess acceptability of the manoeuvre. The fact that the children in the present study performed manoeuvres alone at home after training, may account for some of the differences. The huge variability in flow at low lung volumes may have arisen from a lack of supervision. These flows are very

dependent on sustained effort and maximal FVC. Machine set reproducibility criteria

should have excluded any manoeuvres which did not meet ATS criteria [99]. Much of the

work concerning sensitivity of different measures of lung function contrasts so called large

airway measures such as FEV_1 and PEF smaller airway flows like FEF_{25} [101]. Studies

comparing relative sensitivity of FEV_1 and PEF often compare values obtained from

different equipment or manoeuvres [157,158]. Values for PEF and FEV_1 were recorded during

a spirometric manoeuvre and the resulting values for a single manoeuvre were directly

compared. The unsupervised nature of these manoeuvres may be responsible for the

increased sensitivity of PEF when compared with FEV_1. It is possible, but unlikely that the

children developed techniques for performing the manoeuvre which led to sub-maximal

effort which was repeatable. Reduced effort, incomplete or slow inhalation or pause at

TLC would be expected to impact on both PEF and FEV_1 [94,95].

11.5.4 Relative sensitivity of lung function versus symptoms

Behaviourally defined episodes demonstrated that children responded to increasing

symptoms. The present study suggests that symptoms were more sensitive than any

objective measure of lung function, during an episode (Chapter 7) and at other times

(figures 10.3.2, 10.3.3). A recent study of peak flow diaries from school children

demonstrated that peak flow recording is inaccurate and unreliable [151]. This evidence,

coupled with data from the present study to suggest that for management, peak flow is less

sensitive than symptoms. Malo et al [56] used a crossover design to consider the role of peak

flow in asthma management and concluded that recording symptoms in a diary was as

effective as monitoring peak flow in detecting "flare-ups". The GRASSIC [40] study of

community patients argued that peak flow-based self-management was not effective for

community patients, although they felt that more severe patients may benefit from routine

monitoring. Only one adult study demonstrated the benefits of peak flow when directly

compared with symptoms. Cowie et al [57] directly compared peak flow and symptom-based management and found a reduction in emergency treatment needs in the peak flow group.

If children responded to changes in lung function results, the choice of thresholds is critical. The present study used thresholds of 70 & 50% of patients recent best PEF, measured using the spirometer. The group mean PEF fell for both groups below the 80% level prior to children increasing their inhaled corticosteroids (chapter 7). Higher thresholds, such as those suggested by Charlton *et al*[41] may be more appropriate in this population. However, the risks of over-treatment highlighted by Douma *et al* [76] are demonstrated by the fact that the group mean PEF for the children in the present study was maintained at around 80% (figure 6.6.2.1.3). This suggests that a number of children, if they had responded to PEF, would have required additional therapy.

All of the evidence suggests that overall, small changes in lung function (both PEF and FEV_1) accompany clinically significant increases in symptoms (Figs 10.3.2 & 10.3.3 and Table 10.3.2). This simply reiterates the evidence that families responded mainly to symptoms, at the time of an exacerbation. The reasons are speculative. It is likely that symptoms represent the sum of a host of asthma related sensations and perceptions over the course of the night or day, whereas lung function represents only an instant. Moreover, lung function may be affected by recent bronchodilator use and may be less reliable under unsupervised conditions.

Conclusions

This randomised trial did not demonstrate a beneficial effect within guided self-management of monitoring peak flow on a regular basis. This does not support the hypothesis that the routine incorporation of peak flow monitoring into guided self-management protocols for school children with asthma improves the outcome. This relatively stable group of asthmatic school children made treatment changes based on symptoms and increased reliever use. However, these children were able to alter treatment in response to changes in condition suggesting that as young as seven years old, children can participate in asthma self-management.

This study does not preclude a benefit for PEF or spirometric monitoring under the more controlled and supervised conditions of the asthma clinic, hospital ward or accident and emergency department. The applications of such data are quite different from those of day-to-day monitoring of asthma at home.

11.6 Summary of future work

In light of differences in symptom perception, the finding that children managed their asthma based on symptoms, rather than peak flow warrants further investigation. The next stage is to determine which children are poor perceivers of symptoms. My future work will involve studying children with asthma. Children who have a self-management plan which they understand and follow will record twice daily spirometry and symptom scores electronically until they experience an acute exacerbation. They will complete the study at the conclusion of their acute episode. No spirometric data will be available to the children during the study. All medications used during the study will be chronologued to allow objective assessments of compliance. This study will enable us to determine the following:

(i) Objective assessment of compliance with medications and diary completion

(ii) Which children do not respond to declining lung function until they are experiencing lots of symptoms

(iii) Which children increase treatment in response to small changes in lung function, before symptoms are obvious to others

APPENDICES

Appendix 1 –Quality of Life Questionnaires

Appendix 2-The Self-Management Plan

Appendix 3 - Letter to Families from General Practices Involved in the Study

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