INVESTIGATING HOW EASILY AN INHALER NAÏVE INDIVIDUAL CAN LEARN HOW TO USE AN ASTHMA INHALER THROUGH VIDEO EDUCATION

- A comparative study of four dry powder inhalers

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Abstract

This study aims to address how easily an individual with no prior inhaler experience can learn to use a dry powder inhaler (DPI) through video education. This is a comparative study of four DPIs (Diskus, Easyhaler, Ellipta and Turbuhaler). Different properties affecting ease of use, patient preference as well as educational videos as a method of providing inhaler instructions were investigated. The study used a triangular methodology. The sample consisted of 31 individuals (24-35 years). All participants were considered inhaler naïve. After watching the video education material for a particular inhaler the participants' demonstrated the use of it. Educational videos for all four inhalers were watched and use of all placebo inhalers was demonstrated in a random order. These demonstrations were videotaped. The demonstrations were thereafter checked against a predefined checklist and all mistakes were recorded.

Only 33 % of inhaler demonstrations were completed without the participants making any mistakes that could compromise the efficacy of the inhaled medication in a real-life situation. The frequency of error varied greatly between different types of inhalers. Ellipta proved to be most often used correctly with 55 % demonstrating use without making any mistakes. This was closely followed by Diskus for which 48 % demonstrated correct use. The difference between the average error frequency for Ellipta and Diskus was statistically insignificant. With Easyhaler 19 % percent of participants were able to demonstrate correct use, the corresponding percentage for Turbuhaler was 16 %. When comparing participants' demonstrations for Easyhaler and Turbuhaler, the difference in average error frequency between the devices were not statistically significant. The average frequency of error was lower when using Ellipta in comparison to Easyhaler and Turbuhaler (statistically significant). The same indications were found when comparing average frequency of error for Diskus, to those for Easyhaler and Turbuhaler. Comparing the participants self-reported correct use against the actual numbers it is clear that participants often thought they were using the inhaler correctly when they in fact were not. When asked to rank the inhalers from most preferred to least preferred, Ellipta emerged as a favorite. Turbuhaler received the second highest scores, Diskus the third and Easyhaler was least preferred. However, only the difference between preference scores for Ellipta and Easyhaler was deemed statistically significant.

The high frequency of error suggests that even though participants generally considered the inhalers intuitive and easy to use, they would have required more comprehensive inhaler education in order to achieve correct inhaler technique. Further, the results indicate that video demonstrations are not ideal for providing inhaler education for first time inhalers users. The most prominent problem with video education is that it provides no feedback to the user regarding their inhaler technique. This may present real problems as the results of this study show that participants tended to overestimate their own inhaler technique. Patient education plays a central role in asthma care and needs to be given proper attention even though the inhalers might be considered intuitive and easy to operate. Interesting areas for future research include investigating interactive learning videos as a way of improving video education on inhaler technique.

Keywords

Dry powder inhaler, ease of use, frequency of error, inhaler preference, adherence, asthma, ideal inhaler

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Syftet med denna studie är att undersöka hur lätt en individ utan tidigare erfarenhet av inhalatorer kan lära sig att använda en pulverinhalator (DPI) med hjälp av videoinstruktioner. Studien jämför fyra inhalatorer (Diskus, Easyhaler, Ellipta och Turbuhaler). I studien undersöks olika egenskaper hos inhalatorer som påverkar användarvänligheten och patientpreferensen. Samtidigt undersöks utbildningsvideon som ett sätt att erbjuda användarinstruktioner för inhalatorer. Studien tillämpade en triangulär metod. Samplet bestod av 31 individer (24-35 år). Alla deltagare saknade tidigare erfarenhet av inhalatorer. Deltagarna visades en instruktionsvideo, varefter de uppvisade användningen av den inhalator vars instruktionsvideo just visats. Deltagarna tittade på utbildningsvideon för alla fyra inhalatorer och uppvisade användningen av placeboinhalatorerna i slumpmässig ordning. Deltagarnas inhalatoranvändning videofilmades. Därefter kontrollerades deltagarnas inhalatorteknik mot en på förhand definierad lista och alla fel registrerades.

Endast 33 % av inhalationsuppvisningarna genomfördes utan några misstag som kunnat påverka effekten av det inhalerade läkemedlet i en verklig situation. Felfrekvensen varierade kraftigt mellan olika inhalatortyper. Ellipta var den inhalator som oftast användes rätt och 55 % av uppvisandena genomfördes utan fel. Därefter följde Diskus för vilken 48 % av deltagarna visade korrekt inhalationsteknik. Skillnaden mellan de genomsnittliga felfrekvenserna för Ellipta och Diskus var inte statistiskt signifikanta. Vid uppvisning av inhalationsteknik för Easyhaler genomfördes 19 % av uppvisningarna utan fel. För Turbuhaler var den motsvarande siffran 16 %. Skillnaden mellan de genomsnittliga felfrekvenserna för Easyhaler och Turbuhaler var inte statistiskt signifikanta. Den genomsnittliga felfrekvensen var lägre vid användning av Ellipta i jämförelse med Easyhaler och Turbuhaler (statistiskt signifikant). Samma resultat erhölls då man jämförde den genomsnittliga felfrekvensen för Diskus med de genomsnittliga felfrekvenserna för Easyhaler och Turbuhaler. Då deltagarnas självrapporterade användning jämfördes med de verkliga resultaten framkom det tydligt att deltagarna ofta trodde att de använt inhalatorn korrekt då de i verkligheten hade gjort ett eller flera fel. När deltagarna ombads rangordna inhalatorerna från mest omtyckt till minst omtyckt framkom Ellipta som favorit. Turbuhaler fick de näst bästa poängen, Diskus kom in som trea och Easyhaler framkom som minst omtyckt. Dock var endast skillnaden i preferens mellan Ellipta och Easyhaler statistiskt signifikant.

Den höga felfrekvensen antyder att även om deltagarna i allmänhet tyckte inhalatorerna var intuitiva och lätta att använda skulle de ha behövt mer omfattande träning för att uppnå korrekt inhalationsteknik. Vidare tyder resultaten på att videodemonstrationer inte är ideala för att ge instruktioner i inhalatorteknik då inhalatorn används för första gången. Ett stort problem med videoinstruktioner är att användaren inte får någon feedback på den egna inhalationstekniken. Detta kan innebära problem eftersom resultaten från denna studie visat att deltagare ofta överskattade den egna inhalationstekniken. Patientutbildning spelar en viktig roll i behandlingen av astma och måste uppmärksammas även om inhalatorer kan anses vara intuitiva och lätta att använda. Framtida forskning kunde undersöka hur interaktiva utbildningsvideon skulle kunna användas för att förbättra utbildningsvideon om inhalationsteknik.

Nyckelord: Pulverinhalator, användarvänlighet, felfrekvens, astma, ideal inhalator, inhalator preferens

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Abbreviation	Full name
DPI	Dry powder inhaler
LABA	Long-acting beta-2-agonists
SABA	Short-acting beta-2-agonists
BDP	Beclomethasone diproprionate
FEV1	Forced expiratory volume in 1 s
FVC	Forced vital capacity
FPF	Fine particle fracture
FPM	Fine particle mass
TED	Total emitted dose
THL	The National Institute for Health and Welfare
GSK	GlaxoSmithKline
AZ	Astra Zeneca
FPD	Fine particle dose
API	Active pharmaceutical ingredient
CFD	Computational fluid dynamics
PIF	Peak inspiratory flow
PEF	Peak expiratory flow

1. Introduction

In recent years there have been many studies investigating incorrect use of asthma inhaler and the effect this has on asthma therapy and the patients' health. Before market entry inhalers undergo rigorous testing in randomized controlled trials (Haughney et al. 2010). These trials generally exclude patients who exhibit suboptimal inhaler technique. This may create a distorted perception of inhaler use and handling errors patients face in everyday life. Inhaler errors among asthma patients are common and it has been stated that a majority of asthma patients make mistakes while using their inhalers (Onyedum et al. 2014). The frequency of error varies between different studies but it is estimated that between 50 – 94 % of asthma and COPD patients make at least one mistake when using their inhalers (Crompton et al. 2006; Lavorini et al. 2008). The incidence of errors during inhaler use is highly dependent on which inhaler is used and the frequency of error may therefore vary greatly between different studies (Crompton et al. 2008).

Improper inhaler technique can lead to decreased efficacy, if it results in reduced disposition of the active substance in the lungs (Price et al. 2012). As such, inhaler technique plays a vital role in successful treatment of asthmatic patients. Demonstrating correct inhaler technique has not only been proved to be hard for patients, but also health care professionals have been found to struggle with this issue. A study by Self et al. (2007) among others showed that a majority of health care professionals displayed lack of skill when asked to demonstrate the correct use of various asthma inhalers. This is an alarming statistic as health care professionals usually are the ones instructing patients on how to use their inhalers correctly. Poor inhaler technique has been associated with increased asthmatic symptoms, higher costs and reduced effect on lung function (Price et al. 2012). It has also been suggested that it could lead to patients experiencing more side effects and less adherence to therapy.

