UCL School of Pharmacy

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The Use of Multiple Inhalation Devices for Chronic Obstructive Pulmonary Disease: A Study of Older Patients in Primary Care

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Thesis submitted in accordance with the requirements of the University College London (UCL) for the degree of Doctor of Philosophy by

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Plagiarism statement

This thesis describes research conducted in the UCL School of Pharmacy during the period between January 2011 and June 2014 under the supervision of Professor Felicity Smith and Professor Kevin Taylor. I certify that the study described is original and that many part of the work which was conducted by collaboration are clearly indicated. I also certify that I have written all the text herein and have clearly indicated by suitable citation any part of this thesis that has already appeared in publication.

_____ _____

Signature Date

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Abstract

Background

Chronic obstructive pulmonary disease (COPD) is a long term condition characterised by progressive narrowing of the airways and premature ageing of the lungs. By 2020, it is estimated to be the third biggest cause of death in the UK, after heart disease and stroke. COPD imposes a large financial burden on health services and is among the most costly diseases in the UK. Inhalation therapies are central to the management of COPD; they include pressurised metered dose inhalers (pMDIs), dry powder inhalers (DPIs), and nebulisers. Although, findings from previous studies reveal suboptimal use and a wide range of problems with inhaler handling among COPD patients, very little is known about how and why problems arise. Therefore, the aim of this study was to examine how older patients made decisions regarding the use of inhalers especially when combination of inhalation devices were used at home, how those decision and difficulties contributed to suboptimal outcomes and treatment failures.

Method

A cross-sectional study design using semi-structured face to face interviews, observations of inhalation device users, with patients in their own homes, was conducted with 46 patients. Based on previous studies among patients with respiratory diseases, it was anticipated that the sample of 60 patients would enable us to achieve the study objectives and would be able to reach saturation level, additionally, this sample size was achievable within the time and resources of the study. Patients were recruited from Pinn Medical Centre and identified by the staff through patients' medical notes. All COPD patients, registered at Pinn Medical Centre, and prescribed a combination of at least two different inhalation devices were invited to participate. The practice

population includes patients of different ages, duration and experience of inhalation therapies, ethnicity and disease severity. The data were audio recorded for verbatim transcription. Qualitative and quantitative analysis were conducted using Nvivo and SPSS programme, respectively. The study was approved by Newcastle & North Tyneside 2 Research Ethics Proportionate Review Sub-Committee.

Results

46 patients have been interviewed. Male (N=24) and female (N=22), the mean age was 77 years (63-100). Two-thirds of participants (N=31), 67%, used a combination of both pMDIs and DPIs, 10 participants (22%), used a combination of DPIs, three participants (7%) used three different kinds of inhalation devices (pMDIs, DPIs, and nebulisers), whereas the least used group was a combination of pMDIs with just two participants (4%). Differing expectations of treatment (e.g. regarding immediacy and extent of response), and preferences for different type of device were expressed. Treatment failures were of concern to patients who had experienced multiple episodes of exacerbation. The study identified factors which were potential contributors to treatment failures. These included adherence decisions which were influenced by their beliefs about inhalation therapies and concerns of side effects, especially with the long term such as steroids, and willingness to use devices in public. The study findings also revealed practical and technical issues in manipulation and cleaning the inhalation devices especially with the use of DPIs.

Discussion and Conclusion

Treatment failures are a major concern for COPD patients. Most patients experienced problems with inhalation devices used at home. To improve treatment, continuous education and follow up needs to be done for COPD

patients in order to provide all the necessary assistance in the future tailored to each patient who is at high risk of treatment failures and/or experiencing problems.

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Abbreviations

ASH	Action on Smoking and Health
ATS	American Thoracic Society
BLF	British Lung Foundation
BMQ	Beliefs about Medicines Questionnaire
BNF	British National Formulary
BTS	British Thoracic Society
CFC	Chlorofluorocarbon
COPD	Chronic Obstructive Pulmonary Disease
DH	Department of Health
DPI	Dry Powder Inhaler
ERS	European Respiratory Society
FEV_1	Forced Expiratory Volume
FEV_1/ FVC	Forced Expiratory Volume/ Forced Vital Capacity
FVC	Forced Vital Capacity
GOLD	Global Initiative for Chronic Obstructive Lung Disease
HFA	Hydrofluoroalkane
ICS	Inhaled Corticosteroids
LABA	Long Acting β_2-agonist
LAMA	Long-acting Muscarinic Antagonist

MDI	Metered Dose Inhaler
MMAS	Modified Morisky Adherence Scale
MRC	Medical Research Council
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
PEFR	Peak Expiratory Flow Rate
PFTs	Pulmonary Function Tests
p-MDI	Pressurized Metered Dose Inhaler
QOF	Quality and Outcomes Framework
SABA	Short Acting β_2-agonist
SAMA	Short-acting Muscarinic Antagonists
WHO	World Health Organization

List of Publications

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1 Chapter One: Literature review and background

This chapter outlines the process of developing and informing the research questions and discusses the rationale for conducting this study among the group of patients selected. It also provides an introduction to chronic obstructive pulmonary disease (COPD) including its definition, classification and management.

1.1 The rationale for conducting this study

1.1.1 Why COPD?

COPD is one of the most prevalent diseases in the world, and its prevalence is increasing every year not only in the UK but also around the world. As reported by the Quality and Outcomes Framework (QOF) (DH, 2010), in England in 2008, 15.4 million people had a long-term condition, including COPD which was the third most common after coronary heart disease and diabetes. By 2020, COPD is estimated to be the third biggest cause of death in the UK, after heart disease and stroke (Mannino et al., 2006; BTS, 2008). In the UK, it has been estimated that there are about three million patients with diagnosed COPD, plus a further half million who have the condition without diagnosis (BLF, 2008). There are about 900,000 patients with diagnosed COPD in England and Wales. After allowing for under-diagnosis, the true number of individuals is likely to be about 1.5 million (BLF, 2008).

COPD imposes a large financial burden on health services and is among the most costly diseases in the UK. COPD is the second largest cause of emergency admission in the UK (Healthcare Commission, 2006), with one in eight (130,000) acute adult medical admissions per year. It is estimated that the direct cost of COPD is almost £500 million a year; more than half of this

cost relates to the provision of care in hospital (NICE, 2011). In addition, COPD and other lung conditions cost business 24 million working days in sick leave, while the indirect costs from lost productivity are £3.8 billion (DH, 2011).

Given the high prevalence of COPD and the healthcare costs, it was decided to conduct this study among COPD patients in the UK to determine the needs of this patient group, consider how to optimise their use of medicines, and identify ways to reduce risks of treatment failures and financial costs to the NHS due to unnecessary GP visits, hospital readmission and care.

1.1.2 Why study the use of medication among COPD patients?

Adherence to therapy is usually an important aspect of medication use, specially the treatment of chronic conditions such as COPD (Chisholm-Burns et al., 2003). The World Health Organisation (WHO) offers a definition of adherence: "The extent to which a person's behaviour taking medications, following a diet, and/or execution of life style changes corresponds with agreed recommendations from a health care provider" (WHO, 2008). Medication non-adherence has been identified as a major public health problem that imposes a considerable financial burden on healthcare services (Vermeire et al., 2001). This burden has been estimated worldwide to cost $100 billion each year (Vermeire et al., 2001). The WHO estimates that the average non-adherence rate is 50% among those with chronic illnesses including COPD (Chisholm-Burns et al., 2003). Non-adherence to inhalation therapy was identified in more than 50% of COPD participants in seven different studies (Melani et al., 2001; Boyter et al., 2005; George et al., 2005; Mehuys et al., 2010; Trivedi et al., 2012; Huetsch et al., 2012; Cecere et al., 2012). Among lung diseases, patients with COPD have significantly lower adherence to treatment than asthmatic patients (James et al., 1985; Dolce et al., 1991; Cochrane., 1992; Haupt et al., 2008). Strategies to improve

adherence to inhalation therapy among patients (e.g. patient instruction and education) have been shown to work among patients with asthma (Put et al., 2003; Onyirimba et al., 2003), whereas, in COPD patients, these strategies were less successful (Rand, 2005; Restrepo et al., 2008). Therefore, adherence is a recognised problem among this group of patients, which may lead to suboptimal outcomes and treatment failures.

Despite the sufficient evidence found in the literature supporting the fact that medication taking among COPD patients was found to be suboptimal, caution must be taken before drawing a conclusion due to the wide differences in the estimated rate of non-adherence of COPD patients, which range from 28% to 80% (see Chapter two: a review of the literature for more details). This variation may be due to differences in patient populations, definition of non-adherence, methods employed, disease status, or respiratory conditions included in each study, as some studies included a variety of lung diseases such as asthma and COPD (see Chapter two: a review of the literature).

Non-adherence to medication remains an unresolved problem despite decades of research, and is a factor resulting in suboptimal clinical outcomes and poor disease control. Therefore, it was decided to study in detail whether COPD patients are taking their inhaled drug regimens at home as directed or not. If not, why they do not adhere, what beliefs they have about their medicines which may affect medication taking. In addition, what problems are faced by patients that may make them stop taking their medicines as recommended, and how can this be resolved.

What are the differences between this study and previous studies and what are the gaps in the knowledge in regards to medication use?

The difference between this study and all other previous studies is that, although all methods of adherence measurements have their advantages and disadvantages (see Chapter two: a review of the literature), adherence in these studies was evaluated mainly quantitatively, by measuring the amount of medicine taken over a given time period (Van Grunsven et al., 2000; Melani et al., 2001; Barta et al., 2002; Boyter et al., 2005; George et al., 2005; Mehuys et al., 2010; Agh et al., 2011; Trivedi et al., 2012; Huetsch et al., 2012; Cecere et al., 2012; Khdour et al., 2012); whilst this study is one of very few studies that has measured and examined medicine taking and how patients make decisions to use their inhalation therapy quantitatively and qualitatively – quantitatively, to determine either adherence/non-adherence behaviours to COPD medicines and qualitatively to examine patients' health decision-making processes and the reasons for these decisions, thereby contributing answers to questions that were not clearly addressed by quantitative data.

Almost all studies in adherence research among patients with COPD have measured patients' adherence using only one self-report questionnaire on medication utilisation (Melani et al., 2001; Barta et al., 2002; George et al., 2005; Mehuys et al., 2010; Agh et al., 2011; Cecere et al., 2012; Huetsch et al., 2012; Khadour et al., 2012), whilst this study combined different approaches, tools and methods to gather the data from different sources to maximise the validity of the findings. These tools were the previously validated self-report adherence measure (Morisky) and open/close-ended questions in regards to medication consumption.

One of the most striking reasons for the lack of progress in adherence research is the absence of the patient's perspective (Vermeire et al., 2001).

Therefore, this study will examine the use of inhalation therapy from patients' perspectives, which has been understudied in previous research (Vermeire et al., 2001).

This study is unique in examining the relationship between using multiple inhalation therapies of all medication classes and/or devices and medication adherence and decision to use the therapy together, which will enable examining patterns to different medication classes used within the same patient. Studies that have examined adherence to inhaled medications have been restricted to only one (van Grunsven et al., 2000) or three medications (Cecere et al., 2012; Huetsch et al., 2012). Additionally, many previous studies of medication adherence in COPD patients were performed prior to the common use of long-acting medications, and included only short-acting medications (Dolce et al., 1991, Rand et al., 1995; Turner et al., 1995; Corden et al., 1997).

The potential benefits of this research into the use of medications

Examining how patients made decisions regarding the use of inhalers especially when a combination of inhalation devices was used at home, and how those decisions and difficulties contributed to suboptimal outcomes and treatment failures will help in recognising that collaboration should occur between healthcare professionals and patients to improve patients' use of their medicines in order to achieve optimal health outcomes and minimise the number of treatment failures and healthcare costs.

1.1.3 Why study the use of devices among users?

In regards to the devices used by patients in their homes, the review of the literature in Chapter two reveals that incorrect use of inhalation devices is

very common among patients with COPD, being frequently associated with the use of pressurised metered dose inhalers (pMDIs) and dry powder inhalers (DPIs) (Lenney et al., 2000; Hesselink et al., 2001; Khassawneh et al., 2008; De Moraes Souza et al., 2009; Rootmensen et al., 2010). Suboptimal inhalation technique will lead to suboptimal drug delivery. Therefore, users may receive lower benefits from their treatment, which may result in the prescription of unnecessarily high doses and higher healthcare costs. It has been estimated that $5 to $7 billion in the United States is wasted every year because of inhaler misuse (Fink and Rubin, 2005). The rate of incorrect inhalation technique with the use of inhalation devices reported in five past studies ranged from 2.9% (Ho et al., 2004) to 94.2% in previous studies (De Moraes Souza et al., 2009). The review reveals suboptimal use and a wide range of problems with inhaler handling. However, very little is known about how and why problems arise and what practical and technical issues COPD patients faced when using multiple inhalation devices in combination. Therefore, there is a need for more studies to examine how patients practically use their inhalation devices and what are the frequency and range of problems experienced by patients in terms of the technical aspects of inhaler use, cleaning and maintenance of devices that may lead to suboptimal care or treatment failure.

What are the differences between this study and previous studies and what are the gaps in the knowledge in regards to devices' use?

The majority of past studies (N=6) have assessed the inhalation technique among patients with a number of lung diseases, including asthma and COPD (Hesselink et al., 2001; Ho et al., 2004; De Moraes Souza et al., 2009; Rootmensen et al., 2010**;** Hämmerlein et al., 2011; Melani et al., 2011), whereas this study is one of very few studies (N=3) that included only patients with COPD, to focus on their problems and specific needs, which may differ from those of patients with asthma (Lenney et al., 2000; Wilson et al., 2007; Khassawneh et al., 2008). In addition, other past studies have

included only one class of devices in the assessment process, i.e. pMDIs only (Ho et al., 2004) or DPIs only (Wilson et al., 2007). This study included all classes of inhalation devices, including nebulisers, which have not been assessed previously in studies of COPD patients' use of devices.

The decision to include only patients with COPD in the assessment process in this study was because, despite the fact that both asthmatic and COPD patients are prescribed multiple inhalation therapies to be used daily or when required, the characteristics of COPD as a disease and its treatment differ. For example, in asthma patients the airflow limitation is reversible with the use of therapy, whereas this limitation is irreversible in COPD patients even with the use of medication, which may affect patients' use of their therapy. Unlike COPD, asthma is episodic and is rarely a life-threatening disease. These factors, including the nature of the disease and the treatment, were found to influence patients' use of inhalation therapy (Horne et al., 1999).

Previous studies have reported that incorrect inhalation technique was common among both asthmatic and COPD patients. However, three previous studies reported that COPD patients made or were more likely to make more deviations from the recommended inhalation technique when using their inhalers than those with asthma (Buckley, 1989; De Morales Souza et al., 2009; Melany et al., 2011), and that up to 94% of inhalation devices users with COPD used their devices incorrectly (De Moraes Souza et al., 2009), which may result in suboptimal drug delivery and therefore treatment failures.

Additionally, all previous studies have only measured the practical errors or deviations made by COPD patients when performing the inhalation technique, without paying attention to the technical issues experienced by

users with the device itself (i.e., if there is a problem in the device itself or its manufacture that may affect the drug delivery and therefore patients' choices and use). In addition, no study has been focused on examining inhalation technique among patients with COPD using nebulisers. Previous studies have considered only certain devices and included one aspect of assessment, which is the inhalation technique. Since adequate disease control relies on the appropriate use of the inhalation therapy or devices, there is a need for more studies to examine how these patients practically use their devices.

The potential benefits of this research into the use of devices

To our knowledge, this is the only study that has examined and described the problems encountered by COPD participants with all aspects of the use of multiple inhalation devices, including technical and practical issues of the operation, cleaning and maintenance of inhaler equipment for all classes of devices, including pMDIs, DPIs and nebulisers. By highlighting these issues, which may affect patients' use of their medicines, information will be available which will help inform healthcare professionals in their support of these patients in their use of such medicines at home, and therefore optimise medicines' use.

1.1.4 Why study the informal care provided for COPD patients?

Managing COPD can be complex because it usually occurs with other chronic illness, each of which may require following pharmacological and non-pharmacological recommendations (Pinto et al., 2007). In addition, COPD mainly affects people over the age of 40 and becomes more common with increasing age. The average age when it is formally diagnosed is around 67 years (Trivedi et al., 2012). This age can be associated with physical and

functional limitations which may affect the use of medication among these patients, suggesting an important role for carers.

The terminology used to refer to carers is unclear (Barnes et al., 2006). For example, the phrase “family caregiver” was coined by Houts, et al. (1996) and refers to the people who provide some assistance or help at home for patients and are not getting paid by any caregiving services (Houts et al., 1996). In 2006, the Department of Health in the United Kingdom adopted and employed the term ‘carer’ to distinguish between the formal care provided by health and social care professionals and the informal care provided by family members, friends and neighbours (DH, 2006).

The majority of care that is delivered to patients with chronic illnesses including COPD has shifted from secondary care (e.g. hospitals) towards patients’ homes, as a result of the trend towards community-based care (Spence et al., 2008). Assets and Health Dynamics among the Oldest Old (AHEAD) data suggest that most caregivers are family members (informal carers) (72%) (Clipp and Steinhauser, 2003). The care value provided by informal carers such as family members has been estimated to exceed the cost of care from nursing homes and paid healthcare (Schreiner et al., 2006). It is estimated by the Office of National Statistics that about five million individuals are providing informal care in the UK (The Information Centre for Health and Social Care, 2010).

In 2011, the Department of Health published a report entitled ‘An Outcomes Strategy for People with Chronic Obstructive Pulmonary Disease and Asthma in England’ to ensure that people with COPD receive safe and effective care which reduces the disease progression and enhances their independence (DH, 2011). However, the few existing studies that have

examined the informal care provided for COPD patients have focused on carer experiences and needs (Bergs 2002; Simpson and Rocker, 2008; Spence et al., 2008; Caress et al., 2009), and have neglected the needs of the patients and the important role of informal carers in disease management. Therefore, the nature of informal support provided for COPD patients with their medication in their homes remains understudied. There is a need to know if COPD patients are getting the required help or assistance with their medicines, and how the carer helps – in which activity or tasks and how often.

The potential benefits of this research into the care provided for patients with COPD

Understanding the range and extent of care provided by informal caregivers in relation to the use of inhalation therapy at home is crucial to support and empower carers to fulfil their roles, and to ensure the effective use of COPD medication by patients.

1.2 Definition of chronic obstructive pulmonary disease

Chronic obstructive pulmonary disease (COPD) is a long-term condition characterised by progressive narrowing of the airways and premature aging of the lungs. The obstruction of the airways may be partially reversible or irreversible (BTS, 2008). The World Health Organisation (WHO) defines COPD as “not a single disease but an umbrella term used to describe chronic lung diseases that cause limitations in lung airflow, such as emphysema and chronic bronchitis” (WHO, 2008).

Emphysema is characterised by destruction of the lung tissue, mainly air sacs (alveoli). The smallest airways also narrow, lose their elasticity, and tend to collapse during exhalation (Barnes, 2004; Porth, 2005). Chronic bronchitis is an inflammation of the airways causing the glands that line the airways to produce an excessive amount of thick mucus, which in turn causes further obstruction of breathing. The result is often a chronic cough that produces mucus or sputum and shortness of breath (Barnes, 2004; Porth, 2005). The more familiar terms ’chronic bronchitis’ and ’emphysema’ are no longer officially used, but are now included within the COPD diagnosis (WHO, 2008).

1.3 Pathophysiology and aetiology of chronic obstructive pulmonary disease

The mechanisms involved in the pathogenesis of COPD usually are multiple and include inflammation and fibrosis of the bronchial wall, hypertrophy of the submucosal glands and hypersecretion of mucus, and loss of elastic lung fibres and alveolar tissue. All these changes cause mismatching of ventilation and perfusion. Destruction of the alveolar tissue decreases the surface area for gas exchange and loss of elastic fibres, which normally

provide traction and hold the airways open, impairs the expiratory flow rate, increases air trapping, and predisposes to airway collapse (Barnes, 2004; Porth, 2005).

Cigarette smoking is the most important etiological factor in the development of COPD. Smoking is suggested to account for 90% of cases, and while decline in lung function after the age of 35 is part of the aging process, the decline is two times faster among ‘at risk’ smokers (Alhadad, 2011). In the UK, smoking is attributed as the main cause of COPD in 87% of males and 84% of females (Smeltzer and Bare, 2010). Smoking depresses the activity of scavenger cells and affects the respiratory tract’s ciliary cleaning mechanism, which keeps breathing passages free of inhaled irritants, bacterial and other foreign matter. When smoking damages this cleaning mechanism, airflow is obstructed and air becomes trapped behind the obstruction. The alveoli greatly distend, diminishing lung capacity. Smoking also irritates mucus glands, causing an increased accumulation of mucus, which in turn produces more irritation, infection, and damage to the lung (Smeltzer and Bare, 2010).

Although genetic factors have been suggested to play a role in developing COPD among smokers, previous studies on these factors have not provided full, clear explanations (Alhadad, 2011). The well-documented genetic risk factor is deficiency of alpha-1 antitrypsin (A1AT) which is an enzyme inhibitor that protects the lung parenchyma form injury. This deficiency of alpha-1 antitrypsin predisposes young people to rapid development of emphysema, even if they do not smoke (Smeltzer and Bare, 2010).

Age and gender are other risk factors of COPD. The frequency of COPD increases with age, with prevalence rates of 2% in men aged 45-65 years

and 7% in men over 75. Men are more likely to be affected than women (Smeltzer and Bare, 2010). The prevalence of COPD is 1.7% in men compared to 1.4% in women. However, in some European countries there is no gender difference in prevalence rates because these rates for women are rising more rapidly than for men. This is in part related to the change in their smoking habits and it also appears that women are more susceptible to tobacco smoke. Women who smoke are estimated to be 13 times more likely to develop COPD than a non-smoker (Smeltzer and Bare, 2010). Other risk factors include: certain jobs with occupational risk factors and air pollution.

1.4 Classification of chronic obstructive pulmonary disease

This section describes the classifications of COPD based on disease severity, in order to identify patients who were enrolled in this study as mild, moderate, severe and very severe, based on the chosen classification from the guidelines. The assessment of the severity is based on the FEV_1 value and has implications for therapy and prognosis.

In clinical practice, there are different classification methods used to categorise the stages of COPD and its severity. Firstly, the severity of airflow obstruction in COPD can be categorised according to the degree of reduction in FEV_1% predicted, which is defined as the maximum amount of air that can be expired in one second following a full inspiration (NICE, 2010). However, there is no international agreement in terms of classification of severity and classifications and guidelines to follow are different between countries – for instance the National Institute for Health and Care Excellence CG101 for COPD, which is used in the UK (NICE, 2010), and the Global Initiative for Chronic Obstructive Lung Disease (GOLD), which is used within Europe, and the American Thoracic Society (ATS) and European Respiratory Society (ERS) classifications, which are used in the USA and Europe respectively.

The similarities and differences between the guidelines are shown in Table 1-1.

Table 1-1: Classification of airflow obstruction in COPD according to different guidelines. Values shown are all FEV_1%predicted and in all categories post bronchodilator FEV_1/ FVC<0.7. Source: NICE, 2010

		ATS/ERS (2004)	GOLD (2013)	NICE (2010)
FEV_1% Predicted (The maximum amount of air that can be expired in 1 second following a full inspiration)	Post-bronchodilator FEV_1/FVC (The percent volume of air that can be expired in 1 second relative to the maximum expiration)	Severity of airflow obstruction		
≥ 80%	< 0.7		Stage 1 – Mild	Stage 1 – Mild*
50–79%	< 0.7	Mild	Stage 2 – Moderate	Stage 2 – Moderate
30–49%	< 0.7	Moderate	Stage 3 – Severe	Stage 3 – Severe
< 30%	< 0.7	Severe	Stage 4 – Very severe**	Stage 4 – Very severe**

*With compatible symptoms or symptoms should present to diagnose COPD in people with mild airflow obstruction.
**Or when FEV_1 < 50% with respiratory failure.

Another classification for the disease severity is the Dyspnoea scale, which is a method of recording patients' self-report of activities that cause them breathlessness (see Table 1-2). The Dyspnoea scale is the most widely used scale of activity limitation resulting from breathlessness, and was developed by the Medical Research Council (MRC) (NICE, 2010). This particular tool is graded from 1 to 5 and allows the patients to rate their breathlessness according to the level of exertion required to induce their breathlessness (NICE, 2010).

Table 1-2: Severity of COPD based on the Dyspnoea scale. Source: NICE, 2010

Severity	Score	Degree of Breathlessness Related to Activities
None	1	Not troubled with breathlessness except with strenuous exercise
Mild	2	Troubled by shortness of breath when hurrying or walking up a slight hill
Moderate	3	Walks slower than people of the same age due to breathlessness or has to stop for breath when walking at own pace on the level
Severe	4	Stops for breath after walking approximately 100 meters or after a few minutes on the level
Very severe	5	Too breathless to leave the house or breathless when dressing or undressing

The Dyspnoea scale is an easy tool to use and record but each grade is fairly broad and may not be sensitive enough in some cases to measure the effect of a treatment (Smeltzer and Bare, 2010).

In order to determine the severity of the disease of each participant enrolled in this study, patients' medical records in Pinn Medical Centre were accessed to obtain this information (if specified, mild, moderate, severe and very severe). If the disease severity was not specified by Pinn Medical Centre staff, the FEV_1% predicted or FEV_1/FVC ratio were obtained, in order to identify patients who were enrolled in this study as mild, moderate, severe and very severe, based on the NICE guidelines classifications. The NICE guidelines classifications were used in this study because the guidelines were recently published in 2010 when the study was started in 2011, and the guidance outlines recommended therapy for COPD within the National Health Service (NHS) in the UK.

1.5 Management of chronic obstructive pulmonary disease

Despite the fact that COPD imposes a large financial burden on patients, carers and healthcare system, it remains under-treated (BTS, 2008). Although COPD cannot be cured, optimal disease management can provide control of symptoms and slow the progression of the disease (Kaplan et al., 2005; Rodriguez-Roisin et al., 2005). Effective disease management is crucial to combat the huge impact of this condition on patients, carers and healthcare system.

One of the objectives set out in the 'Outcomes Strategy for Chronic Obstructive Pulmonary Disease' was to assure that safe and effective care is

delivered to individuals with COPD, in order to reduce the progression of the disease and encourage independence (DH, 2011). It is therefore advised in the Outcomes Strategy to initiate treatment through evidence-based use of pharmacological and non-pharmacological interventions that are tailored to the patient's choice and are often reviewed. In order to meet this goal; implementing evidence-based guidelines on the effective management of COPD is recommended. The National Institute for Health and Care Excellence (NICE) in 2004 first issued clinical guidelines to treat patients with COPD. These guidelines were reviewed and replaced with an updated version (NICE, 2010). In 2010, the National Institute for Health and Care Excellence (NICE) issued guidelines on the care and management for patients with COPD. Pharmacological and non-pharmacological approaches are recommended. The pharmacological strategy mainly consists of bronchodilators and/or corticosteroids (Figure 1-1), whereas a non-pharmacological strategy includes smoking cessation, influenza vaccinations, oxygen therapy and pulmonary rehabilitation programmes. This study has focused on the pharmacological strategy of managing COPD, as previous studies have shown suboptimal use and a wide range of problems with inhaler handling among COPD patients, and very little is known about how and why such problems arise. Therefore, in this section the pharmacological aspect of managing COPD will be discussed in detail to outline the therapies available for the management of COPD, and the current policies and guidelines implemented in the UK.

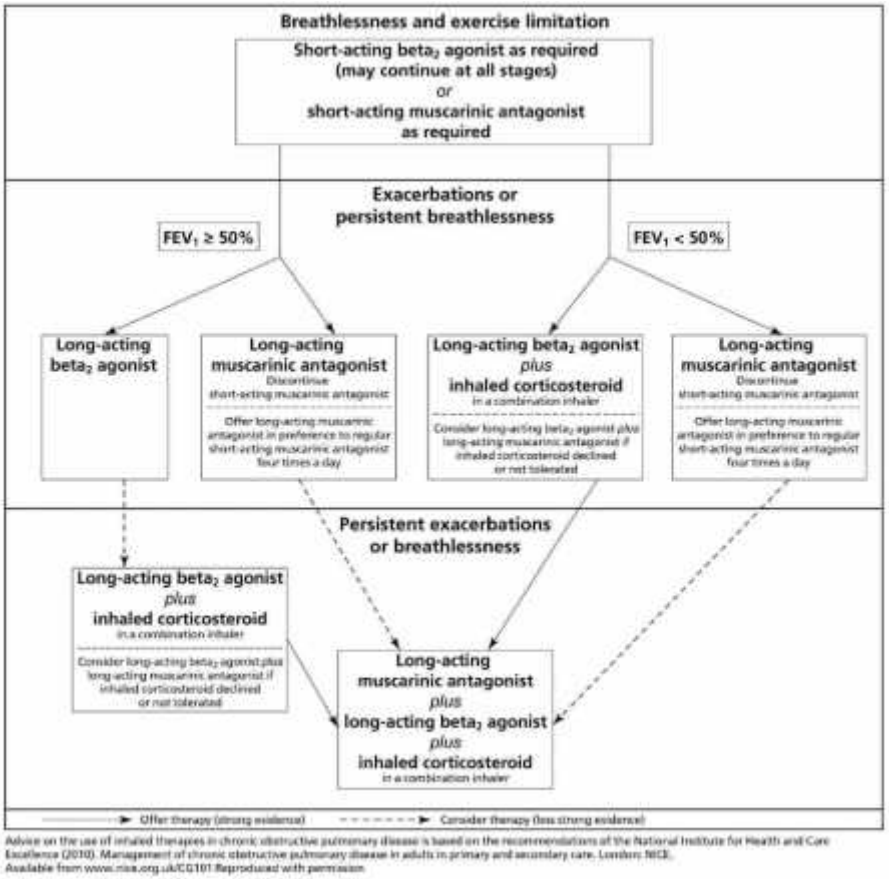


Figure 1-1: Step-care pharmacotherapy in COPD. Source: British National Formulary (BNF), 2013.

1.5.1 Pharmacological management

1.5.1.1 Bronchodilators

Inhaled bronchodilators are the mainstay of treatment in COPD because they reduce breathlessness and improve exercise capacity (Clark, 2004; Howland, 2006). They include short- and long-acting therapy, such as β_2-agonists and antimuscarinic agents. β_2-agonists bind to the β_2-adrenoceptor which is present in the cell membrane of a number of airway cells including smooth muscle cells, causing relaxation of the airway smooth muscles (Howland, 2006). Antimuscarinic agents are muscarinic receptors' (e.g. M_1 and M_3) antagonist, which inhibit cholinergic reflex bronchoconstriction,

causing bronchodilation. In addition, antimuscarinic agents reduce mucus hypersecretion by inhibiting M_3 receptors (Howland, 2006).

A. Short-acting inhaled bronchodilators

Short-acting bronchodilators are the most commonly used therapy for COPD (NICE, 2010; BNF, 2013). Bronchodilators relax the muscles in the airways (bronchioles), causing the airways to open and dilate. They include β_2-agonists (e.g. salbutamol and terbutaline), which have been the mainstay bronchodilator agents used for the management of COPD, and anti-cholinergic agents (e.g. ipratropium).

These drugs have a rapid onset of action (usually within five to 10 minutes) and duration of action of three to four hours, and are given to be used when needed for quick relief of symptoms. They can also be used before exercise to increase exercise tolerance or to relieve breathlessness (Clark, 2004; Howland, 2006; BNF, 2013).

Some older patients may become less responsive to β_2-agonists and may achieve better improvement with anti-cholinergic agents. Short-acting anti-cholinergic agents have a slower onset of action (15-30 minutes) than short acting β_2-agonists (five minutes) but the results of most comparative studies suggest that they are equally effective in achieving symptom relief (Clark, 2004; Howland, 2006; BNF, 2013). In addition, they are both well tolerated, but may cause tremor of the hands or palpitations (rapid and irregular heartbeat) (BNF, 2013).

B. Long-acting bronchodilators

Long-acting bronchodilators have similar effects on lung function to those of short-acting bronchodilators. However, they are more effective in maintaining relief from breathlessness than short-acting bronchodilators; their effect continues for 12 hours compared with up to four hours for the short-acting agents. Long-acting agents reduce breathlessness and give better exercise tolerance (Clark, 2004; Howland, 2006; Beier and Beeh, 2011; BNF, 2013). They are recommended to be given to people with stable COPD who remain breathless or have exacerbations (exacerbations often occur where there is a rapid and sustained worsening of symptoms beyond normal day-to-day variations) despite using short-acting bronchodilators as required (NICE, 2010). Patients should be also given long-acting beta agonists (LABAs: formoterol or salmeterol) or long-acting muscarinic antagonists (LAMAs: tiotropium) as maintenance therapy especially if the FEV1 ≥ 50% predicted (NICE, 2010). Long-acting bronchodilators are usually safe. However, some adverse effects may emerge with the use of these therapies, including palpitation, tremor, headache, muscle cramps and low potassium level in the bloodstream, which are usually caused by LABAs, whereas dry mouth, nausea, palpitation, headache and visual difficulties are caused by LAMAs (BNF, 2013).

1.5.1.2 Inhaled steroids

Inhaled steroids (ICS) should be considered in those with more advanced disease and repeated exacerbations (NICE, 2010). Although these therapies do not have a big impact upon improving lung function or symptoms, they may reduce the frequency of exacerbations. The most commonly used inhaled steroids in COPD are beclometasone, budesonide and fluticasone (BNF, 2013).

Inhaled steroids can cause adverse effects to appear within the mouth and throat such as oral thrush or alteration in voice quality (e.g. voice hoarseness), which can be avoided by gargling or brushing the teeth after using them or using a spacer device, which will be described later. In addition, prolonged use of high doses of steroids may cause the skin bruising and osteoporosis (BNF, 2013).

1.5.1.3 Inhaled combination therapies of LABAs and ICS

ICS should not generally be used alone in COPD; they are most often given along with a LABA in a single inhaler. According to the NICE guidelines, the addition of long-acting bronchodilators (LABA) to inhaled corticosteroids (ICS) (in a combination inhaler) should be considered in people with COPD who remain breathless or have exacerbations. Despite using SABAs as required, patients should be given a combination therapy of LABA with an ICS in one inhaler as maintenance therapy, especially if FEV_1<50% is predicted (NICE, 2010). Combined therapy may produce greater improvements in exercise tolerance and a greater degree of bronchodilation than either drug used separately (NICE, 2010). In addition, patients may find this more convenient and adherence may be enhanced (Clark, 2004; Howland, 2006).

1.5.1.4 Oral corticosteroids

The NICE guidance recommends that oral corticosteroids (e.g. prednisolone) are only indicated for the treatment of exacerbations of COPD as they have been found to reduce the severity and the duration of the episode (NICE, 2010). They should be considered in the following cases: firstly, in the absence of significant contraindications, oral corticosteroids should be given in addition to other therapies to all patients admitted to hospital with an exacerbation, or in patients in the community who have an exacerbation with

a significant increase in breathlessness which interferes with daily activities. However, in these cases, the dose of oral corticosteroids should be kept as low as possible and the therapy should be monitored for the development of any side effects such as osteoporosis (NICE, 2010). Steroid tablets may be prescribed for one or two weeks to deal with exacerbations and reduce inflammation. They should not be used on a maintenance basis (Clark, 2004; Howland, 2006; NICE, 2010).

1.6 Inhalation devices used for the treatment of COPD

Inhalation therapies are central to the management of COPD. A broad range of inhaler devices is available in practice, generally categorised pressurised metered dose inhalers (pMDIs), dry powder inhalers (DPIs), and nebulisers, according to the method used for drug dispersion (see Figure 1-2). Figure 1-2 includes inhalation devices which were most used by participants in this study.

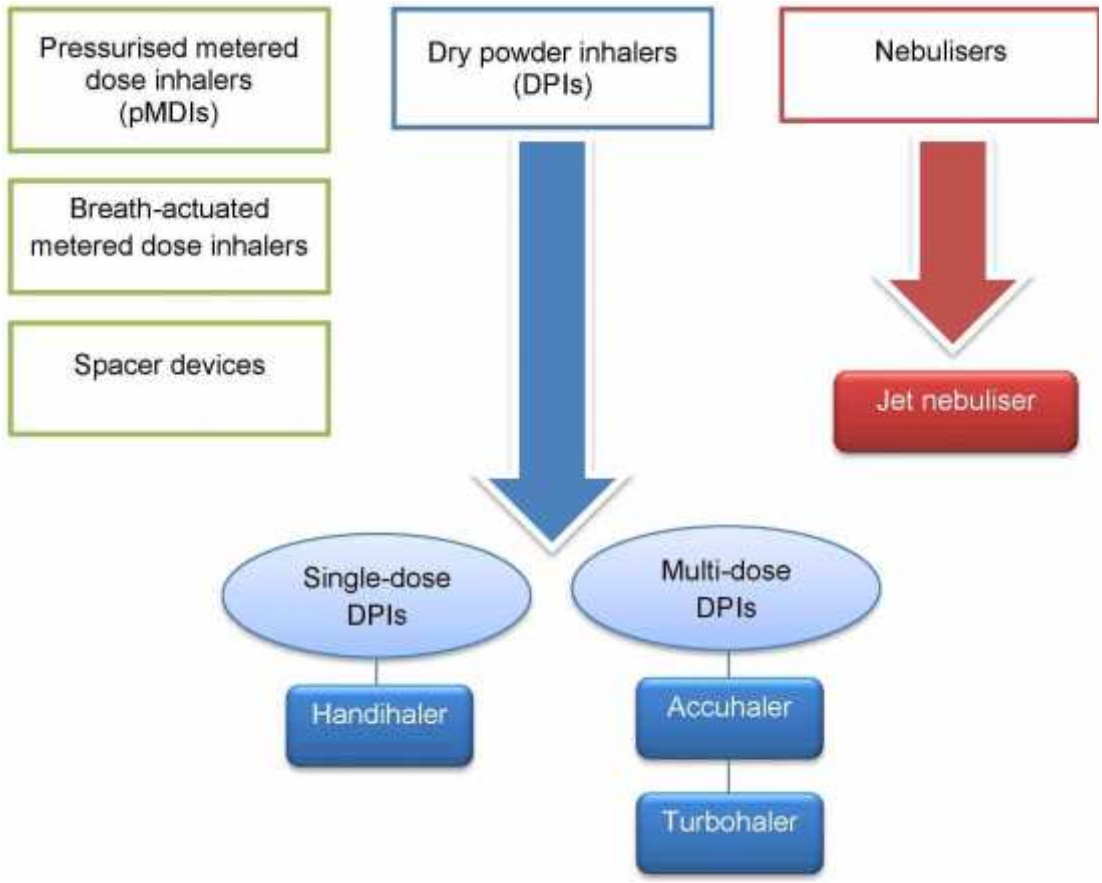


Figure 1-2: Inhalation devices currently available

The pMDI is the most commonly used and prescribed inhaler compared to dry powder inhalers (DPIs) and nebulisers (Child et al., 2002; Chystyn et al., 2003; Rees, 2005; Taylor, 2013). When choosing a suitable inhaler, a patient's ability to use a device should be assessed as it forms an important factor which determining the choice (Barrons et al., 2011), as successful disease management totally relies on the patient's ability to use the inhalation devices properly and efficiently (Lannefors, 2006). There is great variation between the available inhalers in the design and functionality, each of which has advantages and disadvantages, which are considered below.

1.7 The aerosol delivery system

1.7.1 Pressurized metered dose inhalers (pMDIs)

The component parts of the pMDI

The standard pressurized metered-dose inhaler (Figure 1-3) is the most commonly used device for delivering inhaled drugs, especially bronchodilators (BNF, 2013; Taylor, 2013), and in 2002 approximately 500 million were produced and their production is increasing annually (Brown, 2002). pMDIs contain a drug that is either dissolved or suspended in a propellant under pressure which is manually actuated (Beaucage and Nesbitt, 2002). Therefore, a good inhalation technique is required.

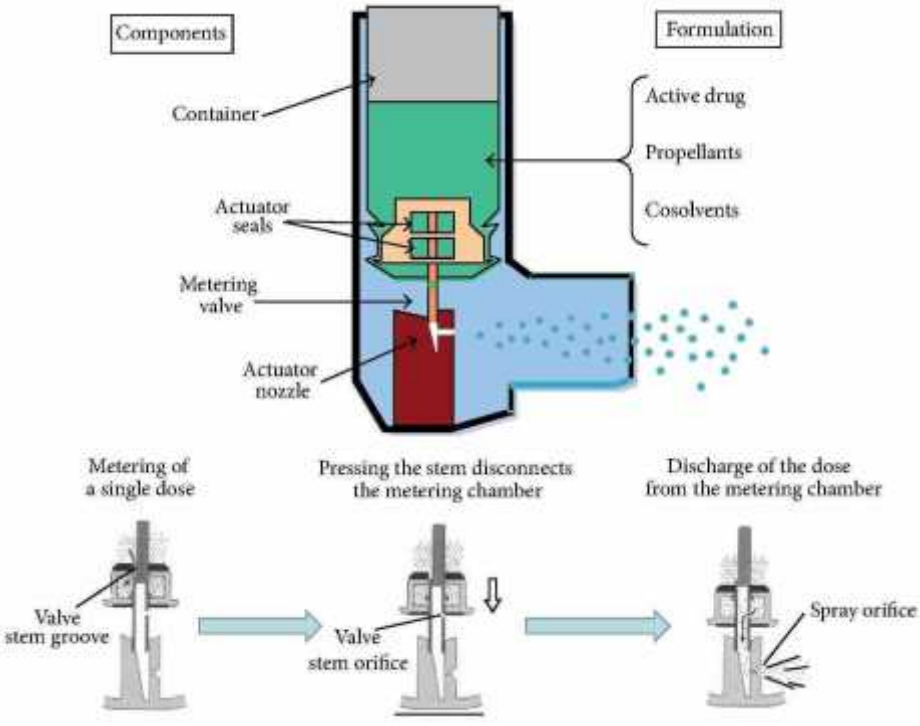


Figure 1-3: Schematic of a typical standard pressurized metered-dose inhaler. Source: Lavorini, 2013.

The pMDI comprises several components, each of which is important to the success of the whole device. These components are container, propellants, drug formulation, metering valve, and actuator (Newman, 2005; Lavorini,

2013). In pMDIs, the drug is either dissolved or suspended in liquid propellant(s) such as hydrofluoroalkanes (HFAs) or chlorofluorocarbons (CFCs), together with other excipients, liquid surfactants, and presented in a pressurized canister fitted with a metering valve. A predetermined dose is released as a spray on actuation of the metering valve. When released from the canister, the formulation undergoes volume expansion in the passage within the valve and forms a mixture of gas and liquid before discharge from the orifice. The high-speed gas flow helps to break up the liquid into a fine spray of droplets (Taylor, 2013). Table 1-3 gives more information about how a pMDI device is operated and the optimal inhalation technique.

Table 1-3: Inhalation technique for standard and breath-actuated pMDIs

Correct technique	pMDI type	Explanations and references
1. Remove the cap	All	None
2. Shake inhaler (the canister) well before use.	All	Some formulations are in a suspension, and when not in use, the particles within it separate or settle. Therefore, it is very important to shake before each use to ensure a homogeneous and uniform dose. Some products which are in the form of solutions do not require shaking (Beaucage, 2002; Fink et al., 2005)
3. Attach a spacer or valved holding chamber (pMDI with spacer only) to the pMDI	Only pMDIs with a spacer or valved holding chamber	None
4. Holds inhaler upright (p-MDIs), (p-MDIs with spacer); with index finger on top and thumb on the bottom, support the spacer with other hand.	All	The device should be held upright to get an adequate dose (Beaucage, 2002) and prevent the oropharyngeal drug disposition which may cause side-effects (Colombo, 2012)
5. Prepare the device according to the manufacturer's instructions	Breath actuated pMDIs	None
6. Breath out before firing	All	None
7. Place mouthpiece/ or the spacer between teeth and close the lips around it	All	None
8. Actuate while breathing in deeply and slowly.	All	Actuation before 1 second of inspiration decreases the inhaled mass and the drug deposition deep in the lungs. Similarly, actuation after the inhalation can lead to exhalation of drug before it can enter the target airways (Fink, et al., 2005; Colombo, 2012). If a patient breathes in too quickly, the drug will hit the back of the throat and mouth instead of reaching the airways due to a tendency to impact in the upper airways.
9. Continue to inhale after firing.	All	None
10. Hold breath for about 5-10 seconds	All	Breath holding increases the residence time of particles in the lungs, thus increasing drug deposition by means of sedimentation and diffusion (Beaucage, 2002)

Advantages and limitations of the conventional pMDIs

pMDIs have the practical benefits of small size, portability, convenience and they are relatively inexpensive. In addition, pMDIs are multi-dose which means that a dose is immediately available when required. A dose can be delivered in a few seconds, unlike nebulisation therapy, which typically takes several minutes to be inhaled. Since the inhaler is pressurized, the contents are protected from the entry of both moisture and pathogens. These factors provide powerful reasons why the pMDI has been successful for a long period of time (Beaucage and Nesbitt, 2002; Newman, 2005; Karotkin, 2011).

Conversely, the limitations of pMDIs have also been recognised for decades. One of the main disadvantages of the pMDIs is that the drug delivery is highly dependent on the patient's inhalation technique. Reports of pMDI misuse are commonplace in the literature, and failure to co-ordinate or synchronise actuation with inhalation is said to be the most common problem patients have with the use of pMDIs, which can result in a very poor drug delivery, leading to suboptimal outcomes (Giraud and Roche, 2002; Karotkin, 2011; Lavorini, 2013). Another problem with some pMDIs is that, even with good inhalation technique, the drug disposition in the lungs from the pMDIs is less than 20% of the dose, with most of the dose being deposited in the oropharynx (Newman, 1991; Karotkin, 2011). High oropharyngeal deposition of some medication can cause localised adverse effects (Newman, 1991; Karotkin, 2011). See Table1-4 for more information about the main advantages and disadvantages of the pMDIs.

Table1-4: Advantages and disadvantages of standard pMDIs. Adapted from: Newman, 2005 and Taylor, 2013

Advantages	Disadvantages
Small, portable, unobtrusive	Difficult to deliver high doses
Quick to use	Drug delivery highly dependent on good inhaler technique
Convenient	Possible to get no drug in lungs with very bad technique
More than 100 doses contained	Most products have low lung deposition
Usually inexpensive	Most products have high oro-pharyngeal deposition
Pressurization of contents protects against air moisture and microorganisms	

1.7.2 Spacers

Spacers are generally prescribed to enhance drug delivery from pMDIs for those who find it difficult to coordinate inhalation with actuation (Taylor, 2013). Spacers make the pMDIs easier to use, because both coordination and 'cold Freon' problems (Freon is the registered trademark of CFCs, in which the arrival of the cold propellant spray on the back of the throat causes the patient to stop inhaling) are reduced. The dose of pMDI is discharged directly into the reservoir prior to inhalation. This reduces the initial droplet velocity, large droplets may be removed by impaction, and efficient propellant evaporation occurs and the need for actuation/inhalation coordination is removed (Taylor, 2013). Additionally, this may reduce adverse effects of inhaled steroids such as oral thrush. The disadvantage of traditional spacers is that they may be cumbersome due to their large volume, e.g. Volumatic® and Nebuhaler®, although smaller, medium-volume spacers are now available, e.g. Aerochamber Plus® (Taylor, 2013) (Figure 1-4).

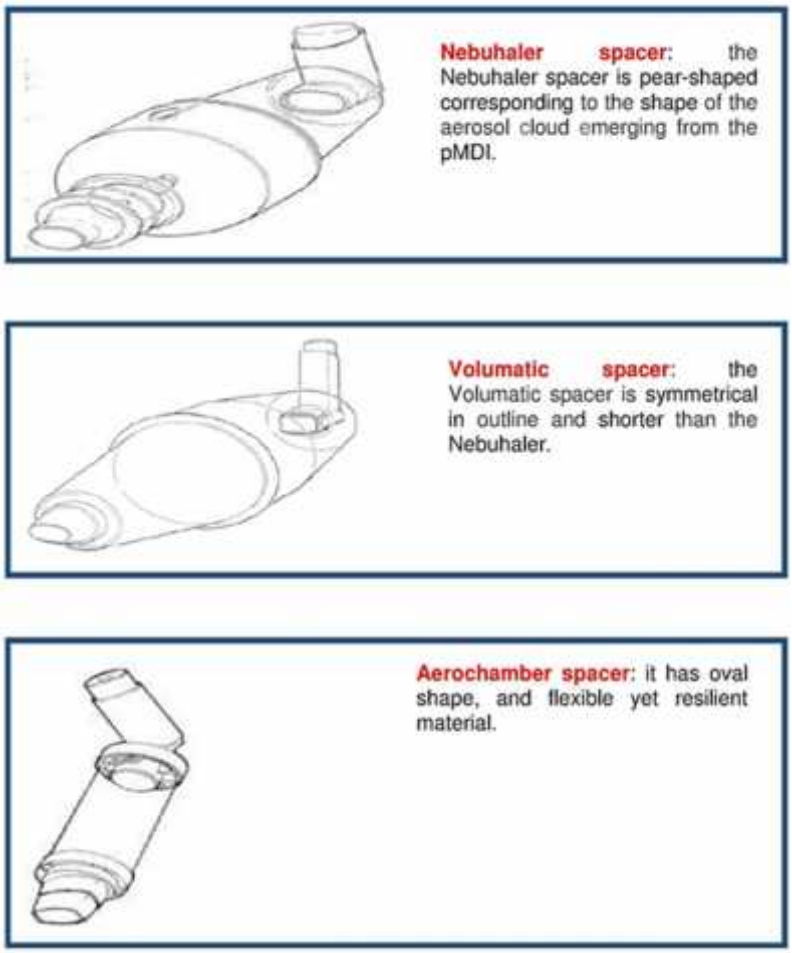


Figure 1-4: Spacer devices prescribed for COPD participants. Source: Global Initiative for Asthma (GINA), 2013.

1.7.3 Breath-actuated metered dose inhaler

These devices are alternatives to the standard pMDIs. They were introduced to improve coordination of actuation of standard pMDIs with inhalation. They are designed to actuate automatically as the patient inhales through them, e.g. Autohaler and Easi-Breath (Newman, 2005; Karotkin, 2011; Grammer et al., 2012).

The concept of a breath-actuated metered dose inhaler is good, because it automatically releases the drug when a patient is inhaling, which resolves the problem of patient coordination of actuation with inhalation (O'Callaghan and

Wright, 2002). Patients seem to find breath-actuated MDIs easier to use than standard pMDIs and may prefer them over other devices (Lenney et al., 2000). This will be discussed in later chapters.

Advantages and limitations of breath-actuated pMDIs

Because some patients may have difficulty coordinating inhalation and device actuation, breath-actuated pMDIs were developed to overcome this problem. Table 1-5 gives more information about the advantages and drawbacks of breath-actuated pMDIs (Berger, 2009).

Table 1-5: Advantages and disadvantages of breath-actuated pMDIs. Adapted from: Berger et al., 2009

Advantages	Disadvantages
Given for patients who are unable to use standard pMDIs or coordinate inhalation and actuation.	Patients may incorrectly stop inhalation at actuation.
May be particularly useful in the elderly.	Patients should be able to perform a maximal exhalation followed with a slow inhalation.
Improves lung disposition.	Cannot be used with spacer devices

1.7.4 Dry powder inhalers

In the dry powder inhaler (DPI) system, the drug is inhaled as a cloud of fine particles. The drug is either preloaded in an inhalation device or filled into hard gelatine capsules or foil blister discs which are loaded into the device prior to use. These devices are propellant-free and usually do not contain any excipient, other than a carrier, which is usually lactose (Taylor, 2013). They are breath-actuated, avoiding the problems of inhalation/actuation coordination encountered with pMDIs (Taylor, 2013).

Advantages and limitations of the dry powder inhalers

DPIs comprise both single and multi-dose models (Table **1-7**). All currently marketed DPIs are breath-actuated and no propellants are needed to generate the aerosol (Smyth, 2003). In general, DPIs are very portable and quick to use. In addition, spacers are not necessary with DPIs. Multi-dose DPIs incorporate dose counters and are easier to use than pMDIs (Broeders et al., 2009). Table 1-6 gives more information about the main advantages and drawbacks of the DPIs. Table **1-7** demonstrates some examples of the most used DPI devices by COPD participants in this study.

Table 1-6: Advantages and disadvantages of DPIs. Adapted from: Broeders et al., 2009

Advantages	Disadvantages
Small and portable	Needs moderate to high inspiratory flow required
Breath-actuated available for most substances and convenient (multi-dose devices)	Not suitable for delivering large doses
Do not contain propellants, so less patient co-ordination required and usually higher lung deposition than a pMDI	May not be appropriate for emergency situations and many patients cannot use them correctly (e.g. capsule handling problems for elderly)
Short treatment time	Most types are moisture sensitive

Table 1-7: Examples on the most used dry powder inhalers devices by COPD participants in this study

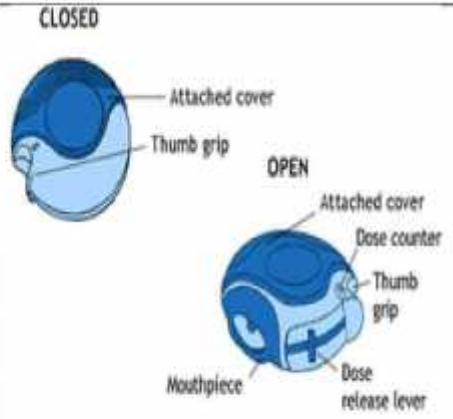
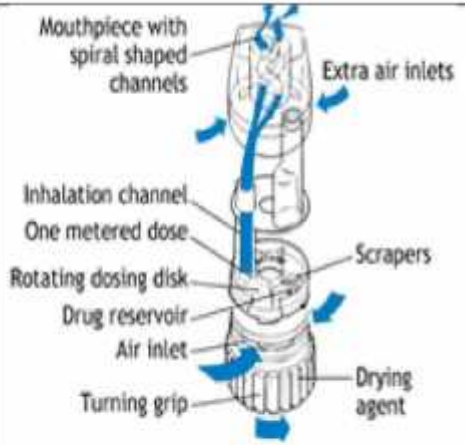
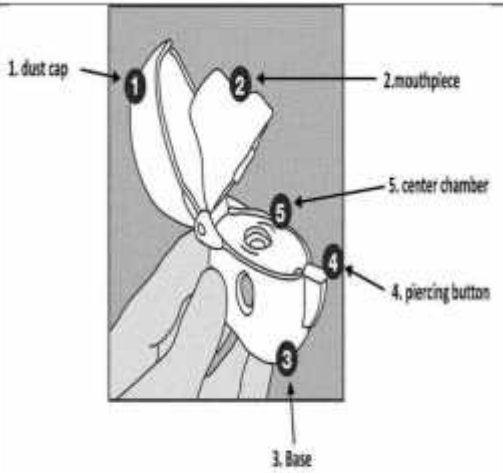
DPIs	The Accuhaler ®	The Turbohaler®	The Handihaler®
Diagram of the device	 The components of the Accuhaler; source: GlaxoSmithKline	 The components of the Turbohaler; source: AstraZeneca	 The components of the Handihaler; source: Pfizer
Description	A multi-dose DPI: it contains several single doses which are individually sealed and discharged each time the device is actuated without the need to manually replace spent cartridges or capsules. The Accuhaler contains the drug with additional lactose excipient.	A multi-dose DPI: it contains a bulk supply of drug from which individual doses are released with each actuation. The Turbohaler contains the drug which is located within this inhaler and is formulated as a pellet of a soft aggregate of micronized drug which may be formulated with or without lactose excipient.	A single-dose DPI in which each dose is loaded before use. The single-dose device contains the drug which is formulated as a micronised powder in a lactose excipient and is supplied in individual single-dose gelatine capsules which must be inserted into the inhaler before use.
Drugs available	B2-agonists and corticosteroids separately and in combination.	B2-agonists and corticosteroids separately and in combination.	Antimuscarinic agents such as tiotropium.