The costs associated with asthma are substantial from both a health care and societal point of view. In Finland the overall costs of asthma are estimated to be roughly 240 million euro (Reissel et al. 2010). Research seems to indicate that costs increase significantly with increasing asthma severity (Price et al. 2012; Godard et al. 2002). The American TENOR

study concluded that the health care expenditure for an uncontrolled asthma patient was as much as twice as high as the health expenditure for a patient with controlled asthma (Sullivan 2005). It appears that decreasing the amount of inhaler errors and subsequently increasing the degree of adherence among patients could help to contribute to a higher quality of life among some patients through factors such as decreased asthmatic symptoms and higher lung function. Furthermore this could be a step towards reducing the asthma related costs from both a healthcare and societal point of view. With the cost pressure in pharmacies and hospitals increasing, time allocation changing and the demonstrated lack of skill among health care professionals taken into consideration an educational videotape can be considered cost efficient way of providing easily accessible and standardized inhaler education to asthma patients. The foundation for this thesis is the idea that easily accessible education in combination with a patient friendly and intuitive inhaler device that leaves little room for mistakes could be a step towards reduced inhaler error frequency and increased adherence among asthma patients.

The purpose of this study is to examine how a naïve subject without inhaler experience finds the use of an inhaler after receiving a short video education. The study measures how frequent inhaler errors are for each inhaler type after this type of demonstration. This is measured through videotaped inhaler demonstrations where the participants' inhaler performance is scored according to a predetermined checklist. The study evaluates the user friendliness of the most frequently sold dry powder inhalers in Finland, as well as the most recent newcomer to the Finnish market. As another dimension for measuring user friendliness the participants filled in forms evaluating different characteristics of the inhalers and educational material used in this study. Research by Small et al. (2011) suggests that the level of satisfaction patients have with their inhaler device is observed to have a positive influence on the treatment goals for asthma through its association with improved adherence. Based on this, the study aims to address the participants' personal preferences and perception of the inhalers they try. Finally the study aims to evaluate videos as a method of providing inhaler education with the purpose of teaching individuals how to correctly use an asthma inhaler. As this is a comparative study of four inhalers, the results for each aspect of this study will be compared between the inhalers used by the participants.

2. Definitions

The terms compliance, concordance and adherence are commonly used to describe the patient's medicine-taking and how they follow treatment instructions (Horne 2005). Concordance, adherence and compliance are sometimes used interchangeably (McDonald et al. 2002). There are, however, a subtle differences between the terms and they should not be used synonymously (Mäkelä et al. 2013; Horne 2005; Bell et al. 2007). This study will mainly focus on adherence sometimes touching upon compliance.

Compliance and adherence are terms that both concern the medicine-taking behavior of the patient (Bell et al. 2007). Compliance was for long the most widely used term. *Compliance* is defined as "the extent to which the patient's behavior matches the prescriber's recommendations" (Haynes et al. 1979). *Adherence* is defined as the extent to which a patient's activities and behavior, in terms of taking medication, following a diet, adjusting habits or executing a lifestyle, corresponds to the medical or health advice given to them (Lamas et al. 1992; Haynes et al. 1979). The term compliance generally infers a lack of patient involvement and adherence is therefore generally considered the preferred term (Mäkelä et al. 2013).

Non-adherence refers to a state in which the patient adhered from the medical or health advice described to them. Non-adherence can be separated into several categories. There are three common categories of non-adherence to therapy: *overuse*, *underuse* and *improper use* (Restrepo et al. 2008). This study will focus on adherence that stems from improper use. Additionally one can distinguish between *intentional non-adherence* and *unintentional non-adherence* (Wroe 2002). Intentional non-adherence refers to a situation in which the patient misses/alters doses to suit their needs, whereas unintentional non-adherence refers to a situation where the patient for example forgets to take their medication or unintentionally adheres from the medical or health advice prescribed to them.

Critical inhalation errors are defined as all errors in the use or handling of the inhaler that is expected to significantly impair the delivery of a sufficient amount of medication (Price et al. 2013). Critical errors they have been documented for all types of inhalers.

Dry powder inhalers (DPIs) are devices that deliver dry powder formulations of an active drug for local or systemic effect via the pulmonary route (Islama & Gladki 2008). *Multi-dose DPI devices* are defined as DPIs that contain more than one dose (Chrystyn 2007). *Multi-dose reservoir devices* are inhaler devices that release individual doses with each actuation from a bulk supply of the pharmaceutical held within the inhaler device (Chrystyn 2007).

Fine particle fraction is defined as the fine particle dose divided by the dose that is actually delivered (Savolainen 2010). The *fine particle dose* is defined as the dose, which is delivered in particles that are smaller than 5 μm in diameter (Savolainen 2013).

The term *aerosolization* refers to the dispersal of i.e. a medicine in the form of an aerosol (Merriam Webster 2015). *Inspiratory flow rate*, which is expressed in L/min, is defined as the maximum instantaneous airflow that a person can achieve during forced inspiration.

3. Structure and delimitations

The remainder of this thesis is divided into four sections. First some background information and previous research is reviewed and presented with the intention of forming a base and initial framework for the study. The literature review examines previous research of asthma as a disease, the effects of in-adherence, the most common mistakes for inhalers, patient preference, inhaler education and ease of use. Thereafter general specifics of dry powder inhalers, factors related to inhaler handling, their design and are presented. Finally the four inhalers that are a part of this study are presented in more detail.

Next, the research method applied to this study is introduced and discussed. The chosen methods are explained and clarified. The approach of the study is discussed and the research design is presented. Thereafter the data collection process is presented and the

methods for data collection are described. Finally the reliability and validity of the study and the chosen method are discussed from a critical perspective.

In the sixth chapter the empirical findings are presented and analyzed. Finally the findings of this study are discussed based on the theoretical framework. A conclusion to the study, including applied recommendations for future asthma inhalers and inhaler education is presented. An overview of the structure and process of this thesis is presented in Figure 1.

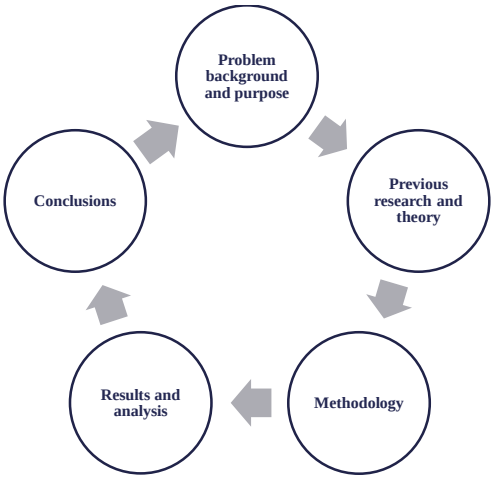


Figure 1: Structure of the study.

This thesis will be limited to inhalers used in the treatment of asthma. There are a great number of asthma inhalers available on the Finnish market. In this study I will focus solely on dry powder inhalers. More specifically the study will include the three most frequently sold dry powder inhalers in Finland, as well as the most recent newcomer in the category of dry powder inhalers on the Finnish market. The inhalers that will be a part of this study are Diskus (GSK), Ellipta (GSK), Easyhaler (Orion) and Turbuhaler (Astra Zeneca). Some of the inhalers used in this study may also be prescribed for the treatment of COPD, but since they are primarily classified as asthma inhalers, the study will focus on this point of view.

When discussing adherence this study will solely focus on unintentional adherence in the form of incorrect inhaler use. All other forms of non-adherence will be excluded from this study. There are several forms of inhaler education. For the purpose of this thesis the

focus will be solely on educational videos. Other forms of inhaler education, such as face to face instructions and interactions will be excluded.

4. Literature review

4.1 An overview of asthma

Asthma is a chronic disease that affects 235-300 million individuals worldwide (Accordini et al. 2008; Masoli et al. 2004). Chronic respiratory diseases, such as asthma and chronic obstructive pulmonary disease (COPD) signify up to 5 % of the total disease burden and 8.3 % of chronic disease burden worldwide and globally asthma is considered to be a central cause of mortality, morbidity and economic burden (WHO 2013).

In Finland 7-10 % of the population suffers from asthma. Additionally it is estimated that approximately 5 % of the population occasionally suffer from asthma-like symptoms (Haahtela 2013). Asthma is characterized by symptoms such as repeated attacks of breathlessness and wheezing (WHO 2013). The severity of asthmatic symptoms and their rate of recurrence vary among patients. Even though the root causes of asthma are not fully understood to date, some risk factors have been identified. These include a combination of genetic disposition and exposure to inhaled substances and particles that may provoke allergic reactions or cause irritation in the airways. At the time of an asthma attack the lining of the bronchial tube start swelling (WHO 2013). This causes the airways to narrow, reducing the airflow to the lungs.

Asthma has become a major public health problem, especially among inner city populations (Moormarn et al. 2007; Gupta et al. 2006; Wisnivesky et al. 2005). Urbanization has been linked to the increasing incidence of asthma, the precise nature of this relationship, however, remains unclear (WHO 2013). Asthma has a comparatively low rate of fatality in comparison to other chronic diseases, such as COPD. Asthma is nowadays rarely fatal in developed countries (Price et al. 2013). The majority of asthma-related deaths today take place in countries with low- and lower-middle income (WHO 2013).

Asthma symptoms are periodic and patients can experience long symptom-free periods. The treatments available for asthma include effective controller and reliever therapy.

Asthma is most often treated with inhaled therapies (Svedsater et al. 2013). Asthma treatment through inhaled therapies facilitate high lung disposition of the drug with minimized systemic bioavailability. This significantly reduces the chance of possible systemic drug interactions (Lavorini et al. 2008). The primary target of asthma medication is to treat the inflammation that is occurring on the mucous membrane (Käypähoito 2012).

The main objective of contemporary treatment guidelines for asthma is to attain clinical control (Accordini et al. 2008). This encompasses a combination of symptom control and maintenance of normal activity levels for the treated patient (Accordini et al. 2008). Despite of the fact that asthma treatment guidelines have been both extensively published and are easily available, there appears to be a significant gap between the aims of treatment and the actual level of asthma control among patients (Gillissen 2004). Incorrect inhaler use has been suggested as a contributing factor to this problem. This study aims to address this issue by gaining a deeper understanding of the frequency of error for common DPIs on the Finnish market.

The clinical picture of asthma as a disease places clear requirements on the inhalers used for treatment. One of these requirements is user-friendliness during an asthma attack as well as during the long time treatment of the disease (Lavorini et al. 2008). Price et al. (2012) states that one of the factors that signifies an ideal inhaler is that it is easy to both teach and learn how to use. Other important properties of asthma inhalers that have been considered key factors are minimal requirements for cooperation and coordination, minimal cleaning and high patient preference (Lavorini et al. 2008). Inhalers play an important part in achieving asthma control, and therefore the needs set up by the disease need to be taken into careful consideration when developing inhalers. The properties of asthma inhalers that affect patients will discussed further on in this thesis.

4.2 The effects of in-adherence

Despite evidence demonstrating clear therapeutic benefit for adhering to the prescribed therapy many patients fail to take their medicines as advised (Rolnick et al. 2013). Adherence seems to be an important issue in the treatment of most chronic diseases and it is estimated that approximately 50 % of individuals suffering from chronic diseases in developed countries adheres to prescribed therapy (Price et al. 2013). Asthma is no exception in the statistics and it is estimated that nearly 50 % of patients do not take their medication as prescribed.

A study among Korean asthma patients found a considerable discrepancy between prescription refill adherence and self-reported adherence to therapy. The self-reported adherence to therapy was reported to be much higher than the actual adherence. In this study the adherence was measured through the refill of asthma medication prescriptions for patients (Bae et al. 2009).

Non-adherence to therapy increases the risk that patients will not receive the intended benefits of the therapy and the risk of developing secondary consequences of their original condition (Rolnick et al. 2013). Suboptimal adherence to treatment also negatively affects patients by contributing to an impaired quality of life (Price et al. 2013; Barnes et al. 1996; Bahadori et al 2009; Kong et al. 2005). Furthermore, research seems to suggest that non-adherence in the long run is likely to lead to higher overall health care costs (Roebuck et al. 2011). The increase in health care expenditures stem from accumulated costs of wasted medication, emergency care and hospitalizations that could have been avoided through proper control of the disease (Price et al. 2013a; Barnes et al. 1996; Bahadori et al. 2009; George et al. 2005).

The costs associated with asthma are substantial from both a heath care and societal perspective. In Finland the overall costs of asthma are estimated to be approximately 240 million euros (Reissel et al. 2010). Research seems to indicate that costs increase signifi-

cantly with increasing asthma severity (Price et al. 2012; Godard et al. 2002). An American study concluded that the health care expenditure for an uncontrolled asthma patient is as much as twice as high as the health expenditure for a patient with controlled asthma (Sullivan 2005). It is estimated that out of an assessed $25 billion spent on asthma inhalers per year, $5–7 billion is wasted due to inhaler misuse (Fink & Rubin 2005).

In addition to the in-adherence that arises from incorrect inhaler use there are many other root causes for non-adherence in the treatment of asthma (GINA-report 2014). The global initiative for asthma reports that around 50 % of asthma patients do not take their controller medication as prescribed. Reasons behind unintentional non-adherence in asthma care include forgetfulness, costs and misunderstandings whereas the underlying reasons for intentional non-adherence may stem from factors such as not perceiving the need for treatment, fear of side-effects, cultural issues or cost (GINA-report 2014).

Inadequate use of inhaler devices has been recognized as one of the leading reasons for not achieving asthma control (Melani et al. 2011). The frequency of misuse is dependent on the type of inhaler device (GINA-report 2014). Properties of the inhalers used for treatment have been shown to affect patient adherence (Hoppentocht et al. 2014). Robustness, ease of handling and convenience are fundamental inhaler properties for achieving correct inhaler use and therapy adherence among patients (Hoppentocht et al. 2014). Non-adherence that stems from improper inhaler technique will be described in further detail in the next chapter.

4.3 Defining the most common inhaler errors

Inhaler use is affected by a number of diverse factors, such as, the device itself, the patient or consumer as well as health care professionals (Price et al. 2012). All inhalers require that the patient exhibit a certain level of physical skill, dexterity, manipulation, hand-strength and lung capacity in order to achieve the intended therapeutic effect. Correct inhaler technique plays a crucial part in achieving this. This section will focus on inhalation errors that may compromise the therapeutic benefits for the patient. These errors are

called critical errors. Critical errors are exhibited when a patient performs an error, displays flawed technique or lacks knowledge of the usage/ maintenance of the inhaler device that is likely to significantly impair the delivery of adequate medication on all occasions of drug administration.

According to comprehensive literature review regarding inhalation technique the most frequently occurring error among patients using DPIs, was not remembering to exhale before using their devices (Lavorini et al. 2008). This error was made by 12–77 % participants depending on the type of inhaler used. The second most common handling error was failure to hold breath after inhalation; this mistake was made by 0–73 % depending on the inhaler. In addition to differences between inhaler types the large range can also be attributed to the fact that different studies used different methods of assessment.

Another common handling error observed in the review article was failure to forcefully and deeply inhale through the device, a mistake made by 0–48 %, depending on inhaler type and study. The great range can also be explained by the fact that different types of inhalers present different requirements for forceful inhalation. Some inhalers can achieve sufficient drug delivery with a smaller inspiratory flow rate whereas other inhalers require much more forceful inhalation in order to achieve optimal drug delivery. Other common inhalation errors included incorrect dose metering (1–46 % of users), incorrect rotation sequence during loading (i.e. rotation of grip until 'click' is heard), a mistake made by 0–45 %); incorrect inhaler position (0–44 % of participants); failure to breathe out slowly after inhalation (2–43 %); and finally, incorrect mouthpiece position (i.e. not positioning the mouth piece correctly between the lips, 0–35 %). The large range for the results can be attributed to the factor such as varying frequency of error for different types of inhaler as well as different methods of assessment used in different studies. (Lavorini et al. 2008)

In addition to the review by Lavorini et al. (2008) other research seems to support that some errors appear to occur more frequently than others. Research by Melani et al. (2004) and Khassawneh et al. (2008) investigated error frequencies for Aerolizer, Turbuhaler and Diskus, and van der Palen's research group focused on the error frequency for Turbuhaler.

In all the mentioned research the patients' inhalation technique was determined based on predetermined steps critical in the patients' inhalation technique. The results were given points and gathered in a table. All participants in these studies were patients who suffered from asthma and had prior inhaler experience. Table 1 lists the most common mistakes made by participants in three different studies regarding inhaler technique for DPIs'.

The errors in Table 1 can all contribute to decreasing the therapeutic effect of the inhalers used. Holding the inhaler in the right position is especially important for reservoir inhalers such as Easyhaler and Turbuhaler. It is essential that they are held in an upright position as the dosing mechanism of the inhalers depends on gravity to fill the dose metering cup (Chrystyn 2007). As such, incorrect inhaler positioning can lead to the patient not receiving the correct dose. As can be seen in Table 1, this error occurred especially for the Turbuhaler, with 37 % of participants using Turbuhaler in the study by Khassawi et al. (2008) and 31 % of participants in a study by van der Palen et al. (1995) making this mistake. Errors related to the breathing technique such as exhaling before inhalation, holding breath after inhalation and not inhaling forcefully enough during the inhalation are all factors that may affect the drug delivery to the lungs (Chrystyn 2007; Lavorini 2013).