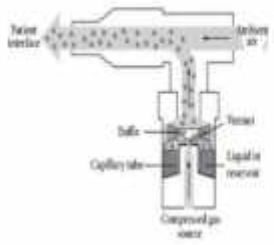
Table 1-7 continued.

DPIs	The Accuhaler ®	The Turbohaler®	The Handihaler®
Operation and loading the device	The Accuhaler device comprises 5 parts; the cover that slides to open, a thump grip that uncovers the dose-release lever, the dose-release lever, a mouthpiece and a dose counter. To load the device; hold the Accuhaler at its base using one hand; put the thumb of the other hand on the grip; open the Accuhaler by pushing the thumb grip around until it clicks; slide the lever until it clicks (Taylor, 2013).	The Turbohaler device comprises 4 parts; the cover, a coloured grip to load the dose, a mouthpiece and a dose counter. To load the device; unscrew the cap; twist the colored grip of the Turbohaler; twist it all the way back until it clicks and now it is ready to use (Taylor, 2013).	The Handihaler device comprises different parts; the cover, mouthpiece, base, green piercing button and centre chamber. Open the cover. Separate only one of the blisters from the blister card; then open the blister; insert the capsule and close the mouthpiece firmly against the grey base until you hear a click; press the green piercing button once until it is flat against the base, then release (Taylor, 2013).
Inhalation technique	• Hold inhaler in correct orientation. • Breathe out away from the inhaler as exhaling into the device will introduce humidity into the system, leading to obstruction. This is because of contact between the powder and humidity, the result being that subsequent doses will be inexact or unobtainable. In addition, the dose may be lost if insufficient breathing rate was used (Beaucage et al., 2002). • Place the mouthpiece between the teeth and close the lips around it. • Breathe in quickly and deeply to create turbulent flow to break up the particles (Beaucage et al., 2002). • Hold the breath for about 5-10 seconds.	• Hold inhaler in correct orientation. • Breathe out away from the inhaler. • Place the mouthpiece between the teeth and close the lips around it. • Breathe in quickly and deeply. • Hold the breath for about 5-10 seconds.	• Hold inhaler in correct orientation. • Breathe out away from the inhaler. • Place the mouthpiece between the teeth and close the lips around it. • Breathe in quickly and deeply. • Hold the breath for about 5-10 seconds.

1.7.5 Nebulisers

Nebulisers deliver relatively large volumes of drug solutions and suspensions and are frequently used for drugs that cannot be conveniently formulated into pMDIs or DPIs, or where the therapeutic dose is too large for delivery with these alternative systems (Taylor, 2013). Nebulisers also have the advantage over pMDI and DPI systems in that the drug may be inhaled during normal tidal breathing through a mouthpiece or facemask, and thus they are useful for patients who cannot use pMDIs or DPIs (Murphy, 2007). Although there are different types of nebulisers, including jet, ultrasonic and mesh nebulisers, this study has been focused only on the Jet nebuliser, as participants in this study used only this type. Therefore, it will be discussed in greater detail in this chapter. Table 1-8 gives information about jet nebulisers.

Table 1-8: Jet nebulisers.

Nebuliser	Jet nebuliser
Diagram of the device	 Jet nebuliser. Source: Lavorini. 2013
Description	Jet nebulisers use compressed gas (air or oxygen) from a compressed gas cylinder, hospital air-line or electrical compressor to convert a liquid (Usually an aqueous solution) into a spray (Taylor, 2013).
Drugs available	Bronchodilators, corticosteroids and antibiotics.
Operation and loading the device	The jet of high-velocity gas is passed through a narrow Venturi nozzle. An area of negative pressure, where the air jet emerges, causes liquid to be drawn up a feed tube from a fluid reservoir. Liquid emerges as fine filaments, which collapse into droplets as a result of surface tension (Taylor, 2013).
Inhalation technique	• Place the nebuliser on a steady horizontal surface. To comply with the manufacturer's instructions and ensure prolong the life span and prevent it from falling and breaking. • Assemble the nebuliser apparatus and plug in power source. • Place medicine in the specified dose in the nebuliser chamber (the medication tank) and close it. • Using a diluent or more than one nebule in the same nebuliser chamber, if required. Most of the frequently prescribed nebulized solutions are compatible and therefore can be mixed together in the nebuliser cup as long as the recommended capacity of the nebuliser used is not exceeded. Examples of compatible solutions include salbutamol, ipratropium bromide, and budesonide (Beaucage et al., 2002). • Attach the top portion of nebuliser chamber to mouthpiece or to mask. • Connect the bottom of nebuliser chamber with tubing to the air compressor. • Place mask over face or mouthpiece in to mouth. Masks should fit properly to prevent loss of medication (Beaucage et al., 2002). • Turn on the compressor. • Sit upright. To ensure maximum drug distribution within the lungs and reduce the quantity of medication that is deposited within the nose and upper airways (Beaucage et al., 2002). • Breathe through the mouth. • Complete the treatment and turn off the compressor. The treatment duration for a single dose of medication is approximately 10 minutes whereas multiple medications may take up to 20 minutes to administer (Beaucage et al., 2002).

Advantages and limitations of the nebulisers

When comparing nebulisers to pMDIs and DPIs, the nebulisers offer some advantages including: they are independent of patient inhalation technique. Thus, they are generally recommended for use by elderly patients who are unable to use hand-held devices correctly and in case of emergency with confused patients (Boe et al., 2001; Murphy, 2007). In addition, COPD patients who are too ill will be able to self-administer drug therapy via a nebuliser. Moreover, nebulisation delivery system is still the preferred administration route in some situations. According to the Nebuliser Project Group of the British Thoracic Society Standards of Care Committee and the Quebec Pharmacology Advisory Board (Boe et al., 2001; Beaucage and Nesbitt, 2002; Murphy, 2007), nebulisers are indicated for the following circumstances:

- For those patients who are unable to use other types of inhalation devices, for example, those who suffer from physical or cognitive deficits.
- In hospital settings for severe dyspnoea and when high doses of medication must be administered.
- Nebulisers can administer other drugs such as antibiotics which are not available in other inhalers.

Despite their advantages, nebulisers have some drawbacks including: nebulisation therapy is more expensive than treatment with hand-held devices. Other disadvantages include: high maintenance of the nebuliser device is required; it is a time-consuming process; nebulisers are usually noisy, depend on outside power sources (electricity), and are less portable than pMDIs and DPIs (Boe, et al., 2001; Murphy, 2007).

To summarise, this chapter has provided information about the background and literature review of COPD which was done to build up the case for conducting this study. It has defined the disease and illustrated the type of

medications' devices available for the management of COPD to help the reader later on to understand the outcomes and the issues that have emerged in this study. However, this was not sufficient. Therefore, the researcher decided to conduct a review aiming to identify and select the research evidence and provide a basis to refine the research objectives. Another reason for conducting a review is that the identified articles and evidence may allow the researcher to establish a theoretical framework in relation to what has been done in this area, and help her in designing the methodology of the study and in the selection of research tools which will be used to meet the study objectives.

2 Chapter Two: Review of the literature regarding medications and devices use

The aim of this chapter is to review the research into how COPD patients use inhalation devices to manage their disease in the context of their daily lives. The objectives were, firstly, to establish the extent to which COPD patients' behaviour regarding adherence to inhalation therapy has been studied and review evidence regarding how they make decisions about the use; and, secondly, to identify all research evidence relevant to problems COPD patients have with inhalation devices in the operation, cleaning and maintenance of inhaler equipment and to identify behaviours which may lead to treatment failures or exacerbations.

2.1 Methods

2.1.1 Search strategy and eligibility criteria

The articles were selected through their titles and abstracts by the researcher. The criteria for relevant studies were: (1) patients with COPD; using multiple inhalation devices; in primary care; (2) studies reported in the English language. The inclusion criteria were generated in order to achieve the aim of the review and to help the researcher to determine the most appropriate articles to best address the review questions. Therefore, only articles that addressed the review questions and met the inclusion criteria were included.

The review commenced with three main keywords/phrases: 'chronic obstructive pulmonary disease', 'inhalation devices', and 'adherence' (or) 'COPD' (or) 'inhalation technique' (or) factors. Lists of search terms associated with each keyword were generated from MeSH (medical subject heading) terms in PubMed and term mapping database in Embase (Ovid), to

provide a consistent way to retrieve information that may use different terminology for the same concept, for instance ‘chronic obstructive pulmonary disease’ and/or ‘COPD’ and/or ‘bronchitis’. Identifying COPD studies was challenging due to different terms used to describe COPD. Moreover, some studies described the use of respiratory medicines for a mix of respiratory diseases including COPD and asthma in the same study, which makes the analysis and data extraction challenging. As a result, the first attempt was to identify suitable search terminologies; therefore, a number of terms were required for searching, including: ‘chronic obstructive pulmonary disease’, ‘COPD’, ‘bronchitis’, ‘emphysema’, ‘inhalation devices’, ‘puffer’, ‘pressurised metered dose inhaler’, ‘pMDI’, ‘dry powder inhaler’, ‘DPI’, ‘nebuliser’, and ‘vaporiser’. Keywords not listed as MeSH or Map Terms were searched as phrases using the free text search mode. To ensure a scientific evidence base this review includes only peer reviewed journal articles.

2.1.2 Data sources

Electronic databases of PubMed (Medline), Embase (Ovid) and International Pharmaceutical Abstract (Ovid) were conducted for the period from 2000 to 2013, as this period witnessed the introduction of many therapeutic agents and higher technological devices for inhalation therapy, especially with the introduction of the patient-friendly devices DPIs. In addition, there was a systematic review published in 2001 by Brocklebank, comparing the effectiveness of inhaler devices in asthma and chronic obstructive airways disease. Therefore, the researcher decided to take this review further to find out how COPD patients and their behaviours have changed with regard to their use of their medicines or devices since that review (Brocklebank et al., 2001). The selected databases are large multidisciplinary bibliographic and citation databases with extensive journal coverage especially in behavioural medicine and modern respiratory treatment, including inhalational therapies.

2.1.3 Process of data extraction

Electronic databases were searched and duplicate articles were removed. All articles were reviewed manually by title, abstract and/or full-text for relevance. The reference lists of retrieved articles were manually examined for further applicable studies. Full text manuscripts were retrieved either electronically or as hard copy for assessment. Information was extracted into a proforma which included: primary author name and date of publication, country of the study, study settings, sample, methods employed, measures used and results. Studies of medication-taking behaviours of multiple inhalation therapy and the technical aspects of operation of the inhalation devices studies among COPD patients are attached as Appendix 1 and Appendix 2 respectively.

2.2 Results

The electronic database search retrieved a total of 326 articles of which 29 were duplicates. Screening of titles, abstracts and/or full texts for the remaining 297 identified that 19 were related to the review questions. A hand search of retrieved articles from the electronic database and journals led to identification of a further four articles. Therefore, a total of 23 studies were included in this review. Of those, 12 studies examined patients' behaviour regarding adherence to inhalation therapy (Van Grunsven et al., 2000; Melani et al., 2001; Barta et al., 2002; Boyter et al., 2005; George et al., 2005; George et al., 2006; Mehuys et al., 2010; Agh et al., 2011; Trivedi et al., 2012; Huetsch et al., 2012; Cecere et al., 2012; Khdour et al., 2012) (Appendix 1). Eleven studies examined the aspects of operation of inhalation devices and showed the frequency and range of problems experienced by COPD patients when using their inhalation devices (Lenney et al., 2000; Hesselink et al., 2001; Molimard, et al., 2003; Ho et al., 2004; Sestini et al., 2006; Wilson et al., 2007; Khassawneh et al., 2008; De Moraes Souza et al.,

2009; Rootmensen et al., 2010; Melani et al., 2011; Hämmerlein et al., 2011) (Appendix 2).

These studies were mostly based in outpatient clinics (N=11) (Lenney et al., 2000; Hesselink et al., 2001; George et al., 2005; Khassawneh et al., 2008; De Moraes Souza et al., 2009; Rootmensen et al., 2010; Agh et al., 2011; Melani et al., 2011; Huetsch et al., 2012; Cecere et al., 2012; Khdour et al., 2012), and patients' home (N=6) (Van Grunsven et al., 2000; Melani et al., 2001; Barta et al., 2002; Boyter et al., 2005; George et al., 2006; Sestini et al., 2006). Others were based in community pharmacies (N=3) (Mehuys et al., 2010; Trivedi et al., 2012; Hämmerlein et al., 2012). Most of these studies were conducted in Europe, especially the UK (N=6) (Lenney et al., 2000; Barta et al., 2002; Ho et al., 2004; Boyter et al., 2005; Wilson et al., 2007; Khdour et al., 2012), followed by Italy (N=3) (Melani et al., 2001; Sestini et al., 2006; Melani et al., 2011), and the Netherlands (N=2) (Van Grunsven et al., 2000; Rootmensen et al., 2010), Belgium (N=1) (Mehuys et al., 2010), Hungary (N=1) (Agh et al., 2011), France (N=1) (Hesselink et al., 2001), Germany (N=1) (Hämmerlein et al., 2011), the USA (N=3) (Cecere et al., 2012; Huetsch et al., 2012; Trivedi et al., 2012), Australia (N=2) (George et al., 2005; George et al., 2006), Brazil (N=1) (De Moraes Souza et al., 2009) and Jordan (N=1) (Khassawneh et al., 2008). The majority of studies that measured and examined medication-taking behaviours were conducted among patients with COPD alone (N=10) (Melani et al., 2001; Barta et al., 2002; Boyter et al., 2005; George et al., 2006; Mehuys et al., 2010; Agh et al., 2011; Cecere et al., 2012; Huetsch et al., 2012; Khdour et al., 2012; Trivedi et al., 2012), or a mix of lung diseases including COPD, asthma, bronchiectasis and other lung conditions (N=2) (Van Grunsven et al., 2000; George et al., 2005). The studies that examined the aspects of operation of inhalation devices and identified the frequency and range of problems experienced in their use were conducted mostly among patients with asthma and COPD (N=8) (Hesselink et al., 2001; Molimard et al., 2003; Ho et al.,

2004; Sestini et al., 2006; De Moraes Souza et al., 2009; Rootmensen et al., 2010; Hämmerlein et al., 2011; Melani et al., 2011), or COPD only (N=3) (Lenney et al., 2000; Wilson et al., 2007; Khassawneh et al., 2008).

2.2.1 Measures employed for data collection on medication-taking behaviour

Adherence among COPD patients has been found to be suboptimal. However, caution must be taken before drawing conclusions due to the wide variation in the estimated rates of non-adherence reported in previous studies, which ranged from 28% (Van Grunsven et al., 2000) to 80% (Huetsch et al., 2012). As a result, treatment failures were a major concern for patients with COPD. However, this variation regarding the rate of non-adherence could be due to the differences in patient populations, definition of non-adherence, methods employed, disease status, or respiratory conditions included in each study, as some studies included a variety of lung diseases such as asthma and COPD.

The majority of research that has investigated medication-taking behaviours (adherence) among COPD patients has employed quantitative approaches (N=11) (Van Grunsven et al., 2000; Melani et al., 2001; Barta et al., 2002; Boyter et al., 2005; George et al., 2005; Mehuys et al., 2010; Agh et al., 2011; Trivedi et al., 2012; Huetsch et al., 2012; Cecere et al., 2012; Khdour et al., 2012), by measuring the amount of medicine taken over a given time period. There is a paucity of qualitative studies (N=1) that have investigated patients' adherence to their COPD medications; they have done so by considering variables such as adherence decisions which were influenced by patients' beliefs about inhalation therapies and concerns of side effects (George et al., 2006).

There are a number of ways to measure adherence among patients with COPD, and each method has its strengths and limitations. Most studies focused on assessing medication adherence using self-report questionnaires on medication utilisation (Melani et al., 2001; Barta et al., 2002; Boyter et al., 2005; George et al., 2005; Agh et al, 2011; Khdour et al., 2012); others used prescription refill rate by reference to pharmacy records of dispensed prescription or manual recording of collected prescriptions (Mehuys et al., 2010; Cecere et al., 2012; Huetsch et al., 2012; Trivedi et al., 2012). One study used a semi-structured questionnaire (George et al., 2006) to explore factors associated with adherence from COPD patients' perspectives. To measure the adherence, these studies included either multiple COPD medications (Van Grunsven et al., 2000; Melani et al., 2001; Barta et al., 2002; Boyter et al., 2005; George et al., 2005; George et al., 2006; Mehuys et al., 2010; Agh et al., 2011; Khdour et al., 2012), or certain drugs such as long-acting beta-agonists (Trivedi et al., 2012; Huetsch et al., 2012; Cecere et al., 2012), corticosteroids (Huetsch et al., 2012; Cecere et al., 2012), or ipratropium bromide (Huetsch et al., 2012).

The most commonly used self-report methods to measure the COPD medication adherence were the Morisky scale (Agh et al., 2011; Khdour et al., 2012) and the Medication Adherence Rating Scale (MARS) (George et al., 2005), which are well-validated tools used widely for all chronic conditions including COPD (see Chapter four for more information about the strengths and weaknesses of different approaches and methods).

2.2.2 Non-adherence rates among patients with COPD

Previous reports have identified non-adherence to inhalation therapy in more than 50% of COPD participants in seven different studies (Melani et al., 2001; Boyter et al., 2005; George et al., 2005; Mehuys et al., 2010; Trivedi et al., 2012; Huetsch et al., 2012; Cecere et al., 2012), whereas four studies

reported adherence at >50% of the sample (Van Grunsven et al., 2000; Barta et al., 2002; Agh et al., 2011; Khdour et al., 2012). As a result, treatment failures might be a concern for patients with COPD.

2.2.3 Patients' identification as adherent/ non-adherent

Three studies defined adherence to COPD medication as taking 80% of doses as prescribed (Appendix 1) (Trivedi et al., 2012; Huetsch et al., 2012; Cecere et al., 2012). Another method was based on the definition used by previously validated questionnaires such as 4-item Morisky (patients scoring 3 or above were classified as 'adherent') (Agh et al., 2011; Khdour et al., 2012), or the MARS score (a score of 25 indicates perfect adherence) (George et al., 2005).

2.2.4 Factors contributing to medication use among COPD patients

The use of inhalation therapy was found to be influenced by patients' decision, which in turn was guided by many factors. The most frequently reported factors that influenced the use of medicines among COPD patients were actual and perceived efficacy and safety of the inhalation therapy (Barta et al., 2002; George et al., 2005; Huetsch et al., 2012; Cecere et al., 2012; Khdour et al., 2012), socio-demographic factors, including age (Mehuys et al., 2010; Agh et al., 2011; Trivedi et al., 2012; Huetsch et al., 2012; Cecere et al., 2012), educational level (Cecere et al., 2012), and ethnicity (Cecere et al., 2012), in addition to the complexity of drug regimen (George et al., 2006; Mehuys et al., 2010; Agh et al., 2011; Cecere et al., 2012). Other reported factors include: smoking status (Agh et al., 2011; Cecere et al., 2012; Khdour et al., 2012); disease severity (Huetsch et al., 2012; Cecere et al., 2012; Khdour et al., 2012); presence of other co-morbidities (Huetsch et al., 2012; Khdour et al., 2012); running out of medications (George et al., 2006); forgetfulness (Melani et al., 2001); and presence of symptoms (Barta et al., 2002; Cecere et al., 2012); in addition to social supports (Trivedi et al., 2012).

All these factors were found to have an influence on patients' decisions on not to use the inhalation therapy, which might put patients with COPD at risk of treatment failures.

2.2.5 Problems encountered with the use of inhalation devices in regards to the inhalation technique

Eleven studies were found in the literature examining and identifying the frequency and range of problems experienced by COPD patients in terms of operation of the inhalation devices and performing the inhalation technique, including: pMDIs alone or with large-volume spacers (Ho et al., 2004), DPIs alone including Accuhaler, Turbohaler, Handihaler, and Aerolizer (Wilson et al., 2007), or a combination of both pMDIs and DPIs (Lenney et al., 2000; Hesselink et al., 2001; Sestini et al., 2006; Khassawneh et al., 2008; De Moraes Souza et al., 2009; Rootmensen et al., 2010; Melani et al., 2011; Hämmerlein et al., 2011). In all studies, COPD patients were found to be using a combination of inhalation devices either from the same class (Ho et al., 2004; Wilson et al., 2007), or different classes (Lenney et al., 2000; Hesselink et al., 2001; Sestini et al., 2006; Khassawneh et al., 2008; De Moraes Souza et al., 2009; Rootmensen et al., 2010; Melani et al., 2011; Hämmerlein et al., 2011). These devices were commonly used to deliver mainly the following: salbutamol by pMDIs, salmeterol/fluticasone by Accuhalers; terbutaline and formoterol/budesonide by Turbohalers; salbutamol, salmeterol/beclometasone or fluticasone by Accuhaler; formoterol by Aerolizer and tiotropium by Handihaler.

2.2.6 Checklists for the inhalation technique assessment

Most previous studies have adopted checklists for the inhalation technique assessment among COPD patients. They have been based on previously published checklists or by using checklists given by pharmaceutical companies or medical leaflets (Lenney et al., 2000; Molimard, et al.,

2003;Sestini et al., 2006; Wilson et al., 2007), or previously published criteria by Newman checklist, 2005 (Melani et al., 2011), or Van der Palen and Beerendonk checklists in 1995 and 1998 (Rootmensen et al., 2010), or Plaza et al., 1998; Steier et al., 2003; Molimard et al., 2003; Muchão et al., 2008 (De Moraes Souza et al., 2009), or Connolly, 1995 (Ho et al., 2004). Two other studies developed their own checklists, based on information from the drug information centre of the German Association of Pharmacists (Hämmerlein et al., 2011), or the Dutch Asthma Foundation (Hesselink et al., 2001).

2.2.7 Definition of inadequate inhalation technique

The majority of studies (N=9/11) defined the essential steps for optimal delivery of the active drug into the lungs for each device. When one or more deviations were made regarding these essential steps, the inhalation technique was defined as inadequate or incorrect, potentially resulting in suboptimal drug delivery to the lungs (Lenney et al., 2000; Hesselink et al., 2001; Molimard, et al., 2003; Ho et al., 2004; Sestini et al., 2006; Wilson et al., 2007; Khassawneh et al., 2008; Rootmensen et al., 2010; Melani et al., 2011). Despite the importance of defining the adequate inhalation technique, past studies have not used validated instruments when assessing the inhalation technique. Only one study (Rootmensen et al., 2010) used a validated scoring method, which involved viewing and assessing a video-recorded inhalation demonstration by participants using device-specific checklists and mutually agreed scoring rules by raters. Many past studies have assessed inhalation technique among patients with a number of lung diseases including asthma and COPD (Hesselink et al., 2001; Ho et al., 2003; De Moraes Souza et al., 2009; Rootmensen et al., 2010; Hämmerlein et al., 2011; Melani et al., 2011). Two of those have shown that COPD patients made or were more likely to make more deviations from the recommended inhalation technique when using their inhalers than those with asthma (De Moraes Souza et al., 2009; Melani et al., 2011). Some other past

studies have included only one class of device in the assessment process, such as pMDIs only (Ho et al., 2004) or DPIs only (Wilson et al., 2007). No previous study assessed the inhalation technique using all three classes of inhalation devices to examine what device was associated with more errors or deviations when assessing the technique.

To maximise the accuracy of the findings, some studies included more than one rater in the assessment process (Lenney et al., 2000; Molimard et al., 2003; Sestini et al., 2006; Wilson et al., 2007; Rootmensen et al., 2010; Melani et al., 2011), whilst others included only one rater (Ho et al., 2004; De Moraes Souza et al., 2009; Hämmerlein et al., 2011).

2.2.8 Deviations and problems encountered by COPD participants when using their inhalation devices

In past studies, participants using pMDIs and DPIs were found to handle their inhalation devices erroneously as the percentage of participants with COPD who made at least one deviation from the recommended technique ranged from 2.9% (Ho et al., 2004) to 94.2% (De Moraes Souza et al., 2009). The percentage of COPD participants who made at least one deviation from the recommended inhalation technique was greater among pMDIs users than DPIs users (Lenney et al., 2000; Hesselink et al., 2001; Khassawneh et al., 2008; De Moraes Souza et al., 2009; Rootmensen et al., 2010). However, different studies by Melani et al (2011) and Ho et al (2004) reported that pMDIs were correctly used by most patients, especially with large volume spacers (Ho et al., 2004; Melani et al., 2011). Three studies found no significant difference between the pMDIs and DPIs; therefore, they were handled similarly by all patients (Lenney et al., 2000; Ho et al., 2004; Hämmerlein et al., 2011). Examining the inhalation technique among COPD patients with different devices is important, to detect whether users are using them effectively or not, as suboptimal techniques affect the drug delivery and

moderate the efficacy of the therapy and are a cause of treatment failures and poor clinical outcomes (Rootmensen et al., 2010).

For the pMDIs, the steps concerning shaking inhaler (the canister) well before use and actuating while inhaling deeply and slowly were the most frequently performed incorrectly, with the inhaler not being shaken (N=7) (Hesselink et al., 2001; Molimard, et al., 2003; Ho et al., 2004; Sestini et al., 2006; Khassawneh et al., 2008; Rootmensen et al., 2010; Melani et al., 2011), or the device being fired before start of inhalation or after end of inhalation (N=4) (Ho et al., 2004; Sestini et al., 2006; Khassawneh et al., 2008; Rootmensen et al., 2010). For the DPIs, the most common errors were in not exhaling away from the inhaler before inhalation or exhaling into the mouthpiece (N=5) (Molimard, et al., 2003; Sestini et al., 2006; Rootmensen et al., 2010; Melani et al., 2011; Hämmerlein et al., 2011), and no/short holding of breath for less than five seconds (N=4) (Molimard, et al., 2003; Sestini et al., 2006; Melani et al., 2011; Hämmerlein et al., 2011).

Further studies of inhalation technique in DPIs (Accuhaler, Turbohaler, Aerolizer, Handihaler and Diskhaler), reported that the percentage of COPD participants who made at least one deviation from the recommended inhalation technique when using DPIs was more when using single-dose DPIs such as Handihaler (Wilson et al., 2007) and Aerolizer (Wilson et al., 2007; Khassawneh et al., 2008; De Moraes Souza et al., 2009) than when using the multiple-dose DPIs such as Turbohaler and Accuhaler. These findings were contradicted by two other studies documenting that the essential errors which compromise treatment efficacy were made more among Turbohaler users than other DPI users using Aerolizer and Accuhaler (Molimard et al., 2003) or Handihaler and Accuhaler (Melani et al., 2011).

2.3 Discussion

This review brought together the information in the current literature regarding how COPD patients use inhaled medicines or inhalation devices. In previous studies, medicine taking or adherence to COPD medicines was found to be suboptimal, influenced by several factors, such as patients' perceptions about the efficacy and safety of the inhalation therapy. However, careful attention must be paid before coming to such a conclusion because of the wide discrepancy reported in the rates of non-adherence to COPD medication, which ranges from 28% to 80%. This variation can be explained by the dissimilarities in COPD population (e.g. age, disease severity, smoking history, etc.), the differences in adherence/non-adherence definition and the variation of methods employed. The results are also limited by the duration of some studies, which ranged from two weeks (Boyter et al., 2005) to six months (Cecere et al., 2012; Huetsch et al., 2012), and 12 months (Mehuys et al., 2010). Although a number of instruments and methods have been used to measure adherence, there was no gold standard method for measuring medicine taking due to the advantages and disadvantages of each method. For example, the easiest way to measure medicine taking is to collect information from the patients themselves through questionnaires. However, self-reporting methods may overestimate adherence (Smith, 2010). Therapeutic drug monitoring also may overestimate adherence because some patients tend to comply better for a short period of time before the drug test (Smith, 2010).

The use of inhalation therapy was found to be influenced by patients' decisions, which in turn were guided by many factors. However, the most frequently reported factor that influenced the use of medicines among COPD patients was actual and perceived efficacy and safety of the inhalation therapy. However, there were some contradictory results among these studies. For example, in four studies, it was found that, as complexity of the medical regimen increases (e.g. the number of medications, frequency of

dosage, etc.), medicine taking decreases (George et al., 2006; Mehuys et al., 2010; Agh et al., 2011; Cecere et al., 2012), whereas the same factor was not a significant predictor of non-adherence in George et al.'s, study (2005). Other studies have shown that disease severity or the decline in the FEV1% may be either not (Agh et al., 2011) or negatively (Cecere et al., 2012; Khdour et al., 2012) related to medicine taking. Others have shown that adherence is related to age: some authors found that, among adults, older age had a positive association with medicine taking (Mehuys et al., 2010; Agh et al., 2011), while others (Mehuys et al., 2010; Agh et al., 2011; Trivedi et al., 2012; Huetsch et al., 2012; Cecere et al., 2012) found that older age had a negative association with medicine taking due to risk of memory loss and cognitive impairment, which are associated with age and may adversely affect adherence.

This review demonstrates that incorrect use of inhalation devices is very common among patients with COPD and is more frequently associated with the use of pMDIs than DPIs. This review reveals suboptimal use and a wide range of problems with inhaler handling among COPD patients. However, very little is known about how and why problems arise. Therefore, there is a need for studies that examine how patients make decisions regarding the use of inhalers especially when a combination of inhalation devices is used at home, and how those decisions and difficulties may contribute to suboptimal outcomes and treatment failures.

2.4 Conclusion

Despite the extensive research, the review has illustrated that adherence to COPD medications was suboptimal among COPD patients. Therefore, COPD patients might be at risk of treatment failures, as the non-adherence misuse of inhalation therapy remains an unresolved problem. Most published studies have found that patients had many problems with inhalation

technique, but this is different based on the used device. Therefore, the research questions of the main study were:

- How do COPD patients use their multiple inhalation devices in the management of their condition?
- How do they use their COPD medication in the context of their daily lives and what beliefs and perceptions do they have in regards to the efficacy and safety of the inhalation therapy.
- What are the frequency and range of problems experienced by COPD patients in technical aspects of the operation, cleaning and maintenance of inhaler equipment that may lead to suboptimal care or treatment failure?
- What is the role of carers and what are the types of assistance with medicines provided for COPD patients by family and friends.
- What are the priorities and concerns for patients in the context of current and potential future service provision?

In addition to the evidence provided by previous research which informs the research questions, preliminary fieldwork and discussion with Pinn Medical Centre staff about this study were conducted, to identify the initiatives that will be focused on in this study to contribute to the existing literature in regards to the use of multiple inhalation devices by COPD patients in their homes and to highlight the priorities and concerns of healthcare prescribers in regards to the use of COPD medicines by COPD patients.

3 Chapter Three: Preliminary fieldwork and discussion with Pinn Medical Centre Staff

This chapter describes the preliminary fieldwork which was conducted to identify the priorities and concerns of healthcare prescribers in regards to the use of COPD medicines and/or devices by patients.

3.1 The study aim

The study aim was to examine the use of multiple inhalation devices by COPD patients in the management of their disease in the context of their daily lives and to consider how patients may most effectively be supported. To achieve this aim five objectives were written.

3.2 The study objectives

- To examine the use of multiple inhalation devices used in combination by COPD patients in the management of their condition.
- To examine COPD patients' use of their medication in the context of their daily lives, information requirements, beliefs and perceived effectiveness and safety of therapy.
- To identify the frequency and range of problems experienced by COPD patients in technical aspects of the operation, cleaning and maintenance of inhaler equipment that may lead to suboptimal care or treatment failure.
- To document the role of carers and the assistance with medicines that patients receive from family and friends.

- To identify the priorities and concerns for patients in the context of current and potential future service provision.

Before the study was formally designed preliminary fieldwork was done, included discussions with professionals from the Pinn Medical Practice. The discussion concerned some of the issues identified in the literature or in practice relating to the use of inhalation therapy by COPD patients and the feasibility of conducting the study.

3.3 Preliminary field work and discussion with Pinn Medical Centre

This work is in partnership with Pinn Medical Centre.

3.3.1 The aim of preliminary field work

The aims of the preliminary fieldwork were the following:

- To consider healthcare professionals' views, thoughts and concerns on the proposed subject when designing the work.
- To review the study aim and objectives and/or suggest any other aspects of which the researcher was unaware to build up the study aim and objectives, as healthcare prescribers may have rich experience of the issues that COPD patients had in the past which would help to raise the researcher's awareness of the possible issues.
- To identify the number of COPD patients who are registered at Pinn Medical Centre and are currently using multiple inhalation devices at home including pMDIs, DPIs and nebulisers.
- To obtain some information on what inhalers were the most commonly prescribed or used by patients at home.
- To discuss the feasibility of conducting the study and inform on suitable methods for collecting data and recruiting participants from the perspective of potential participants.
- To help the researcher in preparing and reviewing the documentation such as the invitation letters, the questionnaire and the reply slip.

3.3.2 Meeting with healthcare professionals at Pinn Medical Centre

The respiratory specialist at Pinn Medical Centre, Dr. Tricia Robertson, was contacted by the researcher and a formal meeting was arranged with her and the research team at Pinn Medical Centre on the 7th of September 2011. Discussions at the meeting were focused on the following: the total number of COPD patients who are registered at Pinn Medical Centre and are currently using multiple inhalation devices at home including pMDIs, DPIs and nebulisers, in addition to approaches to recruit COPD patients, the data collection process, and the selection and assessment of COPD patients.

3.3.3 The impact of the preliminary fieldwork on the development of the study

The preliminary fieldwork informed the development of the study methods (Figure 3-1) and the instruments that should be used in this study to meet the study objectives. After consulting with academics and the respiratory specialist, it was decided to recruit COPD patients from Pinn Medical Centre as it is considered as a large medical practice that serves 20,000 patients and covers a large geographic area of North West London. It includes people of different different age groups, ethnicity, disease status and smoking history. This would confer some generalizability. Preliminary discussion with collaborators and medical staff indicated that Pinn Medical Centre has 116 patients with COPD who are prescribed a range of inhalation devices and are eligible for this study. Therefore, it was decided to target those who are using a combination of pMDIs, DPIs, and nebulisers. Based on the information obtained on the day of the meeting, the most appropriate way to approach these COPD patients was to send an invitation letter to their home address asking them to take part in this study. In addition to that, interviewing COPD patients in their homes was seen as the most suitable method for data collection and this will be described in depth in the next chapter. Therefore, the preliminary fieldwork along with the literature review helped in developing the study objectives and informing the choice of methods.

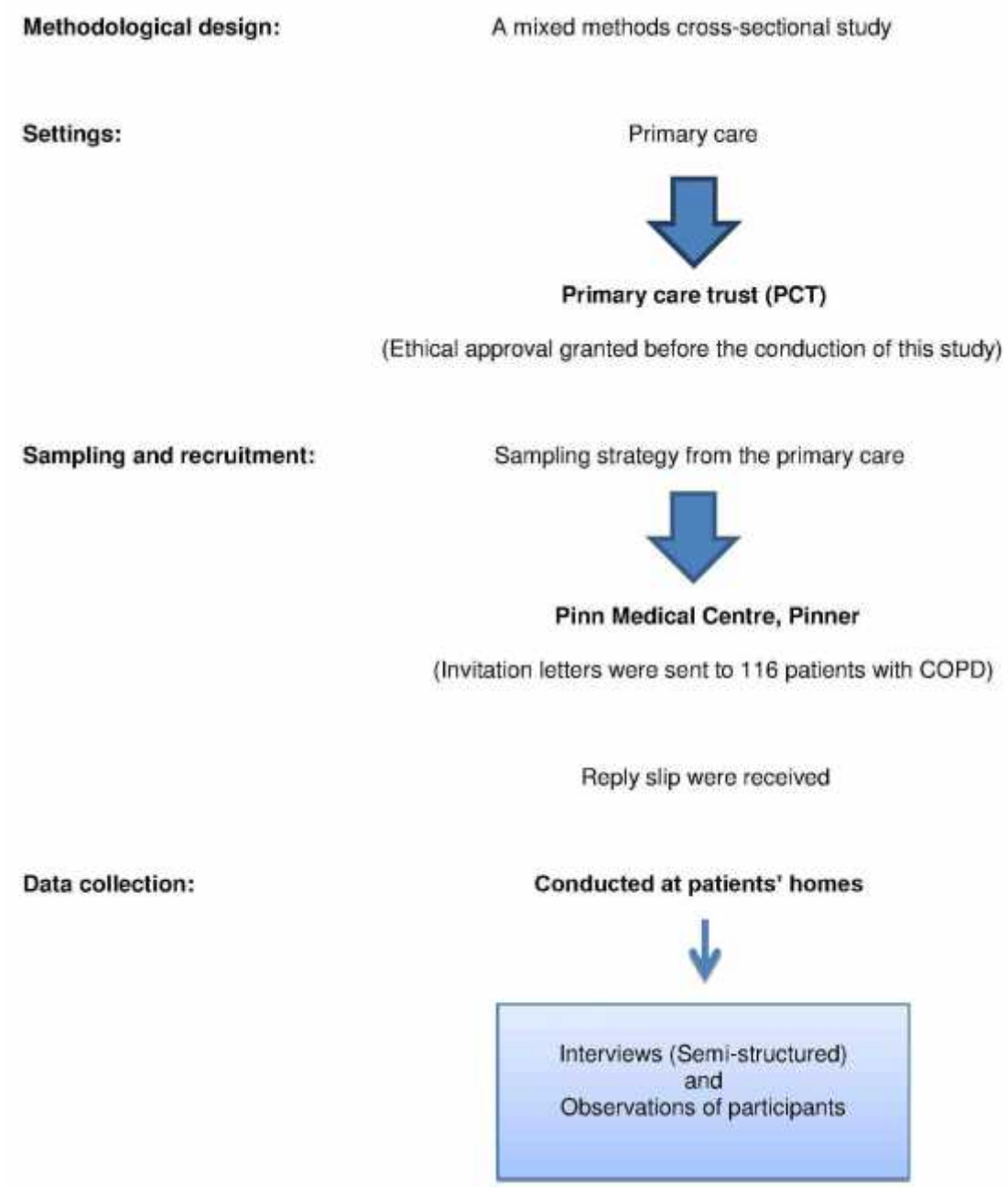


Figure 3-1: Methodological design employed for the main study.

4 Chapter Four: Research context and methodology

This chapter lists the aim and objectives of the main study and explores what methods were the most appropriate to be used to meet the study aim and objectives. In addition, it discusses the different methods used for data collection and highlights the purpose of selecting a specific method over others, followed by a discussion of how the data collection process was carried out and the approaches taken to data analysis.

4.1 The study aim

From the review of the available literature, the study aim was to examine the use of multiple inhalation devices by COPD patients in the management of their disease in the context of their daily lives and to consider how patients may most effectively be supported. To achieve this aim, five objectives were written. These are:

- To examine the use of multiple inhalation devices used in combination by COPD patients in the management of their condition.
- To examine COPD patients' use of their medication in the context of their daily lives, information requirements, beliefs and perceived effectiveness and safety of therapy.
- To identify the frequency and range of problems experienced by COPD patients in technical aspects of the operation, cleaning and maintenance of inhaler equipment that may lead to suboptimal care or treatment failure.
- To document the role of carers and the assistance with medicines that patients receive from family and friends.

- To identify the priorities and concerns for patients in the context of current and potential future service provision.

4.2 Study design

The study was undertaken during the period between February 2011 and May 2014. This was a cross-sectional study design that took a mixed methods approach using qualitative and quantitative methods and observations of inhalation devices' use with patients in their own homes. The qualitative method included conducting semi-structured interviews with COPD patients, in order to examine how patients make decisions regarding the use of inhalers especially when a combination of inhalation devices were used at home, and how those decisions and difficulties may contribute to suboptimal outcomes and treatment failures to optimise medicine use, therefore improving treatment outcomes. The quantitative method involved administering questionnaires to measure the extent or the rate of non-adherence (8-item MMAS) among COPD patients, patients' beliefs about their COPD medicines (BMQ), and inhalation technique assessment for each patient individually using device-specific checklists. A retrospective review of patients' medical records in the surgery, including patients' clinical data, was also conducted to complement and validate the results obtained from the face-to-face interviews. The data were collected from May 2012 to December 2012. Table 4-1 shows a summary of the methods used to fulfil research objectives.

Table 4-1: Summary of the used methods

Method	Determinant question(s)	Rationalisation
Triangulation method was used: Semi-structured interviews using a questionnaire. Patient's GP records review	Q2,Q3	To get an overview of what COPD medications patients use to manage their condition, what they are using at the moment, for what and what they had been using in the past, to manage their condition.
Triangulation method was used: Semi-structured interviews using questionnaire. Morisky scale and Beliefs about medicines questionnaire (BMQ scale).	Q2,Q3,Q4,Q5, Q6,Q7, Q9, Q10, Morisky scale, Beliefs about medicines questionnaire (BMQ scale)	To find out how patients feel about using different devices, what they like or dislike about them, how they make decision about the use, and what problems did they have in the past, what works and what does not work and to understand why some patients act in a certain way. For example, why some patients do not take their medicines as prescribed and what kind of problems do they face that stop them from taking their drug regimen as recommended.
Triangulation method was used: Semi-structured interviews using questionnaire Observational method using inhalation technique and cleaning check-lists with comment boxes.	Q8,Q9	Looking for problems experienced by COPD patients in technical aspects of the operation, cleaning and maintenance of inhaler equipment that may lead to sub-optimal care or treatment failure
Semi-structured interviews using questionnaire.	Q14,Q15	Looking for kind of assistance received by COPD patient from family and friends and any other assistance or help with medicines that COPD patient's need.
Semi-structured interviews using questionnaire.	Summary of all questions.	Looking for the priorities and concerns from patients' perspectives in the context of current and potential future service provision.

4.3 Rationale for the chosen methods

4.3.1 Rationale behind choosing mixed methods approach (Qualitative and quantitative)

The term "mixed methods research" refers to the type of research in which a researcher combines elements of qualitative and quantitative research approaches (Smith, 2010). Using a mixed method approach in a study was useful because it enables generation of new knowledge and enhances the validity of the research by, firstly, collecting the data from a variety of sources qualitatively and quantitatively, which leads to greater validity than when

either was used alone (Richey and Klein 2007); and, secondly, by answering the research questions from a number of perspectives and confirming that there was no gap in the data collected which cannot be met with the use of one method (Smith, 2010; Hunter, 2011).

A mixed methods approach was used in this study in order to collect qualitative and quantitative viewpoints, data and techniques for the reason of developing broadness and a more complete knowledge and understanding of the use of multiple inhalation devices by chronic obstructive pulmonary disease patients in primary care, in order to develop or test theories, compare groups or make strong predictions about the reasons for treatment failures. This method was selected when the researcher and her team believed that neither qualitative nor quantitative approach alone would answer the research questions. Therefore, one method will inform the other.

A mixed method approach to research was referred to as triangulation. In the construction of this research, the data were triangulated after collecting the information from different sources, to ensure the validity of the data and allow more accurate assessment (Smith, 2010; Hunter, 2011). In research this was referred to as ‘triangulation’, which is defined as the use and comparison of two or more methods of data in the same study, to make sure there was enough evidence to make valid claims (Smith, 2010).

A triangulation was used in this study by collecting data through the following sources: semi-structured interviews using a questionnaire comprising open and closed questions, patients’ GP records’ review, and observational method using inhalation technique and cleaning checklists with comment boxes. When conducting this study, participants were observed and asked questions to provide different perspectives on a set of issues related to the

study aim and objectives. For example, it was aimed to examine how COPD participants use and operate their inhalation devices, what they like or dislike about them, what kind of problems they had with different inhalers, what worked and what did not work, and how they clean and store their inhalers. Therefore, to answer these questions, COPD participants were asked and observed by the researcher to operate their devices and conduct the inhalation technique, and to show and explain how these devices were usually cleaned and stored using device-specific checklists with comment boxes to be filled out by the researcher, to identify whether these participants have any difficulties or problems when operating their devices. In addition to this, participants were asked different questions through a questionnaire about how they use their inhalers and whether they have/had experienced any problem when using their devices in their homes.

Another example for triangulation was that when participants were asked about their current COPD medicines and what they had been using in the past, the data obtained from the interviews were compared with data obtained from medical notes in the GPs' surgery to see if participants were accurate about what they had said. Moreover, in regards to patients' adherence and beliefs about their COPD medicines, the data obtained from interviews were compared to the data obtained from the self-reported questionnaires such as Morisky scale and BMQ to ensure data validity by comparing data on the same variables that have been obtained in different ways, which enables more reliable estimates to be made (Smith, 2010).

4.3.2 Rationale behind choosing face-to-face semi-structured interview method

Although there are a diversity of methods and approaches involved in collecting qualitative data, interviews seemed to be the most appropriate method to meet the aims and objectives of this research. Face-to-face

interviews are an efficient and practical way of obtaining data about things which cannot be easily noticed such as how people use their inhalers in real life and in action (e.g. when assessing the inhalation technique). The interviews provide direct contact between the interviewer (the researcher) and the participants (respondents), making it easier to build a relationship with the respondents and obtain more meaningful, detailed information and considered responses. Moreover, these direct interactions could have allowed the interviewer to gain direct access to participants who might not otherwise have been willing or able to take part due to the severity of their disease or the existence of other illnesses which may have prevented their participation. As an example, if a patient was given a survey or a structured instrument to complete, literacy problems would have had to be addressed (Scanlan, 2002). Further, it is recognised by Hunter (2011) and Smith (2010) that this method generally has high validity through allowing the respondents to talk about their use of medicines and any problem they have with their COPD medicines in detail and depth (Hunter, 2011), and because the data obtained from respondents were 'first hand', which means they did not depend on others' reports of what they see or do, which might or might not be accurate (Smith, 2010). In addition, it was also recognised by Bowling and Ebrahim (2005) that interviews may have a higher response rate than questionnaires as they are a less formal method and allow immediate data collection (Scanlan, 2002).

Another advantage of this type of interview is that it is often conducted in a natural setting (patients' homes), which allows important detailed valuable information to be gathered because patients will be more comfortable talking about their medicines if they are sitting at home. In addition, the response rate is known to be generally higher with face-to-face interviews, compared to telephone interviews or surveys that are sent through the post (Hunter, 2011). Receiving a questionnaire through the mail can be ignored due to lack of personal touch (Hunter, 2011). Moreover, semi-structured interview can

make use of prompts: questions which were used in this study to clear up any confusion or misunderstandings about complex questions. Furthermore, it allows the interviewer (researcher) to act as an observer, giving him/herself the opportunity to focus on non-verbal cues and to record the interview using audiotapes (Hunter, 2011).

Like any other methods, face-to-face interview has disadvantages: firstly, it depends on the interviewer's skills and his/her ability to question during the interview and follow. Secondly, although this method has high validity because the information is obtained directly from its original source (the patient), the interviewer has no real way of knowing if the respondents answered truthfully. However, respondents may not intentionally misinform but they may have imperfect recall. For example, if they were being asked to remember what COPD medicine(s) they used in the last 24 hours, they might remember very little about what happened, thus giving inaccurate and incomplete information (Hunter, 2011). Thirdly, in terms of reliability, in this project the data were gathered on one occasion because it was sometimes difficult to do the interview more than once with the same focus group using face-to-face interview and also the sample size of this kind of method is usually not big, ranging from 30 to 60 participants. Fourthly, this research was conducted in the Pinner area (Zone 5 in London). The travel time was between 40 and 50 minutes and the travel ticket cost more than £8 per day; thus, it was expensive and time consuming.

Interviews were then selected as the most suitable method to examine the use of multiple inhalation devices by COPD patients in the management of their disease in the context of their daily lives, from their perspectives, and to consider how patients may most effectively be supported.

There are a variety of methods that can be used for data collection in a qualitative approach such as in-depth structured, semi-structured and unstructured interviews which can be used in interviews, group discussion or focus groups, and participant and non-participant observational studies (Bowling and Ebrahim, 2005). However, the semi-structured research technique was seen as the most appropriate method to be used to meet the study objectives. Semi-structured instruments consisted of pre-prepared questions related to domains of interest (COPD disease and medicines) applied to a representative sample of COPD participants to identify factors or variables to be analysed (Smith, 2010).

The reason for choosing a semi-structured technique was because this technique is the most commonly used qualitative method as it is a flexible tool which enables the researcher to set an agenda for the interview to discuss interesting replies further and to clarify points of ambiguity in participants' answers to any given question (Pope and Mays, 2006). Another reason for selecting a semi-structured instrument was because, firstly, it can make use of both close-ended questions (quantitative data) (e.g. Do you sometimes forget to take your regular COPD medicines?) and open-ended questions (qualitative data) (e.g. How many times in the last week have you missed a dose of your regular COPD medicines and why?), which allows quantitative and qualitative analysis to be undertaken. In this project this method was considered to gather information about respondents' adherence and beliefs about COPD medicines using predetermined structured measures (close-ended questions) and more detailed examination of how COPD patients use their current inhalation therapy to manage their condition, what they were using at the moment or what they had been using in the past, what they feel about using different devices used in combination, what they like or dislike about them, how they make decision about the use, what problems did they have in the past with different inhalers, what works and what does not work, using predetermined unstructured measures (open-

ended questions). Qualitative approaches (open-ended questions) are known to be the most appropriate for ‘how’ and ‘why’ questions (Smith, 2002). It helps to illustrate the way people act and think; additionally, it explores patterns and barriers in people’s thoughts and behaviours. This sharply contrasts with quantitative research, in which the researcher may be testing a hypothesis, or explaining phenomena by collecting numerical data that are analysed using mathematically based methods (Seidman, 2012).

Secondly, this method is used in exploratory studies to collect a substantial amount of information by setting up an interview and talk (like a conversation) following an interview schedule, which draws on principles of qualitative and quantitative approaches (Smith, 2002). All questions in the interview guide or interview schedule were prepared in advance; however, some of which may raised by respondents during the interview. Therefore, the actual direction and content of the interview, in terms of issues discussed, were determined by the respondents’ viewpoints and answers. Thus, the researcher was prepared to consider new issues and ask questions throughout the interview process, in order to get a deeper understanding of phenomena of interest in context of patients circumstances or environment and with their reasoning (Smith, 2010; Seidman, 2012), emphasising the point that semi-structured interviews allow the researcher to observe and ask questions that lead to a deeper understanding of phenomena (e.g. How many times in the last week have you missed a dose of your regular COPD medicines?/Why do you miss a dose of your regular medicines?) in the context of which they occur and to clarify any unclear responses (Smith, 2010). In regards to this study, this flexibility from the semi-structured instrument would not have been obtained if a structured interview or self-completion questionnaire had been used and a totally unstructured interview approach would not have ensured that the same topics were discussed and covered by all participants (Scanlan, 2002).

4.3.3 Rationale behind choosing self-reported Morisky 8-items medication adherence scale (MMAS)

Eight-item Morisky was chosen in this study in order to evaluate the extent and rate of non-adherence to the inhalation therapy among patients with COPD and therefore provide recommendations and feedback to healthcare professionals first and patients second and the required interventions for the purpose of maximising patients' adherence especially that adherence plays an important role in determining the successful disease management, since inadequate adherence can lead to treatment failures, suboptimal health outcomes and increase healthcare costs. Therefore, accurate assessment of adherence behaviours to COPD medicines is an essential component for successful management of the condition.

Various self-report tools have been used in previous studies to measure adherence behaviours and associated health beliefs and attitudes in both general and specific patient populations. However, there is no "gold standard" measure of medication adherence (Kim et al., 2000), but in the last 20 years the most commonly used tool to measure patients' adherence to medication is perhaps the 4-item original Morisky scale (Lichtenberg, 2010).

Although a direct self-report method such as a questionnaire may overestimate adherence and may be subject to memory biases, it was chosen as the method for assessing adherence in this study due to its simplicity and feasibility for most settings including home settings (Smith, 2002). According to Horne et al., when selecting a self-report tool for adherence assessment, a readily reliable and valid questionnaire must be used because it is the most efficient, cost-effective, and time-saving method of assessing adherence, related beliefs and attitudes (Horne et al., 1999). From a clinician's point of view, self-reports are the most workable and useful measures of adherence (Turner et al., 1995), as they can identify the reasons

behind non-adherence along with its detection, which could then help in addressing those underlying issues. When self-report and clinical observations are combined, they have been shown to have better accuracy than self-report alone (George et al., 2006).

From the researcher's point of view, each method has advantages and disadvantages; some are preferred in one setting than others. For example, using direct measures which use drug metabolite in the urine or blood can be useful in hospital settings where the laboratory can be accessed easily to obtain the result, whereas prescription refill rate might be good for pharmacy-setting studies where the patients' drug history can be accessed as well. Others such as patient self-reports and pill count can be more useful in home-setting studies that involve treatment that the patient carries out at home, by asking the patient several questions about medicine taking to get the answer or counting the medication left in the patient's drug bottle. However, using patient self-report method or pill count does not guarantee the accuracy of the result because some patients may want to please the healthcare professional or the researcher by giving them incorrect information about medicine taking maybe deliberately or in-accidentally.

This study was conducted in patients' homes; therefore, the patient self-report method was considered. Although pill count seems more reliable than self-report method because the researcher will count the medication left without relying on patients' stories, it is a time-consuming process and there is no assurance that the medicines missing from the inhalers were actually taken by patients. As a result, it was decided to use the patient self-report method to gather the information on adherence (Fairly et al., 2005).

Having chosen self-report as the preferred method for assessing adherence, the next step was to select which self-report questionnaire to include. Various self-report tools have been used for studying adherence behaviours, and associated health beliefs and attitudes in both general and specific patient populations. However, it was decided to use the Morisky scale to measure adherence as it is the most commonly used measure of adherence and can distinguish between intentional and non-intentional non-adherence (George et al., 2006). Moreover, the Morisky scale has shown to be correlated with other measures of adherence (O'Donohue and Levensky, 2006) such as pill count (Haynes et al., 1980) and pharmacy records (Fairly et al., 2005).

The Morisky scale was developed by Morisky and colleagues in 1986. It was originally developed to measure adherence to antihypertensive medications using a validated 4-item scaled questionnaire. After that, it has been used to evaluate adherence across a wide variety of health conditions including asthma and COPD (Agh et al., 2011). The Morisky instrument was validated in a number of studies and shown to have good psychometric properties, and adequate internal consistency (α=0.61), sensitivity (81%), and specificity (44%) (Morisky et al., 1986). The four-item scale consists of the following questions:

1. *"Do you ever forget to take your medicine?"*
2. *"Are you careless at times about taking your medication?"*
3. *"When you are feeling better, do you sometimes stop taking your medications?"*
4. *"Sometimes if you feel worse, do you stop taking your medications?"*

To score the Morisky scale, each question that is answered with a "no" receives a score of 1 and each "yes" answer receives a score of 0. The possible scoring range is therefore 0 to 4. Patients who answer "no" to four of these questions are classified as high adherence; those with two to three "no" responses are classified as medium adherence; and those who answer "no" to none or one of these questions are classified as low adherence.