Exhalation into a DPI is accompanied by several problems (Basheti et al. 2005). First and foremost exhaled gas can blow the powder out of the chamber, making it unobtainable for inhalation. Secondly exhaled gas is highly humid; this may cause the carrier and/or drug to cake or agglomerate, reducing its ability to break up into individual respirable particles during inspiration.

The final critical error that can be identified in Table 1 is related to the actual loading of the device. Loading the device is a step that assures that the medication is divided into doses and ready to be delivered to the lungs upon inhalation. If this phase is done incorrectly, there is a risk that the parts of the medication, or in some cases even all of it, is not delivered to the lungs and the therapeutic effect is not fully achieved (Chrystyn 2007).

Table 1: The table shows the most common mistakes made by the subjects' during use of dry powder inhalers (%). The error of frequency represents the percentage of participants that made the specified errors in each study.

Error type	**Error frequency in study A (n^1=32)**	**Error frequency in study B (n^1=523, n^2=450)**	**Error frequency in study C (n_1=146, n_2=103)**
The inhaler is not held in the correct position	31 %	27.7 %[1]/ not measured [2]	25.3 % [1]/ not measured [2]
Insufficient emptying of the lungs before inhalation	66 %	24.3 %[1]/ 24.4%[2]	-
Insufficient holding of breath	41 %	47.1 %[1]/ 52.9 %[2]	-
Exhalation into the mouth piece after the inhalation	16 %	21.7 %[1]/ not measured [2]	-
Inhalation is not strong enough	6 %	16.6 %[1]/ 21.7 %[2]	13.7 %[1]/ 3.9 %[2]
Loading the device	-	8.1 %[1]/ 5.9 %[2]	24 %[1]/ not measured[2]

n^1=Number of patients using Turbuhaler, n^2= number of patients using Diskus.
Source: A=van der Palen et al. (1995), B=Melani et al. (2004), C=Khassawneh et al. (2008)

4.4 Ease of use

The most essential criteria to consider when selecting inhalers for patients is ease of use. No matter how exceptional pharmaceutical performance a device has displayed in terms of drug output it will be rendered ineffective, if the device is not used properly. Some research has found ease of use during an asthma attack to be the most important features of an ideal inhaler when patients were asked (Serra-Battles et al. 2002). Chrystyn (2007) argues three main points that affect the ease of use of an inhaler device. These are: the amount of steps needed in order to actuate the device, low requirements on inhaler training and the amount of manual dexterity needed in order to operate the device. In addition to ease of use, patient satisfaction and the patients' abilities such as their lung capacity are important factors that influence the use of the inhaler.

The characteristics and needs of patients who use inhalers are often of such nature that simplicity of operation is of great importance (Serra-Battles et al. 2002). A study assessing the inhalation technique of patients their prescribed DPI or pMDI found that nearly 90 % of patients made at least one mistake in their inhalation technique (van Beerendonk 1998). This research, among others, highlights the importance of providing training for asthma patients with the goal of teaching them to use their DPI correctly. Research has shown that effective training increases the patients' ability to use their inhaler properly (Serre-Batles et al. 2002; Branco Ferreira et al. 1999).

Much of the research available on inhaler technique has been done under clinical conditions and clinical studies often require participants to display good inhaler technique as a prerequisite for participation in the study (Chrystyn 2007). Consequently, real-life studies may be more relevant when evaluation the ease of use of DPIs. When designing an inhaler, it is essential to maximize the simplicity of use for patients in order decrease the possibility for errors. Well-documented comparisons between devices are few, although some data is available. Another problem arises through the fact that many of the available studies have been sponsored by pharmaceutical companies. The results of the studies may therefore have to be examined critically.

Due to the fact that Ellipta is a newcomer to the market very few articles are available regarding its ease of use. The few studies available on Ellipta´s ease of use indicate that the inhaler has been perceived to be easy to handle by patients and inhaler naïve subjects (Svedsater et al. 2013; Svedsater et al. 2014; Komase et al. 2014). The ease of use in asthma patients is most clearly found in an observation from week four of the clinical trials for Ellipta (Svedsater et al. 2014). Participants were asked to fill in a questionnaire regarding the ease of use for the inhaler. A total of 1 050 people participated in the trials, and 94 % of these people completed the questionnaire regarding ease of use. Out of the respondents 65 % stated that the inhaler was very easy to use, and 94 % of respondents reported that it was either easy or very easy to use. Merely 1 % of the respondents expressed had been difficult or very difficult to use. It is important to note that these are self-reported statements by the users from a clinical trial. This may distort the answers in comparison to third party, real life observations.

The perception of Ellipta's ease of use was supported by two comparative studies in inhaler naïve individuals. The first compared the Breezehaler to the Ellipta and Ellipta was preferred based on its ease-of-use features (Komase et al. 2014). Furthermore, it was associated with fewer handling errors. The second study assessed the handling of Ellipta in comparison to the Diskus and Turbuhaler (Sharma et al. 2014). The study showed that an overwhelming majority of users were able to use the Ellipta correctly on their first attempt after reading a leaflet. When the Diskus was demonstrated for the first time 38.2 % of users exhibited one or more mistakes, and for the Turbuhaler 83 % exhibited one or more mistakes upon inhalation. This study was sponsored by GSK.

Many studies have tried to evaluate the ease of use of different inhalers and highlighted the incorrect use of different devices (Chrystyn 2007). Since Turbuhaler and Diskus appear to be among the most widely used DPI's, it is only natural that there would be a large number of studies available, comparing these two inhalers. Most available studies seem to indicate that fewer mistakes where exhibited when using Diskus in comparison to the Turbuhaler (Clay et al. 1994; Backman et al. 2001; Arossa et al. 1998; van der Palen et al. 1998). Many of these studies suggest that the difference in errors among the two inhalers was partially or entirely caused by not loading the Turbuhaler accurately (Backman et al. 2001; Arossa et al.1998; van der Palen et al. 1998). The frequency of error varies greatly between studies. A clinical study by Clay (1994) found that 74 % of patients were able to use the Diskus correctly after a single demonstration in comparison with just 32 % of patients who were able to use the Turbuhaler (Clay 1994). After two training sessions 99 % were able to use the Diskus in comparison with 88 % for the Turbuhaler. In contrast, a randomized crossover comparison of Diskus and Turbuhaler with regards to patient ease of use found that 92 % of participants made no essential inhalation maneuver errors when using the Diskus in comparison with 74 % success rate for the Turbuhaler. The difference can be attributed to the fact that different studies used different methods of assessment as well as other differences in the methodology.

Comparisons of Easyhaler's ease of use to the other inhalers in this study were quite scarce. One study, comparing the inhalation technique for of seven different dry powder inhalers, including Diskus and Easyhaler was, however, found. The study included 72

patients suffering from either asthma or COPD. The lowest level of critical handling errors was observed for the Diskus, the highest numbers were observed for the Easyhaler as well as the Jethaler. The participants of the study all inhaled two times with each inhaler. The first inhalation occurred after reading the device leaflet, and the second after the handling of the device was carefully explained by the investigator. When using the Diskus, 25 % of participants displayed errors during the first inhalation demonstration and 13.9 % during the second one. The corresponding numbers for the Easyhaler was 72.2 % for the first inhalation and 47.2 % for the second one. Device handling for all inhalers improved after instruction was given by the investigator (Schulte et al. 2008).

Finally one study comparing three of the four inhalers used in this study was found. This study compared the Diskus, Easyhaler and Turbuhaler. The results of this study were also interesting due to the fact that they results differed from the previously mentioned comparisons of Diskus and Turbuhaler, as well as Diskus and Easyhaler. The study was a 4 week, phase four, randomized multicenter parallel group trial, comparing the acceptability and correct use amongst 326 inhaler naive asthmatics/symptomatic individuals (Rönmark et al. 2005). The study found no statistically significant difference between the inhalers (Rönmark et al. 2005). After the first demonstration in the trial the following proportion of subjects were able to use the devices without making any mistake: Turbuhaler, 51 %, Easyhaler, 45 %; Diskus, 43 %. During the end of the four week trial, during which additional training was given, the corresponding figures were 89 % for the Diskus, 84 % for the Easyhaler and 81 % for the Turbuhaler.

4.5 Patient preferences and inhaler satisfaction

Patient preference is an important factor to be taken into consideration when determining treatment for an asthma patient. It has even been argued that patient preference might be the most important factor to consider when prescribing a treatment, as even the most effective treatment will not lead to disease control if it is not followed, or if it is used inaccurately (Chrystyn 2005). Some factors regarding treatment preference and adherence of asthma patients can be linked to the intrinsic nature of asthmatic symptoms (Price et al. 2013). One of these factors is considered to be easy access, use and fast relief from an

inhaler in the event of an asthmatic attack. An uncomplicated treatment regimen, preferably with once daily medication, would seem to be desirable for a majority of asthma patients (Price et al. 2011).