Although the original Morisky scale illustrated the ability to predict adherence, it was not formed to describe patient's long-term continuation of therapy, which is considered to be an essential factor in the long-term management of chronic diseases. Also, the Morisky scale was not originally designed to categorise patients into a low/high continuum for motivation and knowledge. As a consequence, additional items were added to better capture barriers surrounding adherence behaviour (Morisky et al., 2008). A new 8-item self-report Morisky Medication Adherence Scale (MMAS) includes the following questions

5. *Do you know the long-term benefit of taking your medicine as told to you by your doctor or pharmacist?*
6. *Sometimes do you forget to refill your prescription medicine on time?*
7. *Taking medication every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan?*
8. *How often do you have difficulty remembering to take all your medications? (Please circle the correct number).*

All questions on the 8-item MMAS are answered on a "yes" or "no" scale except question number 8 which is answered on a "Never/Rarely", "Once in a while", "Sometimes", "Usually" or "All the time" scale. Each "no" answer to items 1-7 receives a score of 1 and each "yes" answer receives a score of 0 except question number 5 where a "no" answer receives a score of 0 and a "yes" answer receives a score of 1. Question number 8, which asks participants to rate the difficulty remembering to take all their medicines, is scored as follows (never/rarely = 4, once in a while = 3, sometimes = 2, usually = 1, all the time = 0). Item 8 was standardised by dividing this item by 4. The MMAS scores can range from 0 to 8, which have been categorised as high, medium and low adherence (MMAS score of 8, 6 to <8, and <6, respectively) (Morisky et al., 2008).

The new scale has been determined to have a higher reliability and better psychometric properties compared with the 4-item scale (α=0.83 vs. α=0.61) (Morisky et al., 2008). As the 8-item self-report Morisky Medication Adherence Scale (MMAS) showed a good reliability and favourable psychometric properties and had been validated in a large patient population with chronic conditions (Morisky et al., 2008), it was decided to use it for measuring participants' adherence in this study.

4.3.4 Rationale behind choosing Beliefs about Medicines Questionnaire (BMQ)

In this study, the researcher aimed to know what patients think about their COPD medicines in terms of overall drug necessity and concerns from their perspective. Therefore, patients' beliefs about the necessity of their COPD medication and concerns about adverse effects were measured and examined.

To improve adherence to treatment and therefore clinical outcomes, it might be important to consider patients' beliefs about medicines, especially given that patients' beliefs have been associated with medication adherence (Horne et al., 1999). Therefore, it was crucial to examine beliefs of patients with COPD about their therapy and investigate if these beliefs had any influence on patients' decisions to use or not to use the inhalation therapy, which may lead to treatment failures and suboptimal outcomes. The beliefs that patients have about their medicines have been shown to be an important factor that influences medication-taking behaviours among COPD patients in previous studies (Barta et al., 2002; George et al., 2005; Huetsch et al., 2012; Cecere et al., 2012; Khdour et al., 2012). Therefore, measuring patients' beliefs about medicines can also provide a new angle and important knowledge which may be used in optimising medicine taking, and it can be a good reference for future intervention studies aiming at improving medicine

taking in patients with COPD, resulting in optimising medicine use and improving treatment outcomes.

To measure the above domain (beliefs about medicines), it was agreed to adapt a suitable questionnaire from the literature which provides a reliable response and a valid reflection of the issues to be measured as well as being efficient and effective in collecting data of interest (Smith, 2002). Therefore, the Beliefs about Medicines Questionnaire (BMQ) was considered.

The BMQ was developed by Horne in 1999, to assess commonly held beliefs about medicines, and was validated on several medical samples including COPD. This scale is comprised of two sections, the BMQ general and the BMQ specific. The first section (the BMQ general), relating to beliefs about medicines in general, also comprises two factors, general-overuse (beliefs that medicines are overused by doctors) and general-harm (concerning beliefs regarding the harmful effects of medicines). The second section (the BMQ specific) comprises two factors, specific-necessity and specific-concerns; both are related to beliefs about necessity of prescribed medication and concerns about adverse effect. A patient with COPD is usually given complex medication regimens including multiple drugs (inhalers or tablets) with different frequencies and dosing schedules, some of which may have many adverse effects, such as steroids, which might cause a burden in medicine taking. In this study, it was decided to use the BMQ specific tool because choosing a disease-specific instrument was preferred to focus on a single specific disease and the personal beliefs patients have about the necessity of prescribed COPD medication and concerns about adverse effects.

The BMQ is a reliable tool, and has been validated for use across a range of different diseases including asthma, renal, cardiac and general medical illnesses (Horne and Weinman, 1999). In the BMQ, participants were asked to rate their agreement with a specific statement using a 5-point Likert scale (1=strongly disagree, 2= disagree, 3=uncertain, 4=agree, 5=strongly agree). The scores of each subscale were computed from the sum of all items within that particular subscale and range from 5-25 from both subscales – BMQ necessity and BMQ concerns. In addition, the necessity-concerns differentials were computed by subtracting the total BMQ concerns subscale score from the total BMQ necessity subscale score. A positive differential score indicates that participants perceive the benefits of their medication to outweigh their concerns about the risk of the medication. In contrast, a negative differential score indicates that participants perceive the risk of taking their medication to outweigh the benefits. The differential scores range from -20 to 20 (Horne and Weinman, 1999).

4.3.5 Direct observation

From previous studies, it was seen that a high number of COPD patients use their inhalers inappropriately and made many deviations when performing the inhalation technique from what is recommended by the published guidelines. The percentage of participants with COPD who made at least one deviation from the recommended technique ranged from 2.9% (Ho et al., 2004) to 94.2% in previous studies (De Moraes Souza et al., 2009). Any deviation from the published guidelines in regards to the recommended inhalation technique may lead to insufficient drug delivery thus reduction in the clinical effectiveness of the inhalation therapy and treatment failures. Therefore, in this study, participants were asked to provide a practical demonstration of their inhalation technique for the most difficult device used at home. If none, they were asked to provide a practical demonstration for the most used device at home using a placebo device. This was done under the supervision of or by direct observation from the researcher. This was done to see what

inhalers were more frequently associated with an incorrect inhalation technique for the most used device at home among COPD patients; and, additionally, to identify the frequency and range of problems experienced by COPD patients in technical aspects of the operation which may lead to suboptimal care or treatment failure.

One of the advantages of direct observation is that data were 'first hand' which means they do not depend on individuals' reports of what they see or do, which might or might not be accurate (Smith, 2010). However, it is often not feasible especially for studies that involve large samples because an observer (the researcher) can be present only in one site at a time. A further disadvantage is that the validity of data collected might not be good because of the 'Hawthorne effect', which is defined as a form of reactivity whereby subjects modify or improve an aspect of their behaviour being experimentally measured simply in response to the fact that they know they are being seen or studied (Smith, 2010).

4.3.5.1 Obtaining placebo devices from pharmaceutical companies

Pharmaceutical companies were approached by the researcher with the aim of obtaining placebo devices for an independently funded study. Placebo devices were used in this research for two reasons: firstly, to identify the frequency and range of problems experienced by COPD patients by observing how patients use their inhalation devices in their homes and how they perform the inhalation technique correctly and effectively without inhaling the actual dose or the active drug; secondly, to minimise the risk of cross-infection if the same device was used by different patients. Therefore, an attempt was made by the researcher to contact the medical information officers of all relevant pharmaceutical companies (e.g. GlaxoSmithKline, Pfizer, and AstraZeneca), to ask them to provide a number of placebos such as pMDIs, Accuhaler, Handihaler, and Turbohaler (see Appendix 3).

Before considering delivery of placebo devices, some companies asked for a full protocol which should be approved by the UK Research Ethics Committees. In addition, the researcher stated that any gift of placebo devices from any source will be acknowledged in the PhD thesis, or in any publications arising from it. After providing all the necessary documents and explanations, AstraZeneca responded immediately and the request was actioned in a few days. Therefore, a pack of 20 Turbohalers was sent to the researcher. After a couple of weeks, no response was received from the other companies. Therefore, a reminder email was sent. Although the response was very slow and many communications were made over the telephone, eventually the researcher was given all the placebos she requested from each company (see Appendix 4)

4.3.5.2 Developing checklists for the inhalation technique assessment

In developing check-lists to assess the inhalation technique for each device, the researcher must ensure that these check-lists are effective in gathering the data for the study objectives, and that they are workable, feasible and acceptable in the study settings (Smith, 2010). Three device-specific check-lists (Appendix 5), were developed for all classifications (pMDIs with or without spacer, breath-actuated pMDIs; DPIs, device specific check-lists; and nebulisers), to identify the frequency and range of problems experienced by COPD patients in technical aspects of the operation and cleaning of inhaler equipments that may lead to suboptimal use or treatment failure. These check-lists were then reviewed by the researcher supervisor Prof. Taylor (Professor in Clinical Pharmaceutics), who has been actively involved in the preparation and characterization of formulations for delivery from nebulisers, pMDIs and DPIs, to ensure that they are accurate, feasible and workable.

Assessment of the inhalation technique was done using the previously developed checklists for each inhaler. These checklists were developed based on the previously published literature, guidelines set by different professional organisations, and the package leaflet of each inhaler from the pharmaceutical companies. These steps were divided into three columns that contain yes, no, and a comment box to specify and give a description of the problem. The number of errors made by the COPD participants was compared for each device separately using SPSS program. The quantity of errors made by COPD participants when using different devices was also compared (see Chapter six).

Five types of inhaler device were examined for inhalation technique assessments: three types of dry powder inhalers, Diskus/Accuhaler (GlaxoSmithKline, UK), Turbohaler (AstraZeneca, Sweden), Handihaler (Pfizer, USA), the pressurised metered-dose inhalator (pMDI) with or without a spacer, and nebulisers. Briefly, the method of assessment consisted of a direct observation of inhalation demonstrations, one time, for each patient, using device-specific checklists.

4.4 Study setting

The study was conducted in patients' homes in the Pinner, North Harrow, Northwood and Northwood Hills areas of North West London. Using homes as an interview site can be time consuming for the researcher. However, conducting this research in patients' homes had many advantages: firstly, patients talked freely about their problems and needs due to being interviewed in a familiar, more peaceful and nonmedical environment (Smith, 2010). Patients in their own homes may feel more relaxed to talk and give details on how they use their medicines, problems they face and how they

were dealing with them in the context of their real environment. However, only a limited number of studies have been conducted in patients' homes among patients with COPD (N=6) (Van Grunsven et al., 2000; Melani et al., 2001; Barta et al., 2002; Boyter et al., 2005; George et al., 2006; Sestini et al., 2006).

Despite all these advantages, there was an ethical challenge raised by the Research Ethics Committee (REC), when applying for approval for this research, which required special consideration when conducting this research in patients' home. This challenge was related to the researcher's safety when visiting patients in their homes. In response to this and in compliance with the ethical requirements, the researcher was asked to notify another person from the research team of the time and location of the home visit and carry a mobile phone to report when the visit had been completed. In addition, participants have to be known to the collaborator or surgery staff at the medical centre.

4.5 Sampling strategy

The aim of the sampling strategy was to obtain a sample which would meet this study's objectives. A sample was needed that would provide an understanding of medication-taking behaviours of patients using multiple inhalation devices for COPD.

Justification of the chosen medical centre and representativeness:

The selection of participants was conducted in Pinn Medical Centre by medical centre staff through patients' medical notes. Pinn Medical Centre is a large medical practice that serves 20,000 patients and covers a large geographic area of North West London. In addition, it includes people of

different age groups, ethnicity, disease status and smoking history. This would confer some generalisability. Moreover, preliminary discussion with collaborators and medical staff indicated that Pinn Medical Centre has 116 patients with COPD who were prescribed a range of inhalation devices and were eligible for this study. Therefore, it was seen that this site would be enough to achieve the targeted sample size.

Justification of the sample size:

1. Based on previous studies among patients with respiratory diseases, it is anticipated that the sample of 60 patients would enable us to achieve the study objectives and will be able to reach saturation level (i.e., sampling to the point at which no new information is obtained). However, the researcher determined the sample size when no new topics, themes and issues emerged from the data (when reaching saturation level).

2. This sample size of 60 patients is achievable within the time and resources of the study. However, issues of availability and willingness of patients to participant in this study affected the sample size.

3. The sample size and potential recruitment rate was based on discussions with a member of practice staff and the research supervisors' experience of supervising a previous PhD project looking at the use of nebulisers in this patient group: Alhadad, 2011, University of London.

4. The sample size was not based on probability statistics because this study took a mixed methods approach, which means including some descriptive or qualitative data. Therefore, the sample size of this kind of research is often limited.

The later sections will discuss patient's eligibility to enrol in this study, the sampling procedure, recruitment of participants from primary care and interview procedure for subjects with COPD.

4.5.1 Inclusion criteria

For COPD patients:

- Patients with a confirmed diagnosis of COPD from medical notes.

- Patients who are over 18 years old.
- Patients who are prescribed at least two inhalation devices including p-MDIs, DPIs and/or nebulisers.
- Patients who use their inhalers in their own home.
- Patients who are able to speak and understand English.

4.5.2 Sampling procedure and recruitment of participants from primary care

Recruitment of patients from primary care:

Potential participants were identified by medical centre staff through patients' medical notes. Patients' information was obtained from their medical notes after identification (Appendix 6). The following information was needed:

- Patients' current and previously prescribed medicines: to get an overview on what COPD medications patients use to manage their condition, what they were using at the moment, for what, and what they had been using in the past to manage their condition, and to compare the information obtained from the medical notes in the GPs' surgery with data collected from COPD patients themselves to see if this corresponded with what they said and if they were taking their medicines as prescribe.
- Presence of other conditions: to get an overview of what other diseases or conditions COPD patients have which generally result in more complex treatment regimens that may lead to problems with medicines' use.
- Patients' details such as age and smoking status (if recorded).

All documentation and information packs were prepared by the researcher. After identification of the potential participants, an information pack was sent to eligible patients. The information pack included an invitation letter (Appendix 7), information sheet (Appendix 8), and patient consent form (Appendix 9). The patient consent form had to be read carefully, understood and signed before the interview date. A reply slip (Appendix 10) with a pre-paid envelope was also included in the information pack to be returned indicating patients' willingness to take part. The information sheet informed potential participants of the purpose of the study, study procedure and how it would be conducted, possible disadvantages and benefits from taking part,

sponsorship, confidentiality of data and the researcher's contact details. The pack included a photograph of the researcher so that participants knew who to expect if they participated in the study. In addition, if the participants required any further information, all contact details of the researcher were provided on all forms to give participants the opportunity to ask any question before the interview date.

Patients who returned the reply slip indicating their willingness to take part were contacted by the researcher to arrange a suitable date and time for a home interview. The interviews with patients were conducted on one occasion at their home.

4.6 The interview topic guide

The interview topic guide (Appendix 5) was informed by the literature and designed to examine COPD patients' use of their medication in the context of their daily lives, information requirements, beliefs, and perceived effectiveness and safety of therapy. In addition, these questions were developed after consulting with academics and a respiratory specialist. Respondents were invited to express their views regarding:

- How do COPD patients used their medicines to manage their condition?
- What were they using or what had they been using in the past?
- What did COPD patients feel about using different devices used in combination; what did they like or dislike about them?
- How did they make decisions about the use?
- What problems were experienced by COPD patients in technical aspects of the operation, cleaning and maintenance of inhaler equipment did they have? What worked and what did not work?
- What medicine-taking behaviours and beliefs about medicines did they have?
- What kind of assistance with medicines did patients receive, if any?

The interview schedule consisted of open and close-ended questions that defined the aim and objectives of this study. Closed questions were used to

gather factual data (e.g. do you sometimes forget to take your regular COPD medicines?), whereas open questions were used to expand the participant's viewpoints and experiences that were relevant to the topic of interest (e.g. for your regular medicines, people often do not take their medicines exactly as prescribed for different reasons, thinking of the medicines you use for your COPD, when was the last time you did not take the dose of your regular medicines and why?). Probing questions, on the other hand, were also used during the interviews to gather more details regarding any important issues or views outlined by the respondents, as recommended by Smith (2002). For example, when was your (COPD/ bronchitis/emphysema) diagnosed? (Which year or how long ago?). Leading questions were avoided as they could introduce bias. In addition, participants were allowed to talk freely without particular order (Smith, 2002). This allowed the exploration of topics according to the importance placed on them by participants.

4.7 Permission to use the questionnaires

In order to comply with the copyrights of the developers for the chosen instruments, a permission to use the questionnaires in this study was sought from the developers. Authorisation to use the MMAS and BMQ were granted free of charge from their developers.

4.8 Ethical approval

The required documents to apply for the Research Ethics Committee (REC) were prepared ahead of the scheduled committee meeting on the 23rd of December 2011 and enclosed with a cover letter for review. The sent documents included the following: interview schedules, copies of the questionnaires, letter of invitation, patients' information sheet and all other relevant materials. The IRAS form was also submitted to the REC and the committee advised the researcher to respond to their emails and queries to

provide further clarifications if needed. A copy of the Research Ethics Committee (REC) application form, a list of questions, queries and issues raised by the REC (North East REC centre) are attached in Appendix 11 and Appendix 12.

The study was then independently reviewed and approved by Newcastle & North Tyneside 2 Research Ethics Proportionate Review Sub-Committee (North East REC centre) [11/NE/0392]. In addition, the study has also been approved by [R&D of local PCT]. The letter of favourable opinion from NHS REC or the provisional decision letter from NHS REC is attached as Appendix 13.

4.9 Data collection

On the day of the interview with each participant, the researcher was wearing an identification badge and introduced herself to the patient, explained the study's aim and objectives and read the information sheet with the participant. The participant was given the chance to ask any question prior to starting the interview. The participant was asked to sign the consent form, after reading and understanding the patient information sheet if they had not already done so. The researcher then asked the patient if the interview could be audio-recorded. If the patient did not wish the interview to be audio-recorded, field notes only were taken. Permission was sought to record information about participants' COPD such as FEV1, FVC, FEV1/FVC ratio and all prescribed medicines on their medical notes at the surgery. Participants were assured that only the research team will have access to this information, which will be kept in a coded format during the study and destroyed after completion of the study, and that they will be not identified in the final report. Prior to the commencement of the interview, written consent was obtained.

Each interview with COPD participants took 45-60 minutes and followed a semi-structured schedule. Firstly, participants were asked to show the researcher all medicines they were using for their COPD and document the use of each and report what they had been using in the past. Secondly, they were asked about decisions they made to use/not use their therapy or devices, missed doses, and technical and practical problems experienced previously with the use of their devices. Thirdly, device-specific checklists were used for all types to assess participants' inhalation technique, so patients were asked to provide a practical demonstration of their inhalation technique for the most difficult device used at home. If none, they were asked to provide a practical demonstration for the most used device at home using a placebo device. This was done under the supervision of or by direct observation from the researcher. Fourthly, they were asked about the assistance or help they received from others especially informal carers (family or friends). Finally, two validated instruments of adherence (Morisky scale) and beliefs about COPD medicines (Beliefs about Medicines Questionnaire [BMQ]) were applied. This enabled qualitative and quantitative data to be collected as required by the objectives of the study.

The interview questions were read by the researcher to minimise the degree of bias and to subject each participant to standard interview conditions. Enough time was given to each participant in order to answer each question. In addition, prompts and probes were also used in the interview to expand the question that was answered to cover the topic broadly. Any unexpected ideas or responses made during the interview were also followed up by the researcher and a note of this was made on the interview schedule. If participants agreed, interviews were audio-recorded to allow data analysis, but this was not a requirement to take part.

4.10 Data protection

The data collected were handled with confidentiality throughout the study period and kept in a coded format without the name of the patients, and locked all the time in a designated cabinet storage for this purpose. Data were stored in university computers where all files were password protected and only the research team was allowed access. Storage was the responsibility of Prof. Felicity Smith. Data will be destroyed at the end of the study period (after publication).

4.11 Use of computer software

A qualitative data indexing software package, Nvivo 10, was used to facilitate coding and retrieval of the qualitative data. This software allowed storing of the transcribed text in an organised form, searching and retrieving particular segment of texts for inspection after coding segments of texts, and linking relevant data to form categories. This was all done in English. In addition, a quantitative data software package, SPSS 21, was also used to interpret the quantitative data.

4.12 Analysis and presentation of the interview data

4.12.1 Transcription of the data

All interviews were conducted by the researcher in English. Of the 46 interviews, 40 were audio-recorded for verbatim transcription, whereas three participants stated their unwillingness to be audio-recorded. Therefore, their interviews were written by hand. Subsequently, all interviews were transcribed. All the stages of the data analysis including development of themes and codes were undertaken in English.

4.12.2 Thematic framework

To enable the data analysis, a thematic framework was used in this study. Thematic framework was developed by the National Centre for Social Research (NatCen), UK in the 1980s for policy research for which the information requirement is known in advance. Although diverse qualitative methods are available for data management, a framework approach was selected to support data analysis. Firstly, the framework approach is especially fit for analysing cross-sectional descriptive data, enabling different aspects of the phenomena under investigation to be captured (Spencer and Ritchie, 2003). Secondly, moving from data management to developing the analysis effectively to answer research questions may be a difficult and confusing task for researchers. Thus, the interlinked stages in the framework approach simply describe the processes that guide the researcher through the systematic analysis of data from initial management to the development of descriptive to explanatory accounts (Spencer, 2003).

Qualitative data analysis can be done deductively or inductively. A deductive approach can be done by developing a theory, which begins with establishing objectives. For example, when the study objectives are identified, key definitions and assumptions should be stated. After that, a logical structure should be generated to accomplish the objectives, based on the definitions and assumptions. This methodology is often described as going from the general to the specific (Hinkin, 2005). The deductive approach is widely used for data analysis in qualitative research. One of the main advantages is that it can test or expand an existing theory by searching systematically for patterns to give a detailed description of a phenomenon, which enables developing of meaningful themes (Braun and Clarke, 2006). In addition, if properly conducted, it will assure the data validity in the final scale. In most situations where the theory does exist, the deductive approach would be appropriate (Clark, 2011).

When developing the themes of this study, a single method approach to qualitative data analysis was considered. This approach was an inductive approach by building up a theory from the ground, derived from the data obtained from COPD participants (grounded theory) (Hinkin, 2005). Therefore, the researcher developed these themes and sub-themes based on a series of factors that were raised by COPD participants during the interviews. This approach is useful to guide the researcher when conducting exploratory research (Clark, 2011).

After audio-recording the interviews for verbatim transcription, they were fully transcribed and typed into a Word document. After that, they were printed out and read many times to manage the data and reach data familiarisation, which means becoming familiar with the data by reading and re-reading it. This stage was very important to gain richness and depth and glean insights into the data, and therefore to identify initial themes (Roe, 2008). After reading the first seven interviews, the researcher was able to see and identify some common themes and issues. After reading and re-reading all transcripts, the key themes were marked and identified for a range and diversity of coded data upon the topic under discussion (e.g. the timeline of the condition=1, COPD medicines=2), using Nvivo. The major key themes were then created as codes or nodes, and each transcript was read on the screen and coded. Each key theme was subdivided into related sub-themes. Some quotes were coded twice because they were covering several codes or sections. A coding matrix was then generated and the codes from each theme that was generated from the data were lined or grouped based on the study objectives seeking wider application of concepts and themes (Roe, 2008). During the coding process, when any new theme arose from the data, it was incorporated into the coding matrix (see Table 4-2).

4.12.3 Data management using a case- and theme-based approach

An initial sample of 10 participants, who were firstly interviewed, was selected from the whole sample and their interview transcripts were read several times to identify the recurring themes and concepts. Codes and categories were developed considering each line, phrase or paragraph of the transcript as an attempt to summarise the findings. The process initially involved using printed versions of the transcripts with key phrases highlighted and comments written in the margins to gather preliminary thoughts. After that, a conceptual framework was developed for the 46 participants into more formal ideas from which a coding matrix was generated to ensure clarity at conceptual level of the issues and to represent a range of experiences. Transcripts were then entered into the NVivo sheet to generate the codes. Each NVivo code initially formed a potential category but, as coding progressed and the number of categories developed, they were grouped together into broader categories. Similar categories were eventually brought together to form initial themes. These categories and themes formed a ‘coding index’ that was used as a means of organising the whole dataset (Table 4-2).

Table 4-2: The coding themes

Categories	Themes	Sub-themes
1. **The time-line of the condition**	1.1 Experience of symptoms over time	
	1.2 Causes of symptoms	1.2.1 External Factors (Weather) 1.2.2 Emotion/ stress 1.2.3 Smoking
	1.3 Experience of COPD medication use over time	1.3.1 Changes in COPD medication over time 1.3.2 Changes in dosing frequency over time 1.3.3 Changes in inhalation devices over time
	1.4 Acceptance and denial of illness and living with the disease	
	1.5 Knowledge about the disease and its prognosis	
2. **COPD Medication**	2.1 Experience of the effectiveness of the inhalation therapy in symptoms management over time	2.1.1 Positive experiences 2.1.2 Negative experiences
	2.2 Participants' beliefs and perceptions about the effectiveness of inhalation therapy.	
	2.3 Participants' decisions regarding using of inhalation therapy	2.3.1 Symptoms that lead to use 2.3.2 Other reasons that lead to use
	2.4 Participants' adherence/ non-adherence to the prescribed COPD medicines	2.4.1 What they missed 2.4.2 Reasons for missing 2.4.3 Approaches for not missing (Compliance aids)
	2.5 The use of multiple inhalation devices by COPD participants on their daily lives	2.5.1 Dosing regimen 2.5.2 The number of puffs 2.5.3 The frequency of doses 2.5.4 The sequence of administering the inhalation devices and the reason behind it 2.5.5 Emergency prescription and/or medications
	2.6 Fitting the COPD medicines with their daily lives and activities.	
	2.7 Medication-specific comments	2.7.1 Bronchodilator 2.7.2 Inhaled steroids
	2.8 Experience of potential side effects of inhalation therapy over time	2.8.1 Type of side effects 2.8.2 Self-guided 2.8.3 Professionally guided
	2.9 Participants' beliefs and concerns about the safety and side effects of inhalation therapy.	
	2.10 Concerns of possible side effects	

3.	**The inhalation devices**	3.1 Comparing devices	3.1.1 Effectiveness 3.1.2 Convenience 3.1.3 The frequency of dosing 3.1.4 Overall preference 3.1.5 Operating aspects
		3.2 Device-specific comments	3.2.1 pMDIs 3.2.2 Breath-actuated pMDIs 3.2.3 DPIs 3.2.4 Nebulisers
		3.3 Operating the inhalation devices	
		3.4 Cleaning and maintaining the inhalation devices	3.4.1 How do they clean it 3.4.2 How often 3.4.3 Participants' perceptions about cleaning and maintaining of the inhalation devices
4.	**The informal carers**	4.1 The care and support provided for COPD patients	4.1.1 What kind of help is received 4.1.2 Who is providing this support 4.1.3 How often?
5.	**Healthcare services**	5.1 Accessing the healthcare services and the advice given to participants	5.1.1 How often 5.1.2 Reasons for accessing the healthcare system 5.1.3 Kind of advice 5.1.4 Who provided this advice or information?
		5.2 Satisfaction with healthcare system and its service	
		5.3 Faith in healthcare professionals	
		5.4 Patients participation in decision-making in regards to their prescribed COPD medicines	
		5.5 Obtaining information, prescriptions and/or medicines about medicines and its sources	

4.12.4 The validity and reliability of the data

The validity of the data refers to the extent to which the chosen method measures what it is intended to measure (Polit, 1991), whereas the reliability refers to the degree of consistency between measures (Polit, 1991). The following discussion aimed to outline the validity and reliability issues related to this study.

The validity refers to the extent to which the research findings present reality (Scanlan, 2002). The literature review in two formed the basis for the validation of this study. Past studies have been taken into consideration when designing this research to aid ensuring that this research included all problems, issues and difficulties in regards to the use of inhalation therapy and/or devices among COPD patients. Therefore, the review highlighted the area of importance in regards to COPD and its therapy. These included how older patients made decisions regarding the use of inhalers, and how those decisions and difficulties contributed to suboptimal outcomes and treatment failures.

The review also helped to ensure that the data collection instruments covered all angles and topics which belonged to COPD and its therapy. Themes that were repeatedly found in the review were considered significant and questioning about these topics was included in the interview schedule, such as the use of inhalation therapy by patients in terms of adherence and inhalation technique and issues related to them. In this way, it will be ensured that the data collection instruments had content validity, which means being a measure that the data collection instrument covered all angles and domains of the topic under investigation (Scanlan, 2002).

At the end of this study a comparison was carried out between its findings and the existing knowledge, theories or established literature of the use of inhalation therapy by COPD patients, in order to validate the accuracy of the findings of this study, despite using different methods to gather the data. The findings were checked and discrepancies between this study and data obtained from previous studies were compared before and during analysis.

In this research, data were gathered from different sources and a triangulated methodology applied, to validate the data and to allow a more accurate assessment. Triangulation is defined as the use of two or more methods of data in the same study. It is a way; the chances of obtaining a true picture of events are high (Scanlan, 2002), in another word to make sure there is enough evidence to make valid claims (Smith, 2010).

To increase the validity of the findings of this research, it was decided to conduct face-to-face semi-structured interviews, which enabled the researcher to follow any interesting points and gave the participants the opportunities to add any further information that they felt was crucial or was missing from the schedule in order to ensure that the interview covered all topics of relevance to the study and participants. As reported by Scanlan in 2002, exploration of issues in this manner means that participants' answers were placed in context and the researcher was able to probe the exact meaning of the patient's response. In this way participants were able to tell their own stories, which enhanced the study validity.

In this study the threats to the validity were minimised in the following ways:

- The literature review and preliminary fieldwork were conducted to ensure that the study covered the relevant data collection domains. In addition, after the researcher had conducted a literature review and developed the

interview schedule, Pinn Medical centre staff including healthcare providers were asked to review and give advice on the methodology used in this study and the interview schedule, including wording of the questions and the way of questioning, to ensure the inclusion of all relevant issues concerning the phenomena. As a result, the interview schedule and the methodology were advised.

- The checklist for each device was also seen and reviewed by the researcher's team to ensure that it is workable and applicable for all COPD participants. Checklists were used to standardise the collected data during patient observations.

- The review of the literature was used in the data analysis and discussion of this study. These reviews provided concepts which can be checked using our actual data.

- To ensure the validity of the data obtained from participants' interviews the following procedure was undertaken:
    - Two courses regarding discussion and training in conducting a qualitative research and the use of questionnaires in research were attended by the researcher at the University of Surrey and the University of London before conducting the study. In addition, the researcher was taught how to conduct a qualitative research and the use of questionnaires in research, in relation to previous MSc research undertaken by the researcher at the University of Strathclyde, Scotland.

    - Different books on interviewing techniques (e.g. Conducting your pharmacy practice research project: a step-by-step guide by Felicity Smith; Research methods in pharmacy practice by Felicity Smith; Interviewing as qualitative research: A guide for researchers in education by Irving Seidman) were read by the

researcher, which informed the development of the methods and helped the researcher to make the best choice regarding the instruments that should be used to answer the research questions.

- The choice of instruments for the quantitative data, which includes measuring adherence and beliefs about COPD medication, was based on previously published reports of the validity and reliability of these instruments (Morisky scale and BMQ) by other researchers among the same group of patients to ensure the validity of the quantitative data.

- The data was audio-taped and transcribed verbatim to assist in applying analytical procedures. One way to assure the reliability and the validity of the data collected was audio-recording the patients' interview, which has been used widely within qualitative research, replacing the researcher's handwritten notes. This was done to review and transcribe the conducted interviews at a later date; additionally, to verify the questions asked during the interviews. When using the audio-recording responses, this will ease the analysis by ensuring that no points were missed and that the researcher has not unintentionally paraphrased the participants' responses. This ensures that the data collected is true and comprehensively reflects their issues (Scanlan, 2002).

- After conducting the first three interviews, the findings obtained from the interviews were examined and reviewed by the researcher's team to ensure that these findings were accurate and representative.

- The collected data from each interview was independently coded and the coding was compared and reviewed by the researcher's team for agreements, which is known as assessing reliability for ensuring accuracy of the data. The results showed close agreement on the main themes.

- Using a computer indexing software package, Nvivo 10, was useful to ensure the validity of the findings, by identifying all data relating to issues of interest for inspection or to support theory building.

- Whenever a new code was added, all the previous interviews were rechecked for relevance of this code, which ensured consistency and carefulness of coding.

- At the end of this study a comparison was done between the findings of this study and the existing knowledge, theories or established literature on the use of inhalation therapy by COPD patients.

In terms of the reliability, as identified by Scanlan (2002), the reliability of the study relies on the reproducibility of the findings and the assumption that if the data were collected using identical techniques or methods at the exactly the same point in time the same findings would be obtained, and if the data were analysed using the documented method of data analysis the same conclusion to the study would be drawn. To ensure this, a number of considerations were made when designing this study to reduce threats to the reliability, including:

- The data collection process was clearly documented and research procedures were followed as per the data collection protocol during the research process.

- To ensure that participants considered the same topics during the home visits, a semi-structured interview technique was undertaken using prepared questions which involve prompts and probes.

- To assure the consistency of each participant's responses, the interview questions were read out loud by the researcher and only one researcher was used throughout the research to do the interviews with

participants, to limit the bias and to avoid different approaches to the interview.

To summarise, the methods employed in this study were to enable collecting of extensive data both quantitatively and qualitatively to meet the study objectives. The collected data that were obtained from different sources were triangulated and considered using a matrix approach to analyse, validate and complement the study findings.

5 Chapter Five: Characteristics of participants, their disease and medicines

This chapter reports the response rate of the study sample and summarizes the study participants' characteristics and participants' disease characteristics (e.g. demographics and clinical characteristics) and participants' COPD medicines, which are essential for interpretation of the results. In addition, it summarizes non-participants' characteristics.

5.1 Response rate

A total of 116 COPD patients were invited to participate in this study by sending an invitation letter to their home address. Of those who responded by sending back the reply slip stating their willingness to take part, 46 respondents were eventually interviewed. The response rate following an initial mailing was 28%, as only 33 patients responded following an initial mailing. Twenty-six patients with COPD declined to participate and no reply was received from 57 patients.

To increase the participation rate, a reminder letter was sent to those who had not yet responded (N=57), asking them for the second time to take part. In response to the reminder letter, 13 patients agreed to take part and were subsequently interviewed. Of the 44 remaining patients, 15 declined to take part in the study and 29 did not respond despite being invited and sent the reminder letter. To summarize, a total of 41 patients declined to participate and 29 did not reply. The remaining 46 participants who met the criteria and

agreed to take part were all enrolled in this study and interviewed (response rate 40%).

5.2 Characteristics of the sample

The characteristics of the 46 participants, who met the inclusion criteria and agreed to take part, were entered into a data base in SPSS v.21. The mean age of the 46 participants was 77 years (SD = 8), and median was 76 years (Interquartile range IQR = 72-83 years). Participants ranged in age from 63 to 100. Almost an equal number of participants from each gender (Male=24 and Female=22), were included.

Smoking is a leading cause of COPD; most participants who enrolled in this study were current smokers or ex-smokers. Three-quarters of the participants (N=34) were ex-smokers, whilst seven participants were still smoking. Regarding their living arrangements, two-thirds of participants (N=31) were living either with a spouse or family (see Table 5-1)

5.3 Participants' disease characteristics

Participants' information and clinical characteristics obtained from the clinical notes and during the interviews are presented in Table 5-1.

Table 5-1: Characteristics of the participants and participants' disease (N=46)

Parameter	Mean (SD); Median
Age (years)	77 (8.23); 76
Number of regular medicine	7 (2.84); 7
Number of years since the diagnosis	12 years (9.69); 10
Number of COPD medicines	3 (0.79); 3

Continue Table 5-1: Characteristics of the participants (N=46)	
Parameter	N (%)
Gender	
Male	24 (52%)
Female	22 (48%)
Ethnicity	
White (English, Welsh, Scottish)	39 (85%)
White Irish	4 (9%)
Any other White background (Italian)	1 (2%)
Asian British (Indian)	2 (4%)
Living arrangements	
Lives alone	15 (33%)
Do not live alone	31 (67%)
Severity of the disease according to NICE guidelines	
Mild airflow obstruction (FEV_1= 50-80%)	14 (30%)
Moderate airflow obstruction (FEV_1= 30-49%)	29 (63%)
Severe airflow obstruction (FEV_1<30%)	3 (7%)
Smoking status	
Current smoker	7 (15%)
Ex- Smoker	33 (72%)
Never-smoked	6 (13%)

The mean (SD) and median are given for continuous variable, whereas, numbers (%) are given for categorical variables

In this study, the number of years since the participants were first diagnosed with COPD ranged from 1 to 35 years with a mean of 12 years (SD=9.7). The median of the number of years since the diagnosis was 10 years.

From the surgery records, the FEV_1 (forced expiratory volume in 1 second), was classified in the medical records based on the NICE guidelines classification of the disease severity three categories: mild airflow obstruction (FEV_1 from 50 to 80% predicted), moderate airflow obstruction (FEV_1 from 30 to 49% predicted), severe airflow obstruction (FEV_1 < 30% predicted). Of the 46 participants, nearly two-thirds (N=29) had moderate COPD, whilst, a few participants (N=3) had severe disease status. Although, it was not possible to access different lung function tests for non-participants to compare the generalizability of the sample between participants and non-participants because no consent was obtained, the sample of this study tends to have a

range of people with different disease status comprising mild, moderate and severe COPD status which makes the sample diverse.

5.4 Characteristics of participants' medicines

5.4.1 Inhalation therapy

All the information provided regarding patients' own medications and what they were prescribed for their COPD was taken from patients' medical records in the surgery, their prescriptions or medications checklists and/or memories (see Table 5-2).

Table 5-2: The COPD medications prescribed for use by participants to manage their condition (N=46)

COPD medications	The scientific name	The trade name	Device type	Disease status	Number of patients
Bronchodilator	Short-acting salbutamol	Ventolin	pMDI	SABA was given (up to 8 puffs daily) as an initial empirical treatment for the relief of breathlessness for all patients in all stages.	34
	Short-acting terbutaline	Bricanyl	Turbohaler (DPI)		6
	Short-acting salbutamol	Salamol	Breath-actuated pMDI		3
	Short-acting salbutamol Steri-neb		Nebulizer		3
	Long-acting Formoterol	Foradil	Aerolizer (DPI)	LABA was given to patients with COPD moderate stage (FEV1 ≥ 50% predicted).	1
	Short-acting ipratropium	Atrovent	pMDI	SAMA was given for the relief of breathlessness with or without SABA.	1
			Nebulizer		1
	Long-acting tiotropium	Spiriva	Handihaler (DPI)	1) Given once-daily with LAMA to stable COPD patients who remain breathless or have exacerbations despite using SAMA as required. 2) To those with moderate stage of COPD (FEV1 ≥ 50% predicted). 3) To those with severe stage of COPD (FEV1 < 50% predicted). 4) Given in addition to LABA where ICS is declined or not tolerated.	28
	Aminophylline	Phyllocontin	Tablets	Was used after a trial of short-acting bronchodilators and long-acting bronchodilators	3
Steroids	Beclometasone dipropionate	Clenil modulate	pMDI	Each of these was given in addition to a LABA inhaler in severe COPD status or regular flare-ups (exacerbations) of symptoms to reduce the inflammation.	5
		Pulvinal	Turbohaler (DPI)		2
		Qvar	pMDI		1
		Becodisks	Diskhaler (DPI)		1
	Budesonide	Pulmicort	Turbohaler (DPI)		2
	Prednisolone	Prednisolone	Tablets	Given to some patients with advanced COPD	3
Combination therapy	Formoterol fumarate dihydrate and budesonide	Symbicort	Turbohaler (DPI)	Given to patients with severe stage of COPD (FEV1 < 50% predicted)/ or to those with stable COPD and an FEV1 ≥ 50% who remain breathless or have exacerbations despite maintenance therapy with a LABA.	20
	Salmeterol xinafoate and fluticasone propionate	Seretide	Accuhaler (DPI)		16
Mucolytic Medicines	Carbocisteine	Mucodyne	Tablets	Was used in patients with a chronic cough productive of sputum.	3

According to Table 5-2, all participants (N=46) were prescribed short-acting bronchodilators such as short-acting β_2-agonists (SABA) and short-acting muscarinic antagonists (SAMA), to be used when required. The second most prescribed medicine (N=28) was the long-acting antimuscarinic bronchodilator (tiotropium), followed by the combination therapies of formoterol/budesonide (N=20) and salmeterol/fluticasone (N=16) respectively. These findings are consistent with those of previously published guidelines such as NICE, BTS, ATS/ERS and GODL. All guidelines recommend escalation of inhalation therapy with increasing severity of disease, starting with short-acting bronchodilators used on an as-needed basis, proceeding to scheduled administration of long-acting bronchodilators, and advancing to ICS in patients with severe disease status or exacerbation (ATS/ERS, 2004; NICE, 2010; GOLD, 2013).

5.4.2 Inhalation devices

In this study, COPD participants used a wide range of inhalation devices ranged from two to five inhalers including multiple inhalers of pMDIs only, multiple inhalers of DPIs only, a combination of both pMDIs and DPIs, or a combination of pMDIs, DPIs and nebuliser. The largest number of participants was using a combination of two inhalation devices. For example, of the COPD participants, nearly half (N=22) used a combination of two devices, whereas more than one-third (N=19) used three devices, and five used more than three devices.

From the pie chart (Figure 5-1) it can be seen that two-thirds of participants (N=31), 67%, used a combination of both pMDIs and DPIs, 10 participants (22%), used a combination of DPIs, three participants (7%) used three

different kinds of inhalation devices (pMDIs, DPIs, and nebulisers), whereas the least used group was a combination of pMDIs with just two participants (4%).

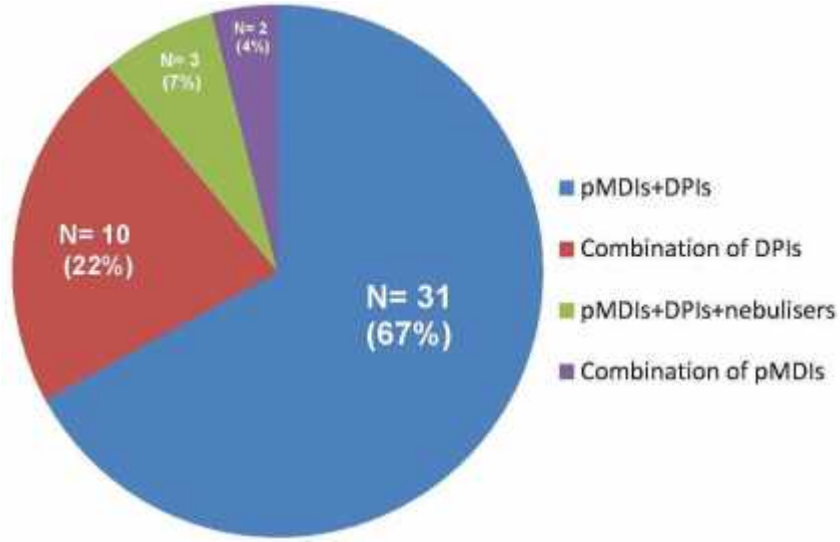


Figure 5-1: The percentage of participants who used different types of inhalation devices in their home (N=46)

Regarding the type of device used, pMDIs were the most frequently prescribed and used devices by COPD participants in this study, whilst, the second most widely prescribed and used devices were the DPIs followed by nebulisers. Among the DPIs, the Handihaler device was the most commonly prescribed and used device, followed by the Turbohaler and Accuhaler (see Table 5-3).

Table 5-3: The number of participants who used each type of device (N=46)

The type of inhalation devices	Spacer	pMDIs	Easi-breathe (pMDIs)	Handihaler	Turbohaler	Accuhaler	Diskhaler	Aerolizer	Clickhaler	Nebuliser
The number of participants who used each type of device	7	43	3	26	20	16	1	1	1	3

According to Table 5-3, the participants were distributed as follows: all participants (N=46) used pressurised metered-dose inhalers including pMDIs and breath-actuated pMDIs; 44 participants used DPIs (Handihaler® (N=28); Turbohaler® (N=20); Accuhaler® (N=16); Clickhaler® (N=1) and Aerolizer® (N=1). Seven used pMDIs with a spacer. For the nebuliser system, three used a side-stream nebuliser. These findings are consistent with the recommendations given by the NICE guidelines which state that for the delivery of bronchodilators and ICS, pMDIs and DPIs are highly advised to be used, with the consideration of a nebuliser device only for those who are unable to use pMDIs and DPIs or who have been diagnosed with severe disease status (NICE, 2010).

5.5 Characteristics of the non-participants

According to the data obtained from the medical records, the mean age of the 70 non-participants was 71 years (SD=16) and the median was 76 years. There was almost an equal number of non-participants from each gender (Male=34 and Female=36). Based on ethnicity, 60 non-participants were from the white ethnic background – English, Welsh, Scottish and Irish – which formed 86% of the non-participants. Asians including Indians (N=8) were the largest minority group (11% of the non-participants), whereas the smallest minority group was other ethnic group including Arabs (N=2).

According to the information obtained from the 41 non-participants who returned reply slips, 15 reported reasons for not participating in the study. The most common reasons given were feeling unwell, time constraints, moving home, being an employee, or out of the country during the period of study.

When comparing the practice population including participants to the non-participants, patients' characteristics appeared similar in age, gender and race. See Table 5-4 for more information on the sample and its representativeness when comparing the practice population including participants to the non-participants:

Table 5-4: Characteristics of non-participants to the participants

Parameter	Non-participants and non-respondents Mean (SD)	Participants Mean (SD)	Statistical Significance (p)
Age (years)	73 years (16)	77 years (8)	0.119
Parameter	**Non-participants or non-respondents N (%)**	**Participants Mean N (%)**	**Ratio**
Gender			
Male	34 (47%)	24 (52%)	1:1.4
Female	36 (53%)	22 (48%)	1:1.6
Ethnicity			
White (English, Welsh, Scottish)	60 (86%)	44 (95%)	1:1.4
Asian British (Indian)	8 (11%)	2 (4%)	1:4
Other ethnic group (Arabs)	2 (3%)	0	1:0

In compliance with the ethical requirements, no data were obtained from the medical records regarding medications and disease characteristics due to the fact that the researcher did not receive written consent from non-participants giving their permission to access their medical records in the surgery. However, based on the available characteristics of non-participants and non-respondents there were no significant differences between the two groups in regards to the age, gender and race, but it should be accepted that there might be some other differences of which we are not aware.

6 Chapter Six: The use of inhalation devices by patients with COPD

This chapter describes how COPD participants operate and maintain different inhalation devices at home. It also identifies the frequency and range of problems experienced by participants in the technical aspects of the operation, cleaning and maintenance of inhaler equipment. The results presented in this section provide insights into participants' inhalation techniques for different inhaler types in terms of preparing the device before taking the dose, inhaling the dose, and maintenance, which includes cleaning, sterilization and replacement of disposable parts if required.

6.1 A description of the inhalation devices

Familiarity with the components of each inhalation device encountered in this study and their product characteristics is a very important stage to be illustrated before describing how these devices were operated and used. A table was constructed by the researcher for the devices which were used most frequently by participants in this study (see Table **1-7**, Table 1-8 and Figure 1-3), in addition to a table summarizing product characteristics (Table 6-1).

Table 6-1: Summary of inhaler characteristics

Type of device	Name of the medicinal product	Qualitative and quantitative composition	Pharmaceutical form and excipients
PMDIs			
Evohaler	Ventolin® Evohaler®	A pMDI delivering 100 mcg of salbutamol sulphate/actuation.	It contains a HFA 134a pressurized inhaler suspension or solution
Evohaler	Seretide Evohaler (25 mcg/ 50 mcg, or 125 mcg, or 250 mcg/ dose pressurised inhalation, suspension).	25 micrograms of salmeterol xinafoate and 50, 125 or 250 mcg of fluticasone propionate (delivered from the valve). This is equivalent to 21 mcg of salmeterol and 44, 110 or 220 mcg of fluticasone propionate delivered from the actuator (delivered dose).	It contains a Norflurane (HFA 134a) pressurized inhaler suspension.
Modulite	Clenil Modulite 50 mcg, or 100 mcg, or 200 mcg, or 250 mcg per actuation pressurised inhalation solution.	Beclometasone dipropionate 50mcg, or 100mcg, or 250mcg per metered (ex-valve) dose.	Pressurised inhalation solution. Clenil Modulite contains HFA 134a and other excipients (e.g. ethanol and glycerol)
DPIs			
Accuhaler®	Seretide® Accuhaler® 50 mcg /100 mcg, or 250mcg, or 500mcg/dose inhalation powder, pre-dispensed.	Each single dose of Seretide provides: 50 micrograms of salmeterol xinafoate and 100, 250 or 500 micrograms of fluticasone propionate.	Inhalation powder, pre-dispensed. Excipients: Lactose monohydrate which contains milk proteins.
Accuhaler®	Ventolin® Accuhaler®	It is a plastic inhaler device containing a foil strip with 60 regularly spaced blisters each containing a mixture of 200 micrograms of micro-fine salbutamol sulphate and larger particle lactose.	Inhalation powder, pre-dispensed. Excipients: Lactose monohydrate which contains milk proteins.

Table 6-1 continued.

Type of device	Name of the medicinal product	Qualitative and quantitative composition	Pharmaceutical form and excipients
DPIs continued			
Turbohaler®	Symbicort® Turbohaler® 200mcg/ 6 mcg/inhalation, inhalation powder.	Each delivered dose (the dose that leaves the mouthpiece) contains: budesonide 160 mcg /inhalation and formoterol fumarate dihydrate 4.5 mcg/ inhalation. Each metered dose contains: budesonide 200 mcg/ inhalation and formoterol fumarate dihydrate 6 mcg/ inhalation.	Inhalation powder. Breath-actuated metered dose powder inhaler. Excipients: Lactose monohydrate (which contains milk proteins).
Turbohaler®	Bricanyl® Turbohaler®, 0.5mg/dose, inhalation powder	Terbutaline Sulphate 0.5 mg/dose.	Inhalation powder. Breath-actuated metered dose powder inhaler.
Handihaler®	Spiriva® 18 microgram, inhalation powder, hard capsule	Each capsule contains 22.5 microgram tiotropium bromide monohydrate equivalent to 18 microgram tiotropium. The delivered dose (the dose that leaves the mouthpiece of the HandiHaler® device) is 10 microgram tiotropium.	Inhalation powder, hard capsule. Light green hard capsules with the product code TI 01 and company logo printed on the capsule. Excipient: Lactose monohydrate (which contains milk protein)
Diskhaler®	Becodisks 400 Micrograms	Beclometasone Dipropionate Monohydrate (Micronised) 414 µg equivalent to 400 µg Beclometasone Dipropionate	Dry Powder for Inhalation via Diskhaler Device

6.2 Sequence of using the inhalation devices and the reason behind each sequence

In this section, it was decided to explore how COPD participants usually administer their inhalation therapy in regards to which order was followed in the administration of their inhalation devices. The study also explored whether a patient's decision to follow a certain order was directed by clinical practice guidelines and/or practitioners' recommendations, or whether it was determined by the patient's personal views. Therefore, 46 participants with COPD who were using multiple inhalation devices in their homes were asked during the interview to state which inhaler they usually used first, second and third. The analysis of the interview data revealed that the sequence of administration of the inhalation devices differed between participants. The majority of participants (N=37) used their inhalation devices randomly, with no identified sequence, having not being informed by their doctor about a specific sequence.

> I do not follow any order. My GP did not tell me that I have to do them in sequence
>
> Female, 76 yrs old, using Ventolin Evohaler pMDI and Clenil Modulite pMDI

The most common followed sequence by participants who reported a specific order was to use bronchodilator inhalers first followed by the inhaled steroid inhalers. For some participants this sequence was not based on scientific evidence or medical recommendations, whereas for others this was due to advice given by neighbours or healthcare providers.

> I take this one first [tiotropium], one inhalation in the morning and after five minutes I take two puffs of that one [Symbicort]. Ammm, I have been on this one [Symbicort] for a few years now and I used to use it first but then my neighbour, who is living across the road and has got the same devices too, told me this is incorrect as the doctor told him to use Spiriva first, then he told me and he said the doctor told him so I never argue.
>
> Male, 68 yrs old, using Symbicort Turbohaler and Spiriva Handihaler

> Amm, I believe I was told by my GP that was the right order [to use the Spiriva before the Symbicort].
>
> Male, 67 yrs old, using Ventolin Evohaler pMDI, Symbicort Turbohaler, Spiriva Handihaler and Phyllocontin tablets

By looking at the mode of action of both drugs, it can be seen that bronchodilators are used to open and relax constricted airways to ease the breathing, whereas steroids are mainly given to minimise the inflammation of the airways. Therefore, it makes sense to use bronchodilators first, followed by inhaled steroids as opening the airways by bronchodilators first may permit enhanced deposition of steroids. However, the evidence regarding the need for a certain sequence when using the inhalation devices is very limited. In addition, there is no strong evidence in the literature suggesting that this sequence alters the outcome of treatment favourably. A previous study of patients with moderate to severe asthma separated them into two groups: those who administered bronchodilators first and then steroids, and those who took steroids first and then bronchodilators, concluded that there was no ideal sequence for administering the inhalation therapy and that the efficacy of both medicines on the lung function and the clinical outcomes were proved completely independent of a particular sequence (Dal Negro et al., 2006). As this is only a single study, further studies are required to provide some evidence on whether following a certain sequence would be effective in improving the lung function and the clinical outcomes or not.

In regards to the device itself, some participants had established their sequence of administration based on two things: firstly, the age of the device and, secondly, the ease of use. For example, four participants declared that the priority was given for the first prescribed inhaler because they had been using it for a long time. One participant tended to use pMDIs first followed by DPIs because pMDIs were much quicker and easier to use than other handheld devices.

> I take one inhalation of Symbicort [Turbohaler] first and I take another inhalation of Spiriva [Handihaler] second. The reason is Spiriva was recently prescribed, just two weeks old.
>
> Male, 76 yrs old, using Ventolin Evohaler pMDI, Symbicort Turbohaler and Spiriva Handihaler

> I always take Ventolin [pMDI] before Seretide [Accuhaler] because Ventolin is easier and quicker to use.
>
> Male, 74 yrs old, using Ventolin Evohaler pMDI with spacer and Seretide Accuhaler

These findings suggest that in general there was no dominant sequence for applying the inhalation therapy; each participant worked out his/her own preferred sequence, which was not based on scientific evidence but on patient's preference and convenience. These sequences were also directed by the type of the prescribed medication and/or advice. In conclusion, due to the lack of evidence proving the effectiveness of using a certain sequence, there were no concerns in terms of the differences in the sequence of drug administration among COPD participants. However, further investigations and experimentations into the sequence of inhalation devices' administration and its effectiveness are needed. If any sequence was proved to be more effective than others, it should then be followed and implemented to maximise the efficacy of therapy and therefore the clinical outcomes.

6.3 Comparing inhalation devices in terms of operation

This was an observational part of the study carried out between May and December of 2012. The sample comprised 46 participants with COPD, treated at Pinn Medical Centre in Pinner, UK. All participants (N=46) were asked to demonstrate and describe how they operate their inhalation devices using a placebo device provided by the investigator. Participants were asked to select the most difficult device to operate at home (from participants' perspective) or the one which they may have a problem using. Some participants claimed that they did not have problems or difficulties in using any inhaler, so they were asked by the researcher to demonstrate the inhalation technique for the device they used most frequently at home. The selection criterion of the included devices in the assessment is potentially

biased because it was based on patient's choices and judgments regarding the definition of the mishandling of each device.

A total of 46 inhalation demonstrations were performed by the 46 participants; DPIs (N=35) including [Turbohaler (N=17), Accuhaler (N=11), Handihaler (N=7)], pMDIs (N=8), and nebulisers (N=3). Although only three participants demonstrated the inhalation technique using a nebuliser, among those no errors were reported. Statistical comparison of other devices with nebulisers was thus not possible since only three participants used nebulisation therapy and no error was made.

For this study, an error in the technique was defined as any deviation from the recommended steps required for optimal drug delivery which are given in the checklists derived from literature provided by pharmaceutical companies for their own devices. The method of assessment was investigated in regards to reliability of the observer and checklists; firstly, the assessment process was performed accurately by direct observation from a properly trained observer (the researcher), who had three sessions of training under the supervision of her academic supervisor Prof. Taylor, who has been actively involved in inhalation aerosol research. In addition, using one observer for the assessment process avoided the possibility of inter-observer variability (defined as a failure to identify or measure the number of deviations made by participants from the recommended technique when using their devices accurately, which results in an error), which may arise from the presence of multiple observers. Secondly, the checklists used in the assessment were developed based on the previously published literature and guidelines set by different professional organisations and the package leaflet of each inhaler from the pharmaceutical companies, and were reviewed by the academic supervisors before use, to ensure that they are accurate, feasible and workable.

Twenty-eight participants (61%) made at least one deviation/ error when using their inhalation device, with only 18 COPD participants (39%) performing all of the steps completely and correctly (Table 6-2).

Table 6-2: Participants who made at least one deviation (error) when using inhalation devices

Type of device	The number of participants who demonstrated this device (N=46)	The number and percentage of COPD participants who made at least one deviation (error) when using the device
pMDI	8	7 (88%)
DPI	35	21 (60%)
Nebuliser	3	0 (0%)

The percentage of participants who made deviations/errors when using specific DPI devices is shown in Table 6-3. The proportion of participants who made at least one deviation was greater for the Handihaler device than when for the Turbohaler or Accuhaler. In addition, the mean number of errors/deviations made by 35 participants when using Handihaler, Turbohaler and Accuhaler devices was 2.7, 1.4 and 1.2 respectively.

Table 6-3: Participants who made at least one deviation/error when using dry powder inhalers

Type of device	The number of participants demonstrated this device (n=35)	The number and percentages of COPD participants who made at least one deviation (error) when using inhalation device
Handihaler®	7	6 (86%)
Turbohaler®	17	10 (59%)
Accuhaler®	11	5 (45%)

The problems encountered by participants, when using these devices are shown in Table 6-4.

Table 6-4: The number of mistakes made by participants per step

Correct technique	Errors in technique	pMDIs with or without spacer N=8	DPIs in general N= 35	Total number of errors/ step
1. Remove the cap (Device specific)	Failure to remove mouthpiece cap	0	0	0
2. Shake inhaler (the canister) well before use (pMDIs only)	Inhaler not shaken	6	N/A	6
3. Attach a spacer or valved holding chamber to the MDI (pMDIs with a spacer or valved holding chamber when required)	Failure to attach a spacer or valved holding chamber to the MDI	0	N/A	0
4. Hold inhaler in correct orientation (Device specific)	Inhaler upside down	4	1	5
5. Prepare or load the device according to the manufacturer's instructions (Device specific)	Failure to prepare device correctly	0	0	0
6. Breath out away from the inhaler	No breathing out	2	12	14
7. Place mouthpiece between your teeth and close the lips around it (Device specific)	Poor seal around mouthpiece	1	0	1
8. Actuate while breathing in deeply and slowly (pMDIs only)	Fast inhalation or firing device before start, at or after end of inhalation	4	N/A	4
9. Breathe in quickly and deeply (breath-actuated inhalers), or slowly (pMDIs)	Weak inhalation	N/A	10	10
10. Continue to inhale after firing (pMDIs only)	Stopping inhalation as device is fired	3	N/A	3
11. Hold breath for about 5-10 seconds (All)	No/short breath-hold	2	11	13
12. Clean the device according to the manufacturer's instructions and allow the device to air-dry completely before the next dose is administered	No cleaning or not according to the manufacturer's instructions	2	14	16
13. Replace the cap after the last dose (All)	Does not replace the cap after the last dose	0	0	0

When comparing the number of errors per step made by pMDI and DPI users, errors were recorded most (N=16) in cleaning the inhalation devices, breathing out away from the inhaler (N=14) and holding breath for less than five to 10 seconds (N=13) (Table 6-4). For the pMDIs alone, the steps concerning shaking inhaler (the canister) well before use and actuating while inhaling deeply and slowly were those most frequently performed incorrectly; with inhaler not being shaken (N=6), the device being fired before start of inhalation, or after end of inhalation (N=4). For the DPIs, the most common errors were in cleaning the device according to the manufacturer's instructions (N=14), exhaling away from the inhaler (N=12) and holding breath for about five to 10 seconds (N=11). Errors in cleaning were reported in not cleaning the device at all or cleaning the device but not according to the manufacturer's instructions. Errors with DPIs in the technique were seen

in not exhaling before inhaling the dose or breathing out into the device, or no/short breath-hold.

In summary**,** the data showed that deviations from the recommended inhalation technique when using the inhalation devices were common among participants (N=28; 61%). The study also revealed that 88% of pMDI users and 60% of DPI users made at least one deviation from the recommended technique. Among the DPIs, the data showed that more patients using the Handihaler device made deviations/errors in the technique compared with those using Turbohaler and Accuhaler. Reasons for the inhalation devices' mishandling can be divided into three categories namely: patient issues, practice issues and device issues. These are addressed.

6.4 Issues encountered by participants using inhalation devices

The clinical effectiveness of the inhalation devices depends not only on the ability of the devices themselves to deliver the medication, but also on the ability of the patient to use these devices properly and effectively.

6.4.1 Pressurised metered dose inhalers

NICE guidelines (NICE, 2010) state that pMDIs are the most prescribed inhalation devices as most medications are available in this form, whereas; the selection of DPIs is limited by the choice of medication because not all devices are available to deliver all drugs. When a patient is first diagnosed with COPD, the pMDI is usually given as a first option to be used to deliver short-acting bronchodilators (NICE, 2010). However, the use of a pMDI device may be problematic for some elderly patients who have impaired handgrip strength, for instance if they have arthritis, or have problems with coordinating inspiration and actuation. In this case, a spacer device and other

hand-held devices should be considered (NICE, 2010). In this study, pMDIs were the most commonly prescribed and used inhalers (N=43). Despite being the most prescribed device and the one that had been used for the longest time, findings of participants' handling of their inhalation devices were in agreement with previous studies which have reported that pMDI devices had higher rates of incorrect handling than DPIs (Lenney et al., 2000; Molimard et al., 2003; Khassawneh et al., 2008; De Moraes Souza et al., 2009; Rootmensen et al., 2010; NICE, 2010). The percentage of pMDI users who made at least one deviation from the recommended inhalation technique when using their pMDIs was 88% compared to 60% of DPIs users.

The correct use of pMDIs by participants was affected by numerous problems, which are listed in Table 6-4. In general, the most frequent errors were: firstly, failure to shake the device before inhaling the dose. The ingredients of some pMDIs in the canister are likely to settle over time. Shaking the pMDI is crucial to ensure that the formulation is appropriately mixed and homogeneous (Fink and Rubin, 2005). The second most common problem was failure to hold the device in upright position. pMDIs should be maintained in the upright position during administrating the dose; failure to do so may cause problems for drug disposition in the mouth or throat, which in turn can cause suboptimal drug delivery and side-effects (Colombo et al, 2012). Thirdly, problems in coordination emerged: patients are required to coordinate actuation at the beginning of inspiration. Actuation before one second of inspiration decreases the inhaled mass and the drug disposition deep in the lungs. Similarly, actuation after the inhalation can lead to exhalation of the drug before it can enter the target airways (Fink and Rubin, 2005; Colombo et al, 2012). Therefore, if there is a delay between actuation and inhalation, or if a participant inhales the dose very rapidly, the drug delivery to the lower airways will be detrimentally affected.

In terms of patients' preferences, the data indicate that participants made judgments in regards to their preferences and needs for using a certain device. However, most participants (N=37) had a conviction that all inhalation devices were the same and there were no differences. In addition, they strongly believed that these devices were given to them by their doctors to be used for their benefit and to meet their needs. Consequently, they had no preference for one device over another, and they believed that they had no choice but to use them even when they experienced difficulties in their use.

In terms of patients' preferences for pMDIs, the results of this study have shown that participants expressed no preference for the pMDIs, especially with the need of good inhalation technique for effective drug delivery. However, this did not affect participant's decision to use the pMDIs, especially because most of the pMDIs (N=34) were prescribed to deliver short-acting bronchodilators to be used when needed, so patients were not using them every day. However, this made pMDIs difficult to use for some patients. Adding a spacer device to the pMDIs may help in eliminating poor hand-lung coordination. However, patients' ability and conviction to use the spacer must be assessed before prescribing.

> Actually, I do not like the fact that I need to inhale while actuating these two [Clenil pMDI and Ventolin pMDI], I rather prefer to take my medicines via this one [Handihaler] because I do not need to go through this complex technique.
> Female, 72 yrs old, using Ventolin pMDI with spacer, Clenil Modulite pMDI and Spiriva Handihaler

This study's results were compared with the findings of previous studies, in regards to the most errors patients make when using their pMDIs. The errors were similar between these studies in terms of the following: inhaler not shaken (Hesselink et al., 2001; Molimard, et al., 2003; Ho et al., 2004; Sestini et al., 2006; Khassawneh et al., 2008; Rootmensen et al., 2010; Melani et al., 2011), and firing the device before the start of inhalation or after the end of inhalation (Ho et al., 2004; Sestini et al., 2006; Khassawneh et al., 2008;

Rootmensen et al., 2010). In addition, in this study, when pMDIs users were asked to explain the reason for disliking their pMDIs, they said that these devices contain propellants which need to be pressed hard to operate; they are unlike breath-actuated inhalers; and they found it difficult to use them correctly especially because of coordination difficulties. Newman's reported similar drawbacks with the use of pMDIs (Newman, 2005).

Although the existence of these difficulties did not stop patients from using their pMDIs, careful attention must be paid to the inhalation technique to ensure the best drug delivery, as the clinical effectiveness of the inhalation therapy depends not only on the efficacy of the devices themselves or patients' decision to use them but also on the ability of the patient to use these devices properly and effectively. Patients' inhalation technique should therefore be assessed regularly to ensure the proper use of pMDIs. However, if any patient is found to be unable to use the pMDI effectively even after receiving educational sessions regarding the use, for instance due to issues such as manual dexterities, other devices should be introduced, such as DPIs or spacers (NICE, 2010).

6.4.2 Spacer Devices

Spacers are generally prescribed to enhance drug delivery from pMDIs for those who find it difficult to coordinate inhalation with actuation (NICE, 2010). Inappropriate use of a pMDI device can lead to insufficient drug delivery, therefore, insufficient lung deposition, subsequently increasing the possibility of treatment failure (NICE, 2010). Adding a spacer to pMDIs improves the inhalation technique and is associated with fewer errors when compared to the pMDIs alone (Connolly, 1995; Ho et al., 2004; Rootmensen et al., 2010).

Seven participants were prescribed spacers to be used with their pMDIs. As reported by participants, spacers were given to ease the administration of aerosolised medication delivered by pMDIs and minimise the local adverse effects such as oral thrush. Participants perceived their spacers were effective in delivering the medication.

> The chemist told me if I use it [Aerochamber spacer] I will get all the good effect and the full amount of the puff of my medicine. I will be telling a lie if I told you it did not work for me.
>
> Male, 74 yrs old, using, Ventolin pMDI with Aerochamber spacer and Seretide Accuhaler

> I was advised by [Dr. Name] to use a spacer. I went to him because I could not get on well with these [salbutamol pMDI or salmeterol/fluticasone pMDI], because of my tongue. When I use these [pMDIs] I feel the medication is going all on my tongue, and I cannot get rid of my tongue [laughs], so when I was telling [Dr. Name], he gave me this [Aerochamber spacer].
>
> Female, 80 yrs old, using AeroChamber Spacer attached to adult comfortSeal mask with the Ventolin pMDI, Seretide pMDI, Seretide Accuhaler and prednisolone tablets

> I think when I started doing it, I think it is a case of you do have to get used to knowing how to use it and [Dr. Name] who I just mentioned to you, she gave me that adapter thing [Nebuhaler spacer] you just adapt to that. She suggested it and I did not know there was such a thing then she suggested I use the spacer with this one [beclometasone pMDI].
>
> Female, 72 yrs old, using Ventolin pMDI with Nebuhaler spacer, Clenil Modulite pMDI and Spiriva Handihaler

The results of this study showed that the pMDI users were prescribed a variety of spacers including Nebuhaler® (N=1), Volumatic® (N=2) and Aerochamber® (N=4) spacers. The data indicated that three participants, who were prescribed either Volumatic or Nebuhaler to be used with their pMDIs, found it difficult to handle these spacers, due to their large size and the lack of a facemask to ease the drug administration.

> I use it [spacer] each time I take Ventolin but I do not take the spacer with me when I go out because it is heavy to carry round and it takes time to administer compared to this one alone [pMDI]
>
> Male, 74 yrs old, using Ventolin pMDI with Volumatic spacer, Symbicort Turbohaler, Spiriva Handihaler and Carbocisteine Capsule

Participants' decision regarding the discontinuation or the intermittent use of spacer devices (Volumatic® and Nebuhaler® spacers) was associated with

device characteristics and properties (e.g. the shape, weight, being generally bulky and difficult to carry around) (Figure 1-4), participants' preference and convenience (e.g. a spacer device can be time consuming to use, particularly if a patient is on multiple medications). These participants who were advised to use a spacer device were unwilling to continue using their spacers (Volumatic® or Nebuhaler®) regularly as advised especially because they were less portable than a pMDI alone and less comfortable to use. Others felt awkward using them, especially when going out. As a result, one participant decided to discontinue using his spacer, whilst two participants stated only intermittent use of their spacers as they acknowledged that they were not using them when they were out of the home and resuming their use when they were at home. In all cases, healthcare providers were not informed about these decisions.

> I found it [Volumatic® spacer] not very comfortable to use and I felt awkward with it, holding it and pushing the centre and I said it does make sense. I can understand what medical people are talking about because they feel that a lot of people like me are not taking the full amount of the puff into their mouth and through this machine you are but the spacer kept falling out or fiddling and something like that. So, I stopped using it without telling my doctor.
>
> Male, 74 yrs old, using Ventolin pMDI with Volumatic spacer, Seretide Accuhaler

> I do not use it [Nebuhaler® spacer] all the time because it not easy to carry around and you cannot use it in public because it looks weird.
>
> Female, 72 yrs old, using Ventolin pMDI with Nebuhaler spacer, Clenil Modulite pMDI and Spiriva Handihaler

Participants who were prescribed and used other types of spacers such as Aerochamber spacer (N=4) reported having no difficulties in dealing with their spacers and stated advantages of the Aerochamber spacer including being small, portable, and having a facemask for use with the spacer. Those acknowledged receiving benefits from the COPD medicines with the use of the Aerochamber device and reported optimal outcomes and good disease control. Aerochamber users were willing to continue using their spacers without any complaint because they felt that they were making best use of their pMIDs.

> I find them [Ventolin pMDI and Seretide pMDI] very easy to use especially after using them with a spacer [Aerochamber® spacer] and a mask, so it [mask] goes over my nose and I feel that I am getting all the contents in. I presume it does me good.
>
> Female, 80 yrs old, using AeroChamber Spacer attached to adult comfortSeal mask with the Ventolin pMDI, Seretide pMDI, Seretide Accuhaler and prednisolone tablets

> I think it [Aerochamber® spacer] is easy to carry around and easy to use.
>
> Male, 84 yrs old, using AeroChamber Spacer with Ventolin pMDI and Symbicort Turbohaler

To conclude, seven pMDI users were prescribed a variety of spacers including Nebuhaler® (N=1), Volumatic® (N=2) and Aerochamber® (N=4). Of those, three had experienced difficulties in handling their spacers especially Nebuhaler® and Volumatic®. Aerochamber users were happy to use their spacers and did not report any problem with the use. They perceived their spacers were effective in terms of drug delivery and had experienced a sign of improvement in their symptoms, when compared to Volumatic and Nebuhaler users. Therefore, Volumatic and Nebuhaler users should be reassessed and re-educated on how to use their spacers properly and other spacer devices should be considered, such as Aerochamber spacer, if appropriate.

6.4.3 Nebulisers

Nebulisers are usually considered in patients with severe disease status or frequent exacerbations (or 'flare up') of COPD (NICE, 2010). In this study, three participants with severe COPD used a jet-nebuliser. These patients were given a nebuliser to administer bronchodilators or saline because they scored FEV_1<30% (severe stage of COPD). They were the only participants who have used all types of inhalation therapy in this study, including pMDIs, DPIs and nebulisers, whereas all the rest (N=43) used a combination of pMDIs and/or DPIs. Therefore, the judgments of these three participants about the inhalation devices and their preferences are considered potentially important as they reported the benefits of a jet-nebuliser, and felt that they

were the best to use of all inhalation devices. Newman's review (2005) reported that nebulisers were the hardest device to prepare and the easiest to perform the inhalation technique appropriately, whereas pMDIs were the opposite. In this study, the three participants using a jet-nebuliser were able to prepare it easily and correctly and performed the inhalation technique efficiently.

There is evidence that a person is most likely to use correctly the device that they prefer (Lenney et al., 2000). Based on the data obtained from the interviews and the observations of the patients' inhalation technique using the jet-nebuliser, it was found that the nebuliser was used correctly by all nebuliser users (N=3), and was preferred over all other hand-held devices. Firstly; using the nebuliser required no specific inhalation technique, as jet nebulisers are fairly intuitive to use and tidal breathing is sufficient. The data obtained from the interviews were triangulated with the findings of the observations of the inhalation technique for each patient when using the inhalation devices. It was found that the jet nebuliser device was used correctly by all three patients, with no recorded errors in the use (Figure 6-1). Additionally, participants considered the ability to mix more than one medication in a nebuliser and deliver them simultaneously as an advantage. By contrast, all nebuliser users criticised their large size and the heavy weight compared to other devices, especially pMDIs, which were considered easy to use and carry around.

> I cannot carry that around [Nebuliser], can I? If I can carry this one [A jet nebuliser] with me I would, because it is easier to use with no specific technique, you just have to breath and that's it.
> Female, 77 yrs old, using Ventolin pMDI, Seretide Accuhaler, Spiriva Handihaler and Salamol Steri-Neb delivered by nebuliser

> I use my nebuliser twice in the morning to take these two [ipratropium and salbutamol] which I like because you can use the same machine to take your medicines.
> Female, 76 yrs old, using Ventolin pMDI, Seretide Accuhaler, Spiriva Handihaler, Salbutamol and Atovent delivered by (Side-stream nebuliser/ Porta-neb compressor)

Another reported advantage of nebulisers over hand-held devices was the benefits of the ability to use very high drug doses, especially antibiotics for seasonal infections in COPD patients, which would be impossible to deliver with a pMDI or DPI. Additionally, no adverse effect was reported with the use of nebulisers unlike other hand-held devices.

> I find the nebuliser very helping especially after my lung infection; I had to take lots of antibiotics. Before I got it, I was complaining of shortness of breath and I used to feel chesty all the time, but, later, I was just fine with using this machine and it does help me breathe better. So, it is the one I prefer most.
>
> Female, 76 yrs old, using Ventolin pMDI, Seretide Accuhaler, Spiriva Handihaler, Salbutamol and Atovent delivered by (Side-stream nebuliser/ Porta-neb compressor)

> Of course, my nebuliser, I find it the most helpful and easy to use. I really cannot live without it but this one [Seretid Accahaler], I do not know if it is doing any good but it loses my voice and makes me cough; it is dreadful, dreadful.
>
> Female, 80 yrs old, using Ventolin Nebul delivered by Side-stream nebuliser/ Porta-neb compressor, Seretide Accuhaler, Spiriva Handihaler, Phyllocontin continus tablets and Carbocisteine Capsule

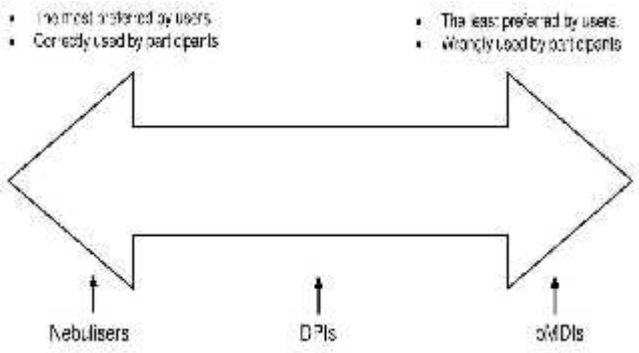


Figure 6-1: Ease of use and operation of the inhalation devices.

According to the NICE guidelines (NICE, 2010), nebulisers have the advantage over other hand-held devices of being independent of inspiratory effort or breathing pattern when a patient has poor coordination or inhalation technique. This means that they are easier to use than hand-held devices. In addition, they also have the advantage of allowing multiple drugs (e.g. bronchodilators and antibiotics) and high doses of medication, to be delivered

safely in patients with severe disease status and during a chest infection (NICE, 2010).

A further preferred advantage expressed by participants when comparing their devices was that nebulisers and pMDIs promote confidence in their use compared to DPIs as they usually generate a visible mist, making participants confident that they were getting the medication, whereas they felt nothing when using some other hand-held devices.

> I think I used to prefer the old Seretide [Seretide pMDI]. I was happy with it and I did not want to stop it but the doctor suddenly told me to stop it and go for the new one [Seretide Accuhaler]. With that one [nebuliser] and the old one [Seretide pMDI] I used to feel something going into my lungs and I have noticed some improvement but with the new one [Seretide Accuhaler] I feel nothing.
>
> Female, 76 yrs old, using Ventolin pMDI, Seretide Accuhaler, Spiriva Handihaler, Salbutamol and Atovent delivered by Side-stream nebuliser/ Porta-neb compressor

To conclude, among nebulisers, the jet-nebuliser was the predominant form that was used by patients at home. Jet-nebulisers were considered the easiest of all the aerosol devices and the most preferred by three participants who had experienced using all types of inhalation devices – pMDIs, DPIs and nebulisers. However, this cannot be extrapolated to all patients, as only three out of the 46 participants in this study used nebulisers. When selecting an inhaler device for a COPD patient, these points (e.g. the likelihood that participants are able to use the device correctly, preferences and adherence) should be considered by the healthcare prescribers to optimize medicine, though nebulisers have a restricted use in the treatment of COPD (NICE, 2010).

As recommended by NICE guidelines, nebulisers should not continue to be prescribed until proper assessment is undertaken to ensure one or more of the following: reduction in symptoms or improvement in lung function, increase in exercise capacity or in the ability to undertake activities of daily

living (NICE, 2010). In addition, they should not be prescribed without examining patient's ability to use them correctly (NICE, 2010). Other recommendations made by the researcher include the following: to maximise the drug delivery and to achieve optimal outcomes, patients' inhalation technique with the use of nebulisers should be assessed periodically or annually. In addition, side effects such as tachycardia or tremor should be assessed or examined when there is regular use of high doses of bronchodilators via a nebuliser. The efficiency of the nebuliser system should be assessed as well because the performance of the nebulisation system may decrease with improper cleaning and/or maintenance.

6.4.4 Dry Powder Inhaler Devices

According to the NICE guidelines, in most COPD cases bronchodilators are best administered by hand-held devices, including pMDIs and DPIs, unless there are some special cases that require nebulisation therapy (NICE, 2010). In this study, most patients (67%) were prescribed a combination of pMDIs and DPIs inhalation devices to deliver the inhalation therapy. In regards to the DPIs, bronchodilators were given to patients either alone by Accuhaler (e.g. salbutamol), Turbohaler (e.g. terbutaline) or Handihaler (e.g. tiotropium), or in combination with inhaled steroids which include Turbohaler (e.g. formoterol and budesonide) and Accuhaler (e.g. salmeterol and fluticasone propionate). The most used DPI devices in order were the Handihaler, Turbohaler, Accuhaler, Diskhaler, Aerolizer and Clickhaler devices. Therefore, it was decided to study whether these devices were used properly and correctly by patients.

As a result of the inhalation technique assessment, it was found that the deviation from the recommended technique was common among pMDIs and DPIs users, though COPD participants made more errors when using the pMDIs than DPIs.

The two most common errors made by participants when using DPIs were exhaling through the mouthpiece device or not breathing out away from the inhaler before inhaling the dose (N=12) and failing to hold a breath for five to 10 seconds post-dosing (N=11) (Table 6-4). Exhalation into the device may cause two issues: firstly, exhaling air into the mouthpiece can lead to blowing of the powder out of the chamber, which makes it unavailable for inhalation. Secondly, this exhalation contains a high amount of humidity, potentially causing aggregation of the drug powder and therefore reducing its ability to disperse during the inhalation process (Newman, 2005; Colombo et al, 2012). The second error regarding no breath-hold for about five to 10 seconds affects the lung deposition; studies found that the lung deposition is better after holding the breath for five to 10 seconds rather than four seconds or less (Newman, 2005; Colombo et al, 2012). Giving a time by breath-holding enables drug diffusion and sedimentation in the lung, which increases the amount of inhaled drug that is deposited (Newman, 2005; Colombo et al, 2012). The first error was defined as a crucial or essential error by Newman (2005), which may result in no drug delivery. However, both errors were common among COPD patients in previous studies (Molimard et al., 2003; Sestini et al., 2006; De Moraes Souza et al., 2009; Rootmensen et al., 2010; Hämmerlein et al., 2011; Melani et al., 2011), as well as this study.

Apart from the inhalation technique, when asking the participants about their preferences for the DPIs, a number of them expressed their preference for the multiple-dose devices (e.g. Accuhaler and Turbohaler), being easier to load and operate when compared to the single-dose devices (e.g. Handihaler), which contain capsules that need to be filled and loaded in the device every time before each use.

> That one [Handihaler] is a bit fussy because you get to go through a long process to clean and use. You have to take the capsule out [from the sealed blister], open this [mouthpiece ridge], put the capsule there [centre chamber] and pierce it. Unlike, this one [Accuhaler], all you need to do is press this [dose release lever] and the medicine comes out.
>
> Male, 95 yrs old, using Ventolin pMDI, Seretide Accuhaler and Spiriva Handihaler

> The Seretide [Accuhaler] is the one I prefer most and I think it is doing me good. I do not have a reason but maybe because it is easier to use.
>
> Female, 84 yrs old, using Ventolin Accuhaler with Aerochamber plus spacer, Seretide pMDI and Spiriva Handihaler

In a previous study that assessed COPD patients' preference and ease of use of a multiple-dose DPI (Accuhaler) and a single-dose DPI (Handihaler), by Moore and Stone (2004), it was found that 79% of Accuhaler users and 46% of Handihaler users were happy to continue using these devices, if this was suggested by their physicians. A preloaded device with a month's supply of medication (e.g. Accuhaler) was preferred to the one that required single doses to be loaded before use (e.g. Handihaler). The Accuhaler was preferred by 67% of users who strongly preferred the preloaded device compared to 33% of users who strongly preferred single doses (Moore and Stone, 2004).

In this study, participants were also asked to state if they had a preference or if they thought that their inhalers were all essentially the same in terms of ease of use; more than three-quarters of the study participants (N=37) had a conviction that all inhalation devices are similar, despite experiencing some specific technical and practical issues. These respondents had no choice but to use their inhalers as suggested. A few participants (N=7) stated their preference for multiple-dose DPIs (e.g. Accuhaler and Turbohaler) over single-dose DPIs (Handihaler), being quicker to load and easier to use because most multiple-dose DPIs hold the powder in a reservoir, from which individual doses are metered, or in individually sealed foil blisters within the device (Newman, 2005).

A further advantage for multiple-dose devices which made them superior or preferred by some participants over the single-dose devices is their use with fewer errors or deviations when performing the inhalation technique. The observations of inhalation technique showed that the percentage of participants who made at least one deviation from the recommended technique when using DPIs was less when using Accuhaler (45%) and Turbohaler (59%) than Handihaler (86%). Previous studies have shown similar findings of a greater number of errors and lower patient preference with single-dose devices compared to multi-dose devices (Moore and Stone, 2004; Wilson et al., 2007).

Moore and Stone (2004) reported that, when asking the patients to rate the most important features of an ideal inhaler device, the three most reported features were: being quick to use, overall ease of use and having a dose counter that tells how many doses are left in the device. This is similar to the findings of the current study, which found that patients' preferences for a certain device depended on being easy to use and load quickly.

> This one is the one I prefer most [Accuhaler]. I do not have a reason but maybe because it is easier to use. Another thing is that this [Accuhaler] has this window which tells you how many doses you have left which is good.
>
> Female, 84 yrs old, using Ventolin Accuhaler, Seretide Evohaler with spacer and Spiriva Handihaler

Participants' decisions to use the inhalation devices were not affected by the type of the prescribed device or by the number of practical or technical problems they experienced when using these devices, but by other factors which were more integrated with patients' perception about the need for therapy, and the actual and perceived effectiveness and safety of the COPD medication, which will be described in detail in the next chapter.

6.5 Device handling

Apart from the inhalation technique, the majority of COPD participants did not report experiencing any technical problems when using their inhalation devices at home. However, a few participants reported some technical issues only with the DPIs at home. These issues are addressed in details bellow and should be taken into account for future practices in order to maximise the medicine use. However, these issues did not affect participants' decisions to use the inhalation therapy as most of these patients were coping with these issues differently, which is also described below. See Table 6-5.

Table 6-5: Technical problems reported by COPD participants with the DPIs

The inhalation device	Where does the problem exist?	The specific device	What is the type of problem?
Multiple-dose devices	The integrated dose counter.	Accuhaler (N=3/16)	Difficulties in reading the numbers of the dose counter that facilitates dose tracking.
		Turbohaler (N=3/20)	Difficulties in seeing the red mark when it comes out which facilitates dose tracking.
	Doubts behind if the active drug is actually released when the device is activated.	Accuhaler (N=1/16) and Turbohaler (N=4/20)	Doubts behind if the active drug is actually released when the device is activated.
	Problems in loading the dose.	Accuhaler (N=2/16)	Problems in hearing the sliding lever when it clicks.
		Turbohaler (N=1/20)	Problems in twisting the coloured grip to release the dose.
Single-dose devices	Problems with the capsule.	Handihaler (N=9/28)	Problems in piercing the capsule (N=5)
			Reports regarding the emptiness of capsule from the inside (N=3)
			The wrong administration of the capsule by swallowing the capsule instead of inhaling it (N=2).

6.5.1 Issues with the Accuhaler devices:

In Moore and Stone's study, 69% of COPD patients had no problems using the Accuhaler device at home as well as this study which showed that three-quarters of Accuhaler users (75%) reported no technical problem with the

use of this device. However, a number of participants (N=6) reported experiencing a problem with the use of Accuhaler device (Figure 6-2). In Moore and Stone's study, the most common issues encountered by participants when using the Accuhaler device were opening the device and sliding the lever (Moore and Stone, 2004), whereas, in this study the most common issues reported were not being able to read the numbers in the integrated dose counter, not being able to hear the click when sliding the lever and doubts behind if the active drug was actually released when the device was used. These issues have not previously been reported in the literature.

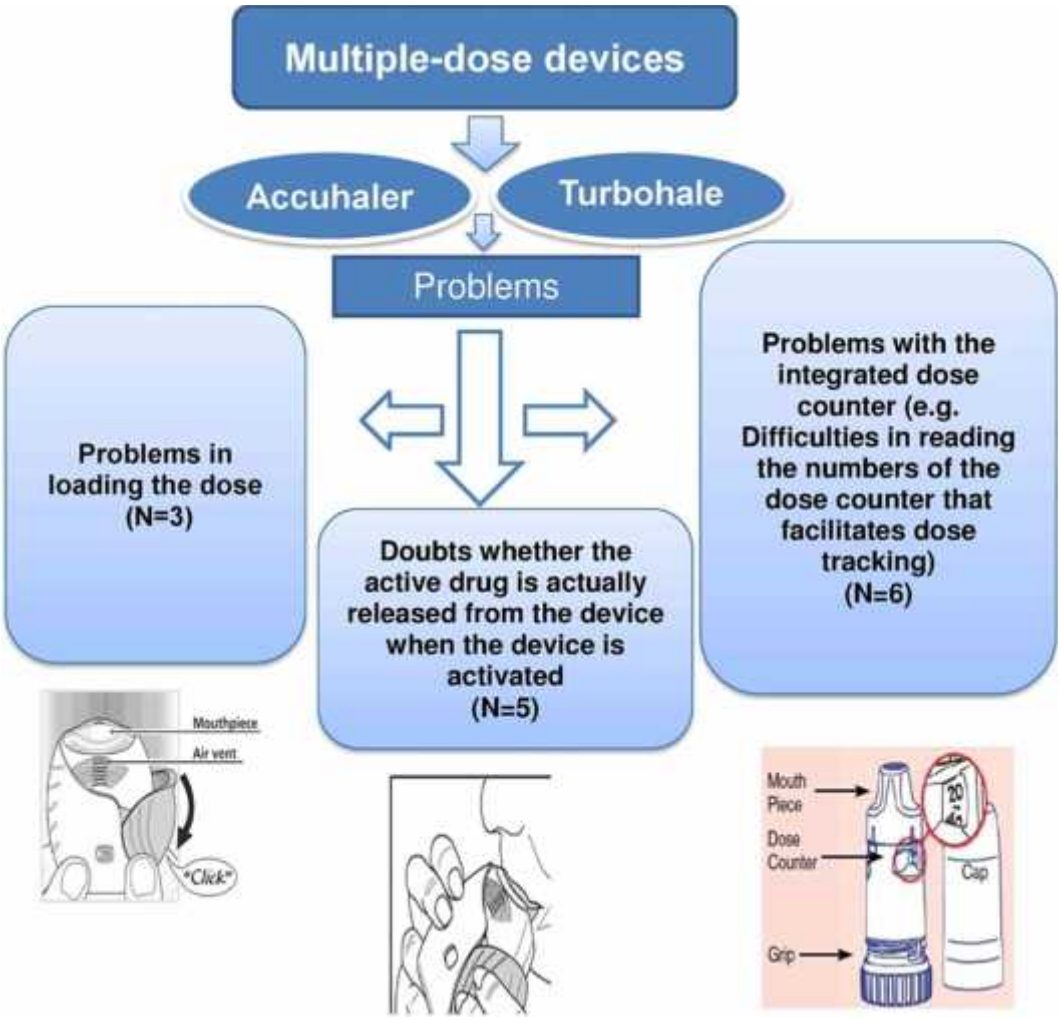


Figure 6-2: Technical problems reported by participants with multiple-dose devices

The integrated dose-counter of the Accuhaler

The dose counter facilitates dose tracking when patients administer multiple doses and reduces the risk of running out of medication. However, reading the dose counter or indicator that records how many doses remain in the device was a problem for three participants using the Accuhaler. They complained about being unable to read the numbers due to poor eyesight, or the small font size on the dose counter. These difficulties arose with aging, as vision continuously worsens, or with the emergence of a new condition, such as a cataract, which in turn influenced their ability to use inhaler devices properly. These patients either used reading glasses or a magnifying glass to help them read the numbers, or they received help from family members.

> Since I had my cataract surgery a few years ago I started using some eye drops and I find it too difficult to read the doses left on that one [Seretide Accuhaler] because these numbers are tiny. So what I usually do is either use my reading glasses or ask my wife to read it for me.
>
> Male, 85 yrs old, using Ventolin pMDI and Seretide Accuhaler

> I just find the number of the doses left is too small to be read [Seretide Accuhaler]. Sometimes, I have got to get my husband to have a look especially if it comes to number two or seven, you know, the red colour [laughs].
>
> Female, 84 yrs old, using Ventolin pMDI, Seretide Accuhaler and Spiriva Handihaler

Having a dose counter that tells how many doses are left in the device was one of the top three attributes of an ideal inhaler rated by patients, in Moore, et al.'s study of 2004. To address these problems, firstly, pharmaceutical companies such as GlaxoSmithKline should consider a larger window and font size for the Accuhaler device to facilitate reading. Secondly, patients' visual acuity should be assessed annually, especially for those who have poor eyesight or cataracts, as this could affect the successful use of the inhalation devices.

Sliding the lever of the Accuhaler until it releases a dose

Two participants aged over 80 years acknowledged that a hearing problem, either tinnitus or poor hearing due to age, affected their ability to hear the click of the Accuhaler device when pushing the lever as far as it goes to release the dose**,** raising the concern of unintentional non-adherence with either no dose or extra dosing. Overdosing was likely for one of them, as he admitted clicking the lever of the Accuhaler twice just to release the drug because he was unable to hear the click the first time.

> I just have more problems with the emergency blue inhaler [Ventolin Accuhaler], I just push my thumb away from me as far as it will go until I hear a click but the problem is I do not hear the click because I have tinnitus you see.
>
> Female, 84 yrs old, using Ventolin Accuhaler, Seretide pMDI with Spacer and Spiriva Handihaler

> Because of my age I have some hearing difficulties so I cannot hear the click of that one clearly [Seretide Accuhaler], so I use hearing aids to listen to the click or ask my wife to make sure that I did it properly. I might click it sometimes twice.
>
> Male, 85 yrs old, using Ventolin pMDI and Seretide Accuhaler

These patients consult their doctors and have their medication reviewed to assess their ability to use the Auccuhaler properly. If appropriate, hearing aids or informal care can be introduced to avoid the misuse of this device by these patients. If these solutions are not possible to be applied, a replacement device may be appropriate, such as the Turbohaler device.

Concerns whether drug is actually released when the device is activated

A further problem stated by one participant who was unable to hear the click when using the Accuhaler device was uncertainty whether the active drug in the Accuhaler was actually released or not. One of the main characteristics of pMDIs is that these devices contain propellants that produce a rapid-moving plume of aerosol, which often feels cold on the back of the throat as the propellants evaporate (Newman, 2005), whereas DPIs do not have this

feature of releasing a small amount of fine powder. For this reason, one participant reported being unsure whether she was using her Accuhaler device correctly because she felt nothing after using it, unlike the pMDI selected and used previously. The Seretide Accuhaler formulation contains lactose (see Table 6-1), but clearly the patient did not experience the taste of the sugar.

> With the old one [pMDI] I used to feel something going into my lungs and I have noticed some improvement but with the new one [Accuhaler] I feel nothing.
> Female, 76 yrs old, using Ventolin pMDI, Seretide Accuhaler, Spiriva Handihaler, Salbutamol and Atovent delivered by side-stream nebuliser/ Porta-neb compressor

This issue may be a psychological matter or result from misuse of the device, not a problem with the device itself, since the same patient reported two technical problems with the same device: being unable to hear the click and feeling nothing after the use. All these issues must be taken into consideration when reissuing the same device to the same patient. In addition, to ensure the greatest adherence to inhalation therapy, participants should understand how a particular device works. If a device does not seem to be working for a participant, non-adherence problems may emerge.

6.5.2 Problems with the Turbohaler device

As for the Accuhaler, the integrated dose counter and the uncertainty about the release of the medication were problems for Turbohalers users. These were common among 11 users of Accuhaler and Turbohaler, raising concerns of device mishandling. Seven users reported experiencing these problems with the use of Turbohaler: being unable to read the number of the doses that are left in the device and uncertainty whether the active drug was actually released (Figure 6-2).

The integrated dose-counter of the Turbohaler

For the Turbohaler, when a red mark first appears in the dose counter window it means that the Turbohaler has 20 doses left, and when it appears at the bottom it means that the device is empty and a new device should be obtained. In this study, three users of a Turbohaler device reported being unable to see the red mark when it first appears. One participant reported using her Turbohaler device for two consecutive weeks without knowing that it was empty because she could not see that the red mark had reached the bottom of the window, indicating an unintentional non-adherence. To overcome this problem, one participant acknowledged disposing of his Turbohaler devices before they get to the red mark, to limit the risk of running out of medicines which would be cost ineffective and causes waste of health resources; whereas another reported receiving help from his wife in regards to this matter.

> The last two weeks I was on and off the Symbicort [Turbohaler] because if I got better you know I do not need to take them every day if I feel ok. I probably missed them five or six times in the last two weeks. Let me show you my Symbicort… Ooooh, it is down to zero. I could not see it. It must be empty then, so I need a new one then.
>
> Male, 71 yrs old, using Bricanyl Turbohaler, Symbicort Turbohaler and Spiriva Handihaler

> For the Symbicort [Turbohaler]: as a design it is not particularly clear how many doses are left, so I tend not to go right down the red because it has got few extra doses over a month. I tend to almost throw it when it gets near the end and start on a new one.
>
> Male, 63 yrs old, using Symbicort Turbohaler, Spiriva Handihaler and Pyllocotincontius M/R tablets

> As I get older, I do have sight problems, so sometimes if I do not have my magnifying glasses I would ask my wife to help me to read this [the doses remaining on the dose counter of the Turbohaler] .
>
> Male, 77 yrs old, using Ventolin pMDI and Symbicort Turbohaler

These patients could be at risk of running out of medications, leading to unintentional non-adherence, if no action is taken to resolve this problem.

Concerns whether drug is actually released when the device is activated

Four Turbohaler users reported uncertainty regarding the release of medication from the Turbohaler. This problem was reported more among Turbohaler users than Accuhaler users (Table 6-5). Despite the Symbicort formulation containing lactose (see Table 6-1), clearly patients did not experience the taste of the sugar, which raised concerns about inhaler mishandling. Participants compared their experience with the pMDI devices when the spray was felt going into the lungs, as well as when using the Handihaler devices, when a rattling sound was heard during use. These experiences assured participants that they had received the dose of their medicines, whilst they felt nothing when using their Turbohalers.

> Well, as I said I do not know about this one [Turbohaler] and what it is doing but this one [pMDI] at least I feel the puff and you feel something going into your lungs.
>
> Female, 78 yrs old, using Ventolin pMDI and Symbicort Turbohaler

> I do not know but with this [pMDI] I used to feel something with it. You know what I mean, but, when I am taking these [Turbohalers], I do not feel anything going in. That is why I did not know if I am using these correctly. But if you use those [pMDIs], and you press in [hpointed on the canister], you can actually feel something, so I think they are better in that way.
>
> Male, 83 yrs old, using Bricanyl Turbohaler and Symbicort Turbohaler

> Actually, with this [Handihaler] I can hear something happening but with that [Turbohaler] I cannot
>
> Male, 63 yrs old, using Symbicort Turbohaler, Spiriva Handihaler and Pyllocotincontius M/R tablets

To assure the greatest adherence to inhalation therapy, participants should understand how a particular device works and what a drug actually does. If an inhaled device does not seem to be working for a participant, other types of inhalation devices can be considered.

Twisting the coloured grip of the Turbohaler device to release the dose

In this study, one participant reported experiencing difficulties in twisting or rotating the grip of the Turbohaler device. Wilson et al. (2007) reported that failure to turn the wheel on the base or the grip was one of the major or fatal errors during assessing the technique which result in no drug delivery (Wilson et al., 2007). The same participant reported cleaning his device inappropriately by washing it with water despite being told not to do so. This resulted in accumulation of powder in the base of the device, which may have affected its performance. A consequence of the lack of knowledge regarding how to clean these devices was that their performance was affected and blockage in the inhalation channels may have been caused.

> Another problem was with the Symbicort [Turbohaler]: I have got one or two of the Symbicort inhalers, so when it was not rotating quite well, then [I] started to use another one. Maybe it is stopped rotating because it seems to be a build-up of some powder or whatever, so what I did is just wash it but it did not work afterwards.
> Male, 67 yrs old, using Ventolin pMDI, Symbicort Turbohaler, Spiriva Handihaler and Phyllocontin tablets

The manufacture's cleaning instructions should be followed and applied step by step as the performance of the inhalation devices and drug delivery could be affected by improper cleaning and maintenance. All users of inhalation devices, including the Turbohaler users, should be taught how to maintain inhalation devices in a good condition. In addition, to obtain optimal results from therapy, inhalation device functionality should be checked and maintained.

6.5.3 Problems with the Handihaler device

When the inhalation technique was observed by the researcher, the percentage of participants who made at least one deviation from the recommended inhalation technique was more when using the Handihaler device (86%) than when using the Turbohaler (59%) and Accuhaler (45%). In addition, when participants were asked about how they handle their devices

and whether they have experienced any technical problem with the use, most problems were reported by Handihaler users. The Handihaler is considered the most complex device to use when compared to the multiple-dose devices, as it involves more preparatory stages to receive medication, so more problems are likely to occur (Moore and Stone, 2004). Other studies have also shown that patients were at a significantly higher risk of making an error when using capsule-based DPIs (Hesselink et al., 2001). However, these issues with the Hanidhaler device that were raised by users were not detrimental to the use the device.

A previous study by Moore and Stone (2004) reported that the most common errors in using the Handihaler device were opening the cover and/or mouthpiece and removing the capsule from the foil. In another study of 30 COPD patients assessing the ease of use of four different DPIs, it was found that failure to press the button to pierce the capsule was the most important error, which would result in no drug delivery (Wilson et al., 2007). In this study, the most common problem experienced by participants with the use of the Handihaler involves the capsules, as illustrated below (Figure 6-3).

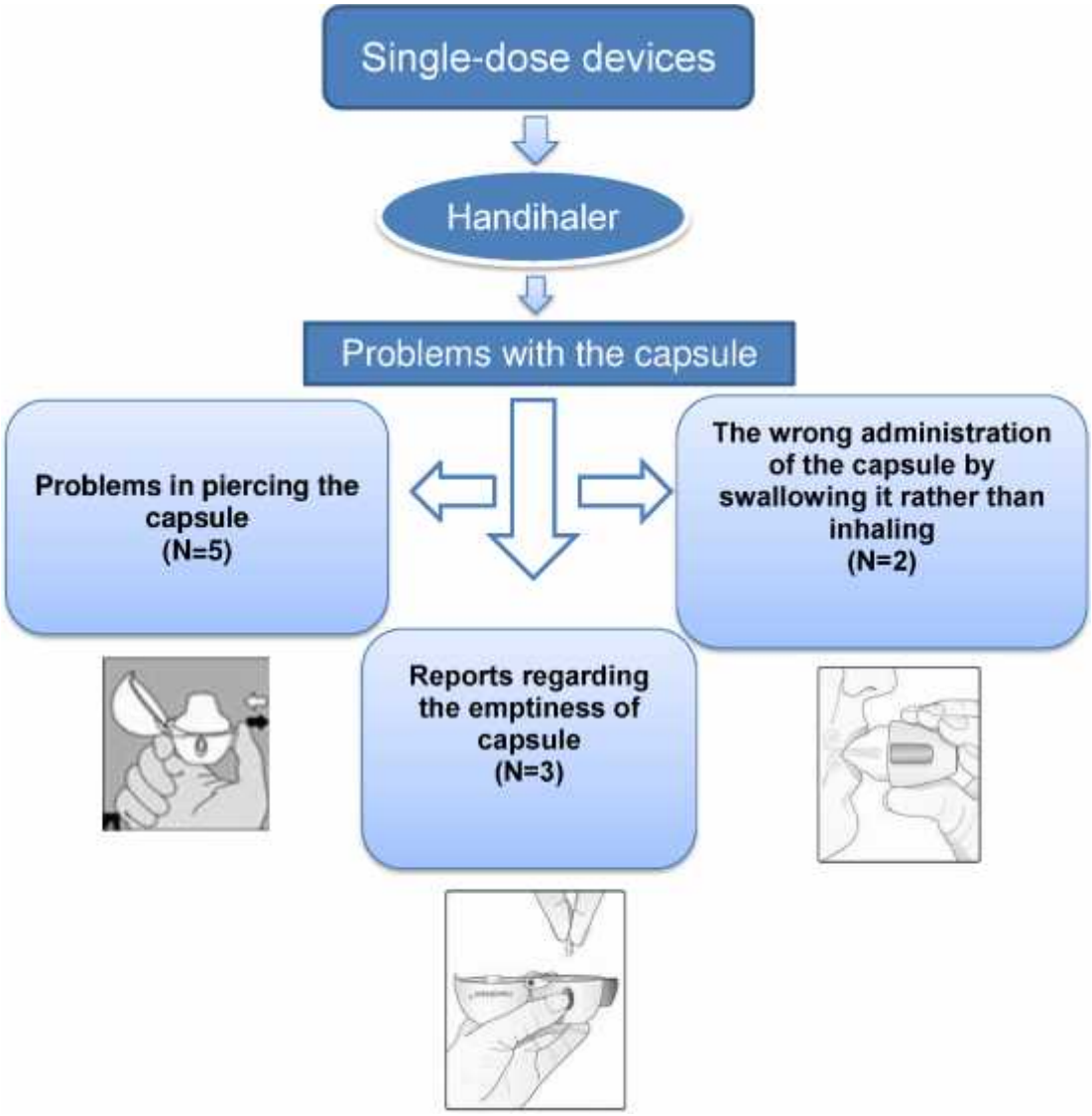


Figure 6-3: Technical problems reported by participants with the Handihaler, single-dose device

Problems in piercing the capsule

With regard to operating the Handihaler device, 10 out of 26 participants who used the Handihaler device reported that it was not working appropriately. The most common problem reported by participants was in piercing the Spiriva capsule (Figure 6-3). For example, five participants stated that when pressing the green button to pierce the capsule and release the dose, it sometimes made the hole too large or fractured the capsule rather than piercing it. This was problematic for some patients who were abroad and had

only a few numbers capsules with them to use. Consequently, some tended to use another capsule, which meant an extra dose was inhaled, leading to overdosing. It can be concluded that inhalers with a complex operator (e.g. Handihaler) can result in medication being misused or wasted when operating the device. The misuse of the inhalation devices can result in the medication being prescribed by physicians with a higher dose or adding other medications to the existed regimens, leading to an increase in the direct and indirect healthcare costs.

> Occasionally with that one [Spiriva Handihaler] I am not actually sure if it makes the hole too large sometimes, so I am not sure if the stuff comes out properly then. It happened maybe once or twice. I am somehow felt it did not feel right. Maybe because it gets a very distinctive noise when it is working, it rattles, so when I checked it out and it did made the puncture hole in it. It did not seem to make it any particularly larger but it definitely had a different sound. So, what I did was I took another capsule put it in and did it again.
>
> Male, 63 yrs old, using Symbicort Turbohaler, Spiriva Handihaler and Pyllocotincontius M/R tablets

> Sometimes it can make the hole bigger or fracture a little bit so you get a little amount inside but I am very careful because then I look at it again and if I feel it is not right.. I inspect it.
>
> Female, 74 yrs old, using Ventolin pMDI, Seretide pMDI and Spiriva Handihaler

> I think this thing [Spiriva Handihaler] does not sometimes puncture a capsule properly. Sometimes it seems to break it rather than puncture it.
>
> Male, 83 yrs old, using Ventolin pMDI, Clenil Modulite pMDI and Spiriva Handihaler

One of the suggested reasons behind the failure in piercing the capsule properly is that Spiriva capsules are made of two-piece hard gelatine capsules, which may pose a problem for some patients of advanced age or who have dexterity problems that may affect the proper use of their inhalers. Another suggested reason is the improper storage of gelatine capsules, which may have caused water loss from the gelatine and made it hard to pierce. Capsules may get dried out when they are exposed to air due to inappropriate storage or because of carelessly peeling back the foil too far and exposing the next capsule to the air as well. All these factors can cause problems when using the Spiriva capsules.

> I have an awful gym to get these capsules out [Spiriva capsules]. I cannot get them out but I have got a pair of scissors to help me get them out, so I cut the

> foil with scissors and leave them out to use them [Spiriva capsules] when I need.
>
> Female, 100 yrs old, using Atrovent pMDI with spacer, Spiriva Handihaler, Pulmicort Turbohaler and Bricanyl Turbohaler

The capsule appears to be empty

Three participants reported that the Spiriva capsule appeared almost empty**,** unaware of the fact that the Spiriva capsule contains only a very small amount of powder; each capsule contains 18 mcg tiotropium blended with lactose monohydrate. The delivered dose (the dose that leaves the mouthpiece of the Handihaler® device) is only 10 mcg (EMC, 2013), the capsule also contains lactose as an excipient. See Table 6-1 for a summary of products.

> I have often suspected that the capsule of the Spiriva [Handihaler] is empty. I cannot really check it before I use it but after each dose I take, I open the capsule and there is a tiny amount of powder left in there, so this obviously has something in it. But occasionally I feel that there is nothing. I suspect that perhaps if there is meant to be 30 capsules in a pack there are only 25 capsules filled with powder and five are false.
>
> Female, 70 yrs old, using Ventolin pMDI and Spiriva Handihaler

> Lately I have had two failures of this one [the capsule of the Handihaler]. Just recently, recently, I do not know if it was different manufacturer. Most unusual but this happened within a week when I went ooooof [he took a deep breath] nothing happened because nothing was in the capsule. That is the problem. The capsule was empty.
>
> Male, 74 yrs old, using Ventolin pMDI, Clenil Modulite pMDI, Spiriva Handihaler and Becotide Diskhaler

One-third of the Handihaler users (N=9) reported experiencing issues with the Handihaler capsule being either empty, hard to pierce or wrongly administered. Great attention must be paid to these points when prescribing a Handihaler device for COPD patients, as these issues can be real and not belong to the patient's psychology. The Handihaler capsule is used as a dose-holding system that allows participants to check if the dose has been administered successfully by opening the capsule to check whether it is empty or not; in addition to that, when the capsule is put into the device and when the dose is taken, participants should feel or hear the capsule vibrate or rattle during inhalation from the Handihaler. In the case of not hearing a

rattling sound, participants are advised by the researcher to open the capsule and put it on a dark surface and if a fine powder comes out that means that the drug was not released or fully taken.

> In the past I opened them [capsules] and put the capsule on a dark surface but the powder was still in there.
> Female, 84 yrs old, using Ventolin pMDI, Seretide Accuhaler and Spiriva Handihaler

To overcome this problem, participants should be educated about the Handihaler device and the content of the capsule and how it can be successful administered and checked to make sure that the device has been used efficiently. In addition, healthcare prescribers should be aware of the consequences or potential problems with the use of the Handihaler. If a certain patient reports experiencing problems with the Handihaler more than once, another device can be considered.

Erroneous administration of the Spiriva capsule

In this study, the unintended oral administration of a Spiriva capsule was reported by two participants. This error stems from the fact that these capsules resemble those taken orally, which is obviously not desirable.

> What I have done on occasions is I swallowed one of these capsules [Spiriva capsule] twice [a laugh].
> Male, 74 yrs old, using Ventolin pMDI, Clenil Modulite pMDI, Spiriva Handihaler and BecotideDiskhaler

> The Spiriva capsule I should be very careful with because it looks very much like a capsule that I need to swallow which I did once, so I mean if I took them out and put them somewhere unless I actually know which tablet I might get mistaken and swallow it. That is why I always keep it separated from all other pills.
> Male, 78 yrs old, using Ventolin pMDI and Spiriva Handihaler

Spiriva capsules should only be used with the Handihaler device and inhaled through the mouth. According to the FDA, in 2005 they received 30 cases regarding the accidental oral consumption of the Foradil Aerolizer and Spiriva Handihaler capsules. Although no adverse event was reported, there were a

few cases that had difficulty in breathing following oral ingestion (Tezky, 2005). Healthcare professionals should be aware of the potential for accidental errors in regards to the unintentional oral administration of Spiriva capsules as this may lead to adverse effects or a delay in the onset of action and minimise the drug efficacy.

As a result, it is suggested that, when prescribing Spiriva to patients with COPD, a cautionary label indicating that this capsule is "for inhalation use only", "for use with inhaler only" or "for inhalation use with special inhaler only" in the principal display panels of the labels, should be provided by the unit-dose section in the pharmacy, if this was not on the manufacturer package. In addition, pharmacists are advised to dispense a Handihaler device for patients every time they collect their Spiriva capsules from the pharmacy, even if a patient did not ask for a new device, to encourage patients to always keep them together, which may be a good way to remind them that this capsule is made for inhalation. This may help in avoiding the misadministration of the capsule.