Researchers have proposed that patients who use their preferred inhaler might obtain a greater degree of satisfaction with therapy (Anderson 2005). This could be an important advantage for both patients and caregiver in regards to the patient's therapy. Furthermore, it has been suggested that higher satisfaction with inhalers may lead to a higher degree of adherence, improved clinical outcomes and thereby reduced healthcare expenditures (Anderson 2005). Data supporting these types of associations are, however, scarce even though some supporting data has been found. Research by Small et al. (2011) indicates that in real-world situations, the majority of patients' who expressed a high level of satisfaction for their inhaler device were more likely to be observed as compliant to their therapy and to experience better outcomes. As such the level of a patient's satisfaction with their inhaler device was observed to have a positive impact on the treatment goals for asthma.

When assessing the patient's preference for an inhaler device it is important to take a number of factors into consideration, these include the clinical benefit of the medicine and adverse effects (drug dependent), economics and sociocultural factors, such as beliefs, knowledge and education, ease of use, dosing schedule, portability and taste, (Small et al. 2011). Lenney et al. (2000) suggest that the delivery of a drug can be maximized by appropriately prescribing, and assessing which devices patients can use efficiently. Patient preference may also be useful for assessing the patient's acceptance, and hence compliance, with the device.

There are some patient preference comparisons available for the inhalers used for this study. All of the previous research has, however, focused on comparing only two or three of the inhalers and to date no research comparing all four inhalers has been found. The fact that many preference studies are being sponsored by pharmaceutical companies needs to be considered when reviewing the results of these studies. Anderson (2005)

found that out of 23 reviewed studies sponsored by the pharmaceutical industry, the sponsor's device was preferred in 19 cases. Since this may influence the results, sponsorships and affiliations with pharmaceutical companies has been stated in the preference reviews below.

Due to the fact that Ellipta is a newcomer to the market there were not many preference studies available. One study was, however, found. The study measured patient satisfaction and preference among asthma and COPD patients through qualitative interviews. Results showed that 71 % of participants with asthma, and 86 % of participants with COPD, preferred the Ellipta to the Diskus. Additionally the study indicated a clear preference for Ellipta over metered dose inhalers and HandiHaler. The study was sponsored by GSK (Svedsater et al. 2013).

Several studies comparing preference for Diskus and Turbuhaler were found. Out of three studies examined one indicated preference for Turbuhaler over Diskus, and two indicated preference of Diskus over Turbuhaler (van der Palen et al. 1998; Schlaeppi et al. 1996; Serra-Batles et al. 2002). The first study was a sequential comparison where 50 % participants expressed preference the Turbuhaler (34 % preferred Diskus and 16 % were undecided) (van der Palen et al. 1998). The results in this study were not significant. In the two other studies preference was determined through and inhaler demonstration an interview (Schlaeppi et al. 1996; Serra-Batles et al. 2002). Both studies indicated preference for Diskus over Turbuhaler (65 % and 60 % preference over Turbuhaler). In all three studies Turbuhaler was preferred over the Diskus regarding factors related to size and the dose counter of the Diskus was preferred over the Turbuhaler (van der Palen et al. 1998; Schlaeppi et al. 1996; Serra-Batles et al. 2002). Findings by van der Palen et al. (1998) showed a preference for Turbuhaler in the number of available dosages. All three studies were sponsored by GSK (Anderson 2005). No studies comparing Turbuhaler and Diskus, sponsored by Astra Zeneca were found. This is most likely due to the fact that Turbuhaler was launched about 7 years earlier than Diskus and that the GSK sponsored studies were conducted in the context of Diskus launching.

Research comparing the Easyhaler to either Turbuhaler or Diskus and Turbuhaler was found. The studies found indicated a preference for Easyhaler in comparison to Diskus or Turbuhaler. When the Easyhaler was compared with Turbuhaler in a group of 79 DPI-naïve asthmatic patients, the results indicated higher preference for Easyhaler (Jeger et al. 2000). In this study 59 % of participants preferred the Easyhaler, 33 % preferred the Turbuhaler, and 7 % of participants rated them the same (Jager et al. 2000). Preference for Easyhaler over Turbuhaler is supported by another study comparing ease of use for the Turbuhaler and the Easyhaler in a group of 32 asthma patients (Zetterström et al. 2000). Results indicate that a majority of patients who reported the Turbuhaler as their own inhaler considered the Easyhaler better, or much better, than the Turbuhaler (Zetterström et al. 2000). All of these comparative studies where sponsored by or affiliated with Orion Pharma.

Finally one study comparing three of the four inhalers used in this study was found. This was a patient preference study judging patient satisfaction for the Turbuhaler, Diskus/Accuhaler and the Easyhaler. The study found Easyhaler to be the most satisfactory for patients. Unlike the other articles examined this study indicated no sponsorship or affiliations with any pharmaceutical company. Out of 30 patients 53 % indicated Easyhaler was their first choice. The corresponding figures were 27 % for Turbuhaler and 20 % for Diskus. The participants of this study habitually used inhaled corticosteroids, and 83 % of participants had prior experience with one of the devices used in the study (Giner et al. 2004).

4.6 Inhaler education and instructions

Patient education plays one of the most important roles in the patients' use and misuse of asthma inhalers (Fink & Rubin 2005). It has been suggested, that inhalers represent technology that is considered to be so intuitive and easy to use, that a large part of patients and prescribers do not receive sufficient training in their use (Fink & Rubin 2005). The cost implications of incorrect inhaler use are many, and manifest themselves in areas, such as doctor visits, hospitalizations and medication. Research suggests that these costs can be reduced by spending more time on the education of inhaler use (Lenney et al. 2000;

King et al. 1991). Many patients are not aware of the fact that they use their inhalers inadequately, and they often overestimate their own abilities (Erickson et al. 1998; Hämmerlein et al. 2011).

Asthma education can provide added value to asthma patients as it empowers them to manage their disease and increase awareness to danger signs (Sanchis et al. 2013). Patients with a positive attitude towards their therapy have been found more likely to adhere to the medical regimen prescribed to them. In a methodical review of educational programs for asthma, education in self-management was associated with better lung function, reduced school absenteeism and less visits to the emergency departments (Guevara et al. 2003). This was a systematic review study focusing on the effects of educational interventions in children and adolescents.

The knowledge of proper inhaler use is often incomplete, not only amongst patients, but also amongst health care professionals (Price et al. 2012: Self et al. 2007). Self et al. (2007), among others, showed that a majority of health care professionals displayed lack of skill, while demonstrating the use of various asthma inhalers. This information ultimately gives rise to the question: If health care professionals are unaware of how to use certain inhalers, how are they supposed to teach patients how to use them. Research has shown that between 28-68 % of patients do not use metered-dose inhalers or powder inhalers well enough to benefit from the prescribed medication (Fink & Rubin 2005). In addition, between 39-67 % of nurses, respiratory therapists and doctors are unable to sufficiently describe, or perform, critical steps for inhaler use. This observation is supported by Price et al. (2013) who suggest that only 15-69 % of health care professionals were able demonstrate correct inhaler use. This can be seen as an alarming statistic as health care professionals play an important role in patients attaining their goal of achieving correct inhaler technique and maintaining it over time.

Many studies regarding the efficiency of different training methods have been made to evaluate, which one is optimal for achieving correct inhaler technique. There are several

different approaches available for training in inhaler technique. These include written instructions, illustrations, audio visual demonstrations, interactive computer programs as well as personal and small group demonstrations (Lavorini 2013: Sanchis et al. 2013).

Roberts et al. (1982) suggest that provision of the manufacturer's instruction sheet alone was ineffective as a method of providing inhaler instructions, partially due to the fact that patients tended to overlook this information. Other studies have shown that this form of training is inefficient, even for those patients who actually read the leaflet (Melani et al. 2004). For instance, a study measuring the technique for Turbuhaler found that only 6 % demonstrated a correct technique with Turbuhaler after receiving the instructions, and after 3 days of use, 36 % were still not able to use it correctly (Nimmo et al. 1993 as seen in Rönmark et al. 2005). The participants of the before-mentioned study were only given the instructions included in the package insert and were not provided any other assistance. Personal instructions provided by a pharmacist have been found more effective than written instruction and inclusion of a physical demonstration were found to improve the instructed patient's inhaler technique (Basheti et al. 2005).

Personal and small group demonstrations of interactive nature have, so far, proven to be the most effective alternatives (van der Palen et al. 1997). These educational methods have proven to be far more effective than, for example, video demonstrations (Lavorini 2013). Periodic retraining is needed as inhaler technique declines over time, it has been found that the technique must be repeated regularly in order to achieve and maintain correct technique (Takemura et al. 2010; O'Bey et al. 1982). Health care professionals play an important role in the achieving correct inhaler technique and maintaining it over time. Wilson et al. (2010) found that the use of video and print interventions also can promote recall on inhaler use in asthma patients. Research suggests patient knowledge and understanding can be improved by combining visual images and words using video technology (Ferguson 2012). A lack of videos that are sensitive to health literacy [1] makes routine cost-effective implementation difficult.