To conclude, it is important to consider the problems encountered by COPD participants with the use of inhalation devices. These problems may result in suboptimal adherence either intentionally (patients' decision to not use a certain device) or suboptimal drug delivery (patient has improper inhalation technique or other technical problems), which may lead to suboptimal disease control or treatment failures.

To summarise, as a result of the inhalation technique assessment, it was found that the deviation from the recommended technique was common among pMDIs and DPIs users, although COPD participants made more errors when using the pMDIs than DPIs. Among the DPIs, it was found that

the deviation from the recommended technique was more common among Handihalers users than Accuhaler and Turbohaler users and this was the same for the technical/practical issues encountered by participants when using the inhalation devices at home. The number of participants who reported experiencing technical issues with the use of DPIs was greater among Handihalers users than Accuhaler and Turbohaler users.

With regards to inhalation technique, only 18 participants performed all the steps correctly when using their inhaled medication, leaving nearly two-thirds of the sample (N=28) at risk of inadequate drug delivery due to their suboptimal inhalation technique. As a result, it is highly recommended to counsel the patients about their inhalation technique in the context of the problems faced at home with these devices, aiming to achieve the best clinical outcomes.

Since adequate disease control relies on the appropriate use of inhalation therapy, it is noteworthy that practical measures may be implemented to reduce the number of deviations from good practice made by participants and maximise the effective use of inhaled medicines. One of the suggested measures is a practical reassessment of user's technique by their healthcare providers, such as a trained nurse during clinic visits, even if a patient claims to know how to use these devices correctly. A second suggestion could be the introduction of short- or long-term structured education programmes for all patients without exception. It is important to check whether the disease is well controlled by the proper use of COPD medication before introducing new and costly therapeutic measures.

6.6 Cleaning inhalation devices

After using the inhalation devices, the manufacture's cleaning instructions should be followed, as the performance of the inhalation devices and medication dose delivery may be affected by improper cleaning and maintenance. Additionally, in the case of the nebulisers there is a high risk of infection due to bacterial colonisation of these devices, which may possibly transmit to patients during their use (Colombo et al, 2012).

> Maybe it [Turbohaler twist grip] has stopped rotating because it seems to be a build-up of some powder or whatever, so what I did is just wash it but it did not work afterwards.
> Male, 67 yrs old, using Ventolin pMDI, Symbicort Turbohaler, Spiriva Handihaler and Phyllocontin tablets

The proper maintenance of inhalation devices includes daily care of cleaning and drying. Manufacturers advise patients to clean their inhalation devices such as nebulisers, spacers and Handihaler device with warm water or warm soapy water, rinsing in tap water and then allowing them to air dry. Others (e.g. pMDIs, Turbohaler and Accuhaler) are recommended to be wiped with a dry tissue or paper towel (Table 6-6 and Table 6-7).

When participants were asked if they cleaned their inhalation devices used at home, more than half of the participants (N=26) indicated that they always did so properly, whereas 20 participants indicated that they never cleaned their inhalers. Those who did not clean their devices were either not motivated to clean them or found it difficult to do so, especially single-dose devices such as Handihaler. Others were unaware of the fact that they should be cleaned regularly or they did not know how to do it. Lack of education regarding cleaning and maintaining of the inhalation devices in a good condition was a reason reported by participants who did not comply with the cleaning and maintenance instructions provided by the surgery or patient information leaflets for each device.

> Now I do not do any cleaning, no, because that one [Spiriva Handihaler] is a bit fussy because you got to go through a long process to clean.
>
> Male, 95 yrs old, using Ventolin pMDI, Seretide Accuhaler and Spiriva Handihaler

> I have never been told how I should clean or store my inhalers and I have never asked for such advice.
>
> Female, 65 yrs old, using Ventolin pMDI and Symbicort Turbohaler

> Well, I do not do that [clean]. I am a bit silly about that. Why, should we clean the inhalers? Are there methods to clean these?
>
> Male, 72 yrs old, using Ventolin pMDI, Pulmicort Turbohaler and Spiriva Handihaler

Another reported reason for not cleaning the inhalation devices, as acknowledged by four participants, was that the devices were limited to single patient use (personal use only). They claimed that, in the absence of the concept of sharing the devices, there was no need to clean the device.

> As nobody else uses them, why should I clean them? So that is one of the reasons why I do not clean them and they do not get dirty or wet or anything like that.
>
> Male, 87 yrs old, using Bricanyl Turbohaler, Symbicort Turbohaler and Bumetanide tablets

Table 6-6: Frequency of cleaning inhalation devices

Frequency of cleaning by participants	pMDI (N=42)	Spacer (N=7)	DPI (Handihaler) (N=28)	DPI (Turbohaler and Accuhaler) (N=37)	Nebuliser (Facemask/ mouthpiece) (N=3)	Nebuliser chamber (N=3)	Nebuliser tube (N=3)
Recommendations	Recommended to be cleaned at least once a week	Recommended to be cleaned once a month	Recommended to be cleaned once per month or as needed	Recommended to be cleaned the mouthpiece once a week or as needed	Recommended to be cleaned once a week		
After each use	1	1	1	1			
Daily	2						
Weekly		2	5	7	1	1	1
Monthly			7		1	0	0
When it gets dirty or when I think of it	5		4	4			
Never	34	4	11	25	1	1	1

Table 6-7: Method of cleaning inhalation devices

Method of cleaning	pMDI (N=42)	Spacer (N=7)	DPI (Handihaler) (N=28)	DPI (Turbohaler and Accuhaler (N=37)	Nebuliser (Facemask) (N=3)	Nebuliser chamber (N=3)	Nebuliser tube (N=3)
Cleaning recommendations	Wipe the mouthpiece inside and outside with a dry cloth, tissue or cotton bud	Take the spacer apart, rinse the parts well in warm water using a mild soap and then in clean water	Open the lid, lift up the mouthpiece and lift up the piercing button to open the base, then rinse it with warm water to remove any powder without using soap	Wipe the mouthpiece with a clean dry tissue	Use a damp cloth	Wash the mouthpiece, nebulizer, tubing and mouthpiece in hot soapy water and washing liquid, rinse under hot running water	
Warm soapy water		2	8		1	1	1
Cleaning it under running tap water	1		5				
Dry tissue	5	1	2	12	1	0	0
Fingers	2		2	0			
Never	34	4	11	25	1	1	1

In this study, the majority of participants were found to either not clean their devices at all or to be non-compliant with the manufacturer's recommendations and guidelines on how to properly clean their devices. This may affect the performance of these devices and therefore the drug delivery, which may lead to treatment failures. Therefore, COPD patients should be aware of current practice guidelines and recommendations provided for the inhalation device in regards to the cleaning and maintenance. Additionally, they have to be encouraged by healthcare professionals to comply with these guidelines and recommendations during each visit.

7 Chapter Seven: The use of medicines in the management of COPD

This chapter addresses the first and the second objectives of this study which concern the use of multiple inhalation therapies by COPD patients in the management of their condition. It also describes patients' use of their COPD medication in the context of their daily lives. In addition, it gives an insight into patients' decision-making regarding using inhalation therapy and the factors that influenced their decisions to use these medicines, in order to provide all the necessary assistance tailored to each patient who is at high risk of non-adherence or treatment failures, which may in turn maximise the use of medicines and reduce the number of treatment failures and healthcare costs.

7.1 The use of multiple inhalation therapies by patients in the management of their condition

Data analysis indicated that participants' positive attitude towards the disease by accepting it as incurable and living with it helped them to be more realistic about the treatment and its outcomes. Participants who accepted their disease and understood the role of medications were using their inhalation therapy as suggested and coped well. On the other hand, denial of illness can be a contributory factor to medication non-adherence and subsequent treatment failures.

> I have no concerns that stop me from taking my inhalers because asthma is not curable. I would like to take nothing but it is not curable.
>
> Female, 78 yrs old, using Ventolin Evohaler pMDI, Seretide Accuhaler and Spiriva Handihaler

> I presume medication is doing me good. It is not curing it because it cannot cure it but it is keeping it at bay.
>
> Female, 80 yrs old, using AeroChamber Spacer Plus with adult comfortSeal mask, Ventolin Evohaler pMDI, Seretide Evohaler CFC-free, Seretide Accuhaler and Prednisolone tablets

In terms of medication use, the data showed that the majority of participants accepted their medication regimens after questioning and evaluating the need for therapy and did not articulate any worries or concerns about taking-medication, especially when their condition was well controlled by the regimen. They were happy to continue on their current drug regimens, despite in some instances making some alterations to the drug regimens (see section 7.3)

> Actually my COPD is stable on the current regimens. It is usually not at all a problem.
> Male, 67 yrs old, using Ventolin Evohaler pMDI, Symbicort Turbohaler, Spiriva Handihaler and Phyllocontin tablets

> In general I am happy with what I am using and they [COPD medications] are doing what they are supposed to do.
> Female, 74 yrs old, using Ventolin Evohaler pMDI, Seretide Evohaler and Spiriva Handihaler

In contrast, a few participants were not using their COPD medications as suggested because they either had worries or concerns about taking these medications or considered their medications as a 'poison' or 'harmful substances', and therefore tried to avoid them as much as possible. This was articulated by three participants who tried to either tolerate the symptoms, or looked for alternatives or returned to the doctor asking for advice or changes to the current regimens.

> My own doctor felt I should have taken more medicines but I did not really like taking it and you know it is a drug, is it not?
> Female, 78 yrs old, using Ventolin Evohaler pMDI, Seretide Accuhaler and Spiriva Handihaler

> I did not want to have steroids. Steroids are artificial products inside your body.
> Female, 65 yrs old, using Symbicort Turbohaler and Ventolin Evohaler pMDI

> I went to see the person who does the COPD but I was not impressed by him because he told me I need to take two of these inhalers twice a day [she pointed to Spiriva and Seretide] but when I went to see my doctor in my old surgery and told her about what happened, she said, "No you only need to take this one once" [she pointed on Spiriva] and I said, "Well that is what he said". She said, "He should not have told you that".
> Female, 77 yrs old, using Ventolin Evohaler pMDI, Seretide Accuhaler, Spiriva Handihaler and Salamol Steri-Neb

Participants made judgments and alterations to their current COPD medicines based on different factors (Figure 7-2). Participants were therefore questioned to see whether they were adherent to their prescribed regimens, what alterations were made, what medication(s) was/were not taken as suggested and what the reasons were behind their actions. As a result, adherence to COPD medications was measured using the self-report Morisky Medication Adherence Scale (MMAS). In addition to enhancing the validity of the data, and examining and gaining insights into medication-taking behaviours among these participants, participants were asked to answer some open questions regarding their medication use (e.g. for your regular medicines, people often do not take their medicines exactly as prescribed for different reasons. Thinking of the medicines you use for your COPD, when was the last time you did not take the dose of your regular medicines? How many times in the last week have you missed a dose of your regular COPD medicines and why did you miss them?) to understand the unanticipated results from quantitative data (Morisky scale) and to identify issues behind non-adherence to COPD medicines.

The eight-item MMAS usually scores range from 0 to 8, which have been categorised as high, medium and low adherence (MMAS score of 8, 6 to <8, and <6, respectively) (Figure 7-1). However, in this study participants were identified as ‘adherent’, if they scored eight in MMAS, whereas, if a participant scored less than eight in the Morisky scale, their adherence was classified as suboptimal. According to the MMAS scores, 24 participants were adherent to their COPD medicines (scored 8), whereas 22 (48%) participants had suboptimal adherence (scored<8). Therefore, close attention should be paid to those with suboptimal adherence, to see what medication(s) was/were not taken as required and why, to optimise the use of medicines in this group.

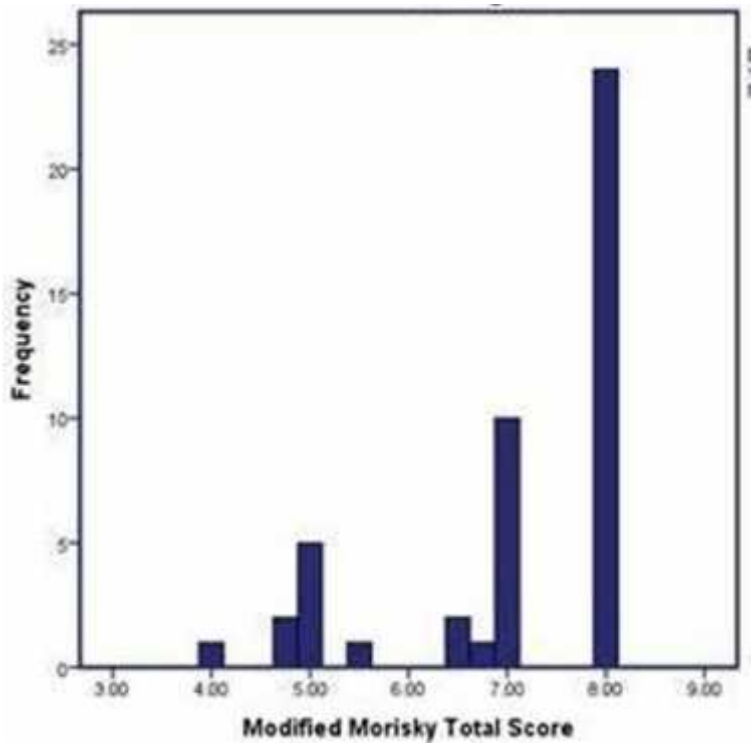


Figure 7-1: The total adherence score of the MMAS scale

When participants started inhalation therapy, they tended to make some amendments or alterations to their prescribed regimens (e.g. discontinuation or adjustments to therapy or intermittent use of therapy). These behaviours were directed by the balance of an individual's reasons for and against taking medication. Intermittent or discontinued use of COPD medicines was associated more with the long-term use of long-acting bronchodilators and inhaled corticosteroids, or adjusted to meet certain needs, especially with the use of short-acting bronchodilators. Short-acting bronchodilators were over-used as a preventative approach, to prevent symptoms from getting worse and prolong symptom-free periods, which exceeds the use based on the symptoms to include taking a prophylactic dose as a precautionary measure (see section 7.3). This behaviour was related to the perceived immediate benefit of short-acting medication on symptom relief.

> Well, I take this one as a preventative [salbutamol] when I will probably be climbing stairs or something like that because it gives me instant relief.
>
> Male, 83 yrs old, using Ventolin Evohaler pMDI, Clenil Modulite pMDI and Spiriva Handihaler

Adherence to long-acting bronchodilators and ICS was found to be suboptimal with those who reported suboptimal medication adherence. This resulted from the prolonged efficacy provided by long-acting bronchodilators and ICS on the symptom's relief.

> Probably I do not need that [tiotropium] but I take it sometimes. Those two [beclometasone and tiotropium] are something that does not affect you as soon as you take them. Does it? You need to give it time but if I took Ventolin [salbutamol] it would help immediately, so I take it but neither of those [beclometasone and tiotropium] is going to help me immediately if I was in a bad way.
>
> Female, 72 yrs old, using Ventolin Evohaler pMDI with spacer, Clenil Modulite pMDI and Spiriva Handihaler

> This one [salbutamol] might make an improvement because it has immediate effect whereas this [tiotropium] does not have an immediate effect, so I am not sure whether it does me good or not and whether I should use it.
>
> Male, 95 yrs old, using Ventolin Evohaler pMDI, Seretide Accuhaler and Spiriva Handihaler

Among the LABA and ICS users, more concerns expressed for ICS. The reason for these concerns is that some participants responded better and quicker to the LABA than the ICS and, for this reason, preferentially used the LABA. In addition, experiencing side effects or fears of side effects with the use of ICS was greatest among participants (see section 7.3).

> The doctor decided to put me on Seretide [salmeterol /fluticasone] and he said try this but it was painful for the first week because it gives you cramps and everything else like that, so I stopped it for a while until these signs disappeared.
>
> Male, 63 yrs old, using Ventolin Evohaler pMDI, Clenil Modulite pMDI, Mometasone furoate nasal spray, Seretide Accuhaler and Carbocisteine Capsule

The next sections give further information on the factors that influenced medication use among patients with COPD. Understanding these factors and addressing patients' adherence issues may help in optimising medicine use and improve treatment outcomes.

7.2 Factors affecting patients' decision to use the inhalation therapy

Various factors were found to affect patients' decision making to use the inhalation therapy (Figure 7-2).

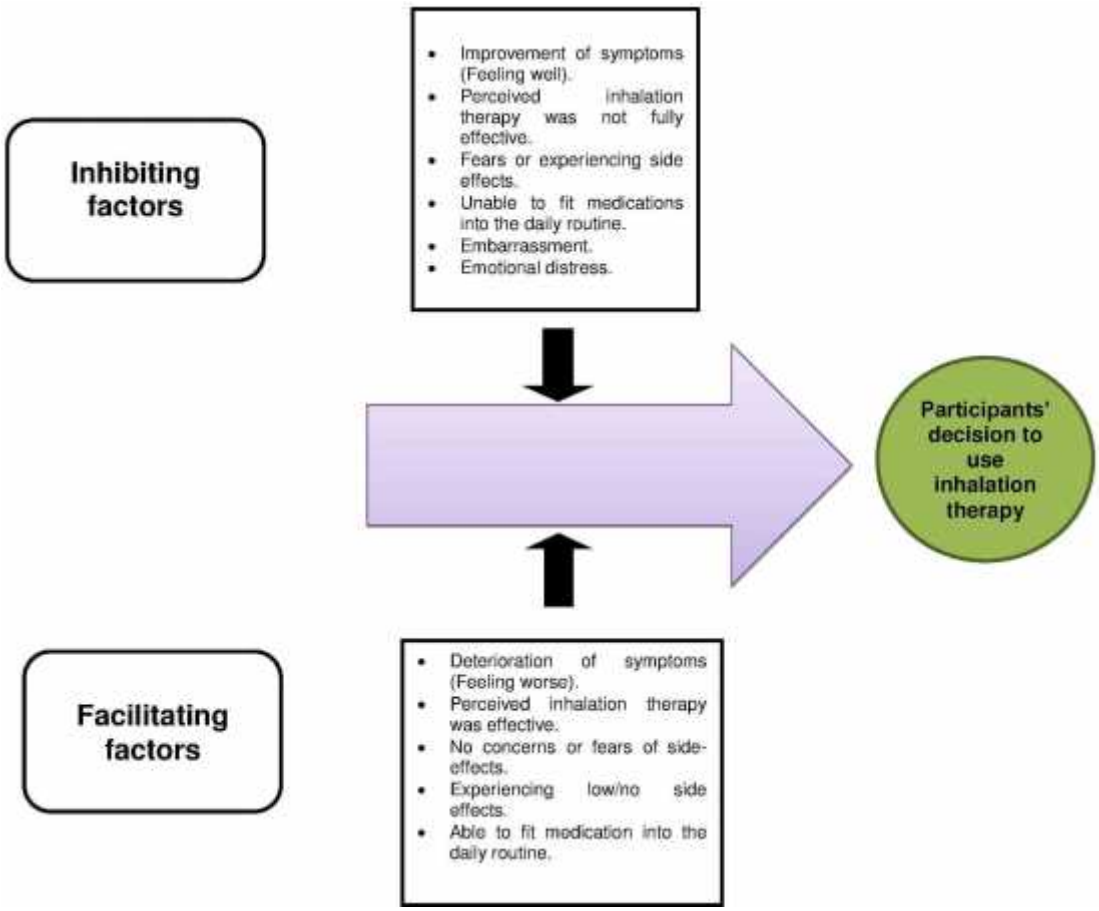


Figure 7-2: Factors which affected patients' decision to use their inhalation therapy

7.2.1 The presence of symptoms

Some participants reported using inhalation therapy in response to their symptoms, with intermittent dosing usually in response to worsening symptoms. Lack of COPD symptoms (feeling well) for some participants resulted in discontinuation of inhalation therapy or some alteration in dosing frequency, as at such times medication was seen as unnecessary.

> I have not used any inhaler today or yesterday because I felt good and I do not need to take any. Whether I have missed… I missed a bit, maybe half a dozen [six doses] because as I said I just used them as an emergency.
> Male, 83 yrs old, using Bricanyl Turbohaler and Symbicort Turbohaler

> I stopped using it [salbutamol] without telling my doctor because I felt it was unnecessary
> Male, 74 yrs old, using Ventolin Evohaler pMDI with Volumatic spacer, Seretide Accuhaler

> In the past I have reduced some doses of my COPD medicines especially the Clenil [beclometasone] because I felt good. You know sometimes you do self-medicate yourself, increase or decrease doses based on your condition.
> Female, 72 yrs old, using Ventolin Evohaler pMDI with spacer, Clenil Modulite pMDI and Spiriva Handihaler

Participants stated that their decisions to use inhalers, timing, and frequency of dosing depended on their views and perceived needs for COPD therapy. Participants reported using their inhalation therapy at less or more than the prescribed dose frequency based on their judgments. Underuse of medication was identified more in asymptomatic patients or in those who have noticed signs of improvement in their symptoms. Some asymptomatic participants reduced doses, stopped medication for a while, or decreased dosing frequency. Participants made such judgments based on what they thought would benefit their respiratory condition.

> I usually take one inhalation in the morning and one inhalation in the evening of this one [formoterol/ budesonide]. If my case gets bad, I take two puffs twice a day instead.
> Female, 65 yrs old, using Symbicort Turbohaler and Ventolin Evohaler pMDI

> They suggest using this [beclometasone] morning and evening but I feel if I am feeling ok, you know, I do not bother to use it. I only use it for necessary things. I usually take two puffs when I feel bad, giving a little time between each one.
> Female, 76 yrs old, using Ventolin Evohaler pMDI and Clenil Modulite pMDI

In contrast, overuse of medication was reported more for symptomatic patients who experienced deteriorations in their symptoms. In response to this some participants reported taking more than one formulation or increasing the dosing frequency to compensate.

> Sometimes I get very breathless or if I go upstairs I feel wheezy, so I take one inhalation more of the Symbicort [formoterol/ budesonide] and I feel better.
> Female, 67 yrs old, using Ventolin Evohaler pMDI and Symbicort Turbohaler

Other participants reported using their inhalation therapy preventatively to prevent symptoms worsening, especially when doing activities such as walking up hills, climbing stairs or when sleeping at night. Participants worked out a new dosing schedule to prolong the symptoms-free period.

> I use it [formoterol/ budesonide] first thing in the morning when I get up whenever the time is and then last thing in the evening before I go to bed I take a couple of puffs because it stops the congesting during the night.
> Male, 77yrs old, using Ventolin Evohaler pMDI and Symbicort Turbohaler

> Generally, if I go walking with a friend I take two puffs of the Ventolin [salbutamol] before I go out and I even carry it with me. I would not go anywhere without it. But if I am going to exercise, I do it [take a dose] before, you know. I sometimes need to use it again.
> Female, 78 yrs old, using Ventolin Evohaler pMDI and Symbicort Turbohaler

> Sometimes when I go upstairs, you know if I am busy and I am up and down the stairs, then I find sometimes I use those [COPD medicines].
> Female, 76 yrs old, using Ventolin Evohaler pMDI and Clenil Modulite pMDI

7.2.2 Actual/perceived effectiveness of medication

The actual or perceived effectiveness of inhaled therapy was found to influence a participant's decision to use the therapy. Participants were likely to exhibit medication non-adherence especially if the medication was perceived as not fully effective, or as unnecessary (see section 7.3). Such participants deliberately skipped some daily doses, or discontinued therapy, especially if not considered effective.

> The only one I skipped deliberately is the Spiriva [tiotropium], because I do not think it does any good quite honestly. It is not making any difference, no.
> Male, 83 yrs old, using Ventolin Evohaler pMDI, Clenil Modulite pMDI and Spiriva Handihaler

Section 7.3 gives more information on patients' perceptions regarding effectiveness of therapy and their influence on medication-taking behaviours.

7.2.3 Actual/perceived safety of medication

The actual or perceived side effects of therapy were also found to influence participants' decision to use the inhaled medication. Individuals were more likely to be non-adherent if the medication was perceived as unsafe or caused unwanted side effects. Previously experienced side effects influenced participants' decision to use the inhalation therapy, especially inhaled steroids. In order to decrease exposure to the inhaled corticosteroid, some participants deliberately decreased dosing and adopted a dosing schedule to decrease their exposure to the drug. Section 7.3 gives more information on the actual and perceived safety of the COPD medication and the influence of these perceptions on medication-taking behaviours.

> I know most people would take Seretide twice a day but I do not. As you know it [salmeterol/ fluticasone] contains steroids and I was already in the past taking lots of steroids, so with that I do believe this amount would kill me at the end.
>
> Female, 78 yrs old, using Ventolin Evohaler pMDI, Seretide Accuhaler and Spiriva Handihaler

7.2.4 Embarrassment at using inhalers

Feeling embarrassed using inhalers in a public place also impacted on decision-making regarding using therapy. Three participants worked out a dosing schedule to use all their inhalation therapy whilst they were at home only. Even if the need arose or the daily dose was due when they were away from home, these participants tended to ignore this dose due to being embarrassed or ashamed to use their inhaled medications in public. They preferred either to miss a dose or sit and wait for the symptoms to resolve or wait until they were able to use their inhalers in private.

> I also sometimes do not use Ventolin in public as I feel embarrassed to use it in public, because COPD is a disease that you feel very guilty about. Even when I am out in a theatre or a party, I carry around my inhaler with me all the time, but I either do not use or use it in a private area because I am very embarrassed about this disease. I know it is stupid.
>
> Female, 71, yrs old, using Ventolin Evohaler pMDI and Seretide Accuhaler

> Sometimes when I am out or visiting friends, my Ventolin will be in my hand bag but I do not like to use it in public because I do not like to draw attention to

> myself or maybe I just go to the toilet and take it as I do not like to make people think that there is a problem with me.
>
> Female, 65 yrs old, using Symbicort Turbohaler and Ventolin Evohaler pMDI

> I should be honest with you. I have never used my inhalers in public even if I felt I need to, except in front of my husband.
>
> Female, 76 yrs old, using Ventolin Evohaler pMDI and Clenil Modulite pMDI

7.2.5 Medication regimen-related factors

The number of COPD medications being used by an individual was found to influence their decision to use the inhalation therapy. A number of participants reported that, when the number of medicines used per day increases, the adherence to the recommended drug regimens decreases.

> I tried to use it [formoterol/ budesonide] for a certain period of time as I was told. But you see I have got so many things wrong with me in the heart and eyes, so it is not a thing you adore, is not it [laughs], and because I have got so many medications, so I stopped it.
>
> Female, 89 yrs old, using Ventolin Evohaler pMDI, Symbicort Turbohaler and Spiriva Handihaler

The greater the complexity of the medication (e.g. the number of medications and the number of doses/day), the less likely the patient was to fit medications into their daily schedule, and, therefore, the less likely to adhere to the medication regimen. One participant, who had a complicated drug regimen with frequent doses, was unable to fit medication taking into his daily schedule, and found medication taking hard to deal with.

> My dosage regimen is such a nuisance because sometimes you have got to take too many medicines during the day and you should take some before meals, some after meals and some with meals, which is so hard and drives me mad.
>
> Male, 87 yrs old, using Bricanyl Turbohaler, Symbicort Turbohaler and Bumetanide tablets

7.2.6 Emotional distress

Three participants reported that significant emotional changes triggered COPD symptoms. For example, emotional incidents, especially deaths of

"dear ones", worsened the condition itself, and compromised COPD medication intake and led to unhealthy lifestyle choices; as the absence of a strong motivational factor influenced patients to be non-adherent to their COPD medication.

> I do have a major problem at the moment; obviously I was a smoker and have been for 15 years. That's what causes this. Two years ago, I stopped smoking for nine months but them a huge thing happened in my life which was a death and it was very emotional. Then I stopped taking my medication for a while and I started smoking and again six weeks ago something else happened in my life which was sad and I have started again. Anyway, if a major thing happened in your like a death you tend to automatically go back to smoking. I know it is not good and not helping and I think that what is probably making my breathing worse.
>
> Female, 71 yrs old, using Ventolin Evohaler pMDI and Seretide Accuhaler

> I found after my husband died I started to get nervous asthma and sometimes I missed a dose or two of my medications [COPD medication]. Anytime that I was actually, you know, very nervous or anxious about anything, I found it hard to breathe. I find since I have got older, I am being anxious about anything. You can get to this stage where things go wrong and you start to kind of feel a bit of anxiety and I have this problem with my grandchildren as well, which causes lots of problems.
>
> Female, 68 yrs old, using Qvar Easi-breathe and Bricanyl Turbohaler

In summary, this study has shown that medication-taking behaviours are dynamic, being directed by different factors which are related to the patient's treatment and disease. These factors had an influence on patients' decisions to use the inhalation therapy leading to treatment failures and poor clinical outcomes. Addressing patient challenges to medication use (adherence), may help in introducing some interventions by healthcare professionals in the future to alleviate some of the issues that prevent patients from using their inhalation therapy as suggested. The next section, 7.3, discusses patients' perception about the efficacy and safety of therapy in greater detail, and how this can affect the patients' use of their COPD medications.

7.3 Participants' views and experiences regarding actual and perceived efficacy and safety of the inhalation therapy

This section describes participants' views and experiences with regards to the actual and perceived effectiveness and safety of the inhalation therapy, and the benefits and drawbacks raised by participants regarding therapy used at home. Providing this information to healthcare services may enable healthcare professionals to assist COPD patients who are using this therapy in their homes in optimizing medicine use and improving treatment outcomes.

7.3.1 Perceptions regarding treatment efficacy

This section provides an insight into COPD patients' perceptions about the inhalation therapy they use at home, what medication was perceived to be not fully effective, and how this affected participants' decisions to continue or discontinue therapy.

7.3.1.1 Efficacy of therapy perceived as suboptimal

To identify the number of participants who perceived their inhalation therapy was effective from those who did not, the following procedure was undertaken: a direct question was asked to all participants (N=46), i.e. what do you think of your regular COPD medicines in regards to their efficacy and which one do you find helpful? The data revealed that three-quarters of participants (N=34) perceived their inhalation therapy to be effective, especially when it was used in combination. Their answers were followed in more depth by asking them to explain in more detail what they meant by being effective or not fully effective.

One-quarter of participants (N=12) reported that they believed their inhalation therapy was not fully effective, leading to treatment failures represented by

recurring symptoms, persistence of symptoms, exacerbations or hospital readmissions.

> I cannot say they are good [COPD medicines]. I do not know, but I wonder if there is one that may have a bit of a stronger effect. It will be preferable because until now I cannot clear up my chest.
> Male, 68 yrs old, using Symbicort Accualer and Spiriva Handihaler

> My case [breathing] is definitely getting worse because the medication does not seem to do that much good I have to say. We have got a park opposite; it is not hilly but there are some light heights which I find difficult to climb. I also meet lots of friends there and I cannot talk due to becoming too breathless.
> Female, 71 yrs old, using Ventolin Evohaler pMDI and Seretide Accuhaler

> I often get a panic attack of asthma. I had a panic attack about a month ago when I could not breathe, so we called the ambulance. They said all I needed was oxygen, I was low on oxygen.
> Female, 77 yrs old, using Ventolin Evohaler pMDI, Seretide Accuhaler, Spiriva Handihaler and Salamol Steri-Neb

The reasons for treatment failures are likely to be due to factors such as disease progression, behaviours that contribute to suboptimal efficacy of the therapy such as smoking, circumstances that contribute to suboptimal efficacy of the therapy, for instance getting a seasonal infection such as influenza, developing resistance to the medication, suboptimal adherence to therapy, which was detected in nearly half of the sample and/or suboptimal inhalation technique, which was detected in more than half of the sample. The result is discontinuation of therapy, the intermittent use of treatment, or decrease in the dosing frequencies, which may lead to a further treatment failure and suboptimal outcomes.

> The only one I skipped deliberately is the Spiriva [tiotropium], because I do not think it does any good quite honestly. Since I used it, it is not making any difference, no.
> Male, 83 yrs old, using Ventolin Evohaler pMDI, Clenil Modulite pMDI and Spiriva Handihaler

<u>Disease progression and persistence of symptoms</u>

The progression of COPD and/or the persistence of symptoms influenced participants' decisions and perceptions regarding treatment and its effectiveness. For example, when adequate control of symptoms was not

achieved, due to increase in the severity of the disease, some cases of treatment failures were registered; consequently alterations to patients' drug regimens were made by healthcare professional adding a new medication, stepping up therapy or switching to another therapeutic group such as from bronchodilators to adding steroids or steroids to adding other steroids.

> I was on Clenil [beclometasone] for 20 years but it was not good. Recently the doctor discontinued this one [beclometasone] because I had a very bad shortness of breath when I was teaching at school and he put me on this [formoterol/ budesonide].
>
> Female, 65 yrs old, using Symbicort Turbohaler and Ventolin Evohaler pMDI

> Well, this Pulmicort [budesonide], which I used to take and this particular night we were going on a holiday on Friday. On Saturday night, I took that one [budesonide] which kept making me sleepy, very sleepy, and I fell asleep and then went for a bath; the following morning I found all my ribs were weakened and I could hardly walk. My breathing was very bad, so it was discontinued by the doctor because I was having some side effects as well and the doctor put me on this one [beclometasone].
>
> Female, 68 yrs old, using Qvar Easi-breathe and Bricanyl Turbohaler

Developing resistance may contributes to suboptimal efficacy of the therapy

Developing resistance to some medication such as salbutamol due to long-term use has made some participants think that their salbutamol is no longer effective. This belief influenced the use of the medication by COPD participants as it was used at a minimum level or was discontinued for a certain period of time, which led to treatment failures. Participants reported that the effectiveness of their salbutamol declined over a prolonged period of time as the symptoms-relieving effect was noticeably less than when salbutamol was first started.

> I used to take the Ventolin first thing in the morning before anything else because initially I used to get a bit of relief with that. Now I do not know; I do not get any relief. Does it seem to change things? I do not know. After a while I did not seem to get any relief so I stopped using it for a while.
>
> Male, 76 yrs old, using Ventolin Evohaler pMDI, Symbicort Turbohaler and Spiriva Handihaler

Suboptimal adherence and/or inhalation technique which may contributes to suboptimal efficacy of the therapy

Suboptimal adherence to inhalation therapy was apparent for nearly half of the sample (48%) and suboptimal inhalation technique for more than half of participants (61%). These factors may cause treatment failures among COPD patients. Nearly one-quarter of patients (N=6) who received tiotropium treatment perceived that their tiotropium therapy was not fully effective. The lack of efficacy reported by these participants could be due to the following: firstly, this medicine was not taken by participants as directed because it was perceived to be not fully effective, as long-acting bronchodilators such as tiotropium have no immediate effect on symptoms. Secondly, when assessing inhalation technique, it was found that the percentage of participants who made at least one deviation from the recommended technique when using the Handihaler device, which delivers the tiotropium, was 85.7% of all participants (see Chapter 6). Treatment failures and worsening of symptoms were reported, and, therefore, participants deliberately missed some daily doses or discontinued tiotropium.

> I do not notice any difference between my inhalers but I was told you must take these continuously. Now and again, in the past a year ago or something like that they found I was not going back to the chemist for the next one [tiotropium] just to see what is going to happen if I did not take it. They did a review in the practice and noticed that I have not been taking it because it was useless.
>
> Male, 76 yrs old, using Ventolin Evohaler pMDI, Symbicort Turbohaler and Spiriva Handihaler

ICS therapies were perceived by some participants to be not fully effective, and lacking in efficacy or causing side effects. Unwanted adverse effects, or concerns about future adverse effects, were a major issue raised by participants who were unwilling to use a particular medicine, especially medicines that contain steroids, such as beclometasone and budesonide.

> I had a small concern when I was first prescribed Symbicort. I do remember that I asked the doctor about whether there is a steroid in it because I did not want to have steroids due to their side effects.
>
> Female, 65 yrs old, using Symbicort Turbohaler and Ventolin Evohaler pMDI

Behaviours that may contribute to suboptimal efficacy of the therapy

One reason for treatment failures, and therefore the perception that the inhalation therapy was not fully effective, was in relation to smoking. For example, some participants who have a smoking history perceived their inhalation therapies were suboptimal. They blamed themselves or spouses for the worsening of their symptoms, or development of their condition into a more severe stage.

> Emphysema is a build-up of smoking because I used to smoke but I am not convinced that smoking… yes it is a contributing factor… but I am not convinced that smoking is totally responsible for lung problems generally and even since I stopped smoking I have not noticed any improvement in my lung function and my medicines do not do that much.
> Male, 76 yrs old, using Ventolin Evohaler pMDI, Seretide Accuhaler and Spiriva Handihaler

> The doctor told me I have got a chronic bronchitis and this is through passive smoking. I gave up smoking but my husband smokes around me all the time that's why I feel sometimes that my inhalers are not helping.
> Female, 78 yrs old, using Ventolin Evohaler pMDI and Symbicort Turbohaler

Circumstances that may contribute to suboptimal efficacy of the therapy

Getting a seasonal infection, such as a viral or bacterial infection, was another reason that participants believed contributed to failure of treatments and therefore participants' views on the suboptimal efficacy of the treatment. Two participants judged their inhalation therapy was not fully effective due to getting chest infections more frequently during the past year.

> Until now I cannot clear up my chest. I also have some difficulties with getting a virus infection every month. Last month I got a viral infection and could not breathe and I thought I am going to die and my medicines did not help at all.
> Male, 68 yrs old, using Symbicort Turbohaler and Spiriva Handihaler

To conclude, participants who perceived their inhalation therapy was suboptimal had either stopped and then restarted their medication, or discontinued it without keeping the doctor informed, due to either the lack of the actual effect or participants' views on the suboptimal effect of the treatment received.

> I stopped using it [salbutamol] without telling my doctor because I felt it was unnecessary
>
> Male, 74 yrs old, using Ventolin Evohaler with Volumatic spacer, Seretide Accuhaler

Providing information for healthcare providers in regards to what medication was perceived to be suboptimal by participants, how these views influenced the use of medicines, and what patients actually did will enable a better understanding of patients decision-making, permitting interventions to correct erroneous views or actions toward treatments, and provide the appropriate education and guidance for patients so that decisions are based on the balanced views of the facts. This may help in optimising medicine use and improving treatment outcomes.

7.3.1.2 Efficacy of therapy perceived to be optimal

The majority of participants (N=34) perceived that their inhalation therapy was effective, especially when used in a combination of drug classes. Participants referred to clinical measures such as FEV_1 or indicators (e.g. relief of breathlessness) to assess the impact and efficacy of their medicines. As reported by participants, the benefit was seen in the relief of COPD symptoms, stopping bronchoconstriction during the night and making it easier to breathe while sleeping, and an increase in their activity levels, in making daily activities possible.

> My COPD medicines are good. Lately I went to the hospital and the nurse tested my FEV_1 and she was happy with the results.
>
> Female, 71 yrs old, using Ventolin Evohaler pMDI and Seretide Accuhaler

> Somehow they [inhaled medicines] relax the muscles and the airways.
>
> Male, 71 yrs old, using Bricanyl Turbohaler, Symbicort Turbohaler and Spiriva Handihaler

> Well, these inhalers make the normal activities possible.
>
> Male, 67 yrs old, using Ventolin Evohaler pMDI, Symbicort Turbohaler, Spiriva Handihaler and Phyllocontin tablets

> I find [salbutamol] helpful and it saves my life. I use it sometimes during the night when I feel tight-chested to help me sleep.
>
> Female, 78 yrs old, using Ventolin Evohaler pMDI and Symbicort Turbohaler

The improvement in patients' symptoms was related to the perceived immediate benefit of short-acting bronchodilators for symptom relief, when used in combination with long-acting bronchodilators, or benefit of the ICS that provide prolonged efficacy with respect to symptom relief. For example, participants who used a combination therapy of short-acting bronchodilators (e.g. salbutamol) and maintenance therapy of LABA and ICS reported that the relief was seen immediately, especially with the use of short-acting β_2-agonist drugs.

> I am happy with the current regimen because the Ventolin [salbutamol] is good and very helpful if you hoover over something or when you do something you should not do like polishing or dusting. Then you instantly take the Ventolin and you feel better after 10 or 15 minutes, and when I take these [fluticasone/salmeterol and tiotropium] later on, they usually take a longer period to act but they add a stronger effect.
>
> Female, 84 yrs old, using Ventolin Evohaler pMDI, Seretide Accuhaler and Spiriva Handihaler

> Well, they both have different functions [Symbicort and Bricanyl]. Symbicort (budesonide/ formoterol) is to combat COPD.. Right! Whereas, Bricanyl (terbutaline) is a reliever, it helps symptoms to disappear not to cure. Do you follow what I am trying to say? I think Symbicort is a very good thing to use because it stops the symptoms from taking over, if you like, whereas, Bricanyl eases my breathing as a reliever.
>
> Male, 87 yrs old, using Bricanyl Turbohaler, Symbicort Turbohaler and Bumetanide tablets

Participants reported that relief was felt immediately with short-acting β_2-agonist drugs, although it was temporary or for a short period of time and the medication needed to be repeated 2 to 4 times during the day to maintain the effect. Some participants stated a gradual relief (happening slowly) with all other COPD medicines, especially products that contained long-acting bronchodilators (e.g. tiotropium and salmeterol) and long-acting corticosteroids (e.g. fluticasone and beclometasone). This gradual effect made some participants uncertain about how effective these medicines were and whether they were doing them any good or not. As a result, doubts were

expressed about the effectiveness of long-acting bronchodilators and inhaled steroids, which may affect patients' use of their medications.

> Those two are something that does not affect you as soon as you take it [beclometasone and tiotropium]. Does it? You need to give it a time but if I took Ventolin [salbutamol] it would help immediately, so neither of those [beclometasone and tiotropium] is going to help me immediately if I was in a bad way.
>
> Female, 72 yrs old, using Ventolin Evohaler pMDI with spacer, Clenil Modulite pMDI and Spiriva Handihaler

> Most helpful, is this Ventolin [salbutamol]. Because after taking it, I feel it calms me because it gives an instant relief. The rest are good but I am just using them as the doctor told me.
>
> Male, 74 yrs old, Ventolin Evohaler pMDI with spacer, Symbicort Turbohaler, Spiriva Handihaler and Carbocisteine Capsule

Some participants, who were unclear of the exact effect of their inhaled medicines, made judgments based on others' (e.g. friends or neighbours) prior experiences with medications. Consequently medicines use was influenced by others' judgments about efficacy and usefulness of therapy. These judgments may change over time based on further experiences.

> I do not think that makes much difference [tiotropium] but people say that's very good. I feel I just need to take it but people say it is really good. I think it is good for COPD practically.
>
> Female, 72 yrs old, using Ventolin Evohaler pMDI with spacer, Clenil Modulite pMDI and Spiriva Handihaler

> Well, I do not use the Ventolin [Salbutamol] these days as they said it is supposed to help you breath but I never found that it did but they said it does, so I used it.
>
> Male, 73 yrs old, using Ventolin Evohaler pMDI, Seretide Accuhaler and Spiriva Handihaler

In summary, the efficacy of inhalation therapy especially in combination was highly appreciated by participants. Providing such information about what participants thought of their COPD medicines, how they actually used them, how this was different from the participants who perceived their therapy as not fully effective, and how this influenced the use of medicines may enable healthcare providers to assist COPD patients who are using inhalation therapy in their homes to optimise medicine use and improve treatment outcomes.

7.3.2 Perceptions regarding treatment safety

All participants (N=46) were asked about their views on the perceived safety of the inhalation therapy they used at home. Almost two-thirds (N=28) reported that they had never experienced any adverse effect since commencing their inhalation therapy, perceiving their inhalation therapy to be safe.

> Usually I have no concern about my medicines and no side effects. They are simply safe.
>
> Male, 84 yrs old, using Ventolin Evohaler pMDI and Spiriva Handihaler

> I am quite happy that they do not cause any harm and I do not think they have a side effect; I have been taking them as a part of my life plan.
>
> Male, 91 yrs old, using Ventolin Evohaler pMDI, Seretide Evohaler and Spiriva Handihaler

On the other hand, more than one-third of the participants (N=18) expressed some concerns regarding experiencing adverse effects in the future, or reported experiencing adverse effects when the inhalation therapy was used, especially with long-term use of steroids. Two participants considered COPD medications in general as ‘poisons’ or ‘harmful substances’, because they believed they were not ‘natural’. They tried to avoid medicines as much as possible and found other ways to compensate, such as undertaking daily exercise.

> My own doctor tried to persuade me to take more COPD medicines. He felt I should have taken more medicines, but I did not really like taking it and you know it is a drug, is it not? So, I put my energy, etc. into running and I became a powerful runner and that helped me and my asthma.
>
> Female, 78 yrs old, using Ventolin Evohaler pMDI, Seretide Accuhaler and Spiriva Handihaler

> I will be honest with you, I am also not a great believer in pills and things because they affect me.
>
> Female, 68 yrs old, using Qvar Easi-breathe and Bricanyl Turbohaler

Unwanted adverse effects or concerns about future adverse effects were a major issue raised by participants who were unwilling to use a particular

medicine, especially medicines containing steroids such as beclometasone and budesonide. These medicines were found to be more prone to misuse because they were used intermittently or not as prescribed. Some inhaled medicines (e.g. budesonide and beclometasone) were replaced due to the untolerated side effects caused by inhaled steroids.

> I know I should take the Seretide twice a day but I only take it once every morning. I know most people would take it twice a day but I do not. As you know, Seretide contains steroids and I was already in the past taking lots of steroids, so with that I do believe this amount would kill me in the end.
>
> Female, 78 yrs old, using Ventolin Evohaler pMDI, Seretide Accuhaler and Spiriva Handihaler

> Previously, I also decided not to use Becotide because it has lots of steroids and I was already on prednisolone. Too much steroids may cause lots of side effects especially on bones, so I did not like it.
>
> Female, 78 yrs old, using Ventolin Evohaler pMDI, Seretide Accuhaler and Spiriva Handihaler

> Actually, I am not happy with steroids. I take it because generally I do everything they tell me but lately I have been suffering from restless legs and Pinn Medical Centre gave me a booklet about restless legs. Then I read some information about the causes and I found that taking steroids is one of the main reasons.
>
> Female, 84 yrs old, using Ventolin Evohaler pMDI, Seretide Accuhaler and Spiriva Handihaler

Participants reported that the adverse effects occurred more often after each use. In most cases, adverse effects were either dose-dependent caused by using a combination of drugs that contained steroids, a double dose or higher strength of steroids, or after a prolonged administration of steroids therapy. Table 7-1 shows more information about the most common side effects experienced by COPD patients due to their medicines.

Table 7-1: The most commonly reported adverse effects with the use of inhalation therapy

Side effect	Number of participants who reported this side effect	Potentially caused by
Shaky hands, tremors, muscle pain and cramps	5	Bronchodilators
Osteoporosis	5	ICS
Persistent cough	4	ICS
Dry mouth and throat irritation	4	Bronchodilators
Voice hoarseness	3	ICS
Oral thrush	3	ICS
Palpitations (increase in heart rate)	1	Bronchodilators
Skin atrophy	1	ICS

- Some participants stated more than one side effect

Medications that contain steroids were the major cause of adverse effects among this group of patients, including dry mouth and oral thrush (overgrowth of fungus in the mouth), caused by not gargling or rinsing the mouth with water, after using inhaled corticosteroids.

> The only concern I had was the thrush which I found nasty but the hospital told me to rinse my mouth after each use, so I use now a mouth wash.
> Male, 83 yrs old, using Bricanyl Turbohaler and Symbicort Turbohaler

> What I do as far as I am concerned is after each dose I swallow it up [steroids left inside the mouth] with water because once when I was in the hospital I caught thrush in my mouth. That was when I was really ill. No one told me to rinse my mouth after each dose but now I do.
> Male, 72 yrs old, using Ventolin Evohaler pMDI, Pulmicort Turbohaler and Spiriva Handihaler

> Yes, the chemist told me once to rinse my mouth with water after taking these inhalers, which I sometimes forget to do and you end up with a very dry mouth.
> Male, 73 yrs old, using Ventolin Evohaler pMDI, Seretide Accuhaler and Spiriva Handihaler

Some participants reported being informed by their doctor to rinse their mouth after each use of inhaled steroids, to minimise the risk of developing adverse effects. However, some participants had developed oral thrush and voice hoarseness, despite rinsing their mouth, whereas some participants did not rinse their mouth after the inhalation of steroids because they were not given enough explanations about the reason behind it.

> I also wonder about the reason for brushing or cleaning my teeth after the Seretide. It does not make much difference and it does not really seem to help, you know, rinsing and sometimes I forget. If it was helping I would stick to it but I thought, "What I am doing this for?"
>
> Female, 84 yrs old, using Ventolin Evohaler pMDI, Seretide Accuhaler and Spiriva Handihaler

> I do gargle it out but still it does irritate me, so I decided to stop it.
>
> Female, 65 yrs old, using Ventolin Evohaler pMDI and Seretide Accuhaler

Persistent cough, voice hoarseness, tremors, muscle pain and cramps were problems raised by participants due to the continuous and prolonged use of steroids or bronchodilators. However, some participants were uncertain about what was causing these adverse effects. In response to this, they decided to go back to the surgery to discuss the issue with their general practitioner. In some instances a decision was made to change their therapy.

> Well, that is a steroid is it not [Seretide] and I am already taking steroid tablets for something else and because of the things I have in my legs and bones. I am not happy with taking all these steroids but I have an appointment with [Dr. Name] on Monday and I hope he is going to cut it back again because he said, "We need to get you off them".
>
> Female, 80 yrs old, using AeroChamber Spacer Plus with adult comfortSeal mask, Ventolin Evohaler pMDI, Seretide Evohaler CFC-free, Seretide Accuhaler and Prednisolone tablets

> Actually, I have an appointment with my doctor on the 16th of this month but I might go earlier because I have got shaky hands and the shake is getting a lot worse and I am wondering what is causing this.
>
> Male, 72 yrs old, using Ventolin Evohaler pMDI, Pulmicort Turbohaler and Spiriva Handihaler

> Well, I have a concern about either one of those [Sympicort and Spiriva] because I have had for years a bad shake, right; I cannot carry more than one cup. I can carry a cup but I cannot carry two and I was told that it is probably the medicine that is causing this. I told the people about my shake but I do not emphasis it too much to the doctor but what I would like is somebody to say, "Oh we can treat that or we can give you something to stop that tremor". Anyway, I have an appointment this afternoon to talk about this issue to see what is causing this.
>
> Male, 76 yrs old, using Ventolin Evohaler pMDI, Symbicort Turbohaler and Spiriva Handihaler

The majority of participants who reported experiencing adverse effect (N=12), accepted and tolerated the adverse effects caused by their medicines, and reported not stopping their regular COPD medicines as a result. For others

(N=6), the experience of adverse effects from COPD medicines impacted their decision to use the therapy, either stopping their therapy, reducing the daily dose, decreasing dosage frequency, or consulting their doctor for alternatives.

> I do not use the Symbicort that often because the twice a day dose seems to burn my throat.
>
> Male, 71 yrs old, using Bricanyl Turbohaler, Symbicort Turbohaler and Spiriva Handihaler

> I usually take two inhalations of Seretide in the morning and sometimes in the evening because if I take the evening dose I cough a lot, so I try not to take it in the evening before I go to bed. I was taking it but it makes me cough.
>
> Female, 65 yrs old, using Ventolin Evohaler pMDI and Seretide Accuhaler

> The Symbicort: I reduce it from two puffs twice a day to two puffs once a day, because it is irritating and congesting my throat.
>
> Male, 71 yrs old, using Bricanyl Turbohaler, Symbicort Turbohaler and Spiriva Handihaler

> My voice is a bit hoarse and it got worse after I took the steroids. I have this problem for quite a while and because this one has doubled the steroids [Seretide 250 mcg] from what I was on [Seretide 125 mcg], that is why I do not take it as prescribed. I was not over-happy about that because ok she [her doctor] is doing this for my benefit but I am not taking double strength and double the amount, so what I have done is take this, one puff in the morning in case I need a heavier dose [Seretide 250 mcg] and I just take one puff at night from the one I used to take [Seretide 125 mcg].
>
> Female, 84 yrs old, using Ventolin Evohaler pMDI, Seretide Accuhaler and Spiriva Handihaler

Two participants reported discontinuing their therapy due to adverse effects such as oral thrush and heart palpitations caused by steroids and bronchodilators respectively. In these two cases, the drug products causing the adverse effects were discontinued after consulting their doctor.

> I went back to my GP and he put me on Symbicort and discontinued the old one [Clenil (beclometasone)]. With this one [beclometasone] when I first used it I got thrush in my mouth and a horrible taste; of course after that I had to use a mouthwash after each use.
>
> Male, 83 yrs old, using Bricanyl Turbohaler and Symbicort Turbohaler

> I had Seretide 200 mcg. I was very unwell earlier this year and my heart rate had increased from it. Then, I saw [Dr. Name], oh she is a lovely, she said, “Could I change your medicine?”, and then I said, “Well yes”, then she put me on Symbicort and took me off the Seretide
>
> Female, 67 yrs old, using Ventolin Evohaler pMDI and Symbicort Turbohaler

In this study, the use of inhalation therapy in general was considered to be safe and well tolerated. However, 18 participants had experienced an actual adverse effect, mainly with the long-term use of steroids including budesonide and beclometasone in particular. As a consequence, six cases of non-adherence to the inhaled steroid were identified with intermittent use of therapy, or discontinuations. The rest of the participants (N=12) had accepted and tolerated the adverse effects caused by their medicines. This section informs the healthcare system about the main concerns and adverse effects that COPD patients experience that may lead them to underuse their medicines, leading to treatment failures. It is important that healthcare providers monitor the effects and adverse effects of the inhaled therapy and try to reduce these adverse effects if possible, and educate their patients about the importance of continuing to use their inhaled medicines for their condition and provide the proper advice and assistance tailored to each patient, to maximise medicine use and treatment outcomes.

7.4 Experience of COPD medication: alterations over time

The findings obtained from the interviews were compared to the data obtained from patients' notes in the surgery regarding participants' experience of COPD medication changes over time. Some changes were made to the patients' dosing regimen and were adjusted over time, as reported by 19 participants and obtained from the medical notes. In regards to the medication itself, the changes were made by medical prescribers by adding a new medication, switching to another group or step-up of COPD therapy from bronchodilators to adding steroids. As acknowledged by participants, these adjustments were made when side effects emerged or were raised by participants, when adequate control of COPD symptoms was not achieved, when the severity of the disease increased, or exacerbations occurred more frequently due to inadequate management.

> I was on Clenil [beclometasone] for 20 years but recently the doctor discontinued this one because I had a very bad shortness of breath when I was teaching at school and he put me on this [Symbicort (formoterol/ budesonide)].
>
> Female, 65 yrs old, using Symbicort Turbohaler and Ventolin Evohaler pMDI

> At the time, which was about a year ago, my chest was very bad, so a lady pharmacist who was in charge of the bronchi-problems gave me a Ventolin [albutamol] which I did not agree with, because it irritated my lungs more rather than making it better. So I went back again, then they gave me a blue one [Bricanyl (terbutaline)] which is to be taken when necessary.
>
> Male, 71 yrs, using Bricanyl Turbohaler, Symbicort Turbohaler and Spiriva Handihaler

Medical professionals were making changes to COPD medication over time. Examining patients' medication history, by exploring what COPD patients are currently using, what they had been using in the past, what the changes were and the reasons for these changes, is a crucial element to be examined. The reason for this examination is to see what worked and what did not work in regards to these alterations and to obtain the information regarding what COPD patients use in the management of their condition, how COPD patients felt after these changes, and whether they were useful or not. The poor assessment of consequences when inappropriate changes are made to patients' drug regimen by their doctors may lead to improper use of COPD medicines and therefore treatment failures.