[1] WHO defines health literacy as "the cognitive and social skills which determine the motivation and ability of individuals to gain access to, understand and use information in ways which promote and maintain good health"

Mechanical or computer-based devices have been found to aid in technique training and these methods could prove to be both useful and time-saving additions to one-on one training sessions with a doctor, nurse or pharmacist (Hardwell et al. 2008). Their value must, however, not be overestimated, as a substantial proportion of patients still have incorrect inhalation technique despite several training sessions. Research of instructional videos in e-learning has found that students who were provided interactive educational videos achieved significantly better learning performance and a higher level of learner satisfaction than those who were provided a non-interactive video or no video at all. The findings of the study strongly indicated that it may be important to integrate interactive instructional video into e-learning systems (Zhang et al. 2006).

4.7 Factors that should influence the selection of an inhaler device

There are several international and national guidelines which have been created to guide patients in the process of their asthma treatment. Despite of this, Dolovich et al. (2005) argue that there are not enough guidelines based on scientific evidence. There are a number of factors that play a part in choosing the best inhaler for a patient. Currently there is no inhaler available on the market that would meet every patient's needs, and therefore the choice of an asthma inhaler has to be tailored to each patient individually taking their characteristics and needs into careful consideration (Hess 2008; Roche et al. 2013).

When choosing the most suitable treatment for a patient there are several factors that need to be taken into consideration. Roche et al. (2013) suggest that based on the patients age and clinical conditions, physicians should aim to choose an inhaler that the patients is able to use correctly. When prescribing inhalers to special populations, such as children or elderly, many distinctive elements need to be considered (Dolovich et al. 2005). These populations often display difficulty with coordination and the triggering of the device. Elderly patients frequently exhibit deteriorated agility in their hands, therefore it may become difficult to operate certain inhaler devices (Hess 2008). Inhalation flow rate is another factor that needs to be taken into consideration when prescribing asthma inhalers

for special populations, such as the elderly and children. This is important as a high enough inhalation flow rate is required in order for the therapy to be efficient.

Some cases of asthma require the patient to use several inhalers. If this is the case it is in the interest of the patient to prescribe as similar inhaler devices as possible (Khassawneh et al. 2008). Patients who use several different inhalers are at a higher risk of getting confused with the instructions, and they usually require more time to learn how to use their devices correctly (Melani 2007). If possible, doctors should try to prescribe combination preparations, rather than separate inhalers for each active ingredient. Combination inhalers decrease the number of doses needed throughout the day (Rau 2005). A lower number of daily doses have been shown to increase the patient's adherence to the prescribed therapy (Rau 2005; Melani 2007).

Research by Melani et al. (2007) suggests that the preferences of the prescribing doctor and the patient play a central part in the patient's adherence to the prescribed therapy. The time it takes for the patient to administer a dose, the ease at which the inhaler device is cleaned and its portability, and durability are also factors that need to be considered when prescribing an inhaler device (Melani 2007; Hess 2008; Chrystyn & Price 2009). The next chapter will examine different inhaler types and their distinguishing properties.

4.8 The characteristics of an ideal inhaler

When aspiring to design an ideal inhaler the needs of the patient should be placed in center of the development process. High levels of device reliability, patient acceptance and clinical efficacy are essential in this process (Ashurst et al. 2000). Many characteristics of the inhaler affect these factors. One major challenge in the development of an ideal inhaler is that needs vary between patients. Schichilone (2015) states that in reality there is no such thing as an ideal inhaler and that one size fits all approaches are not the solution to the problem. Instead an adapted selection of the device based on patient preferences and perceptions should be encouraged and implemented in clinical practice. It is important that the patient is able to achieve and maintain proper inhalation technique as this ultimately effects the efficacy of treatment.

The fact that inhaler needs vary greatly between different patients makes it difficult to develop inhalers. Some characteristics have, however, been established as important to consider when aspiring to develop and ideal inhaler. The inhaler has to be simple to use, easy and convenient to carry around it should contain multiple doses (Ashurst et al. 2000; Newman 2004). The inhaler should also have an audiovisual indicator of doses remaining as this makes use easier for the patient (Ashurst et al. 2000). In order to increase patient acceptance and ease of use the inhaler should also include a feedback mechanism that informs the patient of dose administration (Ashurst et al. 2000; Newman 2004). The design of the inhaler should enable product stability in the device and protect the medicine from moisture (Newman 2004). Cost-effectiveness is another important property of an ideal inhaler (Clark 1995). When looking at factors that influence clinical efficacy and reliability it is important to highlight that the inhaler should display an accurate and uniform dose delivery over a wide range of inspiratory flow rates (Ashurst et al. 2000; Chrystyn 2006; Newman 2004). Moreover the formulation of an ideal inhaler should display optimal particle size of the drug as this is crucial for achieving deep lung delivery (Clark 1995). Finally it is important that an ideal inhaler shows suitability for a wide range of medications and doses (Newman 2004).

Table 2 lists the most important characteristics of an ideal inhaler complied from a number of articles on the subject. In addition to the above mentioned features, an ideal inhaler should contain as few additives, propellant gases and excipients as possible (Melani 2007). Another aspect of an ideal inhaler is that it should not require an external power source or apparatus in order to work, and it should have as little need for maintenance as possible. A final identifying aspect of an ideal inhaler would be that it would have little or no harmful effect on the environment.

Table 2: Characteristics of an ideal inhaler.

Drug delivery
• Excellent drug delivery • Targeted, optimized and reproducible delivery • Little or no delivery active ingredient to the mouth and larynx • Full dose generation even at lower inspiratory flow rates • Fast aerosolization of the dose enabling the possibility of taking a new dose immediately after • Dose precision in all environmental conditions
Inhaler properties
• Multiple doses • Pocket sized and light weighed • Dose counter • Affordable and cost effective • Little or no harmful effect on the environment • Suitable for use in all clinical and environmental conditions • Ability to use with any active ingredient with potent clinical efficacy when administered as an aerosol • No additives, propellant gases or excipients • Suitable for use without requiring external power sources or additional apparatus • Little risk of contamination of active ingredient
Ease of use
• Simple reconstitution process with few steps • Easy to teach and learn • Provides feedback on dose administration • Little of no need for maintenance

Source: Modified from Melani (2007), Ashurst et al. (2000) and Newman & Busse (2002).

4.9 Inhaler devices

Inhalation therapies were initially introduced in the 1950's, when the first a pressurized metered dose inhaler (pMDI) was launched (Islama & Gladki 2008). The first DPI was introduced in 1967 as a single dose device (Islama & Gladki 2008; Crompton 2004). Today DPIs and pMDIs are the most commonly used inhaler devices in the treatment of asthma (Lavorini et al. 2008). Asthma treatment through inhaled therapies facilitate high lung disposition of the drug with minimized systemic bioavailability. This significantly reduces the chance of possible systemic drug interactions (Lavorini et al. 2008).

The technical features of inhaler devices have improved steadily since their introduction to the market (Lavorini et al. 2008). The inhalers used in this study can be seen as representing a part of this development as there has been approximately 25 years between the launching of the first inhaler in this study (Turbuhaler) and the last (Ellipta).

The effectiveness of the delivered dose highly depends on the correct use of the inhaler device. In clinical settings there appears to be no difference between the efficacy a drug delivered though pMDIs or DPIs. Studies from patient use in real life have indicated that pMDIs are more difficult for the patients to use and, hence, are more often used incorrectly (Lavorini et al. 2008; Molimard et al. 2003; Crompton 2004). This ultimately affects the efficiency of the therapy. DPI's were originally developed in an effort to make the inhalation easier for the patient. One of the major benefits of DPIs in comparison to pMDIs is that they enable the patient to inhale the drug without the coordination and actuation required when using pMDIs (Lavorini et al. 2008). Table 3 below shows the advantages and disadvantages of DPIs in comparison to pMDIs.

Table 3: The advantages and disadvantages of dry powder inhalers in comparison to pressurized metered dose inhalers.

Advantages of DPI's	**Disadvantages of DPI's**
• Free from propellants • Less need for patient coordination • Less potential for extractable from device components • Less potential for formulation problems	• More expensive than pMDIs • Design issues, such as device resistance • Dependency inspiratory flow rate and profile of the patient • Potential for problems in dose uniformity

Source: Arshurst et al. (2000)

This study will focus on DPIs and include four inhalers sold on the Finnish market. The next chapter will present the specific characteristics of DPIs and the types of DPIs used in this study.

4.10 Dry powder inhalers

Dry powder inhalers (DPIs) are devices that deliver dry powder formulations of an active ingredient for either local or systemic effect through the pulmonary route (Islama & Gladki 2008). Dry powder formulations are often a mixture of the active pharmaceutical ingredient and an excipient. DPIs use the inspiratory flow energy to deliver the drug dose to the respiratory tract (Crompton 2004). Table 4 lists all of the DPIs that are currently available on the Finnish market.

Table 4: Dry powder inhalers sold on the Finnish market (Pharmaca Fennica 2015; Fimea 2015).

Name *	**Device**	**Manufacturer**	**Number of doses**	**API****
Spiriva	Handihaler	Boehringer Ingel-heim	30, 60 and 90 capsules	Tiotropium
Bricanyl	Turbuhaler	Astra Zeneca	200	Terbutaline
Oxis	Turbuhaler	Astra Zeneca	60	Formoterol
Pulmicort	Turbuhaler	AstraZeneca	100, 200	Budesonid
Symbicort, (also Forte and Mite)	Turbuhaler	Astra Zeneca	60 (Forte), 120	Budesonide, formoterol
Flixotide	Diskus	GSK	60	Fluticasone
Seretide	Diskus	GSK	60	Salmeterol, flutikason
Ventoline	Diskus	GSK	60	Salbutamoli
Relvar	Ellipta	GSK	30	Fluticasone, Vilanterol
Novopulmon	Novolizer	Meda	100, 200	Budesonide
Ventilastin	Novolizer	Meda	200	Salbutamol
Bufomix	Easyhaler	Orion	60, 120	Budesonide, Formoterol
Beclomet	Easyhaler	Orion	100, 200	Beclometasone
Budesonid	Easyhaler	Orion	100, 200	Budesonide
Buventol	Easyhaler	Orion	200	Salbutamol
Fomeda	Easyhaler	Orion	120	Formoterol
Formoterol	Easyhaler	Orion	120	Formoterol
Foradil	Aerolizer	Novartis	30, 60	Formoterol
Asmanex Twisthaler	Twisthaler	Schering-Plough	30, 60	Mometasone
Cycloterol	Cycloterol-inhaler	Laboratoires SMB	60	Formoterol
Formaxa	Formaxa-in-haler	Laboratories SMB	60	Formoterol

* Each medicinal product may have several strengths.
** API - Active pharmaceutical ingredient.

In order to work correctly, all DPIs require an inspiratory flow rate of between 30 l/min and 90 l/min (Al-Showair et al. 2007; Dolovich & Dhand 2011). DPI's with medium resistance to airflow are designed to operate at an optimum inspiratory flow rate of 60 l/min. This rate may, however, not be reached by all patients. Reaching a high enough inspiratory flow rate may prove especially challenging for populations, such as children under the age of six, elderly or patients with gravely impaired lung function (Janssen et

al. 2008; Fink & Rubin 2005).

Each DPI requires a priming procedure, which is specific to the device in question (Sanchis et al. 2013). Understanding and executing the required steps correctly is critical in order to make the drug obtainable for inhalation. The device specific priming steps for the inhalers used in this study will be handled in detail in the methods chapter.

There are several different types of DPIs available on the market. These designs include passive, patient driven devices and active, power-assisted devices (Dolovich & Dhand 2011). Power-assisted devices generally reduce the need for patients to create a high inhalation rate as the power source assists in ensuring delivery on inhalation. Today DPI's represent the most rapidly expanding field in inhaled therapies (Crompton 2004; Islama & Gladki 2008). The phasing out of chloroflurocarbon (CFC) production was thought to have led to increased development of DPIs (Son & McConville 2008; Hendeles et al. 2007). Another factor that is thought to have increased development is the improved availability of drug powders (Dolovich & Dhand 2011).

4.11 Different types of DPI devices and design

There are three main categories of dry powder inhalers; pre-metered single dose inhalers, pre-metered multi-dose inhalers and multi-dose reservoirs (Wright 2009). The inhalers included in this study belong to the two latter categories. As such, these two categories will be explained in further detail below.

4.11.1 Multi-dose DPIs

Multi-dose DPI devices are defined as DPIs that contain more than one dose (Chrystyn 2007). These inhalers can further be divided into two categories: multi-dose reservoir devices and multi-unit devices.

Multi-dose reservoir devices release individual doses with each actuation from a bulk supply of the pharmaceutical held within the inhaler device (Chrystyn 2007). The first

multi-dose reservoir device that was introduced to the market was the AstraZeneca's Turbuhaler, which is used to deliver corticosteroids as well as β2-agonists, either separately, or in combination (Wetterlin 1988). Other multi-dose reservoir inhalers currently for sale on the Finnish market include the Easyhaler (Orion) and the Twisthaler (Schering Plough). These are all newer than the Turbuhaler and throughout their design have been said to focus on minimizing the flow dependent dose emission that has been said to occur in the Turbuhaler (Chrystyn 2007). Another aspect designers have focused on, is adding features that would protect the formulation in the inhaler from moisture during patient use and storage. The Easyhaler has a protective case to protect the inhaler formulation during storage and the hopper on the Easyhaler is designed in order to make it difficult to blow into the inhaler.

Multi-unit dose inhalers are set apart from single unit and reservoir inhalers by the property that they use individually scaled and prepared, sealed doses of drugs (Chrystyn 2007). The first multi-unit dose device introduced to the market was the Aerohaler which contained six unit dose capsules as a magazine. Excipients, such as, lactose are used in multi-unit dose inhalers to improve the dose uniformity. This is achieved by increasing the mass of powder for each dose resulting in minimized inhalation dependent dose emission and improvement of the accuracy of dose metering. Due to the fact that the formulations for these inhalers are sealed into a blister the design offers both a high level of protection against environmental factors like humidity. Because the doses of the pharmaceutical are prepared and separately packaged in the factory, dose uniformity can be secured.

4.12 Dry powder inhalers; the devices used in this study

The four inhalers in this have been chosen as they represent the three most frequently prescribed dry powder inhalers for asthma in Finland; the Diskus, Turbuhaler and Easyhaler, as well as the most recent newcomer to the Finnish market, Ellipta. The inhalers used in this study can be seen as representing a development of DPIs over a 25 year period as there has been approximately 25 years between the launching of the oldest and newest inhaler used in this study. Figure 2 describes the timeline for launching each

of the inhalers used in this study. In this chapter the characteristics for each inhaler will be presented in further detail.

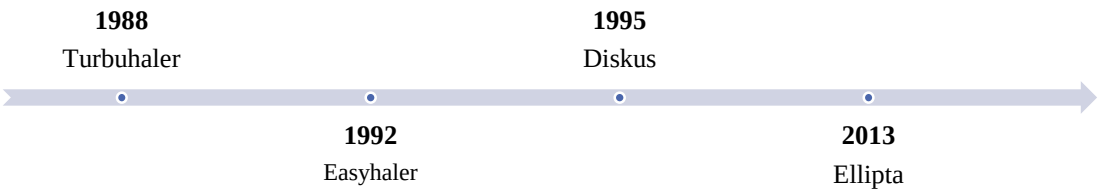


Figure 2: Timeline for when the inhalers used in this study was launched.

4.12.1 Turbuhaler

Turbuhaler was first introduced in 1988 and is today the second most sold dry powder inhaler on the Finnish market (GSK Sales data 2013). The Turbuhaler was the first multi-dose reservoir DPI that was introduced to the market and the inhaler dispenses metered doses from a reservoir inside the inhaler (Wetterlin 1988; Newman & Busse 2002). The drug formulation is used in the Turbuhaler inhalers is agglomerated. When first introduced the Turbuhaler was used to deliver corticosteroids as well as β2-agonists, either separately, or in combination in the treatment of asthma (Wetterlin 1988). During its time on the market the inhaler has been used to deliver formulations of terbutalinesulphate, formoterol, salbutamolorbudesonide or a combination of budesonide and formoterol (Symbicort) (Newman & Busse 2002).

The active ingredient is located within the inhaler in the Turbuhaler it is formulated as a pellet of soft aggregates of drug in its micronized form (Chrystyn 2007). The pellets are approximately 0.5 mm in diameter without any excipient (Newman & Busse 2002). These pellets can either contain lactose monohydrate as an excipient or the active ingredient can stand alone (Chrystyn 2007). Of the medicines using Turbuhaler as a device on the Finnish market, Oxis and Symbicort Turbuhaler both contain lactose monohydrate as an excipient in the pellets, whereas Bricanyl Turbuhaler and Pulmicort Turbuhaler contain no excipients (Pharmaca Fennica 2015). Figure 3 shows the structure of the Turbuhaler and identifies the different components of the inhaler. The blue arrows represent the air flow that is created within the device upon inhalation.