7.5 Strategies in fostering appropriate medication use among COPD patients

COPD patients were prescribed more than one inhalation device to be used at home and had complex medication regimens, with some alterations made to their drug regimen based on disease progression and seasonal changes. The aim of this section is to examine how COPD patients fitted their treatments into their daily routines and describe strategies employed by patients to facilitate the use of their COPD medicines, when several inhalation devices were being used.

Many participants referred to their medication-taking behaviour as a habit due to the long-term use. They had no difficulties in using their COPD medication daily as required. Some made inhalers part of the daily routine (e.g. linking COPD medicines to mealtimes), and had strict and well-organized routines in taking medicines. This allows even complex regimens to be easy to cope with.

> It is more than difficult to keep track of everything but we have our routine to remind us.
>
> Male, 85 yrs old, using Ventolin Evohaler pMDI and Seretide Accuhaler

> Well, I used the usual, one capsule of Spiriva before breakfast first and three inhalations of Symbicort after breakfast and dinner.
>
> Male, 67 yrs old, using Ventolin Evohaler pMDI, Symbicort Turbohaler, Spiriva Handihaler and Phyllocontin tablets

> It is a breakfast routine, everything happens in the breakfast time; I take Spiriva and Symbicort first then all my heart pills followed by the blood pressure tablet and finally my eye drop.
>
> Female, 89 yrs old, using Ventolin Evohaler pMDI, Symbicort Turbohaler and Spiriva Handihaler

For some participants, the daily drug regimen was complicated due to the total number of prescribed medications and the number of doses that should be taken daily in addition to the changes in prescribed drug regimens which occurred over time. These participants developed their own strategies to facilitate the use of COPD medicines to stay well and independent for as long as possible. Firstly, some participants worked out a dosing schedule to make it easier for them to remember to take their COPD medicines. For example, seven participants reported that morning was the easiest time during the day for them to remember to take all their COPD medicines. This was due to minimal distractions that occur in the morning, whereas remembering to take the afternoon or evening doses was problematic for other participants. Those participants tended to take all their COPD medicines every morning and made it like a habit to take them as soon as they stepped out of the shower, or as soon as they got out of bed.

> I take both of these [Seretide and Spiriva] at 7 o'clock in the morning when I wake up but one before the other. I take them first thing in the morning because

> it is more convenient and I can remember the morning doses better with no distractions.
>
> Female, 78 yrs old, using Ventolin Evohaler pMDI, Seretide Accuhaler and Spiriva Handihaler

> I take most of my COPD medications in the morning before taking a shower because I find it easier to remember the morning doses. Sometimes I actually go to the shower and I think, “Oh I have not taken my Spiriva or Seretide”, so I go and take them.
>
> Female, 77 yrs old, using Ventolin Evohaler pMDI, Seretide Accuhaler, Spiriva Handihaler and Salamol Steri-Neb

Others stored their COPD medicines with items that were associated with habitual behaviour (e.g. mobile phones) or in a conspicuous location (e.g. on a kitchen counter) which is visited often (N=9). Others placed their inhalation devices near something they need to deal with on a daily basis such as a wrist watch or toothbrush. Some participants (N=3) set up a visual or auditory reminder (e.g. sticky notes, cell phone alarms).

> I have never forgotten to take the morning dose because it is upstairs on the dressing table in my bedroom, where my mobile, watch and medicines are, looking at me.
>
> Male, 76 yrs old, using Ventolin Evohaler pMDI, Symbicort Turbohaler and Spiriva Handihaler

> I am not very good at remembering but I do keep some sticky notes on the fridge door to remind me to take my medicines.
>
> Female, 78 yrs old, using Ventolin Evohaler pMDI and Symbicort Turbohaler

The participants used memory triggers provided by informal care givers (e.g. a spouse) to remind them to take their COPD medication at the recommended time, and to help them to accommodate their COPD medication within their daily routine and lifestyle.

> My wife does everything starting from making sure that I take my medicines everyday on time because I usually forget.
>
> Male, 89 yrs old, using Salamol Easi-breathe and Seretide Accuhaler

Two participants had developed their own way to avoid missing their medication by using compliance aids or sorting their medications using a mouthpiece cover or cap system. For example, one participant, who was prescribed three puffs of Symbicort to be taken three times daily, reported

placing the Symbicort with three caps on the counter in front of him; each cap represents one puff. As he takes one puff, he places one cap to the left of the counter, making two puffs left. This way he organised the number of puffs that should be taken at the same time by remembering that the number of puffs left for the morning dose, for example, is at the front, whereas the ones he has already taken are to the left.

> I have got to have a system to remember taking my medicines; I have got a box with all my morning, afternoon, and evening medicines, so I never miss.
>
> Male, 72 yrs old, using Ventolin Evohaler pMDI, Pulmicort Turbohaler and Spiriva Handihaler

> I am a very compliant patient I do what I was told. The only problem I had with the Symbicort, and it is nothing to do with the designer, is in the morning if I am making breakfast I usually forget how many inhalations I take but I have devised a system which helps. What I do is I have three things lined up like that [he pointed to three caps lined up together] and when I take the first inhalation I move the cap let's say, so now I have taken one then I take the next one and move the next cap, so I know now I have taken two and then I take the last inhalation; but in the past it has been a problem and that is why I now I take them pretty quickly one after the other.
>
> Male, 67 yrs old, using Ventolin Evohaler pMDI, Symbicort Turbohaler, Spiriva Handihaler and Phyllocontin tablets

Some COPD patients in this study found a way to work out their dosing schedule for fostering medication taking which may in turn optimise medicine use. These strategies were perceived as successful and efficient in promoting medication use, by those with high self-reported adherence. Illustrating patient's medication-taking behaviours and the way they fitted their medication into the daily life may help healthcare providers in the future to suggest some strategies to foster medication taking, especially for those with low self-reported adherence.

7.6 Participants' beliefs about COPD medicines

Similarly to adherence, participants' beliefs were assessed using a triangulation method. Firstly, a direct method was used with a self-report scale (Specific Beliefs about Medicines Questionnaire BMQ) to measure

participants' beliefs about their COPD medicines (Horne et al., 1999). Secondly, semi-structured interviews which consisted of open and close-ended questions were undertaken (discussed earlier in section 7.3). Table 7-2 gives more information on participants' responses to the BMQ-specific scales.

Table 7-2: Mean scores and ranges of participants' beliefs using BMQ-specific scales

*BMQ subscale	Mean score (SD)	Minimum	Maximum
Total necessity	18 (3.23)	10	25
Total concerns	12 (2.85)	5	23
Total differential (necessity-concerns)	6 (4.504)	-8	17

***(Potential range of scores is from 5-25 from BMQ necessity and BMQ concerns: potential range for differential is from -20 to +20)**

During the interview, when participants were asked about their perceptions regarding the treatment efficacy, three-quarters of participants (N=34) perceived their inhalation therapy to be effective, whereas, when they were asked about their perceptions regarding the treatment safety, almost one-third of the participants (N=18) expressed some concerns regarding experiencing adverse effects in the future, or reported experiencing adverse effects when the inhalation therapy was used. Therefore, the number of participants who perceived their inhalation therapy as effective was more than those who had some concerns regarding the treatment safety. When these findings were compared with the BMQ, the same results were found, as a positive differential score of six, which was scored by participants in this study (Table 7-2) indicated that participants perceived the benefits of their COPD medication to outweigh their concerns about the risk of their COPD medications. As a result, more than half of the sample were adherent to their inhalation therapy and scored 8 in the MMAS. See Figure 7-3 and Figure 7-4 for more information regarding BMQ-specific necessity subscale (Figure 7-3) and BMQ-specific concerns subscale (Figure 7-4).

BMQ-specific necessity subscale

The majority of participants responded that they either agreed (57%) or strongly agreed (17%) about the necessity of taking their COPD medicines. However, 22% of participants were not sure whether these medicines are necessary or not. A small proportion of participants 4% disagreed about the necessity of taking COPD medicines. Figure 7-3 illustrates the participant's responses to the 5-items of BMQ-specific necessity subscale.

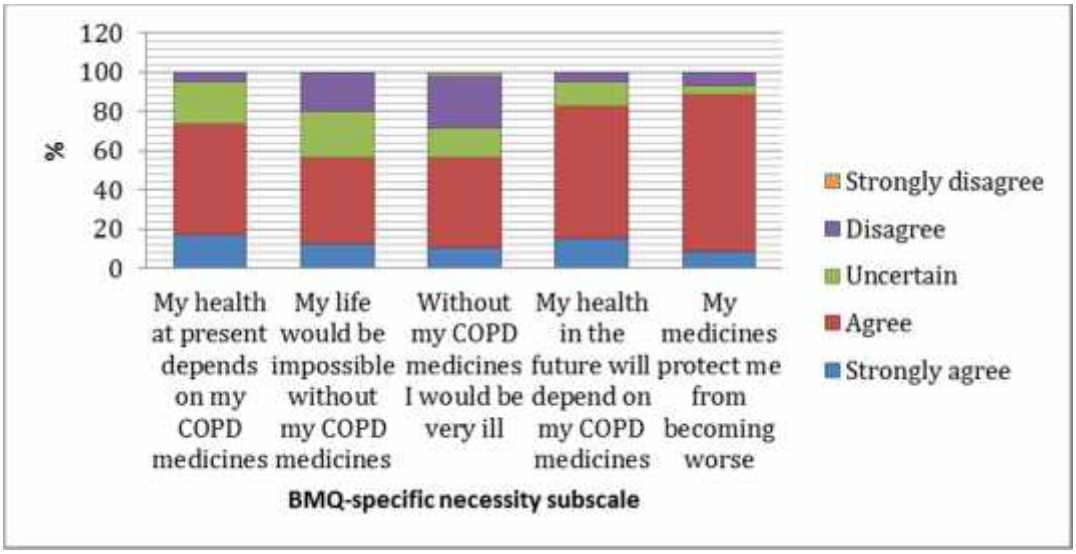


Figure 7-3: Percentage of participant's responses to individual items of the 5-items BMQ-specific necessity subscale

BMQ-specific concerns subscale

Figure 7-4 shows that a larger proportion of participants either disagreed (71.72%) or strongly disagreed (6.1%) that they were concerned about their COPD medicines comparing to those who either agreed (10.42%) or strongly agreed (3.1%) that they had concerns about their medicines.

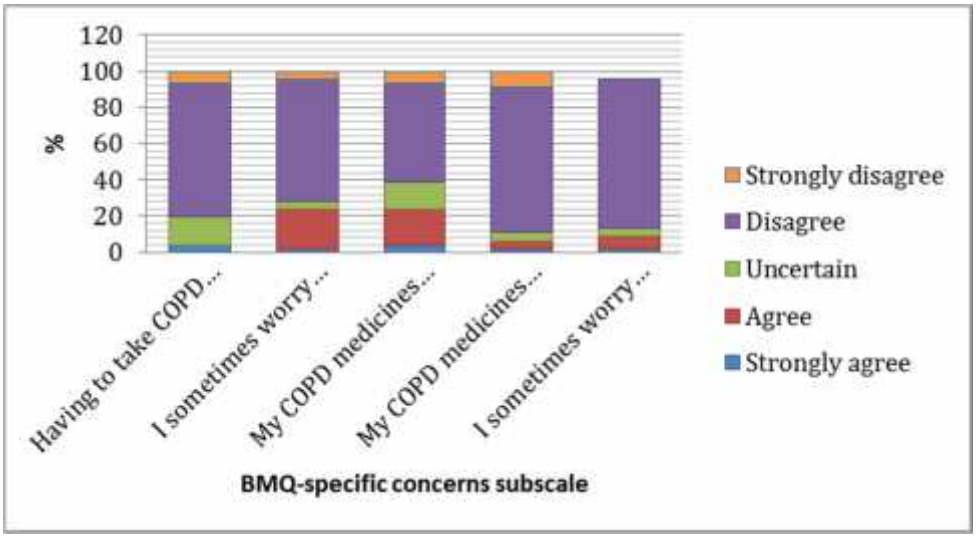


Figure 7-4: Percentage of participant's responses to individual items of the 5-items BMQ-specific concerns subscale

8 Chapter Eight: The care and services provided for patients with COPD

This chapter is divided into two sections. The first section documents the nature of care or support provided for COPD patients with their medication in their homes and the role of informal carers in supporting these patients with their medicines, and how often this help was sought. Providing such information to the healthcare professionals in regards to how informal carers and COPD participants divided tasks and shared responsibilities may help in optimising medicine use and health outcomes. The second section documents patients' priorities and concerns regarding the current and potential future service provision, to enable healthcare providers to introduce interventions if required, to meet patients' needs and expectations to maximise medicine use and health outcomes.

8.1 The informal care provided for COPD participants with their medicines

COPD is a life-threatening illness. It needs constant attention to control its symptoms. Patients with COPD in this study were asked to follow a recommended treatment plan and medication courses; the mean number of all prescribed medicines including COPD was seven (SD= 3), which ranged from two to 12. Patients were also asked to use inhalation devices correctly for an effective drug delivery. Some patients may need some help to use these medications properly; suggesting the potential role of the informal carers.

Forty-six participants were asked during the interviews to declare whether they received help or assistance with their COPD medication and to document the nature of the support provided, how often and in which circumstances or on which occasions help is needed. It was reported that two-thirds of participants (N=32) reported not receiving any help with their COPD medicines; they were able to manage their COPD medications on their own. However, nearly one-third of participants (N=14) claimed to receive help from their informal carers in their homes. However, the frequency of assistance provided by informal carers was only when required or if needed but not on a daily basis.

The next stage was to examine who these informal carers are. As a result, participants who reported receiving help at home with their COPD medicines were asked to name the person who provided such help or assistance. The majority of participants (N=10) who acknowledged getting help from informal carers reported receiving help from family members, especially spouses. A further two participants reported receiving help from friends or neighbours. The remaining two participants reported receiving help from multiple sources including family and friends.

As a result, spouses were the primary carers for COPD participants in this study, as 72% of informal care was provided by them. The findings of the current study regarding receiving major help from spouses are consistent with those of Trivedi et al (2012) who reported that, when examining the association of informal carers and adherence among COPD patients, the major help was received from spouses by providing some medical support (e.g. managing pill-boxes or getting prescriptions refilled). In addition, it was found that the greater involvement of spousal caregivers often translates into closer monitoring of and a greater influence on patient behaviours (Trivedi, et al., 2012). In a secondary analyses, the Lung Health Study reported that

COPD patients who were married were more likely to be adherent to their medications than non-married participants, reflecting the important role of spouses in the disease management (Rand, et al., 1995). In another study conducted among patients with COPD, it was found that most of the caregivers were close family, especially spouses (74%). However, 26% of the patients received help from neighbours or friends regularly (Gautun, et al., 2012).

In this study, participants were also asked to document the nature of assistance or help provided by their informal carers in terms of the following: ordering or collecting the prescription from the surgery or the pharmacy, opening containers, reading labels, understanding, reading or obtaining information, administration (e.g. breaking tablets, measuring, putting in eye drops, etc.), advice on when to take or how much (especially for prn medicines), and advice on need for medicines and/or on side effects. Participants reported receiving help with some activities regarding ordering or collecting prescriptions from the surgery or pharmacy and, to a much lesser extent, helping in obtaining and reading information. The two participants who received help from their informal carer in obtaining or reading information either had poor vision or hearing difficulties, but this was not a major concern because they were receiving help from their informal carers when required. Table 8-1 gives more information regarding the help provided for COPD participants in this study.

Table 8-1: Types, frequencies, and percentages of assistance provided for COPD participants (N=14)

Type of assistance	Number of participants (N=14)
Help received with ordering or collecting prescription from the surgery or pharmacy.	13
Help received with obtaining and reading information	2
Help received with administering COPD medicines	0
Giving advice or a recommendation on a prescribed medicines	0

***Some participants reported receiving more than one type of assistance with their medicines; therefore, the total is more than 100%**

Although these results on the nature of help differ from some published studies (Essue et al., 2010; Trivedi et al., 2012), they are consistent with that of Gautun, et al. (2012), who reported that the most common help provided for COPD patients was practical support in transportation and accompanying the patient to the doctor, hospital, and other healthcare services. Whilst, in the studies by Essue and Trivedi, the nature of support was technical support such as operation of medical equipment (e.g. supplementary oxygen concentrators and medication management (Essue et al., 2010), including filling prescriptions (Essue et al., 2010; Trivedi et al., 2012), and ensuring adherence to the prescribed medication regimen (Essue et al., 2010; Trivedi et al., 2012). The differences between this study's findings and all other previous studies in regards to the frequency of assistance provided by informal carers and the nature of help could be due to the fact that the characteristics of each sample were different; as the sample of this was study characterised by patients with mainly moderate disease status (N=26), with a mean age group of 77 years and a mean number of COPD medicines of three inhalers.

In summary, almost one-third of participants sought help from their informal carer with their medicines and this was mainly in ordering or collecting their prescriptions. This help was mainly sought when required but not on a daily basis. However, it is always important to keep a record of whether COPD patients require help or assistance with their medicines and whether this help is sufficient to meet their needs because informal care is one of the cornerstones of maintaining health and function in many older adults with COPD.

8.2 The priorities and concerns for patients in the context of current and potential future service provision

8.2.1 Accessing healthcare services

Forty-six participants were asked if they had accessed the healthcare services in the last year to speak to a healthcare professional in regards to their COPD and its medicines, the reasons for accessing the healthcare system and how often they did so. All participants (N=46) had accessed the healthcare services in the last year at least once in regards to their condition and/or medication, including primary and secondary care. The data suggest that COPD patients (N=46) were initially managed in primary care (e.g. Pinn Medical Centre, which was the most recent contacted site for most participants), followed by emergency services from secondary care (e.g. Northwick Park Hospital), as reported by participants (N=5). The reasons given by COPD participants for accessing healthcare services are demonstrated in Table 8-2.

Table 8-2: Services accessed by COPD participants during the last year.

1. Physician consultation
+++ cough, shortness of breath (**7**)
Exacerbation of COPD (**3**)
Inhalation technique (**14**)
Follow up/ review appointment (**23**)
2. Nursing consultation
Diagnostic testing (**9**)
3. Hospital visit
Annual review (**2**)
In-patient stay/ hospital admission (**3**)
4. Supply of medication
Repeat medication (**46**)
Antibiotics and steroids (**5**)
Nebuliser medication (**1**)
Other respiratory medications (**13**)

8.2.2 Satisfaction with healthcare system and its service

In this study, COPD participants were generally satisfied with the healthcare services. However, some participants had concerns about accessing the healthcare system and were relatively dissatisfied with their own healthcare

arrangements. Fear of change to the current medication regimens was the first reason reported by two participants who were unwilling to access the healthcare services. Others decided to avoid getting in touch with the medical centre (Pinn Medical Centre) intentionally due to previous bad experience with their doctors.

> Actually, I have a tendency not to phone the surgery too much, you know, asking for advice or help because they might do other changes to my medicines, which I won't be happy with.
>
> Female, 84 yrs old, using Ventolin Evohaler pMDI, Seretide Accuhaler and Spiriva Handihaler

> Actually, I used to have a very regular doctor who was very good and I wanted to keep him as my doctor because he was able to keep my regular medicines without changing them every time and my chest was not bad as it is now. Unfortunately, this doctor is now working part-time because he is about to retire. So, I do not go to Pinn Medical Centre to see doctors like I used to.
>
> Male, 74 yrs old, using Ventolin Evohaler pMDI with spacer and Seretide Accuhaler

> Honestly I am trying very much to keep away from doctors because I am afraid of doctors. I also have had some bad experiences with doctors and things.
>
> Female, 68 yrs old, using Qvar Easi-breathe and Bricanyl Turbohaler

Participants' satisfaction with healthcare services was judged by the amount of time they spend with their doctors in a consultation, keeping their regular doctor, the quantity and the quality of information provided to each one, and the appointment system. Patients expected their doctors to spend enough time with them explaining everything about their disease and medication. Failure to meet these expectations caused dissatisfaction and delayed access to healthcare services, subsequently leading to lack of medical supervision and information, which may lead to treatment failures.

> Sometimes, it is very hard to get an appointment. I mean their [Pinn Medical Centre] appointment system was very poor at one time mainly after they took over that other surgery – that sort of flooded them out, overwhelmed them – but I think now it is improved. However, it is sometimes quite difficult to get any appointment and talk about your medicines.
>
> Male, 83 yrs old, using Ventolin Evohaler pMDI, Clenil Modulite pMDI and Spiriva Handihaler

> Actually, I used to have a very regular doctor who was very good and I wanted to keep him as my doctor because he was able to keep my regular medicines without changing them every time and my chest was not bad as it is now.

> Unfortunately, this doctor is now working part-time because he is about to retire. So, I do not go to Pinn Medical Centre to see doctors like I used to.
>
> Male, 74 yrs old, using Ventolin Evohaler pMDI with spacer and Seretide Accuhaler

> You will get nothing from that surgery... It is useless. If you do not phone them up asking for help they will not do anything without asking. You cannot even get an appointment now!! You have to wait for two weeks for an appointment. Some doctors even rush you through just to finish early. They give you less than five minutes. They cannot be bothered at all.
>
> Male, 85 yrs old, using Ventolin Evohaler pMDI and Seretide Accuhaler

> It is very very difficult to spend time with your doctor and honestly I am trying very much to keep away from doctors because I am afraid of doctors. I also have had some bad experiences with doctors and things; half of the time they have not got the time to listen to you, unfortunately, yeaaah.
>
> Female, 68 yrs old, using Qvar Easi-breathe and Bricanyl Turbohaler

8.2.3 Obtaining information, prescriptions and/or medicines about medicines and its sources

Forty-six participants were asked during the interview if they have received any information from the healthcare providers in regards to their COPD medicines, and who provides such information. More than half of the participants (N=24) claimed that they had not received any information regarding their COPD medicines in the last year. Twenty-two participants reported receiving either verbal or written instructions from a member of the healthcare team on medication dosage, frequency of dosing or how to operate and maintain their devices. In most cases (N=17), these instructions were mainly received when the medication or inhaler was first prescribed and the patient has not followed the instructions. Participants claimed receiving information mainly from their doctors (N=11) and/or a practice nurse (N=6) or a pharmacist (N=5).

Other participants (N=18) reported obtaining this information mostly from the medicine information leaflet or the instruction booklet. However, one participant reported that, although she reads the information leaflet that comes with each device, she had the tendency to forget what she read.

Another participant complained about the small font size provided in the leaflet.

> Not that I recall any advice... Not recently no, I do not think so... I may have... I am not sure but I would like to receive the information if possible. I have read most of the leaflets very carefully but I have forgotten what is in each one [laughs].
>
> Female, 76 yrs old, using Ventolin Evohaler pMDI and Clenil Modulite pMDI

> I now get all this information from a piece of paper in the packet. I just read the packet leaflet and it is so descriptive but too small and not easy to follow or understand.
>
> Female, 78 yrs old, using Ventolin Evohaler, Seretide Accuhaler and Spiriva Handihaler

As a result, it should not be assumed that COPD patients will learn how to use their inhalers only by reading the package leaflets. If participants have the tendency to forget the information they have read over time, it is suggested to keep monitoring patients and to provide continuous education and training about each device.

8.2.4 Faith in healthcare professionals

Faith in healthcare professionals was found to influence participants' decision to follow a recommended treatment plan. Some participants had a strong faith and great trust in their doctors, which made them take their medicines consistently without worrying about the long-term effect of their medicines.

> In the future if I had to go on steroids I would rather not to use it but if the need was there and I was told by my doctor to use it I will, because I trust my doctor completely and simply.
>
> Female, 65 yrs old, using Symbicort Turbohaler and Ventolin Evohaler pMDI

> I do not have any concern because I trust what the doctor prescribed.
>
> Female, 76 yrs old, using Ventolin Evohaler pMDI and Clenil Modulite pMDI

> I mean if the doctor told me that's the one I should use for the rest of my life, that's what I will be on.
>
> Female, 68 yrs old, using Qvar Easi-breathe and Bricanyl Turbohaler

In contrast, losing patients' trust may result in delay in seeking help or advice if needed and further delays in recovery will occur, as was expressed by one participant.

> The last time I went to Pinn Medical Centre was when I first moved here. They said I should go and see the doctor. Anyway, I went to see the person who does the COPD but I was not impressed by him because he told me I need to take two of these inhalers twice a day [she pointed to Spiriva and Seretide] but when I went to see my doctor in my old surgery and told her about what happened, she said, "No you only need to take this one once" [she pointed to Spiriva] and I said, "Well that is what he said". She said, "He should not have told you that", so now I do not go to see him [laughs]. I only have faith in somebody or I do not.
>
> Female, 77 yrs old, using Ventolin Evohaler pMDI, Seretide Accuhaler, Spiriva Handihaler and Salamol Steri-Neb

8.2.5 Patients' participation in decision-making in regards to their COPD medicines

Sharing decision-making with patients regarding their prescribed medicines and involving the patient in the management process were found to give desirable results in medicine taking. The opposite was found to contribute to suboptimal adherence and lead to treatment failure. Four participants reported that, when a decision was made by their doctor to change their current medicines without giving any explanation or without sharing the decision-making with the patient, they were unwilling to follow their doctor's recommendations; therefore, they either continued taking their old medicines when the doctor asked them to switch to something else or decreased the dose when the doctor asked them to double it, without informing their doctor, which of course may lead to treatment filatures.

> I used to see an ordinary GP, but now it has been changed to an asthma specialist. She rang to say that my prescription was made out but she was altering it from this 125mcg to double up and from one puff twice a day to two puffs, also doubling up. I was not over-happy about that because ok she is doing this for my benefit but she only did it on the telephone. Obviously I had a scan few months ago and it was not good, I had severe emphysema and I got a very bad attack.
>
> Female, 84 yrs old, using Ventolin Evohaler pMDI, Seretide Accuhaler and Spiriva Handihaler

> I used to take it [she pointed to Symbicort], as prescribed but I am not using it now because I do not need it. I told the pharmacist of what I need but they over-

> prescribe things [laughs]. Well I suppose they are trying to help me but we are not stupid [laughs].
>
> Female, 89 yrs old, using Ventolin Evohaler pMDI, Symbicort Turbohaler and Spiriva Handihaler

In summary, the majority of COPD participants were generally satisfied with the healthcare services. However, the data suggest that participants' satisfaction with the healthcare services was influenced by different factors such as accessing the service quickly and easily, quantity and quality of information provided, faith in healthcare professionals, and getting the patient involved in the management process by sharing the decision-making. Meeting patients' needs and expectations may enhance the recovery time, whereas failing to meet these needs and expectations caused delays in accessing healthcare services and delays in recovery time.

This study informs healthcare professionals about COPD patients' views and concerns regarding the current and future service provision, to allow them to intervene and try to reduce these concerns and provide the best quality of care which is continuously viewed by patients. This may increase patients' satisfaction and confidence in the healthcare system and therefore maximise the use of medicines by patients, leading to better outcomes.

9 Chapter Nine: General discussion

9.1 Methodological issues

In this chapter, the main findings of this study are summarized, discussed and general conclusions drawn. Furthermore, the strengths and limitations of this thesis are considered and suggestions for further research into the use of COPD medications and/or devices are presented. This chapter concludes with recommendations for COPD patients and policy makers.

9.1.1 Sampling and recruitment

The recruitment process for COPD patients from the Pinn Medical Centre was quick and went smoothly. However, the surgery tended to be very busy and was often unable to provide a private room for the researcher to access the surgery records when needed. In response to the surgery's busy schedule, the researcher requested to complete the recruitment process and identify eligible participants as quick as possible, to maximize the availability of the consultation room available for the GPs to consult their patients. An issue emerged when identifying eligible patients, which was that some patients had recently been diagnosed with COPD according to the records, whilst others were previously diagnosed with asthma and then developed COPD. This created a challenge in identifying the eligible patients. Therefore, it was decided to look through the clinical variables such as record of spirometry test, FEV1, FVC, and smoking history, to confirm the diagnosis, which was a time-consuming process. This caused confusion for some participants, who introduced themselves to the researcher during the interview as asthmatic patients, for example, whereas they were registered in the databases in the surgery as COPD patients. In addition, when the invitation letter was sent to patients asking them to take part, some patients

refused to participate by reporting that they were not aware of being diagnosed with COPD.

Another challenge was that, in order to comply with the ethical requirements set by the local ethics committee, the identification process was undertaken alongside a respiratory specialist based in Pinn Medical Centre. Medical professionals have very little time to conduct such processes due to their busy schedules. However, convenient dates and times were set to help the researcher to identify the eligible participants under specialist supervision. The researcher attended the centre only on Fridays, to be under the supervision of a respiratory specialist when carrying out this process.

9.1.2 Response rate and participants' characteristics

This study comprises a relatively small sample size (N= 46), which is appropriate for a study intending to produce predominantly qualitative data. Qualitative research, which is observation and interview-based, often uses a small sample size (e.g. less than 50), to facilitate the researcher's close collaboration with the participants and ensure that the data collected accurately depict their experiences with their medicines (Richey and Klein 2007; Smith, 2010). A small number also increases the accuracy of the data obtained and in-depth inquiry in naturalistic settings (patients' homes) (Richey and Klein, 2007; Smith, 2010).

The sample of 46 participants comprised individuals from different age groups and ethnicity. In addition, a similar proportion of males and females were recruited with different disease status and smoking history, which would confer some generalizability to the general COPD population.

9.2 Key findings of the study

9.2.1 The use of multiple inhalation devices used in combination by COPD patients in the management of their condition.

There is a lot of information available in the British National Formulary (BNF), the Summary of Product Characteristics (SPC), or other sources regarding the recommended doses and dosing frequency for medicines used to treat COPD. However, little is reported in the literature about the actual drug usage, whether patients are taking their inhaled drug regimens at home as directed or not. If not, why they do not adhere; what beliefs they have about their medicines that may affect medication taking. In addition, what problems are faced by patients that may make them stop taking their medicines as recommended, and how this can be resolved.

This study is unique in examining the relationship between using multiple inhalation therapies of all medication classes, and different devices. Studies that have examined adherence to inhaled medications in COPD have been restricted to only one (van Grunsven et al., 2000) or three medications (Cecere et al., 2012; Huetsch et al., 2012). Additionally, many previous studies of medication adherence in COPD patients were performed prior to the common use of long-acting medications, and included only short-acting medications (Dolce et al., 1991, Rand et al., 1995; Turner et al., 1995; Corden et al., 1997).

In this study, medication taking among COPD participants was found to be suboptimal. Suboptimal adherence to inhalation therapy was identified in almost 50% of the sample, which was consistent with the rate of non-adherence in seven past studies (Melani et al., 2001; Boyter and Carter, 2005; George et al., 2005; Mehuys et al., 2010; Cecere et al., 2012; Huetsch et al., 2012; Trivedi et al., 2012). In contrast, four previous studies showed that the rate of adherence was identified in more than 50% of the sample

(Barta et al., 2002; Chen et al., 2007; Agh et al., 2011; Khadour et al., 2012). This variation may be due to differences in patient populations, definition of non-adherence, methods employed, disease status, or respiratory conditions included in each study, as some studies included a variety of lung diseases such as asthma and COPD. For example, almost all studies in adherence research among patients with COPD have measured patients' adherence using only one self-report questionnaire on medication utilisation (Melani et al., 2001; Barta et al., 2002; George et al., 2005; Mehuys et al., 2010; Agh et al., 2011; Cecere et al., 2012; Huetsch et al., 2012; Khadour et al., 2012; Trivedi et al., 2012), whilst this study combined different approaches, tools and methods to gather the data from different sources to maximise the validity of the findings. These tools were the previously validated self-report adherence measure (Morisky) and open/close-ended questions in regards to medication consumption (Morisky, 2008).

In terms of medication non-adherence, adherence to long-acting bronchodilators and ICS was found to be suboptimal among those who reported low medication adherence (N=22). This was justified by the prolonged efficacy provided by long-acting bronchodilators and ICS on the symptoms' relief.

Among the LABA and ICS users, it was found that participants adhered more to the LABA than ICS. However, the adherence was suboptimal for both classes among those with a low-adherence rate. The reason behind being more adherent to the LABA than the ICS is that some participants responded better and quicker to the LABA than the ICS and for this reason preferentially used the LABA, which provides superior relief. In addition, experiencing an actual side effect or fears of side effects with the use of ICS was greater among participants who used different classes. Factors that influenced adherence to inhalation therapies were different and dependent on the

medication being examined. These findings were in line with Cecere et al.'s (2012) study which reported that, although adherence to LABA was better than ICS, adherence to LABA was suboptimal. However, no explanation was given for the reasons behind these behaviours.

Although there are a variety of classes of agents to be used in COPD, depending on the severity of the disease, one of the most prescribed and used classes of drug were the short-acting bronchodilators, whereas tiotropium was the second most commonly prescribed and frequently used not as prescribed. These findings are consistent with Chen et al.'s study (2007) which investigated patients' attitudes and actions toward their COPD treatment. Within the three months of the study, the most commonly used drugs were short-acting bronchodilators including theophylline (53.7% of patients) and iprotropium (39.8% of patients), whereas the least used drug as prescribed was tiotropium (27.1% of patients). In this study, the main reason identified for the underuse of tiotropium was because nearly one-quarter of participants (N=6) who were prescribed tiotropium treatment perceived their tiotropium therapy was not fully effective. There is no doubt that these changes in the medication dose or dosage regimen were contrary to the recommendations published in the guidelines and the existing literature. The NICE and the GOLD guidelines indicate that tiotropium should be inhaled once daily, not intermittently, because its duration of action is 24 hours (NICE, 2010; GOLD, 2013).

The suboptimal use of COPD medications by almost half of the participants in this study raises a series of concerns for healthcare professionals. Non-adherence to inhalation therapy at this extent may lead to suboptimal management and treatment failures. These findings highlight the need for healthcare professionals to continuously review patients' adherence to their prescribed regimen and provide comprehensive assessment, assistance and

education for patients to maximise medicines' use. In addition, healthcare providers should assess the need for therapy, identify cases when the inhalation therapy is not used as suggested, study the reasons and find appropriate solutions to address concerns and misapprehensions and avoid unnecessary costs.

Examining how patients make decisions regarding the use of inhalers, and how those decisions and difficulties contribute to suboptimal outcomes and treatment failures will help in evaluating and assessing each patient individually to try to maximise the use of therapy and minimise the number of treatment failures. It is therefore advised that all healthcare professionals do the following: firstly, adherence screening, assessment and evaluation should be routinely performed using direct and indirect methods. Secondly, in the event of non-adherence or if non-adherence is suspected, healthcare professionals should identify the nature and the reasons for non-adherence and develop strategies for overcoming this problem, as the disease management is a dynamic process influenced by the presence or absence of these trigger factors. Thirdly, over time adherence may decline, therefore healthcare professionals should be encouraged to provide feedback and counsel their COPD patients about the role of treatment and the importance of adherence, which may in turn enhance patients' adherence. See section 9.5 for recommendation and suggestions to healthcare providers in the context of the current policy.

9.2.2 COPD patients' use of their medication and decision-making regarding using the inhalation therapy, beliefs and perceived effectiveness and safety of therapy.

In this study, numerous factors were found to affect patients' decisions regarding the use of inhalation therapy. The two major influences impacting on the decision-making were patients' perceptions about the efficacy and safety of therapy and their actual experiences using it. These factors are

consistent with the findings obtained from the previous studies (Dolce et al., 1991; George et al., 2005; George et al., 2006; Huetsch et al., 2012; Khdour et a., 2012) in regards to this aspect.

Patient beliefs and experiences with treatment used at home were found to be the most powerful predictors of medication non-adherence (Section 7.3). Patients were more likely to use their inhalation therapy if it was perceived to be effective. Otherwise, patients were found to make changes to their treatment plan in terms of dosing frequency, number of doses and adding or stopping a drug, until they achieve what they consider a satisfactory efficacy level with their medicines.

In regards to the safety of the inhaled therapy, actual or fears of developing adverse effects was found to limit its use. Participants in this study made some alteration to their daily drug regimens, such as reducing the dosing frequency or the number of puffs, as a result of experiencing adverse effects, due to the prolonged use of some medication, particularly steroids. Patients were previously reported to underuse their COPD medication with the emergence of adverse effects, or the existence of fears of adverse effects (Dolce et al., 1991; Barta et al., 2002; Calverley et al., 2007; Khdour et a., 2012), with inhaled steroids (Dolce et al., 1991; Huetsch et al., 2012).

Patients' beliefs and experiences regarding the efficacy of inhaled therapy and/or devices

In this study, the use of multiple inhalation therapy in combination was highly supported by participants. Three-quarters of COPD participants (N=34) perceived their inhalation therapy to be effective especially when it was used in combination. The benefit was seen in the relief of COPD symptoms, the increase in their activity levels, being able to sleep all night and decreased

hospital admissions due to exacerbations. The marked improvement in patients' symptoms was related to the perceived immediate benefit of symptoms' relief for short-acting bronchodilators when used in combination with long-acting bronchodilators or ICS that provide prolonged relief of symptoms.

Participants who perceived their inhalation therapy to be effective reported that the combination of a nebuliser and DPI provided a sustained and adequate control of symptoms at home due to the fact that these devices deliver medication with prolonged efficacy, such as long-acting bronchodilators and/or steroids, whereas the benefit of the pMDI, which delivers mainly medication that provides instant relief such as salbutamol, particularly appeared when they were away from home. Tashkin et al., (2007) conducted a 12-week study among 126 COPD patients using two medications (salbutamol + ipratropium) delivered by a nebuliser and a pMDI. Patients were randomised into three groups: nebuliser users, pMDI users, or concomitant treatment users. It was found that patients who used nebuliser therapy morning and night in combination with a mid-day pMDI (viewed as portable therapy), had great improvements in quality of life. This concomitant regimen combines symptom relief offered by a nebuliser with the convenience of a pMDI when patients were away from home (Tashkin et al., 2007).

During the interview, participants were asked to state one inhaler that they feel is most effective when compared to others. From their perspective, participants (N=3) who had experienced using all types of inhalation devices including pMDIs, DPIs and nebulisers were in favour of the nebulisers based on the current or past experience with the nebulisation therapy. They perceived their nebulisation therapy to be the most effective in terms of immediacy of relieving the symptoms especially when a combination of short-

acting bronchodilators was given and when higher doses were required. Additionally, these participants reported being more confident to use the nebuliser device efficiently and independently at home, when compared to alternative hand-held inhaler devices due to the former being easier to use. These results are in line with two previous studies of nebulisation therapy users who perceived their nebulisation therapy as effective in controlling and managing their respiratory condition; therefore, they were less dependent on healthcare systems (Melani et al., 2001; Barta et al., 2002). Barta et al. (2002) showed 82 COPD patients using home nebulisation treatment (either salbutamol and/or ipratropium), and concluded that patients overwhelmingly reported that the benefit of using a nebuliser at home far outweighed the disadvantages (98.2% vs. 1.8%). The majority of participants agreed that using domiciliary nebulisers made a big difference to their life in reducing their COPD symptoms and in making their daily activities possible, as they felt they could walk further following nebuliser treatment. Three-quarters of the participants found the nebulisers were superior to their inhalers in symptom relief; breathing was commonly reported as much easier after using a nebuliser (Barta, et al., 2002).

However, a systematic review showed no difference in the efficacy between nebulisers and hand-held inhalers (Brocklebank et al., 2001). Using a pMDI with a spacer has also been reported as being as effective as a nebuliser with respect to airways drug deposition, with fewer oral side effects (Cates et al., 2006a, 2006b). However, it should be noted that these studies mainly involved a sample of primary care patients with severe disease status and excluded patients with inadequate or incorrect inhalation technique. Nevertheless, these findings have supported the use of pMDIs and DPIs in preference to nebulisers (NICE, 2010).

Among the hand-held device users (DPIs and pMDIs) (N=43) three-quarters (N=32) perceived their combination therapy of formoterol/budesonide (Symbicort) delivered by the Turbohaler or salmeterol/fluticasone (Seretide) delivered by the Accuhaler as more effective than hand-held devices which deliver a single therapy of either a bronchodilator or inhaled steroid. This was explained in terms of the relief in the COPD symptoms after commencing this treatment, and the increase in their activity levels. These findings are consistent with the findings from earlier research and guidelines. It is highly advised to commence a therapy of LABA in combination with inhaled corticosteroids (ICS), as this combination was approved to improve symptoms and lung function in COPD (NICE, 2010). Furthermore, it is strongly recommended in the management of COPD to add ICS to bronchodilators, as the combination was shown in previous studies to significantly reduce treatment failure rates and length of hospital stays, if they are used correctly (Quon et al., 2008; Lindenauer et al., 2010).

In one study of patients with COPD comparing the efficacy of the combination of long-acting bronchodilator and long-acting ICS (salmeterol/ fluticasone) delivered by Accuhaler device against long-acting anti-cholinergic agent LAMA (tiotropium) delivered by Handihaler device, it was indicated that there were no significant differences in the efficacy of the salmeterol/fluticasone and tiotropium in decreasing the rate of exacerbation in COPD patients. However, the mortality rate was significantly lower in the salmeterol/fluticasone users compared with tiotropium users (Wedzicha et al., 2008). In contrast, in a randomised controlled trial conducted by Aaron et al. among 449 patients with moderate or severe COPD, the exacerbation rates were similar in both users of salmeterol/fluticasone and tiotropium (Aaron et al., 2007). However, the quality of life improved with the use of tiotropium.

When using tiotropium in conjunction with the combination therapy of LABA and ICS, participants perceived their inhalation therapy as more effective than when using the combination of LABA and ICS alone. This agrees with two studies that evaluated the efficacy and tolerability of triple therapy of formoterol/budesonide added to tiotropium in COPD patients. This triple therapy gave greater bronchodilation and decrease in exacerbation rates than occurred with individual components (Singh et al., 2008; Welte et al., 2009). Based on this evidence, it is recommended to add the long-acting anti-cholinergic drug to the combination therapy of LABA and ICS for participants with breathlessness or worsening dyspnoea (NICE, 2010). However, further studies are needed to clarify the impact of inhaling a long-acting anti-cholinergic drug with the combination of LABA and ICS on quality of life and exacerbations. Until then, this regimen is only given to patients at the severe stage of COPD (FEV1 <50% of predicted) or to those who were lately hospitalised or admitted to hospital for an exacerbation (NICE, 2010).

It can be concluded that, based on the participants' perceptions, this study supports the use of multiple inhalation therapies in combination by patients in their homes. The reason behind this was due to the fact that most participants reported that they benefited from their combination therapies used at home; when these multiple therapies were given in combination, they provided a complementary effect in disease management. However, some participants responded differently to medications. After analysing the data, it was shown that patients' perceptions of the effectiveness of the inhalation therapy were different and were influenced by their own or others' previous experiences or expectations with the inhalation therapy. These perceptions and expectations may undergo changes with further experience. This indicates a need for tailoring an individual care plan for each patient, especially given that one-quarter of participants perceived their inhalation therapy was not fully effective, due to treatment failures resulting in recurring symptoms, persistence of symptoms, exacerbations or hospital

readmissions, despite using their therapy. See section 9.5 for recommendation and suggestions to healthcare providers in the context of the current policy.

Patients' beliefs and experiences regarding the safety of inhaled therapy and/or devices

Approximately two-thirds of the participants (N=28) reported that they had never experienced any adverse effects since commencing inhaled therapy, and therefore they perceived their inhalation therapy to be safe. However, one-third of the participants (N=18) reported experiencing adverse effects after using the inhalation therapy, especially inhaled steroids. Systematic and local side effects (e.g. oral thrush, voice hoarseness, persistent cough and osteoporosis) were mostly reported by a number of participants in this study with the long-term use of steroids. These side effects appeared to be dose-dependent and did not disappear with persistent use. This was consistent with a previous study, which found that half of COPD patients who reported one or more side effects with the long-term use of steroids did not develop tolerance to side effects, even after three years of use (O'Driscoll et al., 1997).

Some of the local side effects such as oral thrush and voice hoarseness were dose-dependent, well tolerated, and totally reversible, especially when rinsing the mouth after each use with water or mouthwash. These findings were in line with two previous studies investigating the safety of the inhaled steroids from a patient's point of view (Roland et al., 2004; Park, et al., 2012). In Roland et al.'s study (2004), which was conducted among COPD patients using ICS, long-term use of ICS was found to raise the risk of persistent cough by 4% every year, oral thrush by 9% and voice hoarseness by 2%. These risks would be eliminated by washing the mouth or gargling after each use (Roland et al., 2004). Another side effect reported by participants in this

study was skin atrophy (N=1). The risk of developing skin atrophy was calculated as 1% and of cataracts by less than 1% every year with the continuous use of ICS (Park et al., 2012). Tremor, shaky hands and heart palpitations were other side effects reported by participants resulting from the use of inhaled bronchodilators. However, they were well tolerated by participants, and tolerance to these side effects was developed after prolonged use.

To conclude, the findings of this study suggest systematic or local adverse effects especially with the long-term use of ICS. Therefore, safety concerns exist with the use of inhaled steroids in patients with COPD, particularly when using a combination of drugs that contains steroids, double dosing, or higher strength. To improve patients' use of inhalation therapy, see the recommendations in section 9.5.

9.2.3 The frequency and range of problems experienced by COPD patients in technical aspects that may lead to suboptimal care or treatment failure

This is believed to be the only study that has examined and described the problems encountered by COPD participants with all aspects of the use of multiple inhalation devices, including technical issues with each device and practical issues of the operation, cleaning and maintenance of inhaler equipment of all classes, i.e. pMDIs, DPIs and nebulisers. In addition, it has explored the reasons for mishandling and misuse of the inhalation devices, which may lead to poor drug delivery and potentially failure of disease control. By highlighting these issues, information has been generated which will help inform healthcare professionals, in supporting these patients and their carers in the use of inhaled therapy at home, and optimising medicines' use.

A total of 46 inhalation demonstrations were made by the 46 participants to the researcher: DPIs (N=35), pMDIs (N=8), and nebulisers (N=3). No errors were observed for those demonstrating their use of a nebuliser. Comparison of other devices with nebulisers was thus not possible since only three participants used nebulisation therapy and no error was made. However, they were the only participants who had used all types of inhalation therapy in this study, whereas all the rest (N=43) used a combination of pMDIs and/or DPIs. Therefore, their judgments about the inhalation devices and their preferences are considered potentially important.

The nebuliser users (N=3) performed the inhalation technique completely and correctly without any deviation from the recommended technique. They preferred and perceived their COPD therapy delivered by a nebuliser to be more effective than aerosol therapy delivered by hand-held devices (pMDIs and DPIs), despite nebulisers being less convenient and less portable. The use of a nebuliser was considered simple and easy by the participants because it requires minimal coordination of breathing and was considered less effort to use than hand-held devices. The aerosol of a nebuliser device is continuously produced when the user is sitting and inhaling the dose using normal tidal breathing. Correct use may result from this simple operation and/or due to the NHS providing clear descriptive guidelines regarding the proper use of nebulisers (published in 2003 and updated in 2006) for all users (Morgan, 2003). These guidelines include a guide on how a nebuliser works, its components and the correct use and care.

Considering participants' use of pMDIs and DPIs, it was found that the deviation from the recommended technique was common among users of both types of devices, although COPD participants made more errors when using the pMDIs than DPIs. A general practice study conducted among 558

adults with COPD and asthma showed that the type of inhalation device was the strongest independent determinant of an incorrect inhalation technique (Hesselink et al., 2001). Findings of patients' handling of their inhalation devices were in agreement with previous studies which have reported that pMDI devices had higher rates of incorrect handling than DPIs (Lenney et al., 2000; Molimard et al., 2003; Khassawneh et al., 2008; De Moraes Souza et al., 2009; Rootmensen et al., 2010). In an observational study conducted in the UK among 100 participants with COPD and asthma aged between 22 and 88 years, it was found that, although more than half of the participants (55%) were using the pMDI, the performance scores and participants' preference were highest for the DPIs, including Accuhaler and Turbohaler (Lenney et al., 2000).

In another observational study of 3811 adults with COPD and asthma using pMDIs and DPIs in primary care, deviation from the recommended technique was common for many of the participants, especially those using pMDIs (76% of participants), though for the DPI users also had poor technique but the proportion of deviation was less (49-55%), including those using Accuhaler, Turbohaler and Aerolizer (Molimard et al., 2003). One study found elderly patients with COPD used a dry powder inhaler more correctly than a pMDI, even in combination with a large volume spacer (Ho et al., 2004). A further cross-sectional observational study was conducted by Khassawneh et al. in Jordan among 300 patients with COPD, to see how they handled their inhalation devices. It was found that DPIs had a significantly lower rate of incorrect inhalation technique when compared to the pMDIs (Khassawneh et al., 2008).

However, some previous studies (Melani, et al (2011); Sestini, et al (2006)), have suggested that the ease of use of inhalation devices (e.g. pMDIs and DPIs) was linked to patients' training. The problem of individuals having

inadequate inhalation technique was similar between the pMDIs and DPIs (Accuhaler, Turbohaler and Aerolizer), when participants received appropriate training before using each device (Melani et al., 2011), whilst deviation from recommended inhalation technique was common among users of pMDIs and DPIs, and was associated with lack of instruction in their use by healthcare professionals (Sestini et al., 2006). To ensure the correct use of inhalation therapy whatever the device, appropriate training and education by the healthcare professionals must be given, more frequently to improve the patients' ability to use the inhalation devices correctly. After receiving appropriate teaching in regards to how to perform a complete and correct inhalation technique, there may be no difference in COPD patients' ability to use DPIs or pMDIs (Brocklebank et al., 2001; Melani et al., 2011, Sestini et al., 2006).

Among the DPIs users in this study, the proportion of participants who made at least one deviation was greater for the Handihaler device (86%) than for the Turbohaler (59%) or Accuhaler (45%). In relation to the problems encountered with the use of the Accuhaler device, this study agrees with the findings of Schlaeppi et al. (1996), Sumby et al. (1997) and Molimard et al. (2003) which showed that the Accuhaler device had a consistent performance, being reliable and trusted, and has broad patient acceptance. In a study by Moore and Stone (2004) for patients with COPD who were aged over 60 years, two-thirds were able to use the Accuhaler without a single deviation or mistake, compared with less than 3% of those who used a Handihaler. An observational study in Jordan of 300 patients with COPD found that among the DPIs the Accuhaler device had the lowest rate of incorrect handling (Khassawneh et al., 2008). It can be concluded that amongst the DPIs the Accuhaler is something of a gold standard, although this study has revealed it was inaccurately used by almost half of those whose technique was observed.

When participants were asked to state their preferences for one inhaler, they were not in favour of the Handihaler device. Participants' use of the Handihaler was inferior to other DPIs. This could be due to the complicated procedures associated with the use of the single-dose DPI, starting from loading the dose, which is not easy to accomplish for elderly participants, especially those who have manual or dexterity problems. Therefore, many were not able to perform all the essential steps, from getting the capsule out of the blister pack, loading it, and piercing it. In addition, when a COPD patient is experiencing a sudden attack of shortness of breath and needs immediate drug delivery of short-acting bronchodilator, these devices will not be practical because they do not deliver short-acting bronchodilators and the inhalation process takes time to perform. Previously, it has been shown that participants favoured the use of the Accuhaler over the Handihaler (Moore and Stone, 2004). According to that study, the two top-rated features for an inhaled device were being quick to use when needed, and overall ease of use (Moore and Stone, 2004).

The deviations from correct use or device mishandlings in this study were due to many reasons. Firstly, checking the inhalation technique was not an integral part of the routine management of COPD patients. If participants complained that they were not receiving the therapeutic effect from their inhalation therapy, physicians tended to step up therapy, increase the frequency of dosing or switch to another device instead of investigating the reasons (section 7.4). This indicates that inhalation technique should be regularly assessed, not only provided with the initiation of a new inhaler device. Secondly, the information about how to use the inhalation devices was found to be mostly obtained from the patient information leaflets that come with each device. These are usually written using a medical language that is not easily understood by some patients. Additionally, despite the fact that the pharmaceutical companies tend to give a lot of description in the information leaflet about the use of each inhaler, this information is usually

written in a very small font size accompanied by illustrations, which were hard to read for some of the participants in this study (Section 8.2.3). Therefore, healthcare providers, including medical staff, nursing staff and pharmacists should not assume that patients are able to obtain all the required information in regards to use from reading the package leaflets alone. Healthcare providers need to assist patients on the proper use of each device. In addition, it was acknowledged by some participants that doctors do not usually spend enough time counselling their patients during peak hours at the outpatient clinic. Therefore, doctors should be encouraged to spend adequate time (more than 10 minutes) and provide sufficient resources such as handouts or videos for inhaler technique training.

Another reason for the differences seen in handling the inhalation devices among COPD participants can be due to the differences in the properties in the design of each device and instructions given for each patient, which may be related to patients' manual dexterity problems. If any one of these cases arises, quick action should be taken to evaluate each case individually and find the proper solution. In addition, healthcare prescribers are advised to avoid prescribing a device with a complex design and to consider the ease of use when prescribing inhalation therapy.

To conclude, inhalation therapy is central in the management of chronic obstructive pulmonary disease, and pMDIs and DPIs remain primary devices to manage this condition. Checking inhalation technique and the proper use of the inhalation therapy for each prescribed device need to be an integral part of the routine management of any COPD patient, ensuring the proper use of devices by patients and optimising therapy. In addition, nebulisers should be considered in patients with a severe condition and those with manual dexterity limitations who cannot optimally use hand-held inhalers, because nebulisers require less coordination and no special breathing

manoeuvres are required. The dual use of nebulisers and pMDI or DPI is recommended because it may obtain the best efficacy and convenience. However, continuous review, assessment, training and education are also suggested to minimise any confusion or misuse and maximise the medicine use. See section 9.5 for recommendation and suggestions to healthcare providers in the context of the current policy.

9.2.4 The role of carers and the assistance with medicines that patients receive

This study was conducted to explore the extent of involvement of informal carers in the disease management process for COPD patients, and to address the gap in the literature by describing the nature of support or care provided for COPD patients in their homes. Understanding the range and extent of care provided by informal caregivers regarding inhalation therapy at home is crucial to support and empower carers to fulfil their roles, and to ensure the effective use of COPD medication by patients.

In this study the informal carers were involved in the following activities: ordering and collecting a prescription from the surgery or pharmacy (N=13) and obtaining or reading information (N=2). Women (generally spouses) were the main sources of care for COPD patients with their medicines. These findings are supported by the studies of Essue et al. (2010) and Gautun et al. (2012). In these two studies most support received was practical (e.g. accompanying the patient to healthcare services and getting prescriptions filled). Additional support comprised operation of medical equipment (e.g. supplementary oxygen concentrators and carrying out testing procedures) (Essue et al., 2010; Gautun et al., 2012) and ensuring adherence to the prescribed medication regimen (Essue et al., 2010; Trivedi et al., 2012).

Three studies have previously concluded that COPD patients received inadequate support from the formal care sector; therefore, they have unmet needs that are managed by informal caregivers (Simpson et al., 2008; Spence et al., 2008; Caress et al., 2009), highlighting the important role of informal carers in helping homebound patients with their medicines. The involvement of informal care may substantially improve patient outcomes (Lilleaas, 2003; Gautun et al., 2012).

Understanding the range and extent of care provided by informal caregivers in relation to the use of inhalation therapy at home is crucial to support and empower these individuals to fulfil their roles in supporting of the patients, and to ensure the effective use of COPD medication by patients.

9.2.5 The priorities and concerns for patients in the context of current and potential future service provision

Excluding patients' involvement in the management process of COPD and fears of change regarding the current medication regimens were the main reasons reported by participants who were unwilling to access the healthcare system and follow the medical advice due to being dissatisfied with their own healthcare provider's arrangements. This was in line with the previously published studies. Thomas's study (2009), conducted among 499 patients with asthma, found that 50% of the participants refused to use their DPIs because they had been replaced with a substitute device for no apparent reasons. In a further study which used in-depth interviews of five patients with asthma, four participants were concerned about switching their existing DPIs to another inhalation device, with the presence of confusion about the need for change (Booker, 2005).

Healthcare professionals therefore have to be aware that, when a patient has any concern or confusion regarding switching their inhalation devices, they may not only not request clarification or assistance from professionals, but also continue using the old drug regimen without informing their doctors. Therefore, it is necessary to describe to the patient the need for the change and to educate the patient on the new treatment including the indications, the frequency of dosing and the inhalation technique. Furthermore, it is important to always try to get the patients involved in the management process, to maximise the medicine use.

9.3 Limitations of the study

From a total of 116 COPD patients who were eligible to take part and were invited to participate in this study, only 33 participants responded following an initial mailing. In order to increase the participation rate, a reminder letter was sent to those who had not yet responded. Ultimately, in total 46 participants who met the criteria and agreed to take part were enrolled in this study and interviewed (response rate 40%). This was lower than expected, since the feasibility of conducting this study and the accessibility of COPD patients was examined with Pinn Medical Centre staff in the preliminary fieldwork. Based on the feedback of respondents this could be due to the fact that this study was conducted mainly during the spring and summer seasons, when most non-participants were either working or out of the country. Despite the small sample size, the sample of 46 participants consisted of people from different age groups, ethnicity, disease status and smoking history. In addition, a similar proportion of males and females were recruited with different disease status and smoking history, which would make the sample representative and generalisable to the general population. In addition, it can be applied to a wider population with COPD.

In terms of assessing patients' adherence and beliefs about medicines, this assessment was done at a particular point of time (when the study was conducted). Patients' adherence and beliefs about medicines may undergo changes over time based on further experiences of their own or others' prior experiences with the treatment (George et al, 2006). Therefore, it would be interesting to know whether these beliefs may change over time and whether this affects patients' medication-taking behaviours. As a result, repeated assessment may enable the assessment of the consistency of adherence to and beliefs about COPD medicines over time.

9.4 Contribution to existing knowledge and implication for future research

To our knowledge, this is the only study that has examined the use of multiple inhalation devices (all medication classes and inhalation devices) used in combination by COPD patients in the management of their disease in the context of their daily lives. In addition, this study provides information about how COPD patients made decisions about use of devices, what problems they had in the past with different inhalers, what worked and what did not work. Semi-structured interviews and participant observation were employed together to provide a detailed assessment. This is the first single study to explore the frequency and range of technical and practical problems experienced by COPD patients with all inhalation devices in aspects of their use including operation, cleaning and maintenance of inhaler equipment. Moreover, it is one of very few studies that have explored informal carers' contribution in the assistance of COPD patients with their medicines at home. This study adds to the field of medication use at home in the following ways:

- It has reported the perceived barriers to using the inhalation therapy by COPD patients with the description of the factors that affect the decision-making with regards to the use of inhalation therapy.

- It has reported the actual and perceived effectiveness and safety of the inhalation therapy in regards to symptoms' control and disease management.

- It has identified the frequency and range of problems experienced by COPD patients in technical aspects of the operation, cleaning and maintenance of inhaler equipment that may lead to suboptimal care or treatment failure.

- It has documented the role of carers and the assistance with medicines that COPD patients receive from family and friends, and had identified the priorities and concerns for patients in the context of current and potential future service provision.

- This study made some recommendations to healthcare professionals to optimise medicine use and maximise the efficacy of the therapy, leading to better health outcomes for COPD patients.

Based on the results found in this thesis, further research is suggested with respect to the following:

- Different tools were used previously by researchers to assist the inhalation technique among the pMDIs and DPIs users. As far as we are aware, no tool has been published to assess the nebulisation technique among nebuliser users. This study assessed the nebulisation technique among three nebuliser users. However, more studies are required in this aspect to assess the effective use of the nebulisation therapy among COPD patients in a wider context and examine what problems the nebuliser users had in the past with different nebulisers, what worked and what did not work.

- Future work can be done to investigate the contribution of informal carers in assisting patients with their COPD medicines at home, as very little was found in the literature on what is the nature of support provided for COPD patients in terms of their COPD medication in their homes, from whom and how often this help is sought. Therefore, it can be said that the nature of informal support provided for COPD patients with their medication in their homes remains understudied. The few existing studies that have examined the informal care provided for COPD patients have focused on carer experiences and needs, neglecting the needs of homebound patients with COPD and the important role of the informal carers in disease management among COPD patients. Therefore, there is a need to know if the dependent patient is getting any help or assistance with their COPD medicines, whether formal or informal, and how does the carer help – in which activity or tasks and how often. Understanding the range and extent of care given by the caregivers in relation to the use of inhalation therapy at home is crucial to support and empower carers to fulfil their roles and to ensure the effective use of COPD medication and optimise health outcomes for COPD patients.

9.5 Considerations of the study results in regards to the current policies

- In the last two decades, the profile of COPD as a disease has been raised by a number of British organisations (e.g. NHS, BTS, BLF) trying to decrease the number of treatment failures, exacerbations and hospital admissions (BLF, 2008). In order to accomplish this goal, appropriate medicine usage and the safety of the inhalation therapy in patients' homes need to be assured. This study gives information about the use of multiple inhalation devices by COPD patients in the management of their disease in the context of their daily lives, which gives the healthcare

professionals the opportunity for intervention to optimise medicine use and maximise management of the condition.

- Medication formed a major component of the National Service Framework (NSF) plan, which reported that older people and their carers should be assisted in using their therapy to maximise medicine use. In order to maintain or enhance their quality and duration of life and to avoid deteriorations of symptoms resulted from suboptimal medication use (DH, 2001b). To achieve this goal another document was published to specifically address the medicines component of the standards (DH, 2001a). In this document, the practical aspects of medication use was emphasised in any medication review. However, findings of this study revealed that patients with COPD frequently experienced practical and technical issues with the use of their inhalers.

- It is recommended by the Medical Research Council (MRC) to guide and formulate adherence-enhancing interventions by research findings (MRC, 2008). As a result, findings of this study are used to provide the foundations of program development and help in designing tailored medication adherence interventions among patients with COPD. Suboptimal adherence to inhalation therapy was identified in almost 50% of the sample, which was consistent with the rate of non-adherence in seven past studies (Melani et al., 2001; Boyter and Carter, 2005; George et al., 2005; Mehuys et al., 2010; Cecere et al., 2012; Huetsch et al., 2012; Trivedi et al., 2012). The suboptimal use of COPD medications by almost half of the participants in this study raises a series of concerns as non-adherence to inhalation therapy at this extent may lead to suboptimal management and treatment failures. These findings highlight the need for healthcare professionals to continuously review patients' adherence to their prescribed

regimen and provide comprehensive assessment, assistance and education for patients to maximise medicines' use. In addition, healthcare providers should assess the need for therapy, identify cases when the inhalation therapy is not used as suggested, study the reasons and find appropriate solutions to address concerns and misapprehensions and avoid unnecessary costs. This study examined how each patient made decisions regarding the use of inhalers, and how those decisions and difficulties contributed to suboptimal outcomes and/or treatment failures. Providing this information to healthcare professional may help in evaluating and assessing each patient individually to try to maximise the use of therapy and minimise the number of treatment failures.

- Patients with chronic disease conditions including COPD who use inhalation therapy including bronchodilators, corticosteroids, theophylline, or other related COPD therapy, comprise one of the national targets for the current Medicines Use Review (MUR) services and one of the conditions that was included in the New Medicine Service (NMS) to assess and improve adherence to COPD medicines (HSC, 2013) by educating the patients and reminding them about the chronic nature of their disease and the importance to keep a track of their medicines and use them as suggested (HSC, 2013).

- Using inhaled corticosteroids (ICS) is recommended by NICE and GOLD guidelines, to be used in combination with LABA (e.g. Symbicort or Seretide), as this combination improves symptoms and lung function (NICE, 2010). The majority of participants in this study perceived their combination therapy to be effective in regards to better lung function and condition control. Therefore, this regimen should be continued until patients perceive their drug

therapy to be suboptimal, at which time these cases should be assessed and further investigated.

- The data from the interviews revealed that two-thirds of participants perceived their inhalation therapy to be optimal when delivered by different types of devices including pMDIs, DPIs and nebulisers. This was due to the relief in their COPD symptoms, the increase in their activity levels and being able to sleep through the night. Such findings have led the recommendations to support the use of other hand-held devices, with a preference for nebulisers, and nebulisation therapy discontinued in the absence of a clear benefit to the patients (NICE, 2010). This study shows a clear appreciation by patients of the continued availability of nebulisers for drug delivery in the home.

9.6 Implication of the study findings and recommendations for practice and policy

One of the main values for conducting this research among patients with COPD is to communicate relevant results of patients' perspectives to healthcare professionals, in order to optimise medicines use and maximise treatment outcomes. It was advocated by Health initiatives to commence services incorporate the experiences and views of service users (DH, 2010). The aim of this was to introduce services that are responsive to patients' needs, beliefs and concerns. To support this aim, this section applied the findings of this study to inform healthcare professionals of patients' beliefs, concerns and needs. Additionally, recommendations for healthcare professionals were made in light of the study results to support the use of medicines by COPD patients using multiple inhalation therapy in combination in their own homes, leading to optimizing health outcomes. These recommendations are:

- Healthcare professional should consider using multiple inhalation therapy in combination and a wider use of nebuliser therapy: patients' reports indicated nebuised therapy was perceived to be effective by all users. However, currently nebulisers are considered only in patients with a severe condition and those with manual dexterity limitations who cannot optimally use hand-held inhalers (NICE, 2010), because nebulisers require less coordination and no special breathing manoeuvres are required.

- Based on the participants' perceptions, this study supports the use of multiple inhalation therapies in combination by patients in their homes. The reason behind this was due to the fact that most participants reported that they benefited from their combination therapies used at home; when these multiple therapies were given in combination, they provided a complementary effect in disease management. However, some participants responded differently to medications.

- Nebulisers should be considered in patients with a severe condition and those with manual dexterity limitations who cannot optimally use hand-held inhalers, because nebulisers require less coordination and no special breathing manoeuvres are required.

- The dual use of nebulisers and pMDI or DPI is recommended because it may obtain the best efficacy and convenience. However, continuous review, assessment, training and education are also suggested to minimise any confusion or misuse and maximise the medicine use.

- Healthcare professional should consider the efficacy of therapy used in combination by COPD patients: the data from the interviews

revealed that two-thirds of participants perceived their inhalation therapy to be optimal when delivered by different types of devices including pMDIs, DPIs and nebulisers. This was due to the relief in their COPD symptoms, the increase in their activity levels and being able to sleep through the night. Such findings have led the recommendations to support the use of other hand-held devices, with a preference for nebulisers, and nebulisation therapy discontinued in the absence of a clear benefit to the patients (NICE, 2010). This study shows a clear appreciation by patients of the continued availability of nebulisers for drug delivery in the home.

- After analysing the data, it was shown that patients' perceptions of the effectiveness of the inhalation therapy were different and were influenced by their own or others' previous experiences or expectations with the inhalation therapy. These perceptions and expectations may undergo changes with further experience. This indicates a need for tailoring an individual care plan for each patient, especially given that one-quarter of participants perceived their inhalation therapy was not fully effective, due to treatment failures resulting in recurring symptoms, persistence of symptoms, exacerbations or hospital readmissions, despite using their therapy.

- Treatment failures were of concern to patients who had experienced multiple episodes of exacerbation. The study identified factors which were potential contributors to treatment failures one of which is non-adherence to therapy or misuse of therapy. Therefore, to improve patients' use of inhalation therapy, it is suggested that healthcare professionals should be aware of how individual COPD patients use their inhalation therapy to manage their condition in the context of their daily lives, and what the reasons that guide the use were, to provide all the necessary assistance tailored to each patient, particularly whose is at high risk of suboptimal adherence.

- Adherence screening, assessment and evaluation should be routinely performed by healthcare professionals using direct and indirect methods.

- In the event of non-adherence or if non-adherence is suspected, healthcare professionals should identify the nature and the reasons for non-adherence and develop strategies for overcoming this problem, as the disease management is a dynamic process influenced by the presence or absence of these trigger factors.

- Over time adherence may decline, therefore healthcare professionals should be encouraged to provide feedback and counsel their COPD patients about the role of treatment and the importance of adherence, which may in turn enhance patients' adherence.

- Patients' medical progress and adherence to their treatment should be reviewed and assessed periodically along with a review of the problems experienced by patients in the use of medicines and care.

- To increase adherence to medicines and correct use of devices, patients should get involved in shared decision-making in regards to the treatment and devices alternatives and state their preferences when any alteration is suggested. However, they should be first well educated about the available treatment.

- Increasing the dose or adding a new medication to the treatment plan may achieve better control of symptoms but may in turn lead to more side effects or medication non-adherence. Therefore, negotiating patients' choices, decisions and requests is recommended before making any alterations. Patients may also benefit from continuous

education in regards to each inhalation device and medication and its mode of action, to enable them to distinguish between the immediate and the long-term treatment benefits along with the possible side effects and risks.

- Patients' previous experiences and expertise with medicines used at home should be considered in medical practice, to detect and overcome perceived barriers to adherence.

- When asking patients to follow a treatment plan involving multiple inhalation devices, this plan should be practicable and fit into each patient's daily routine. In addition, instructions should be adapted to each patient's knowledge level and should be clear, simple, personalised and operational in terms of how many to take, what kind and when to use. After receiving advice, patients should be asked to paraphrase their understanding of the given advice and the rationale behind it.

- The findings of this study suggest systematic or local adverse effects especially with the long-term use of ICS. Therefore, safety concerns exist with the use of inhaled steroids in patients with COPD, particularly when using a combination of drugs that contains steroids, double dosing, or higher strength. As a result, it is recommended that patients' fears and concerns should be addressed carefully during each consultation which should be patient-centred, with all their questions answered clearly.

- In regards to the safety of the inhalation therapy, participants have to be counselled during each visit about the possible side effects, and in particular they should be informed about the need to rinse their mouth after each use of ICS, to avoid developing oral thrush due to deposition of the drug in the oro-pharynx. In addition, participants who

experienced side effects with the long-term use of steroids delivered by a pMDI should be encouraged to use a spacer device with their pMDI. Spacer devices are recommended for use with pMDIs to increase drug delivery to the airways, and decrease the side effects resulting from deposition in the mouth or throat (Roland et al., 2004).

- Before stepping up doses or dosing frequencies of the therapy, healthcare providers are advised to make assessment of inhalation technique an integral part of the routine management of COPD patients. Checking inhalation technique and the proper use of the inhalation therapy for each prescribed device need to be an integral part of the routine management of any COPD patient, ensuring the proper use of devices by patients and optimising therapy.

- Inhalation technique assessment should occur at regular intervals, not only with the initiation of a new inhaler device. Therefore, during visits to the surgery, COPD patients should be encouraged to bring their prescribed devices and should be asked to demonstrate their use and maintenance. In addition, adequate time and resources need to be set aside for inhaler technique training, if needed.

- Patients' visual acuity and manual dexterity should be assessed often, especially for those who have tremors, arthritis and coordination problems, as this could affect the successful use of inhalation devices.

- Some participants tended to forget the information they have read or heard with time, due to their age or cognitive problems. Therefore, it is suggested to keep monitoring the patients and to provide continuous education and training, as appropriate.

- When an inhaled therapy is used by patients for a long period of time, it should not be assumed that patients became familiar and proficient in the use of this device. Appropriate assessments should be undertaken.

- After the assessment, if the inhalation devices were handled inappropriately by patients, quick action should be taken (e.g. training or consideration of a spacer device or breath-actuated devices, when use of pMDIs is problematic or an alternative device).

- The training session should provide a clear explanation of why a particular inhaler was prescribed, how it works and the steps needed to use it efficiently. In addition, patients also need to know how and when to clean these devices and how to tell when the device is empty and needs to be replaced.

- Almost one-third of participants in this study sought help from their informal carer with their medicines and this was mainly in ordering or collecting their prescriptions. This help was mainly sought when required but not on a daily basis. However, it is always important to keep a record of whether COPD patients require help or assistance with their medicines and whether this help is sufficient to meet their needs because informal care is one of the cornerstones of maintaining health and function in many older adults with COPD.

- Understanding the range and extent of care provided by informal caregivers in relation to the use of inhalation therapy at home is crucial to support and empower carers to fulfil their roles, and to ensure the effective use of COPD medication by patients.

- Excluding patients' involvement in the management process of

COPD, dissatisfaction with the services provided and fears of change to the current medication regimens were the main reasons reported by participants who were unwilling to access the healthcare system and follow the medical advice due to being dissatisfied with their own healthcare provider's arrangements. Healthcare professionals therefore have to be aware that, when a patient has any concern, confusion or dissatisfaction, they may not only not request clarification or assistance from professionals, but also continue using the old drug regimen without informing their doctors. Therefore, it is necessary to describe to the patient the need for the change and to educate the patient on the new treatment including the indications, the frequency of dosing and the inhalation technique.

- It is also recommended to always try to get the patients involved in the management process, to maximise the medicine use.

- Participants' satisfaction with healthcare services was judged by the amount of time they spend with their doctors in a consultation, keeping their regular doctor, the quantity and the quality of information provided to each one, and the appointment system. Therefore, it is recommended that healthcare professionals spend enough time with their patients in a consultation explaining everything about their disease and medication. Failure to meet these expectations caused dissatisfaction and delayed access to healthcare services, subsequently leading to lack of medical supervision and information, which may lead to treatment failures. A named regular GP is also recommended to coordinate patients' care and in an effort to meet patients' satisfactions.

10 Chapter Ten: The conclusion

Treatment failures were a major concern for COPD patients in this study as almost half of participants reported suboptimal adherence. Therefore, screening of medication taking among patients with COPD should be routinely done on all aspects of management using simple and practical tools. This is required for all COPD patients including those whose non-adherence has not been a concern in the past. However, more time should be spent with patients whose non-adherence is of concern, paying lots of attention to the identification of the nature of non-adherence and the reasons behind this behaviour, which are also critical in clinical practice along with its detection and quantification.

Most patients experienced problems with inhalation devices used at home, especially with the pMDIs and DPIs. Therefore, practical measures (e.g. repeated instruction and supervision on the proper use of an inhaler) should be undertaken to minimise the number of deviations from the inhalation technique made by patients when using inhalation devices, to allow better control of symptoms and optimise the disease management. Further and larger research which is related to the proper use of the inhalation therapy and proper handling of the inhalation devices in real practice with clinical efficacy and disease control is needed.

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Appendix 1:

Studies of medicine taking (adherence/non-adherence) to COPD medicines worldwide

Study/ Setting/ Country	Sample	Definition of patients' adherence/ non adherence	Methods/measures	Study findings and conclusions
Khadour (2012) Outpatient clinics, UK	137 COPD patients	Adherent: patients scoring 3 or above were classified as 'adherent'.	Not clear. Adherence to COPD medications was measured using patients' self-reported questionnaire (4-items Morisky)	Adherence was generally good. Low adherence with medications was present in 29.5 % of the patients only. Variables linked to medicine taking: a range of clinical and psychosocial variables such as perceived severity of the disease and benefits of medications.
Cecere (2012) Outpatient clinics, USA	167 COPD patients, prescribed LABA and ICS	Adherent: took 80% of doses as prescribed	Randomised trial Adherence to COPD medicines was measured using prescription refill rates	Of the 167 patients prescribed LABA, 54% (n=90) were adherent to therapy while only 40% (n=74) of 184 the patients prescribed ICS were adherent. Variables linked to medicine taking: patient perception of their provider as being an "expert" in diagnosing and managing lung disease.
Huetsch (2012) Outpatient clinics, USA	2,730 COPD patients, prescribed ICS,LABA, and IP	Adherent: took 80% of doses as prescribed	A cohort study Adherence to COPD medicines was measured using prescription refill rates	Adherence to medications was poor, with 19.8% adherent to ICS, 30.6% adherent to LABA, and 25.6% adherent to IP. Variables linked to medicine taking highly variable and dependent on the medication being examined.

Table 2-1. Continued.

Study/ Setting/ Country	Sample	Definition of patients' adherence/ non adherence	Methods/measures	Study findings and conclusions
Trivedi (2012) Outpatient clinics, USA	374 COPD patients, prescribed LABA	Adherent: took 80% of doses as prescribed	Non-blinded cluster randomised clinical trial. Adherence to COPD medicines was measured using prescription refill rates	Patient's adherence rate to LABA was poor (43%) of participants. Variables linked to medicine taking: social care.
Agh (2011) Outpatient clinics, Hungary	170 participants with COPD	Adherent: patients scoring 3 or above were classified as 'adherent'.	Cross-sectional observational study. Adherence to COPD medications was measured using patients' self-reported questionnaire (4-items Morisky)	Adherence was good (58.2%). 99 patients reported optimal adherence. Whereas, 71 (41.8%) of those reported suboptimal adherence. Variables linked to medicine taking: age, smoking status, number of medicines, the number of daily doses and quality of life.
Mehuys (2010) Community pharmacies Belgium	555 patients with stable COPD	No clear classification.	Cross-sectional, observational study. Adherence to COPD medicines was measured using prescription refill rates.	53% of patients were non-adherent, 47% were adherent. Variables linked to medicine taking: age and number of drugs.
George (2006) Patients' homes Australia.	28 patients with moderate to severe COPD	The identified themes for medication adherence were agreed among all the pharmacists	Randomized controlled trial study. Factors associated with adherence to disease management interventions were explored using in depth semi-structured questionnaire.	Adherence to disease management programs was complex process driven by 15 major themes (e.g. personal beliefs and experiences which related to patient, treatment, disease, and health professionals).

Table 2-1. Continued.

Study/ Setting/ Country	Sample	Definition of patients' adherence/ non adherence	Methods/measures	Study findings and conclusions
George (2005) Ambulatory care, Australia	276 patients with chronic lung diseases (90.6% with COPD, 5.4% with asthma, 2.2% bronchiectasis, and 1.8% others)	Highly adherent: (a score of 25 indicates), while any other score reports suboptimal adherence.	Cross-sectional descriptive study. Adherence was measured using patients' self-reported questionnaire (MARS). A 30-item Beliefs and Behaviour Questionnaire (BBQ) under three sections: beliefs, experiences, and behaviours were used to determine the factors that are related to medicine taking.	Adherence was generally low (37%). 102 patients reported optimal adherence on MARS. Whereas, 164 (60%) of those reported suboptimal adherence. Variables linked to medicine taking: patients' beliefs, experiences, and behaviours with regards to both disease and treatment.
Boyter (2005) Patients' homes, The United Kingdom	117 patients mainly with COPD, prescribed home nebuliser treatment	Adherent: used home nebulizers at four times a day	A survey study. Adherence to COPD nebulised medications, use and maintenance of equipments were measured and explored by patients' self-reported using anonymous postal questionnaire	Adherence to COPD medicines was generally low (42.5%). Whereas, (57%) of those reported suboptimal adherence.
Barta (2002) Patients' homes, The United Kingdom	75 patients most with COPD, prescribed home nebuliser treatment	Adherent: used home nebulizers at least once a day	A survey study. Adherence to nebulised medications, use, technical issues and concerns about side effects were measured and explored using patients' self-reported anonymous postal questionnaire.	Adherence was generally excellent (60%). Variables linked to medicine taking: feeling worse, less confidence in treatment.

Table 2-1. Continued.

Study/ Setting/ Country	Sample	Definition of patients' adherence/ non adherence	Methods/measures	Study findings and conclusions
Melani (2001) Patients' homes, Italy	1,257 COPD patients, prescribed home nebuliser treatment	Adherent: used home nebulizers at least once a day	Open, multicentre, cross-sectional, observational study. Adherence to respiratory nebulised medications, use, technical issues, and concerns about side effects were measured and explored using patients' self-reported anonymous postal questionnaire.	Adherence was generally low (40%), whereas, (60%) of those reported suboptimal adherence. Variables linked to medicine taking: medication forgetfulness.
van Grunsven (2000) home setting, The Netherland	77 patients with lung diseases (48 with COPD and 29 with asthma), prescribed fluticasone via DPI (Rotadisk).	No clear classification.	Prospective, randomised, placebo-controlled study. Adherence to respiratory medicines was measured using medication count which was done using pill count of Rotadisks returned.	(72%) of patients reported optimal adherence in the early COPD trial. Variables linked to medicine taking: Patient motivation.

***COPD: Chronic Obstructive Pulmonary Disease**
***pMDIs: Pressurised Metered Dose Inhalers**
***DPIs: Dry Powder Inhalers.**
***LABA: long-acting beta-agonists.**
***ICS: inhaled corticosteroids.**
***IP: Ipratropium bromide**

Appendix 2:

Characteristics of studies of inhalation technique assessment among COPD patients worldwide

Study/ Setting/ Country	Sample	Developing check-lists	Definition of incorrect technique	Kind of assessment	Methods/measures	Study findings and conclusions
Hämmerlein (2011), Community pharmacies Germany	757 patients with asthma or COPD using pMDIs and DPIs	21-items checklist was developed to be used for all types of inhalation devices	As a matter of principle, an error probability of less than 5% was demanded ($P < 0.05$), when using independent sample *t*-test	Assessment was made based on a personal view of one rater.	Multi-centre intervention study. Each single step was marked as been performed correctly or incorrectly. However, not all steps were relevant for each inhaler system, for example, shaking the inhaler in case of a DPI; non-relevant steps should be marked as correct.	Almost 80% of patients with chronic lung diseases in ambulatory care made one or more errors when inhaling their medication.
Melani (2011) Outpatient clinics, Italy	1633 patients, most with COPD and asthma, using MDIs and DPIs	Check-lists were adapted from previously published criteria by (Newman, 2005)	If one or more errors were made regarding these essential steps determined by (Newman, 2005)	Assessment was made based on an agreement between multiple raters on set of criteria for the correct use.	Cross-sectional, observational study. Assessment of inhalation technique was done using; a checklist that measures steps required for adequate drug delivery and categorized the steps into 'essential' and 'non-essential' errors and assessed only those 'critical errors or essential steps'.	Critical mistakes were widely distributed among users of all the inhalers, ranging from 12% for MDIs, 35% for Diskus and HandiHaler, and 44% for Turbuhaler. Patients committed more errors when using DPIs than when using MDIs. The COPD group patients committed more errors than asthma patients.

Table 2-2. Continued.

Study/ Setting/ Country	Sample	Developing check-lists	Definition of incorrect technique	Kind of assessment	Methods/measures	Study findings and conclusions
Rootmensen (2010) Outpatient clinics, The Netherlands	156 patients most with COPD and asthma, using MDIs and DPIs	Check-lists adapted from published criteria (van der Palen, et al., 1995; van Beerendonk et al., 1998).	If one or more errors were made regarding these essential steps determined by (van der Palen, et al., 1995)	Assessment was made on an agreement between 3 raters on set of criteria for correct use with the assessment of the total inhalation technique.	Randomized controlled trial. Assessment was done using checklists that measures steps required for adequate drug delivery and categorized the steps into 'essential' and 'non-essential' and only those 'critical errors or essential steps' were measured.	Inhalation technique was judged insufficient in 40% of the patients. Most errors were seen in demonstrations with pMDIs with or without spacer (respectively, 47 and 81%). Essential errors were recorded least in the prefilled Diskus (15%), Turbuhaler (18%), and Diskhaler (21%).
De Moraes Souza (2009) Outpatient clinics Brazil	120 patients with COPD and asthma, using MDIs and DPIs	Check-lists adapted from previously published criteria (Plaza et al., 1998; Steier et al., 2003; Molimard et al., 2003; Muchão et al., 2008).	No clear definition.	Assessment was made based on a personal view of one rater.	Observational study. Measuring the total inhalation technique for each inhaler individually. The quantity of errors committed by the asthma group patients and by the COPD group patients was compared for each device separately.	Inhalation technique was judged insufficient in 94.2% of the patients when using the inhalation device. Patients committed more errors when using MDIs than when using DPIs. The COPD group patients committed more errors when using the inhalation devices than the asthma group patients.

Table 2-2. Continued.

Study/ Setting/ Country	Sample	Developing check-lists	Definition of incorrect technique	Kind of assessment	Methods/measures	Study findings and conclusions
Khassawneh (2008) Outpatient clinics Jordan	500 patients with COPD using pMDIs and DPIs	Not clearly listed	If one or more errors were made regarding these essential steps, leading to indicating little or no delivery of the drug.		Cross-sectional observational study. Measuring steps required for adequate drug delivery and categorized the steps into 'essential' and 'non-essential'. When one or more essential steps were made, inhalation technique was defined as incorrect.	DPIs had a lower rate of incorrect inhalation technique comparing to the pMDIs ($p<0.001$). Among the DPIs, the Accuhaler device had the lowest rate of incorrect handling ($p<0.031$), when compared to Turbuhaler and Aerolizer.
Wilson (2007) Outpatient clinics, London, United Kingdom	30 patients with COPD with evidence of airflow obstruction ($FEV_1/FVC < 70\%$) and had no previous experience of DPIs.	Device-specific checklists were adapted from the package leaflet of each inhaler	If one or more errors were made regarding these essential steps, leading to indicating little or no delivery of the drug.	Assessment was made based on an agreement between two raters on set of criteria for correct use	Randomized controlled trial. Measuring steps required for adequate drug delivery and categorized the steps into 'essential' and 'non-essential'. When one or more essential steps were made, inhalation technique was defined as incorrect.	The numbers of perfect scores were not significantly different between devices, but the number of fatal errors that would result in no drug delivery was significantly more common in Aerolizer, and Handihaler.

Table 2. Continued.

Study/ Setting/ Country	Sample	Developing check-lists	Definition of incorrect technique	Kind of assessment	Methods/measures	Study findings and conclusions
Sestini (2006) Outpatient clinics Italy.	1,126 patients with COPD and asthma, using MDIs and DPIs	Device-specific checklists were adapted from the package leaflet of each inhaler.	A sum score was computed separately for each device, in which each item of the checklist considered as minor was scored as 1, and each one considered as major flaws received a score of 3	Assessment was made based on an agreement between two raters on set of criteria for correct use.	An open, observational study. Measuring steps required for adequate drug delivery and categorized the steps as 'minor' and 'major' errors and only those 'major' errors were measured. When one or more major errors were made, inhalation technique was defined as incorrect.	Prevalent users of either pMDIs or DPIs were, respectively, 644 and 661. Inhaler misuse was common and similar for both pMDIs and DPIs.
Ho (2004) Patients' homes United Kingdom	423 patients use MDIs, MDIs with a large volume spacer and bread actuated inhalers.	Check-lists adapted from previously published criteria (Connolly, 1995).	Major errors were identified using previously published criteria (Connolly, 1995).	Assessment was made based on a personal view of one rater with the assessment of the total inhalation technique.	Cross-sectional study. Measuring steps required for adequate drug delivery and categorized the steps into acceptable (perfect or minor errors not preventing adequate use of the device) or unacceptable (major errors).	Inhalation technique for breath actuated-inhalers was judged insufficient in 27.8% of the patients, compared to 17.9% of patients used p-MDIs alone and 2.9% with large volume spacers.

Table 2. Continued.

Study/ Setting/ Country	Sample	Developing check-lists	Definition of incorrect technique	Kind of assessment	Methods/measures	Study findings and conclusions
Molimard (2003) Outpatient clinics, France	3811 adult with COPD and asthma, using MDIs and DPIs	Device-specific checklists were adapted from the package leaflet of each inhaler.	If one or more errors were made regarding these essential steps, leading to indicating little or no delivery of the drug.	Assessment was made based on an agreement between multiple raters on set of criteria for correct use.	Randomized control clinical trial. Measuring steps required for adequate drug delivery and categorized the steps into 'critical' and 'non-critical' errors and only those 'critical' errors were measured.	Inhalation technique judged insufficient in 49-55% of the patients use breath actuated devices compared to 76% used p-MDIs. 11-12% of patients treated with Aerolizer, Autohaler, or Diskus made critical errors compared to 28% and 32% of patients treated with p-MDI and Turbuhaler, respectively.
Hesselink (2001) Outpatient clinics The Netherland	588 COPD and asthma patients using pMDIs and DPIs	Using the short version, validated inhaler-specific checklist of the Dutch Asthma Foundation	If one or more errors were made regarding these essential steps, leading to indicating little or no delivery of the drug.	Unspecified	Cross-sectional study. The checklist measures the adequacy of the most essential preparation and breathing manoeuvres necessary for optimal drug delivery.	Overall, 24.2% of the patients made at least one essential mistake in their inhalation technique. Compared to users of the Diskhaler (4%) or Cyclohalers (11%), patients using the Rotahaler/Spinhalers more often showed an incorrect inhalation technique (37%), followed by patients using Turbuhalers (31%) and MDI users (30.0%).

Table 2-2. Continued.

Study/ Setting/ Country	Sample	Developing check-lists	Definition of incorrect technique	Kind of assessment	Methods/measures	Study findings and conclusions
Lenney (2000) Respiratory Function Laboratory United Kingdom	100 patients with COPD using MDIs and DPIs	Device-specific checklists were adapted from the package leaflet of each inhaler.	If one or more errors were made regarding these essential steps, leading to indicating little or no delivery of the drug.	Assessment was made based on an agreement between multiple raters on set of criteria for correct use.	Cross-sectional observational study. Inhaler technique was graded in the following way; A. good technique indicating good delivery of the drug; B. poor technique indicating partial delivery of the drug; C. very poor technique indicating little or no delivery of the drug.	Technique was best in 91% of patients using the breath-actuated inhalers (Easi-Breathe and Autohaler), when compared to 79% of patients using pMDIs, despite being the most commonly prescribed devices. The Autohaler came in second position closely followed by the Clickhaler and Accuhaler.

COPD: Chronic Obstructive Pulmonary Disease
MDIs: Metered Dose Inhalers.
DPIs: Dry Powder Inhalers.
FEV1/ FVC: The ratio of forced expiratory volume in one second to forced vital capacity

Appendix 3:

Example of emails sent to the pharmaceutical companies in order to request placebo devices

Appendix 4:

Receiving placebo devices from pharmaceutical companies

Appendix 5:

Interview topic guide

UCL School of Pharmacy
Department of Practice and Policy

NHS Harrow

UCL

Research Questionnaire

Inhalation Devices in the Management of Chronic Obstructive Pulmonary Disease in the Community: A Study with Patients

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The use of inhalers at home
(Interview with the patient)

Notes to Interviewer
Bold: To be spoken out loud to respondent
Italics: Prompts to be used when needed
Standard: Directions to the interviewer

Before we start the interview, I am going to tell you a little bit about the study.

A lot of people like you are using different inhalers to manage their condition at home. We do understand that this can be a complicated task to do.

We would like to know more about your experience with inhalers, any particular aspects you want to raise, any issues related to inhaler use and how your inhaler affects you health and everyday life.

Request permission to tape-record.

Request permission to take photos of the inhalers used.

Ensure consent form is completed.

Stare time of interview: End time of interview:

Section 1: information about your medicines:

1. **When was your (COPD/ bronchitis/emphysema) diagnosed?**
   Which year or how long ago

2. **Could you please show me all medicines you currently use?**

Name of current medications/ strength/ form	Dose from the label/ Intervals	When was first prescribed/ Expiration date	What do you use it for	When do you use it *e.g. Time of day/ in response to symptoms*
1.				
2.				
3.				
4.				
5.				

Complete on a separate sheet

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3. Have you ever used any other type of inhalation devices in the past?

Name of past medications/ strength/ form	Dose from the label	When was it first prescribed	What did you use it for	Why did you stop using it
1.				
2.				
3.				
4.				
5.				

Complete on a separate sheet

Section 2: The use of your medicines

4. **What COPD medicine(s) did you use in the last 24 hours? Why/how much?**

   Morning.....

   .....

   .....

   .....

   .....

   .....

   .....

   Afternoon.....

   .....

   .....

   .....

   .....

   .....

   .....

   Evening.....

   .....

   .....

   .....

   .....

   .....

   .....

5. **For your regular medicines, people often do not take their medicines exactly as prescribed for different reasons, thinking of the medicines you use for your COPD, when was the last time you did not take the dose of your regular medicines?** [State which]

6. **How many times in the last week have you missed a dose of your regular COPD medicines?** [State which]

7. **Why did you miss them?**

Section 3: Operation, cleaning and maintenance of inhaler(s):

8. Inhalation technique assessment [See checklists]

9. Take a photo for the inhalers, see their conditions/cleaning/maintenance and if there is any old/expired medicines

10. What do you think of your regular COPD medicines?
Which one do you find most helpful/ which one do you prefer most/ is there any COPD medicine you decide not to use or you wonder/ concern about/ what do you like or dislike/ have you faced any problem with using your inhalers/ It is hard/easy continuing your normal activities with the use of inhalers.

11. Tell me about any advice you have been given about using your inhaler?
In terms of inhalation technique, cleaning, and maintenance, etc....

12. How and where do you store your inhalers?

13. Do you think your inhaler(s) has to be cleaned? If yes, tell me (how often do you clean it).

Section 4: carer;

14. Do you receive help or assistance with your inhalers from family or friends?
(Ordering or collecting your prescription from the surgery, ordering or collecting you prescription from the pharmacy, opening containers, reading labels, understanding or reading information, obtaining information, administration (e.g. breaking tablets, measuring, putting in eye drops, etc), advice on when to take or how much (especially for prn medicines), advice on need for medicines and/or on side effects, buying medication or other remedies for you, other, Please describe).

- *Yes.*
- *No.*

15. If yes, for each of the above?

Who is this person?	*How does this person help you?*	*How often does this person help you/ which circumstances or occasions help is needed?*

Section 5: Morisky scale (adherence to medicines)

You indicated that you are taking medication for you chronic obstructive pulmonary disease (COPD). Individuals have identified several issues regarding their medication-taking behavior and we are interested in your experiences. There is no right or wrong answer. Please answer each question based on your personal experience with your chronic obstructive pulmonary disease medication (Please circle the correct number).

N	***Questions***	***No = 1***	***Yes = 2***
M1	Do you sometimes forget to take your regular COPD medicines?		
M2	People sometimes miss taking their medications for reasons other than forgetting. Thinking over the past two weeks, were there any days when you did not take your COPD medicine?		
M3	Have you ever cut back or stopped taking your medication without telling your doctor, because you felt worse when you took it?		
M4	When you travel or leave home, do you sometimes forget to bring along with your COPD medication?		
M5	Did you take your COPD medicine yesterday?		
M6	When you feel like your COPD is under control, do you sometimes stop taking your medicine?		
M7	Taking medication everyday is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan?		
M8	How often do you have difficulty remembering to take all your COPD medications? (Please circle the correct number)		
	Never/Rarely.....0		
	Once in a while.....1		
	Sometimes.....2		
	Usually.....3		
	All the time.....4		
TR			

Additional information;

Morisky adherence scale

Source: Morisky DE, Ang A, Krousel-Wood M, et al. (2008). "Predictive validity of a medication adherence measure for hypertension control". *Journal of Clinical Hypertension*, vol. 10, no. 5, pp. 348-354.

Section 6: Beliefs about medicines questionnaire (BMQ)

We would like to ask you about your personal views about COPD medicines prescribed for you. These are statements other people have made about their medicines. Please show how much you agree or disagree with them by ticking the appropriate box. There are no right or wrong answers. We are only interested in your personal view about COPD medicines.

N	*Views about medicines prescribed for your COPD*	*Strongly agree*	*Agree*	*Uncertain*	*Disagree*	*Strongly disagree*
BS1	My health, at present, depends on my medicines					
BS2	Having to take medicines worries me					
BS3	My life would be impossible without my medicines					
BS4	I sometimes worry about long-term effects of my medicines					
BS5	Without my medicines I would be very ill					
BS6	My medicines are a mystery to me					
BS7	My health in the future will depend on my medicines					
BS8	My medicines disrupt my life					
BS9	I sometimes worry about becoming too dependent on my medicines					
BS10	My medicines protect me from becoming worse					
BS11	These medicines give me unpleasant side effects					

The Beliefs about Medicines Questionnaire

Source: Horne R, Weinman J, Hankins M. The Beliefs about Medicines Questionnaire: the development and valuation of a new method for assessing the cognitive representation of medication. *Psychology Health*, vol, 14, pp, 1-24.

Section 7: participant's details;

16. Gender *Male* ☐ *Female* ☐

17. Age .....

18. Smoking status;

- *Current smoker*
- *Ex- Smoker*
- *Never-smoked*

19. What is your ethnic group?

A. White

- English / Welsh / Scottish / Northern Irish / British
- Irish
- Gypsy or Irish Traveller
- Any other White background, write in

B. Mixed / multiple ethnic groups

- White and Black Caribbean
- White and Black African
- White and Asian
- Any other Mixed / multiple ethnic background, write in

C. Asian / Asian British

- Indian
- Pakistani
- Bangladeshi
- Chinese
- Any other Asian background, write in
- Black / African / Caribbean / Black British
- African
- Caribbean
- Any other Black / African / Caribbean background, write in

E. Other ethnic group

- Arab
- Any other ethnic group, write in

Additional information to be completed by the research student:

Complete end time on page 1

20. Was anyone presented at the interview?

- Yes.
- No.

21. If yes, who?
Please make comments about their participation in this interview

.....
.....
.....
.....

22. Was this interview recorded?

- Yes.
- No.

23. If yes, write the code of the interview on the tape.....
.....
.....
.....

24. If no, give reasons below.....
.....
.....
.....
.....
.....
.....
.....

The inhaler technique checklist for p-MDIs

Name of inhaler .....

Correct technique	pMDI type	Yes	No	Comments
1. Remove the cap	**All**			
2. Shake inhaler (the canister) well before use.	**All**			
3. Attach a spacer or valved holding chamber (pMDI with spacer only) to the MDI	**Only pMDIs with a spacer or valved holding chamber**			
4. Holds inhaler upright (p-MDIs), (p-MDIs with spacer); holds the inhaler upright with index finger on top and thumb on the bottom, supports the spacer with other hand.	**All**			
5. Prepare the device according to the manufacturer's instructions	**Breath actuated pMDIs**			
6. Breath out before firing				
7. Place mouthpiece/ or the spacer between teeth and close the lips around it	**All**			
8. Actuate while breathing in deeply and slowly.	**All**			
9. Continue to inhale after firing.	**All**			
10. Hold breath for about 5-10 seconds	**All**			
11. Clean the device and allow the device to (air-dry) completely before the next dose is administered if appropriate.	**All**			
12. Replace the cap after the last dose.	**All**			

The inhaler technique checklist for DPIs

Name of inhaler .....

Correct technique	DPI type	Steps	Yes	No	Comments
1. Remove the cover (Device specific)	**Handihaler**	• Open cap.			
	Diskhaler	• Remove the cover.			
	Turbohaler	• Unscrew the white cover and remove.			
	Accuhaler	• Hold the outer case of the closed Accuhaler in one hand and put the thumb of your other hand on the thumb grip and push your thumb away from you as far as it will go until you hear a click.			
	Others	•			
2. Load the inhaler before usage	**Handihaler**	• Open mouthpiece.			
		• Remove capsule from blister and place in chamber.			
		• Close mouthpiece until it clicks.			
		• Press green piercing button in once and release.			
	Diskhaler	• Raise the lid as far as it goes, to pierce both sides of the medication blister, and then close the lid.			
	Turbohaler	• Turn the base as far as it will go in one direction. Then, turn the base as far as it will go in the other direction.			
	Accuhaler	• Push your thumb away from you as far as it will go until you hear a click.			
	Others	•			
3. Hold inhaler in correct orientation	**All**				
4. Breath out away from your inhaler	**All**				
5. Place mouthpiece between your teeth and close the lips around it	**All**				
6. Breathe in quickly and deeply	**All**				
7. Hold breath for about 5-10 seconds	**All**				
8. Clean the device according to the manufacturer's instructions and allow the device to air-dry completely before the next dose is administered	**All**				
9. Replace the cap after the last dose.	**All**				

The inhaler technique checklist for (Nebulisers)

Name of nebulizer .....

Correct technique	Yes	No	Comments
1. Place the nebulizer on a steady horizontal surface.			
2. Assemble the nebulizer apparatus and plug in power source.			
3. Place medicine in the specified dose in the nebulizer chamber (the medication tank) and close it.			
4. Using of a diluent or more than one nebule in the same nebulizer chamber			
5. Attach the top portion of nebulizer chamber to mouthpiece or to mask.			
6. Connect the bottom of nebulizer chamber with tubing to the air compressor			
7. Place mask over face or mouthpiece in to mouth.			
8. Turn on the compressor.			
9. Sit upright.			
10. Breathe through the mouth.			
11. Complete the treatment and turn off the compressor.			
12. Cleans the nebulizer.			

Appendix 6:

Patient's information from medical notes

UCL School of Pharmacy
Department of Practice and Policy

NHS Harrow

UCL

Patient's information from medical notes

Inhalation Devices in the Management of Chronic Obstructive Pulmonary Disease in the Community: A Study with Patients

Miss Farah Alhomoud
Professor Felicity Smith
Professor Kevin Taylor

UCL School of Pharmacy (Department of Practice and Policy)
University of London,
London, UK
WC1N 1AX

Version 1 Date 18/11/2011 Page 1

Patient's code: .....

Information about patients' medicines:
All current medicines:

Name of current medications/ strength/ form	Dose from the label/ Intervals	When was first prescribed/ Expiration date	What is it for
1.			
2.			
3.			
4.			
5.			

Complete on a separate sheet

Previously prescribed inhalation devices with dates?

Name of past medications/ strength/ form	Dose from the label	When was it first prescribed	What is it for
1.			
2.			
3.			
4.			
5.			

Complete on a separate sheet

Other information:

Other conditions;

Disease severity (If specified):

FEV1:

FEV1/FVC:

Patients' details:

1. **Age .....**
2. **Smoking status (If recorded);**
   - *Current smoker*
   - *Ex- Smoker*
   - *Never-smoked*

Appendix 7:

Invitation letter for participants

The School of Pharmacy
University of London

The School of Pharmacy
University of London

Mezzanine Floor, BMA House
Tavistock Square
London WC1H 9JP

T 020 7874 1270
F 020 7387 5663

www.pharmacy.ac.uk

Invitation Letter for Participants
Research Project: The Use of Inhalation Devices for Chronic Obstructive Pulmonary Disease: A Study with Patients in Primary Care.

Dear Patient,
We are carrying out a study among COPD (bronchitis or emphysema) patients to find out more about their views and experiences of inhalation devices used at home. Findings from previous studies reveal a wide range of problems which may have an impact on the effectiveness of inhaled therapy. This research project is being undertaken by researchers at the School of Pharmacy, University of London.

I would like to invite you to be part of this research. Taking part in this research involves an interview with you about your views and experiences of inhalation devices used at home. If you are happy to participate, the principal researcher will contact you to arrange a convenient time to come and meet you in your home. The interview should take between 45 and 60 minutes.

Enclosed with this letter you will find an information leaflet which will tell you more about the study. You may wish to read and decide if you would like to participate in this study. Whether you are willing to participate or feel unable to do so, I would be very grateful if you would complete the reply slip attached to this letter and return it to the principal investigator in the pre-paid envelope provided.

If you require more information about the study, please do not hesitate to contact the principal investigator by e-mail or on the number shown below:

I look forward to receiving your reply slip,
Miss Farah Alhomoud, Principal Investigator,

Centre for Pharmacy Practice, School of Pharmacy, University of London,
Mezzanine Floor, BMA House,
Tavistock Square. London WC1H 9JP.

[Name and position at GP Practice]
[Signature from surgery]

Appendix 8:

Patient's information sheet

Information Sheet for Participants

The Use of Inhalation Devices for Chronic Obstructive Pulmonary Disease: A Study with Patients in Primary Care

You are being invited to take part in a research study. Before you decide it is important to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends, relatives and your GP if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Whether you are willing to participate or feel unable to do so, we would be very grateful if you would complete the reply slip attached to this letter and return it to the principal investigator in the pre-paid envelope provided.

THANK YOU FOR TAKING TIME TO READ THIS

Part 1:

- **What is the purpose of this study?**

Inhalation therapy is one way of managing a number of conditions which affect breathing and airways. Very little is known about how patients use inhalation devices to manage their COPD (bronchitis or emphysema) on a daily basis, how they make decisions about their use, technical and practical problems in the operation of devices and whether or not this could be improved.

- **Who is doing the study?**

Farah Alhomoud (the principal investigator), is a PhD student, who is carrying out this study as a part of her degree. She is based at the School of Pharmacy, University of London, and is working in collaboration with your GP surgery. Her photograph is included for you to have a look at and know who you may expect when you are visited.

- **Why have I been chosen?**

All patients registered at Pinn Medical Centre using inhalation devices for COPD are invited to take part.

- **Do I have to take part?**

No, taking part is voluntary. If you do decide to take part, you will be asked to sign a patient consent form, and a copy of this will be provided for you to keep. You will have the absolute freedom to withdraw at any time without giving a reason and without your medical care or legal rights being affected.

- **What will happen if you decide to participate in this study?**

The study will involve one interview arranged at your convenience in your home to discuss your use of inhalation devices. In addition, you will be asked to provide a practical demonstration of the inhalation technique for the most used device at home using your own placebo device. However, if you do not have any placebo, you could describe the inhalation technique process without inhaling the actual dose. We expect this to take between 45 and 60 minutes. We would like to audio-record the interview, so we have a complete record of what you say, but if you are not happy with this, notes can be taken instead.
We would also like to make a note of your current medications and medical conditions from your medical notes in the surgery.

- **What are the possible advantages and risks of taking part?**

This study will not affect your treatment or any support that you are receiving with your medicines. However, by sharing your experiences it will help us plan services in the future. A summary of the study findings will be made available to you if you request it.

Part 2:

- **What will happen if I do not want to carry on with the study?**

If you withdraw from the study, we will destroy all your identifiable information, but use the information collected up to your withdrawal.

- **What if there is a problem?**

If you have concerns or complaints about any aspect of the study or its conduct, contact details of members of the research team are provided at the university and your surgery or you can do this though the NHS Complaints Procedure. Details can be obtained from the surgery.

- **What if there was harm?**

It is unlikely that this study will result in any harm to you; however, there is a small chance that during the conduct of the interview you may recall bad or negative experiences. If this occurs, you may stop the interview at any time without giving any reasons and without your care being affected. The principal investigator is also experienced at handling such events. The patient will also be advised to speak to his/her GP.

- **Who is organizing and funding the research?**

The research is being carried out and funded by the School of Pharmacy, University of London. We are an independent establishment involved in education and research; we are not a commercial organisation.

- **Will my taking part in this study be kept confidential?**

In accordance with Data Protection Legislation, all information collected will be kept strictly confidential and will be made anonymous so that you cannot be recognised from it.

- **Involvement of your GP**

As you may already know your GP/Healthcare team is aware that you have been invited to take part in this study. However, no information collected in the study will be disclosed to your GP/Healthcare team without your consent.

- **Who has reviewed the study?**

The study has been independently reviewed and approved by Newcastle & North Tyneside 2 Research Ethics Proportionate Review Sub-Committee (North East REC centre) [11/NE/0392]. In addition, the study has also been approved by [R&D of local PCT].

- **Further information and contact details**

If you would like any further information about the research or if you have concerns or complaints about any aspect during the course please contact:

Farah Alhomoud, the Principal Investigator,
Department of Practice and Policy, School of Pharmacy,
London. WC1H 9JP.
Tel:
E-mail:

Other members of the team;
Felicity Smith, academic supervisor,
Kevin Taylor, academic supervisor,
The School of Pharmacy, London
29-39 Brunswick Square
London, WC1N 1AX

E-mail:
E-mail:

[Name and contact details to be inserted]
The Pinn Medical Centre
37 Love Lane, Pinner, Middx, HA5 3EE
]

Appendix 9:

Consent form for participants

The School of Pharmacy
University of London

Consent form for participants

Study Title:
The Use of Inhalation Devices for Chronic Obstructive Pulmonary Disease: A Study with Patients in Primary Care

Name of researcher:
Farah Alhomoud

To be signed by patient;	Please tick	
	YES	NO
1. I confirm that I have read and understood the information sheet for the above study and I am satisfied with the information provided. In addition, I have had the opportunity to consider the information, ask questions and have had these answers satisfactorily.		
2. I understand that participation is voluntary and I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.		
3. I understand that relevant sections from my medical notes and data collected during the study may be looked at by the research team. Where it is relevant to my taking part in this study, I give permission for these individuals to have access to my records.		
4. I know that a request will be made to audio-record the interview, but agreeing to this is not a requirement to take part in this study.		
5. I give permission to the Principal Investigator to take a photo of my inhalers.		
6. I give permission to the Principal Investigator to inform my GP about me taking part in this study.		
7. I agree to participate in the above study.		

Participant's Name/Identification number	Date	Signature
The Principal Investigator's Name	Date	Signature

The School of Pharmacy
University of London
Mezzanine Floor, BMA House
Tavistock Square
London WC1H 9JP
T 020 7874 1270
F 020 7987 6693
www.pharmacy.ac.uk

Appendix 10:

Reply slip for participants

The School of Pharmacy
University of London

The School of Pharmacy
University of London

Mezzanine Floor, BMA House
Tavistock Square
London WC1H 9JP

T 020 7874 1270
F 020 7387 5693

www.pharmacy.ac.uk

The Use of Inhalation Devices for Chronic Obstructive Pulmonary Disease: A Study with Patients in Primary Care

Reply slip for patient

Name (please print your name).....

I am willing/ I am not willing* to take part in the research study
'The Use of Inhalation Devices for Chronic Obstructive Pulmonary Disease:
A Study with Patients in Primary Care'.

*-Please delete as appropriate

If you are willing to take part in the research please complete the following section so that I can contact you to arrange suitable time for the interview and answer any questions you have

Contact me on: .....
.....

Address;
.....
.....

Types of inhalers I am using at the moment are;
.....
.....
.....

Pleas return this slip in the pre-paid envelope provided (no stamp is required)
Thank you very much for your time

Appendix 11:

Integrated Research Application System Form

NHS REC Form Reference: IRAS Version 3.4

Welcome to the Integrated Research Application System

IRAS Project Filter

The integrated dataset required for your project will be created from the answers you give to the following questions. The system will generate only those questions and sections which (a) apply to your study type and (b) are required by the bodies reviewing your study. Please ensure you answer all the questions before proceeding with your application.

Please enter a short title for this project (maximum 70 characters)
The Use of Inhalation Devices for Chronic Obstructive Pulmonary Disease

1. Is your project research?

(•) Yes ( ) No

2. Select one category from the list below:

( ) Clinical trial of an investigational medicinal product
( ) Clinical investigation or other study of a medical device
( ) Combined trial of an investigational medicinal product and an investigational medical device
( ) Other clinical trial to study a novel intervention or randomised clinical trial to compare interventions in clinical practice
( ) Basic science study involving procedures with human participants
(•) Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology
( ) Study involving qualitative methods only
( ) Study limited to working with human tissue samples (or other human biological samples) and data (specific project only)
( ) Study limited to working with data (specific project only)
( ) Research tissue bank
( ) Research database

If your work does not fit any of these categories, select the option below:

( ) Other study

2a. Please answer the following question(s):

a) Does the study involve the use of any ionising radiation? ( ) Yes (•) No
b) Will you be taking new human tissue samples (or other human biological samples)? ( ) Yes (•) No
c) Will you be using existing human tissue samples (or other human biological samples)? ( ) Yes (•) No

3. In which countries of the UK will the research sites be located? (Tick all that apply)

[x] England
[ ] Scotland
[ ] Wales
[ ] Northern Ireland

3a. In which country of the UK will the lead NHS R&D office be located:

Date: 1 99624/274538/1/783

NHS REC Form Reference: IRAS Version 3.4

(•) England
( ) Scotland
( ) Wales
( ) Northern Ireland
( ) This study does not involve the NHS

4. Which review bodies are you applying to?

[ ] NHS/HSC Research and Development offices
[ ] Social Care Research Ethics Committee
[x] Research Ethics Committee
[ ] National Information Governance Board for Health and Social Care (NIGB)
[ ] Ministry of Justice (MoJ)
[ ] National Offender Management Service (NOMS) (Prisons & Probation)

For NHS/HSC R&D offices, the CI must create Site Specific Information Forms for each site, in addition to the study-wide forms, and transfer them to the PIs or local collaborators.

5. Will any research sites in this study be NHS organisations?

(•) Yes ( ) No

5a. Are all the research costs and infrastructure costs for this study provided by an NIHR Biomedical Research Centre, NIHR Biomedical Research Unit, NIHR Collaboration for Leadership in Health Research and Care (CLAHRC) or NIHR Research Centre for Patient Safety & Service Quality in all study sites?

(•) Yes ( ) No

If yes, NHS permission for your study will be processed through the NIHR Coordinated System for gaining NHS Permission (NIHR CSP).

5b. Do you wish to make an application for the study to be considered for NIHR Clinical Research Network (CRN) support and inclusion in the NIHR Clinical Research Network (CRN) Portfolio? Please see information button for further details.

( ) Yes (•) No

If yes, NHS permission for your study will be processed through the NIHR Coordinated System for gaining NHS Permission (NIHR CSP) and you must complete a NIHR Clinical Research Network (CRN) Portfolio Application Form immediately after completing this project filter and before completing and submitting other applications.

6. Do you plan to include any participants who are children?

( ) Yes (•) No

7. Do you plan at any stage of the project to undertake intrusive research involving adults lacking capacity to consent for themselves?

( ) Yes (•) No

Answer Yes if you plan to recruit living participants aged 16 or over who lack capacity, or to retain them in the study following loss of capacity. Intrusive research means any research with the living requiring consent at law. This includes use of identifiable tissue samples or personal information, except where application is being made to the NIGB Ethics and Confidentiality Committee to set aside the common law duty of confidentiality in England and Wales. Please consult the guidance notes for further information on the legal frameworks for research involving adults lacking capacity in the UK.

8. Do you plan to include any participants who are prisoners or young offenders in the custody of HM Prison Service or

Date: 2 99624/274538/1/783

NHS REC Form Reference: IRAS Version 3.4

Give details of the educational course or degree for which this research is being undertaken:

Name and level of course/ degree:
Department of Pharmacy Practice and Policy, PhD

Name of educational establishment:
School of Pharmacy, University of London 2011

Name and contact details of academic supervisor(s):

Academic supervisor 1

	Title	Forename/Initials	Surname
	Professor	Felicity	Smith
Address	Department of Practice and Policy		
	Entrance A, Mezzanine Floor, British Medical Association (BMA) House		
	Tavistock Square, London		
Post Code	WC1H 9JP		
E-mail	felicity.smith@pharmacy.ac.uk		
Telephone	02078741288		
Fax			

Academic supervisor 2

	Title	Forename/Initials	Surname
	Professor	Kevin	Taylor
Address	3rd floor, the Department of Pharmaceutics		
	29-39 Brunswick Square		
	The School of Pharmacy,University of London		
Post Code	WC1N 1AX		
E-mail	kevin.taylor@pharmacy.ac.uk		
Telephone	02077535853		
Fax	02077535842		

Please state which academic supervisor(s) has responsibility for which student(s):
Please click "Save now" before completing this table. This will ensure that all of the student and academic supervisor details are shown correctly.

Student(s)	Academic supervisor(s)
Student 1 Miss Farah Alhomoud	☑ Professor Felicity Smith ☑ Professor Kevin Taylor

A copy of a current CV for the student and the academic supervisor (maximum 2 pages of A4) must be submitted with the application.

A2-2. Who will act as Chief Investigator for this study?

◉ Student
○ Academic supervisor
○ Other

Date: 5 95624/274538/1/783

NHS REC Form Reference: IRAS Version 3.4

A3-1. Chief Investigator:

	Title Forename/Initials Surname
	Miss Farah Alhomoud
Post	PhD Research Student
Qualifications	BSc in Pharmacy, MSc in Clinical Pharmacy
Employer	Department of Practice and Policy, School of Pharmacy, University of London
Work Address	Department of Practice and Policy
	Entrance A, Mezzanine Floor, British Medical Association (BMA) House
	Tavistock Square, London
Post Code	WC1H 9JP
Work E-mail	farah.alhomoud@live.pharmacy.ac.uk
* Personal E-mail	f_alhomoud83@yahoo.com
Work Telephone	
* Personal Telephone/Mobile	07594326265
Fax	

** This information is optional. It will not be placed in the public domain or disclosed to any other third party without prior consent.*
A copy of a current CV (maximum 2 pages of A4) for the Chief Investigator must be submitted with the application.

A4. Who is the contact on behalf of the sponsor for all correspondence relating to applications for this project?
This contact will receive copies of all correspondence from REC and R&D reviewers that is sent to the CI.

	Title Forename/Initials Surname
	Miss Farah Alhomoud
Address	The Department of Practice and Policy, School of Pharmacy, University of London
	Entrance A, Mezzanine Floor, British Medical Association (BMA) House
	Tavistock Square, London
Post Code	WC1H 9JP
E-mail	farah.alhomoud@live.pharmacy.ac.uk
Telephone	07594326265
Fax	

A5-1. Research reference numbers. *Please give any relevant references for your study:*

Applicant's/organisation's own reference number, e.g. R & D (if available):	
Sponsor's/protocol number:	
Protocol Version:	1
Protocol Date:	18/11/2011
Funder's reference number:	
Project website:	

Additional reference number(s):

Ref.Number Description	Reference Number

Registration of research studies is encouraged wherever possible. You may be able to register your study through your NHS organisation or a register run by a medical research charity, or publish your protocol through an open access publisher. If you have registered your study please give details in the "Additional reference number(s)" section.

Date: 6 95624/274538/1/783

☐ Dissemination of findings
☑ None of the above

Give details of involvement, or if none please justify the absence of involvement.
The aim and objectives of this study are derived by earlier work which was based on interviews with patients use inhalation devices conducted with the British Lung Foundation (BLF) and with patients at home who are using nebulisers.

4. RISKS AND ETHICAL ISSUES

RESEARCH PARTICIPANTS

A17-1. Please list the principal inclusion criteria (list the most important, max 5000 characters).

- Patients with a confirmed diagnosis of COPD from the medical notes.
- Patients who are over 18 years old.
- Patients who are prescribed at least two inhalation devices including MDIs, DPIs and/or nebulizers.
- Patients who use their inhalers in their own home or a residential home.
- Patients who are registered at Prvn Medical Centre.
- Patients who are able to speak and understand English.

A17-2. Please list the principal exclusion criteria (list the most important, max 5000 characters).

- Patients who are under 18 years old.
- Patients who are prescribed only one inhalation device.
- Patients who are unable to speak and understand English.

RESEARCH PROCEDURES, RISKS AND BENEFITS

A18. Give details of all non-clinical intervention(s) or procedure(s) that will be received by participants as part of the research protocol. *These include seeking consent, interviews, non-clinical observations and use of questionnaires.*

Please complete the columns for each intervention/procedure as follows:

1. Total number of interventions/procedures to be received by each participant as part of the research protocol.
2. If this intervention/procedure would be routinely given to participants as part of their care outside the research, how many of the total would be routine?
3. Average time taken per intervention/procedure (minutes, hours or days)
4. Details of who will conduct the intervention/procedure, and where it will take place.

Intervention or procedure	1	2	3	4
Recruitment and seeking consent	1			Potential participants will be identified by medical centre staff through patients' medical notes. All documentation and information packs will be prepared by the principal investigator. After identification of the potential participants, information pack will be sent to eligible patients. The information pack will include an invitation letter, information sheet, and patient consent form. Patient consent form has to be read carefully, understood and singed before the interview date. A reply slip with a pre-paid envelope will be also included in the information pack to be returned indicating their willingness to take part. The information sheet will inform potential participants of the purpose of the study, study procedure and how will it be conducted, possible disadvantages and benefits from taking part, sponsorship and confidentiality of data and the principal investigator's contact details. The pack will also include a photograph of the researcher so that participants know who they will be expecting if they wish to take part in the study. In addition, if the participants require any further information, all contact details of the principal investigator will be provided in all forms to give participants the opportunity to ask any question before the interview date. Patients, who return the reply slip indicating their willingness to

			take part, will be contacted by the principal investigator to arrange a suitable date and time for a home interview.
Data collection	1		On the day of the interview with the patient, the principal investigator will be wearing an identification badge, and will read the information sheet with the patient. The patient will be given the chance to ask any question prior to deciding to take part. The patient will be asked to sign the consent form, after reading and understanding patient information sheet if they have not already done so. A request will be made from the patient to audio record the interview. If the patient does not wish the interview to be audio-recorded, field notes only will be taken. Permission will also be sought to record information about participant's COPD such as FEV1, FVC, FEV1/FVC ratio and all prescribed medicines from their medical notes at the surgery. Participants will be assured that only the research team will have access to this information which will be kept in a coded format during the study and destroyed after completion of the study and that they will be identified in the final report.
The length of the interview	1	45-60 minutes	The interview with COPD patients will be expected to take 45-60 minutes and will follow a semi-structured schedule. This will enable qualitative and quantitative data (structured instruments) to be collected as required by the objectives of the study. If patients agree, interviews will be audio recorded to allow data analysis but this will not be requirement to take part. Prior to the commencement of the interview, written consent will be obtained.
Instruments	1		Open and closed semi-structured questions will be answered by participants, to document COPD medicines and how they are used by patients to manage their disease, additionally, to gather information on how and when they use and how they make decision about their use on a daily basis. • Firstly, participants will be asked to show the principal investigator all medicines they are currently using for their COPD and document the use of each. • Secondly, they will be asked about decisions they make to use/not use devices, missed doses, technical and practical problems in their devices. • Thirdly, patients will be asked to provide a practical demonstration of their inhalation technique for the most used device at home using their own placebo device. However, if they do not have any placebo, they will be asked to describe the inhalation technique process without inhaling the actual dose. This will be done under the principal investigator observation. A standardized check list will be used for all types to assess the patients' technique among COPD participants. • Fourthly, they will be asked about the assistance or help they receive from others especially informal carers (family or friends). • Finally, two validated instruments of adherence (Morisky scale) and beliefs about COPD medicines (Beliefs about Medicines Questionnaire (BMQ)) will be applied. These tools have been widely used in previous studies and extensively validated.

A21. How long do you expect each participant to be in the study in total?

2-8 weeks, to enable the interview to be arranged and conducted at potential participants' convenience.

A22. What are the potential risks and burdens for research participants and how will you minimise them?

For all studies, describe any potential adverse effects, pain, discomfort, distress, intrusion, inconvenience or changes to lifestyle. Only describe risks or burdens that could occur as a result of participation in the research. Say what steps would be taken to minimise risks and burdens as far as possible.

It is possible during the interview that participants may recall some negative experiences or they may find the length of the questionnaire inconvenient. However, if any of these arise, participants will be able to stop the interview at any point without giving any reasons.

A23. Will interviews/ questionnaires or group discussions include topics that might be sensitive, embarrassing or upsetting, or is it possible that criminal or other disclosures requiring action could occur during the study?

☐ Yes ☑ No

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A26. What is the potential for benefit to research participants?

The aim of this study is to inform and improve future practice and consider how patients prescribed inhalation devices for the management of COPD may most effectively be supported. However, if any problem was detected or identified in the use of inhalation devices among participants during the course of the study, they will be advised to speak to their practice staff. But, there will be no interventions and no changes on patients' treatment from this research.

A26. What are the potential risks for the researchers themselves? *(if any)*

None

RECRUITMENT AND INFORMED CONSENT

In this section we ask you to describe the recruitment processes for the study. Please give separate details for different study groups where appropriate.

A27-1. How will potential participants, records or samples be identified? Who will carry this out and what resources will be used? *For example, identification may involve a disease register, computerised search of GP records, or review of medical records. Indicate whether this will be done by the direct healthcare team or by researchers acting under arrangements with the responsible care organisation(s).*

Potential participants will be identified by medical centre staff through patients' medical notes. All documentation and information packs will be prepared by the principal investigator (research student). After identification of the potential participants, information pack will be sent to eligible patients. The information pack will include an invitation letter, information sheet, and patient consent form. Patient consent form has to be read carefully, understood and singed before the interview date. A reply slip with a pre-paid envelope will be also included in the information pack to be returned indicating their willingness to take part. The information sheet will inform potential participants of the purpose of the study, study procedure and how will it be conducted, possible disadvantages and benefits from taking part, sponsorship and confidentiality of data and the principal investigator's contact details. The pack will also include a photograph of the researcher so that participants know who they will be expecting if they wish to take part in the study. In addition, if the participants require any further information, all contact details of the principal investigator will be provided in all forms to give participants the opportunity to ask any question before the interview date.

Patients, who return the reply slip indicating their willingness to take part, will be contacted by the principal investigator to arrange a suitable date and time for a home interview. The interview with the patient will be conducted on one occasion at their home.

A27-2. Will the identification of potential participants involve reviewing or screening the identifiable personal information of patients, service users or any other person?

(●) Yes ( ) No

Please give details below:
Potential participants will be identified by Pinn Medical Centre staff through patients' medical notes.

A27-4. Will researchers or individuals other than the direct care team have access to identifiable personal information of any potential participants?

( ) Yes (●) No

A28. Will any participants be recruited by publicity through posters, leaflets, adverts or websites?

( ) Yes (●) No

A29. How and by whom will potential participants first be approached?

Once the patient identified by the surgery, the potential participants will be first approached by Pinn Medical Centre

staff, by sending them a letter to their home addresses to invite them to take part.

A30-1. Will you obtain informed consent from or on behalf of research participants?

(●) Yes ( ) No

If you will be obtaining consent from adult participants, please give details of who will take consent and how it will be done, with details of any steps to provide information (a written information sheet, videos, or interactive material). Arrangements for adults unable to consent for themselves should be described separately in Part B Section E, and for children in Part B Section F.

If you plan to seek informed consent from vulnerable groups, say how you will ensure that consent is voluntary and fully informed.

All eligible patients will be invited to take part in this study by sending them an information pack. The information pack will include an invitation letter, information sheet, and patient consent form. Patient consent form has to be read carefully, understood and singed before the interview date. A reply slip with a pre-paid envelope will be also included in the information pack to be returned indicating their willingness to take part. The information sheet will inform potential participants of the purpose of the study, study procedure and how will it be conducted, possible disadvantages and benefits from taking part, sponsorship and confidentiality of data and the principal investigator's contact details. The pack will also include a photograph of the researcher so that participants know who they will be expecting if they wish to take part in the study. In addition, if the participants require any further information, all contact details of the principal investigator will be provided in all forms to give participants the opportunity to ask any question before the interview date.

All documentation including the consent form and information packs will be prepared by the principal investigator.

On the day of the interview with the patient, the principal investigator will read the information sheet with the patient. The patient will be given the chance to ask any question prior to deciding to take part. The patient will be asked to sign the consent form, after reading and understanding patient information sheet if they have not already done so. A request will be made from the patient to audio-record the interview. If the patient does not wish the interview to be audio-recorded, field notes only will be taken. Permission will also be sought to record information about participant's COPD such as FEV1, FVC, FEV1/FVC ratio and all prescribed medicines from their medical notes at the surgery. Participants will be assured that only the research team will have access to this information which will be kept in a coded format during the study and destroyed after completion of the study and that they will be identified in the final report.

This consent from includes
1. Reading and understanding the participant information sheet for this study and the satisfaction with the information provided.
2. Understanding that participation is voluntary and they are free to withdraw at any time without giving any reason, without chief investigator present or future medical care being affected.
3. Understanding that relevant sections from their medical notes and data collected during the study may be looked at by the chief investigator. Where it is relevant to their taking part in this study, participants give permission for the chief investigator to have access to their medical records.
4. Agreeing to audio-record the interview, but agreeing to this is not a requirement to take part in the study.
5. Agreeing to participate in this study.

If you are not obtaining consent, please explain why not.

Please enclose a copy of the information sheet(s) and consent form(s).

A30-2. Will you record informed consent (or advice from consultees) in writing?

(●) Yes ( ) No

A31. How long will you allow potential participants to decide whether or not to take part?

Expected start and completion dates of this project is from January 2012 to January 2013, during this period there is no time limitation for participants to take part. They are free to join any time during this year.

A33-1. What arrangements have been made for persons who might not adequately understand verbal explanations or

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written information given in English, or who have special communication needs?(e.g. translation, use of interpreters)

One of the inclusion criteria in this project is to interview patients who are able to consent English.

A35. What steps would you take if a participant, who has given informed consent, loses capacity to consent during the study? Tick one option only.

- ○ The participant and all identifiable data or tissue collected would be withdrawn from the study. Data or tissue which is not identifiable to the research team may be retained.
- ◉ The participant would be withdrawn from the study. Identifiable data or tissue already collected with consent would be retained and used in the study. No further data or tissue would be collected or any other research procedures carried out on or in relation to the participant.
- ○ The participant would continue to be included in the study.
- ○ Not applicable – informed consent will not be sought from any participants in this research.
- ○ Not applicable – it is not practicable for the research team to monitor capacity and continued capacity will be assumed.

Further details:

If you plan to retain and make further use of identifiable data/tissue following loss of capacity, you should inform participants about this when seeking their consent initially.

CONFIDENTIALITY

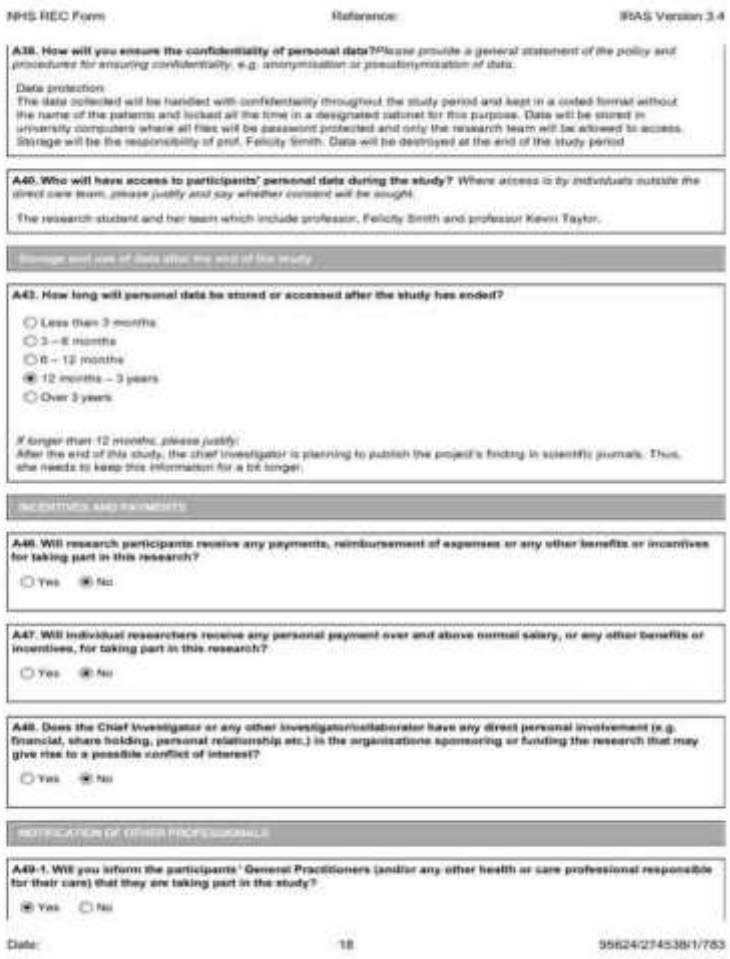
In this section, personal data means any data relating to a participant who could potentially be identified. It includes pseudonymised data (subjects of study linked to a participant through a unique code number).

Storage and use of personal data during the study

A36. Will you be undertaking any of the following activities at any stage (including in the identification of potential participants)?(Tick as appropriate)

- ☑ Access to medical records by those outside the direct healthcare team
- ☐ Electronic transfer by magnetic or optical media, email or computer networks
- ☐ Sharing of personal data with other organisations
- ☐ Export of personal data outside the EEA
- ☑ Use of personal addresses, postcodes, faxes, emails or telephone numbers
- ☑ Publication of direct quotations from respondents
- ☐ Publication of data that might allow identification of individuals
- ☑ Use of audio/visual recording devices
- ☑ Storage of personal data on any of the following:
  - ☐ Manual files including X-rays
  - ☐ NHS computers
  - ☐ Home or other personal computers
  - ☑ University computers
  - ☐ Private company computers
  - ☐ Laptop computers

Further details:



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A38. How will you ensure the confidentiality of personal data?*Please provide a general statement of the policy and procedures for ensuring confidentiality, e.g. anonymisation or pseudonymisation of data.*

Data protection
The data collected will be handled with confidentiality throughout the study period and kept in a coded format without the name of the patients and locked all the time in a designated cabinet for this purpose. Data will be stored in university computers where all files will be password protected and only the research team will be allowed to access. Storage will be the responsibility of prof. Felicity Smith. Data will be destroyed at the end of the study period.

A40. Who will have access to participants' personal data during the study? *Where access is by individuals outside the direct care team, please justify and say whether consent will be sought.*

The research student and her team which include professor, Felicity Smith and professor Kevin Taylor.

Storage and use of data after the end of the study

A43. How long will personal data be stored or accessed after the study has ended?

- ○ Less than 3 months
- ○ 3 – 6 months
- ○ 6 – 12 months
- ◉ 12 months – 3 years
- ○ Over 3 years

If longer than 12 months, please justify:
After the end of this study, the chief investigator is planning to publish the project's finding in scientific journals. Thus, she needs to keep this information for a bit longer.

INCENTIVES AND PAYMENTS

A46. Will research participants receive any payments, reimbursement of expenses or any other benefits or incentives for taking part in this research?

○ Yes ◉ No

A47. Will individual researchers receive any personal payment over and above normal salary, or any other benefits or incentives, for taking part in this research?

○ Yes ◉ No

A48. Does the Chief Investigator or any other investigator/collaborator have any direct personal involvement (e.g. financial, share holding, personal relationship etc.) in the organisations sponsoring or funding the research that may give rise to a possible conflict of interest?

○ Yes ◉ No

NOTIFICATION OF OTHER PROFESSIONALS

A49-1. Will you inform the participants' General Practitioners (and/or any other health or care professional responsible for their care) that they are taking part in the study?

◉ Yes ○ No

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If Yes, please enclose a copy of the information sheet/letter for the GP/health professional with a version number and date.

A49–2. Will you seek permission from the research participants to inform their GP or other health/ care professional?

○ Yes ◉ No

It should be made clear in the participant's information sheet if the GP/health professional will be informed.

PUBLICATION AND DISSEMINATION

A50. Will the research be registered on a public database?

○ Yes ◉ No

Please give details, or justify if not registering the research.

Registration of research studies is encouraged wherever possible.
You may be able to register your study through your NHS organisation or a register run by a medical research charity, or publish your protocol through an open access publisher. If you are aware of a suitable register or other method of publication, please give details. If not, you may indicate that no suitable register exists. Please ensure that you have entered registry reference number(s) in question A5-1.

A51. How do you intend to report and disseminate the results of the study? *Tick as appropriate:*

- ☑ Peer reviewed scientific journals
- ☑ Internal report
- ☑ Conference presentation
- ☐ Publication on website
- ☐ Other publication
- ☐ Submission to regulatory authorities
- ☐ Access to raw data and right to publish freely by all investigators in study or by Independent Steering Committee on behalf of all investigators
- ☐ No plans to report or disseminate the results
- ☐ Other (please specify)

A53. Will you inform participants of the results?

○ Yes ◉ No

Please give details of how you will inform participants or justify if not doing so.

5. Scientific and Statistical Review

A54. How has the scientific quality of the research been assessed? *Tick as appropriate:*

- ☑ Independent external review
- ☐ Review within a company
- ☐ Review within a multi-centre research group
- ☑ Review within the Chief Investigator's institution or host organisation
- ☑ Review within the research team
- ☑ Review by educational supervisor
- ☐ Other

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Justify and describe the review process and outcome. If the review has been undertaken but not seen by the researcher, give details of the body which has undertaken the review:
The research student put the project protocol for discussion among respiratory specialists meeting which is held every Friday in Pinn Medical Centre in Pinn to get their views, opinions, and feedback on the methodology, recruitments, sample strategy applied in this project and any other issues raised by COPD patients we are not aware of to be included in this project. After the meeting, no changes were suggested by the respiratory specialists.

For all studies except non-doctoral student research, please enclose a copy of any available scientific critique reports, together with any related correspondence.

For non-doctoral student research, please enclose a copy of the assessment from your educational supervisor/ institution.

A56. How have the statistical aspects of the research been reviewed? *Tick as appropriate:*

- ☐ Review by independent statistician commissioned by funder or sponsor
- ☐ Other review by independent statistician
- ☐ Review by company statistician
- ☐ Review by a statistician within the Chief Investigator's institution
- ☐ Review by a statistician within the research team or multi-centre group
- ☐ Review by educational supervisor
- ☐ Other review by individual with relevant statistical expertise
- ☑ No review necessary as only frequencies and associations will be assessed – details of statistical input not required

In all cases please give details below of the individual responsible for reviewing the statistical aspects. If advice has been provided in confidence, give details of the department and institution concerned.

Title Forename/Initials Surname

Department
Institution
Work Address

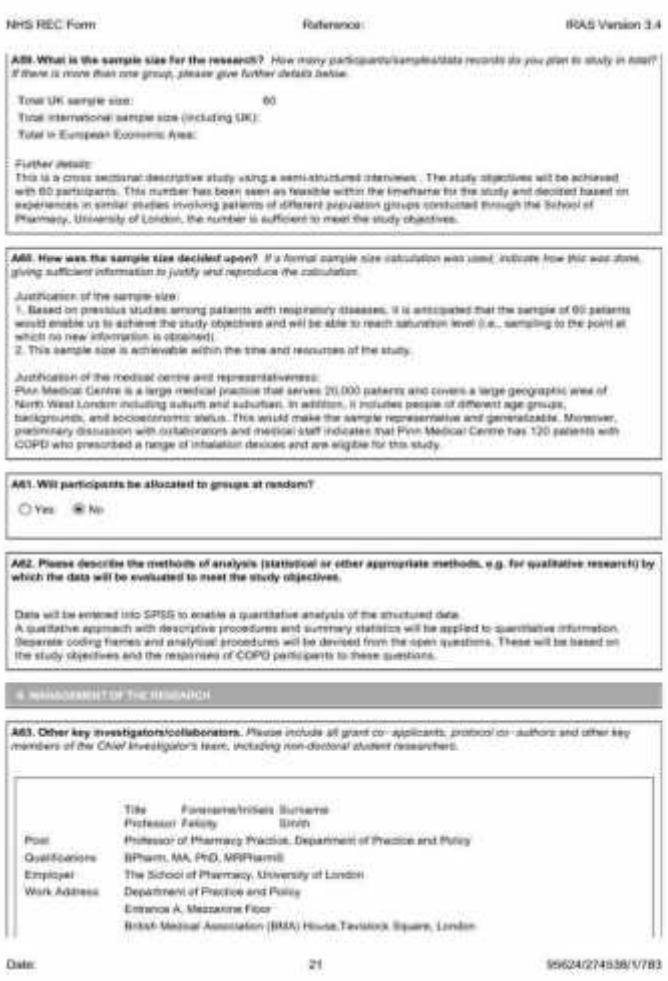
Post Code
Telephone
Fax
Mobile
E-mail

Please enclose a copy of any available comments or reports from a statistician.

A57. What is the primary outcome measure for the study?

Findings from the study will provide a description of the use of different inhalers in the management of COPD from the patient's perspectives, their beliefs, priorities and concerns in relation to medicine use. In addition, it will enable identification of problems that may impact on the effectiveness of the therapy which will provide useful information for local health about the health of COPD patients that will help inform and development of services and improve the health of COPD patients and support them.

A58. What are the secondary outcome measures? *(if any)*



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A59. What is the sample size for the research? *How many participants/samples/data records do you plan to study in total? If there is more than one group, please give further details below.*

Total UK sample size: 60
Total international sample size (including UK):
Total in European Economic Area:

Further details:
This is a cross sectional descriptive study using a semi-structured interviews . The study objectives will be achieved with 60 participants. This number has been seen as feasible within the timeframe for the study and decided based on experiences in similar studies involving patients of different population groups conducted through the School of Pharmacy, University of London, the number is sufficient to meet the study objectives.

A60. How was the sample size decided upon? *If a formal sample size calculation was used, indicate how this was done, giving sufficient information to justify and reproduce the calculation.*

Justification of the sample size:
1. Based on previous studies among patients with respiratory diseases, it is anticipated that the sample of 60 patients would enable us to achieve the study objectives and will be able to reach saturation level (i.e., sampling to the point at which no new information is obtained).
2. This sample size is achievable within the time and resources of the study.

Justification of the medical centre and representativeness:
Finn Medical Centre is a large medical practice that serves 20,000 patients and covers a large geographic area of North West London including suburb and suburban. In addition, it includes people of different age groups, backgrounds, and socioeconomic status. This would make the sample representative and generalizable. Moreover, preliminary discussion with collaborators and medical staff indicates that Finn Medical Centre has 120 patients with COPD who prescribed a range of inhalation devices and are eligible for this study.

A61. Will participants be allocated to groups at random?

○ Yes ◉ No

A62. Please describe the methods of analysis (statistical or other appropriate methods, e.g. for qualitative research) by which the data will be evaluated to meet the study objectives.

Data will be entered into SPSS to enable a quantitative analysis of the structured data.
A qualitative approach with descriptive procedures and summary statistics will be applied to quantitative information. Separate coding frames and analytical procedures will be devised from the open questions. These will be based on the study objectives and the responses of COPD participants to these questions.

B. MANAGEMENT OF THE RESEARCH

A63. Other key investigators/collaborators. *Please include all grant co- applicants, protocol co- authors and other key members of the Chief Investigator's team, including non-doctoral student researchers).*

	Title Forename/Initials Surname
	Professor Felicity Smith
Post	Professor of Pharmacy Practice, Department of Practice and Policy
Qualifications	BPharm, MA, PhD, MRPharmS
Employer	The School of Pharmacy, University of London
Work Address	Department of Practice and Policy Entrance A, Mezzanine Floor British Medical Association (BMA) House,Tavistock Square, London

Date: 21 99624/274538/1/783

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Post Code	WC1H 9JP
Telephone	02078741288
Fax	02073875693
Mobile	
Work Email	felicity.smith@pharmacy.ac.uk

	Title Forename/Initials Surname
	Professor Kevin Taylor
Post	Head of the Department of Pharmaceutics and Professor of Clinical Pharmaceutics
Qualifications	BPharm, PhD, MRPharmS
Employer	School of Pharmacy, University of London
Work Address	3rd floor, the Department of Pharmaceutics,The School of Pharmacy,University of London 29-39 Brunswick Square London
Post Code	WC1N 1AX
Telephone	02077535853
Fax	02077535942
Mobile	
Work Email	kevin.taylor@pharmacy.ac.uk

A64. Details of research sponsor(s)

A64-1. Sponsor

Lead Sponsor

Status: ○ NHS or HSC care organisation Commercial status:
◉ Academic
○ Pharmaceutical industry
○ Medical device industry
○ Local Authority
○ Other social care provider (including voluntary sector or private organisation)
○ Other

If Other, please specify:

Contact person

Name of organisation: School of Pharmacy, University of London

Given name	Maureen
Family name	Boylan
Address	29-39 Brunswick Square
Town/city	London
Post code	WC1N 1AX
Country	UNITED KINGDOM
Telephone	02077535817
Fax	02078373465
E-mail	maureen.boylan@pharmacy.ac.uk

Date: 22 99624/274538/1/783

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Is the sponsor based outside the UK?
○ Yes ◉ No

Under the Research Governance Framework for Health and Social Care, a sponsor outside the UK must appoint a legal representative established in the UK. Please consult the guidance notes.

A65. Has external funding for the research been secured?

☐ Funding secured from one or more funders
☐ External funding application to one or more funders in progress
☑ No application for external funding will be made

What type of research project is this?
○ Standalone project
○ Project that is part of a programme grant
○ Project that is part of a Centre grant
○ Project that is part of a fellowship/ personal award/ research training award
○ Other

Other – please state:

A67. Has this or a similar application been previously rejected by a Research Ethics Committee in the UK or another country?

○ Yes ○ No

Please provide a copy of the unfavourable opinion letter(s). You should explain in your answer to question A8.2 how the reasons for the unfavourable opinion have been addressed in this application.

A68. Give details of the lead NHS R&D contact for this research:

	Title Forename/Initials	Surname
	Dr Tricia	Robertson
Organisation	The Prin Medical Centre	
Address	The Prin Medical Centre	
	37 Love Lane, Pinner	
	Middx	
Post Code	HA5 3EE	
Work Email	tricia.robertson@nhs.net	
Telephone	02088657/06	
Fax	02084280351	
Mobile		

Details can be obtained from the NHS R&D Forum website: http://www.rdforum.nhs.uk

A69-1. How long do you expect the study to last in the UK?

Planned start date: 31/01/2011
Planned end date: 31/01/2014

Date: 23 95624/274538/1/783

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Total duration:
Years: 3 Months: 0 Days: 0

A71-2. Where will the research take place? *(Tick as appropriate)*

☑ England
☐ Scotland
☐ Wales
☐ Northern Ireland
☐ Other countries in European Economic Area

Total UK sites in study:

Does this trial involve countries outside the EU?
○ Yes ◉ No

A72. What host organisations (NHS or other) in the UK will be responsible for the research sites? *Please indicate the type of organisation by ticking the box and give approximate numbers of planned research sites:*

☐ NHS organisations in England
☐ NHS organisations in Wales
☐ NHS organisations in Scotland
☐ HSC organisations in Northern Ireland
☐ GP practices in England
☐ GP practices in Wales
☐ GP practices in Scotland
☐ GP practices in Northern Ireland
☐ Social care organisations
☐ Phase 1 trial units
☐ Prison establishments
☐ Probation areas
☐ Independent hospitals
☑ Educational establishments
☐ Independent research units
☐ Other (give details)

Total UK sites in study: 0

A75-1. What arrangements will be made for insurance and/or indemnity to meet the potential legal liability of the sponsor(s) for harm to participants arising from the management of the research? *Please tick box(es) as applicable.*

Note: Where a NHS organisation has agreed to act as sponsor or co-sponsor, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For all other sponsors, please describe the arrangements and provide evidence.

Date: 24 95624/274538/1/783

☐ NHS indemnity scheme will apply (NHS sponsors only)

☑ Other insurance or indemnity arrangements will apply (give details below)

The School of Pharmacy have an insurance policy (incorporating public liability) with Zurich Municipal until 31 July 2011. Insurance policy number NHE-01CA21-0013

Please enclose a copy of relevant documents.

A70-2. What arrangements will be made for insurance and/ or indemnity to meet the potential legal liability of the sponsor(s) or employer(s) for harm to participants arising from the design of the research? *Please tick box(es) as applicable.*

Note: Where researchers with substantive NHS employment contracts have designed this research, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For other protocol authors (e.g. company employees, university members), please describe the arrangements and provide evidence.

☐ NHS indemnity scheme will apply (protocol authors with NHS contracts only)

☐ Other insurance or indemnity arrangements will apply (give details below)

Please enclose a copy of relevant documents.

A70-3. What arrangements will be made for insurance and/ or indemnity to meet the potential legal liability of investigators/collaborators arising from harm to participants in the conduct of the research?

Note: Where the participants are NHS patients, indemnity is provided through the NHS schemes or through professional indemnity. Indicate if this applies to the whole study (there is no need to provide documentary evidence). Where non-NHS sites are to be included in the research, including private practices, please describe the arrangements which will be made at these sites and provide evidence.

☐ NHS indemnity scheme or professional indemnity will apply (participants recruited at NHS sites only)

☑ Research includes non-NHS sites (give details of insurance/ indemnity arrangements for these sites below)

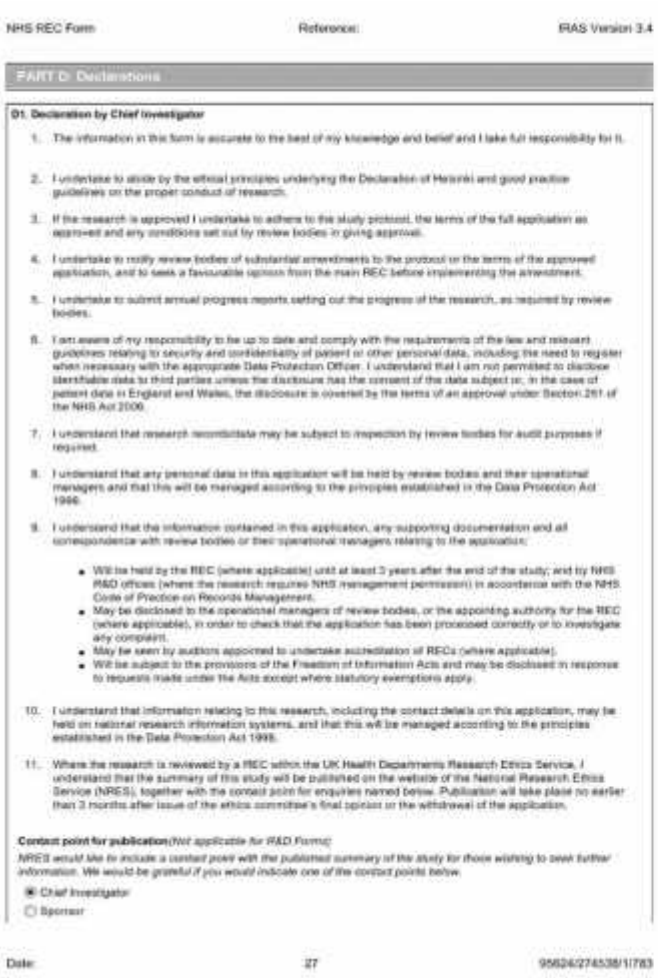
The School of Pharmacy have an insurance policy (incorporating public liability) with Zurich Municipal until 31 July 2011. Insurance policy number NHE-01CA21-0013

Please enclose a copy of relevant documents.

PART C: Overview of research sites

Please enter details of the host organisations (Local Authority, NHS or other) in the UK that will be responsible for the research sites. *For NHS sites, the host organisation is the Trust or Health Board. Where the research site is a primary care site, e.g. GP practice, please insert the host organisation (PCT or Health Board) in the Institution row and insert the research site (e.g. GP practice) in the Department row.*

Investigator identifier	Research site	Investigator Name



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PART D: Declarations

D1. Declaration by Chief Investigator

1. The information in this form is accurate to the best of my knowledge and belief and I take full responsibility for it.
2. I undertake to abide by the ethical principles underlying the Declaration of Helsinki and good practice guidelines on the proper conduct of research.
3. If the research is approved I undertake to adhere to the study protocol, the terms of the full application as approved and any conditions set out by review bodies in giving approval.
4. I undertake to notify review bodies of substantial amendments to the protocol or the terms of the approved application, and to seek a favourable opinion from the main REC before implementing the amendment.
5. I undertake to submit annual progress reports setting out the progress of the research, as required by review bodies.
6. I am aware of my responsibility to be up to date and comply with the requirements of the law and relevant guidelines relating to security and confidentiality of patient or other personal data, including the need to register when necessary with the appropriate Data Protection Officer. I understand that I am not permitted to disclose identifiable data to third parties unless the disclosure has the consent of the data subject or, in the case of patient data in England and Wales, the disclosure is covered by the terms of an approval under Section 251 of the NHS Act 2006.
7. I understand that research records/data may be subject to inspection by review bodies for audit purposes if required.
8. I understand that any personal data in this application will be held by review bodies and their operational managers and that this will be managed according to the principles established in the Data Protection Act 1998.
9. I understand that the information contained in this application, any supporting documentation and all correspondence with review bodies or their operational managers relating to the application:
   - Will be held by the REC (where applicable) until at least 3 years after the end of the study; and by NHS R&D offices (where the research requires NHS management permission) in accordance with the NHS Code of Practice on Records Management.
   - May be disclosed to the operational managers of review bodies, or the appointing authority for the REC (where applicable), in order to check that the application has been processed correctly or to investigate any complaint.
   - May be seen by auditors appointed to undertake accreditation of RECs (where applicable).
   - Will be subject to the provisions of the Freedom of Information Acts and may be disclosed in response to requests made under the Acts except where statutory exemptions apply.
10. I understand that information relating to this research, including the contact details on this application, may be held on national research information systems, and that this will be managed according to the principles established in the Data Protection Act 1998.
11. Where the research is reviewed by a REC within the UK Health Departments Research Ethics Service, I understand that the summary of this study will be published on the website of the National Research Ethics Service (NRES), together with the contact point for enquiries named below. Publication will take place no earlier than 3 months after issue of the ethics committee's final opinion or the withdrawal of the application.

Contact point for publication *(Not applicable for R&D Forms)*

NRES would like to include a contact point with the published summary of the study for those wishing to seek further information. We would be grateful if you would indicate one of the contact points below.

- (•) Chief Investigator
- ( ) Sponsor

Date: 27 9562/274538/1/783

NHS REC Form Reference: IRAS Version 3.4

- ( ) Study co-ordinator
- ( ) Student
- ( ) Other – please give details
- ( ) None

Access to application for training purposes *(Not applicable for R&D Forms)*

Optional – please tick as appropriate:

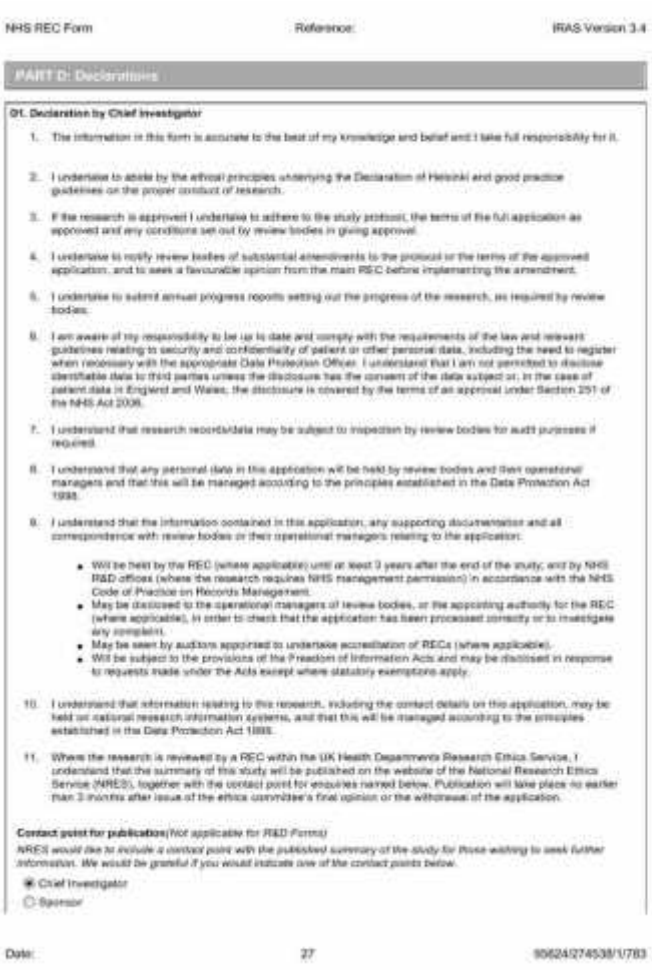
- [x] I would be content for members of other RECs to have access to the information in the application in confidence for training purposes. All personal identifiers and references to sponsors, funders and research units would be removed.

Signature: _____

Print Name: Farah Alhomoud

Date: 21/11/2011 (dd/mm/yyyy)

Date: 28 9562/274538/1/783



NHS REC Form Reference: IRAS Version 3.4

PART D: Declarations

01. Declaration by Chief Investigator

1. The information in this form is accurate to the best of my knowledge and belief and I take full responsibility for it.
2. I undertake to abide by the ethical principles underlying the Declaration of Helsinki and good practice guidelines on the proper conduct of research.
3. If the research is approved I undertake to adhere to the study protocol, the terms of the full application as approved and any conditions set out by review bodies in giving approval.
4. I undertake to notify review bodies of substantial amendments to the protocol or the terms of the approved application, and to seek a favourable opinion from the main REC before implementing the amendment.
5. I undertake to submit annual progress reports setting out the progress of the research, as required by review bodies.
6. I am aware of my responsibility to be up to date and comply with the requirements of the law and relevant guidelines relating to security and confidentiality of patient or other personal data, including the need to register when necessary with the appropriate Data Protection Officer. I understand that I am not permitted to disclose identifiable data to third parties unless the disclosure has the consent of the data subject or, in the case of patient data in England and Wales, the disclosure is covered by the terms of an approval under Section 251 of the NHS Act 2006.
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9. I understand that the information contained in this application, any supporting documentation and all correspondence with review bodies or their operational managers relating to the application:
   - Will be held by the REC (where applicable) until at least 3 years after the end of the study, and by NHS R&D offices (where the research requires NHS management permission) in accordance with the NHS Code of Practice on Records Management.
   - May be disclosed to the operational managers of review bodies, or the appointing authority for the REC (where applicable), in order to check that the application has been processed correctly or to investigate any complaint.
   - May be seen by auditors appointed to undertake accreditation of RECs (where applicable).
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10. I understand that information relating to this research, including the contact details on this application, may be held on national research information systems, and that this will be managed according to the principles established in the Data Protection Act 1998.
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Contact point for publication *(Not applicable for R&D Forms)*

NRES would like to include a contact point with the published summary of the study for those wishing to seek further information. We would be grateful if you would indicate one of the contact points below.

- (•) Chief Investigator
- ( ) Sponsor

Date: 27 99624/274539/1/783

NHS REC Form Reference: IRAS Version 3.4

- ( ) Study co-ordinator
- ( ) Student
- ( ) Other – please give details
- ( ) None

Access to application for training purposes *(Not applicable for R&D Forms)*

Optional – please tick as appropriate

[✓] I would be content for members of other RECs to have access to the information in the application in confidence for training purposes. All personal identifiers and references to sponsors, funders and research units would be removed.

Signature: _____

Print Name: Farah Alhomoud

Date: 21/11/2011 (dd/mm/yyyy)

Date: 28 99624/274539/1/783

NHS REC Form | Reference: | IRAS Version 3.4

D2. Declaration by the sponsor's representative

If there is more than one sponsor, this declaration should be signed on behalf of the co-sponsors by a representative of the lead sponsor named at A64-1.

I confirm that:

1. This research proposal has been discussed with the Chief Investigator and agreement in principle to sponsor the research is in place.
2. An appropriate process of scientific critique has demonstrated that this research proposal is worthwhile and of high scientific quality.
3. Any necessary indemnity or insurance arrangements, as described in question A70, will be in place before this research starts. Insurance or indemnity policies will be renewed for the duration of the study where necessary.
4. Arrangements will be in place before the study starts for the research team to access resources and support to deliver the research as proposed.
5. Arrangements to allocate responsibilities for the management, monitoring and reporting of the research will be in place before the research starts.
6. The duties of sponsors set out in the Research Governance Framework for Health and Social Care will be undertaken in relation to this research.
7. Where the research is reviewed by a REC within the UK Health Departments Research Ethics Service, I understand that the summary of this study will be published on the website of the National Research Ethics Service (NRES), together with the contact point for enquiries named in this application. Publication will take place no earlier than 3 months after issue of the ethics committee's final opinion or the withdrawal of the application.

Signature: .....

Print Name: Ms M F Boylan

Post: Chief Operating Officer and Secretary to Council

Organisation: The Shool of Pharmacy, University of London

Date: 21/11/2011 (dd/mm/yyyy)

Date: 29 9562/4/274538/1/783

NHS REC Form | Reference: | IRAS Version 3.4

D5. Declaration for student projects by academic supervisor(s)

1. I have read and approved both the research proposal and this application. I am satisfied that the scientific content of the research is satisfactory for an educational qualification at this level.

2. I undertake to fulfil the responsibilities of the supervisor for this study as set out in the Research Governance Framework for Health and Social Care.

3. I take responsibility for ensuring that this study is conducted in accordance with the ethical principles underlying the Declaration of Helsinki and good practice guidelines on the proper conduct of research, in conjunction with clinical supervisors as appropriate.

4. I take responsibility for ensuring that the applicant is up to date and complies with the requirements of the law and relevant guidelines relating to security and confidentiality of patient and other personal data, in conjunction with clinical supervisors as appropriate.

Academic supervisor 1

Signature: .....

Print Name: Professor Felicity Smith

Post: Professor of Pharmacy Practice, Department of Practice and Policy

Organisation: School of Pharmacy, University of London

Date: 21/11/2011 (dd/mm/yyyy)

Academic supervisor 2

Signature: .....

Print Name: Professor Kevin Taylor

Post: Head of the Department of Pharmaceutics and Professor of Clinical Pharmaceutics

Organisation: School of Pharmacy, University of London

Date: 21/11/2011 (dd/mm/yyyy)

Date: 30 9562/4/274538/1/783

Appendix 12:

List of questions and emails asked by the sub-committee

Appendix 13:

Ethical Approval

NHS
Health Research Authority

NRES Committee North East - Newcastle & North Tyneside 2

Room 002
TEDCO Business Centre
Rolling Mill Road
Jarrow
NE32 4BW

Telephone: 0191 428 3566
Facsimile: 0191 428 3433

22 December 2011

Miss Farah Alhomoud
PhD Research Student
Department of Practice and Policy
Entrance A, Mezzanine Floor
British Medical Association (BMA) House
Tavistock Square
London
WC1H 9JP

Dear Miss Alhomoud

Study title: **The Use of Inhalation Devices for Chronic Obstructive Pulmonary Disease: A Study with Patients in Primary Care**

REC reference: **11/NE/0392**

The Proportionate Review Sub-committee of the NRES Committee North East - Newcastle & North Tyneside 2 Research Ethics Committee reviewed the above application on 21 December 2011.

Ethical opinion

The sub-committee confirmed that this study has no material ethical issues.

The following issues were raised by the sub-committee and as chief investigator you responded accordingly as follows -

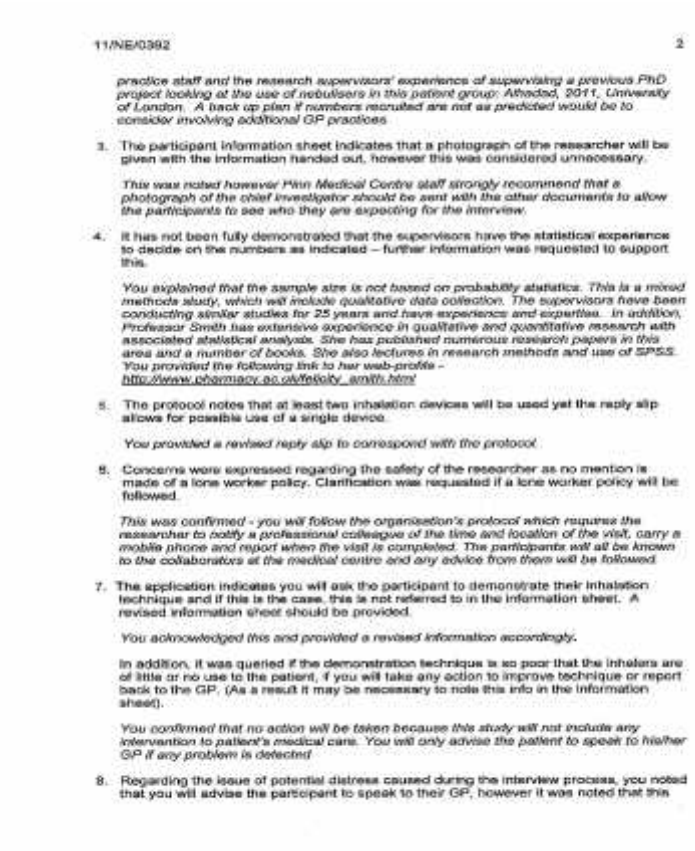
1. The invitation should be issued from the Primary Care practice – therefore an appropriate invitation letter should be provided.

   You informed that it had been agreed with Pinn Medical Centre staff that all documentation and information packs which include an invitation letter will be prepared by the principal investigator and before sending the invitation letter to the patient, it will be signed by a doctor from the Pinn Medical Centre Practice with the header logo of the medical centre.

2. Allegedly there are 120 potential participants and the aim is to recruit 60 – it was questioned if this is feasible as this would involve a 50 percent take-up. If not, then it was queried if you have a back-up plan.

   You noted that previous work in this field with a similar population group achieved a higher response rate. The number of eligible patients has been confirmed. If a difficulty did arise the researchers have discussed the possibility of extending recruitment to a neighbouring practice, but this is not anticipated to be necessary. In addition, the sample size and potential recruitment rate was based on discussions with a member of

A Research Ethics Committee established by the Health Research Authority



11/NE/0392 2

practice staff and the research supervisors' experience of supervising a previous PhD project looking at the use of nebulisers in this patient group: Alhadad, 2011, University of London. A back up plan if numbers recruited are not as predicted would be to consider involving additional GP practices.

3. The participant information sheet indicates that a photograph of the researcher will be given with the information handed out, however this was considered unnecessary.

   This was noted however Pinn Medical Centre staff strongly recommend that a photograph of the chief investigator should be sent with the other documents to allow the participants to see who they are expecting for the interview.

4. It has not been fully demonstrated that the supervisors have the statistical experience to decide on the numbers as indicated – further information was requested to support this.

   You explained that the sample size is not based on probability statistics. This is a mixed methods study, which will include qualitative data collection. The supervisors have been conducting similar studies for 25 years and have experience and expertise. In addition, Professor Smith has extensive experience in qualitative and quantitative research with associated statistical analysis. She has published numerous research papers in this area and a number of books. She also lectures in research methods and use of SPSS. You provided the following link to her web-profile – http://www.pharmacy.ac.uk/fekoby_smith.html

5. The protocol notes that at least two inhalation devices will be used yet the reply slip allows for possible use of a single device.

   You provided a revised reply slip to correspond with the protocol.

6. Concerns were expressed regarding the safety of the researcher as no mention is made of a lone worker policy. Clarification was requested if a lone worker policy will be followed.

   This was confirmed - you will follow the organisation's protocol which requires the researcher to notify a professional colleague of the time and location of the visit, carry a mobile phone and report when the visit is completed. The participants will all be known to the collaborators at the medical centre and any advice from them will be followed.

7. The application indicates you will ask the participant to demonstrate their inhalation technique and if this is the case, this is not referred to in the information sheet. A revised information sheet should be provided.

   You acknowledged this and provided a revised information accordingly.

   In addition, it was queried if the demonstration technique is so poor that the inhalers are of little or no use to the patient, if you will take any action to improve technique or report back to the GP. (As a result it may be necessary to note this info in the information sheet).

   You confirmed that no action will be taken because this study will not include any intervention to patient's medical care. You will only advise the patient to speak to his/her GP if any problem is detected.

8. Regarding the issue of potential distress caused during the interview process, you noted that you will advise the participant to speak to their GP, however it was noted that this