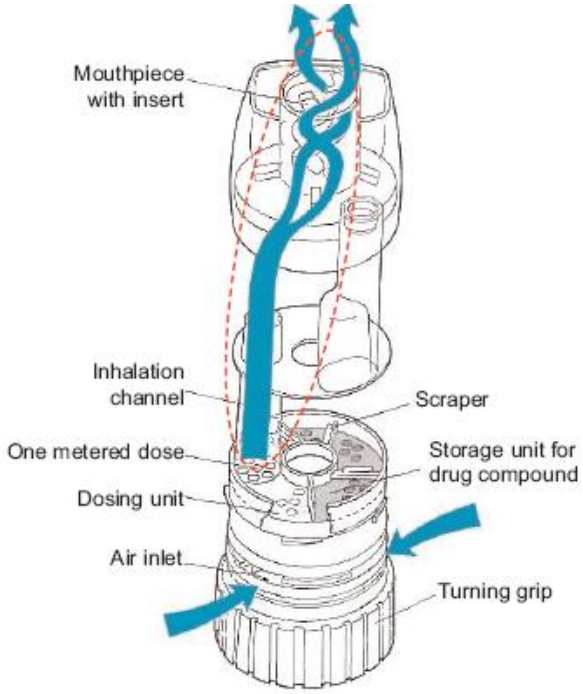


Figure 3: The design scheme of the Turbuhaler. The blue arrows represent the air flow that is created upon inhalation, according to Azouz & Chrystyn (2012).

In order for patients to release a dose from the Turbuhaler patients twists the base of the inhaler, while holding it in a vertical position (Chrystyn 2007). This leads to a dose being shaved off of the pellet. Due to this dosing mechanism it is essential that the Turbuhaler be kept in an upright position. It is essential that the upright position is held for all reservoir DPIs as they depend on gravity to fill the dose metering cup (Chrystyn 2007). The aerosol dispersion mechanism of the Turbuhaler is based so called discharge channels (Frijlink & De Boer 2004). The aerosol is conducted through specifically shaped discharge channel, or channels with helical inserts.

As the patient inhales through the device the dose is dispersed by turbulent airflow (Chrystyn 2007). The energy, which is created by the turbulent air flow then disperse the particles in the emitted dose. These particles are sufficiently small to have a high probability of depositing in the conducting airways (Chrystyn 2007).

4.12.2 Easyhaler

Easyhaler is a multi-unit reservoir dry powder inhaler that can hold up to 200 doses of drug formulation (Newman & Busse 2002). The Easyhaler is marketed by Orion Pharma and has been used to deliver formulations of salbutamol and BDP with lactose monohydrate acting as an excipient. The first Easyhaler was launched into the Finnish market in 1992 (Orion 2015).

Even though the Easyhaler is a DPI reservoir device, the shape and operating sequence of the inhaler is rather similar to those of pMDIs (Smith & Parry-Billings 2003). The Easyhaler consists of seven plastic components and one spring made of stainless steel. The reservoir in the device contains the powdered drug formulation. Below the reservoir there is a metering cylinder with dose cavities that on its surface. The metering cylinder is able to rotate and thereby dose the powder in the reservoir. The Easyhaler utilizes the Venturi effect[2] as its aerosol-dispersion mechanism, and the aerosol passes through narrow tubes, or so called venturi tubes, upon delivery (Frijlink & De Boer 2004).

Picture 1 in Figure 4 shows a cross-sectional cut of the Easyhaler. Picture 2 in Figure 4 depicts how the device functions when the patients performs an inhalation correctly. First the dosing cup is filled up when the patient shakes the device, while simultaneously holding it in an upright position. Thereafter the device actuation rotates the dosing cup into the inhalation channel whereby the dose is ready for inhalation. The inhalation performed by the patient creates a turbulent airflow in the dosage channel. This turbulent airflow causes the drug-carrier complex to break up into its constituents. The inhalation delivers the active ingredients to the lungs where it acts systemically (Chrystyn 2006).

[2] Merriam Webster's dictionary defines the venturi effect as "a short tube with a tapering constriction in the middle that causes an increase in the velocity of flow of a fluid and a corresponding decrease in fluid pressure and that is used especially in measuring fluid flow or for creating a suction (as for driving aircraft instruments or drawing fuel into the flow stream of a carburetor)"

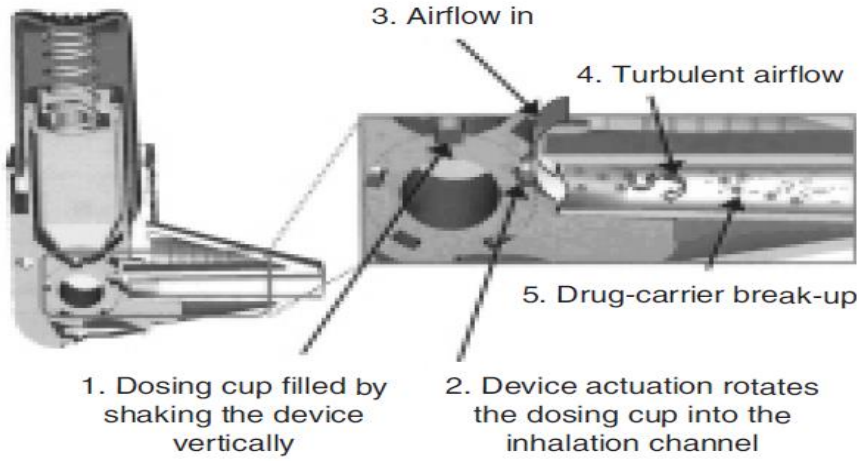


Figure 4: Cross-sectional picture of the Easyhaler inhaler accompanied by a schematic design explaining how the dose is generated during inhalation, Chrystyn (2006).

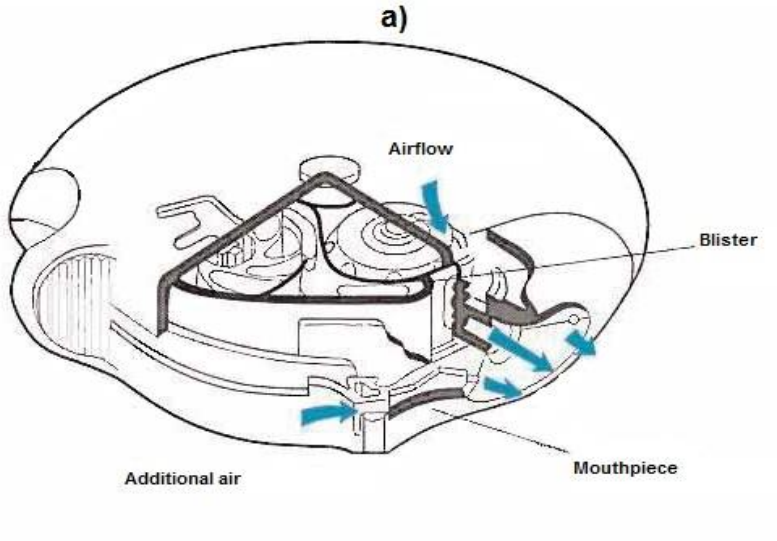
4.12.3 Diskus

Diskus (GSK) is a multi-dose dose device that was first introduced to the market in 1995 and is currently the most frequently sold inhaler on the Finnish market (GSK Sales data 2014). The Diskus is a multi-unit dose device and can be considered a further development of its predecessor the Diskhaler. The Diskus was designed to simplify the use of the Diskhaler by removing the need to manually load the inhaler with cartridges and providing a larger number of doses.

The Diskus contains a coiled strip of 60 individual, pre-metered, double foil-wrapped blister doses that provide up to 1 month's medication (Chrystyn 2007). The double aluminum blister foil assures that each individual dose is protected from environmental factors, such as moisture, dust and light. Each blister contains small drug particles mixed with larger lactose particles that act as a carrier (Borgström et al. 2005). The inhaler has been used to deliver active ingredients, such as fluticasone propionate, salbutamol, salmeterol xinafoate and a combination preparation of fluticasone propionate and salmeterol xinafoate (Newman & Busse 2002). There are several medicines using the Diskus as a delivery device currently available on the Finnish market.

The Diskus is constituted and activated by sliding a lever which transfers the next blister, containing a new dose, into place. The device also contains a ratchet, which causes the inhaler to click when the next dose is positioned properly (Chrystyn 2007). When the device is primed in this way, it leads to the two foil layers being simultaneously peeled apart, thereby exposing the dose and getting the device ready for inhalation. The Diskus also contains a dose counter through which the patient can monitor the amount of doses remaining in the device. Furthermore, the device has an integral outer case which serves the purpose of keeping the inhaler dust free, in addition to resetting the lever. Table 6 lists critical errors that can be made when using the Diskus inhaler.

The Diskus is a so called passive inhaler (Chrystyn 2007). In practice this means that the patient's inhalation disperses the formulation and the therapeutic dose, which reaches the lungs may vary with the strength of the inhalation. Figure 5a shows the different parts of the Diskus and the blue arrows depicts the airflow that occurs during inhalation. Figure 5b shows a cross-sectional schematic design of the inhaler.



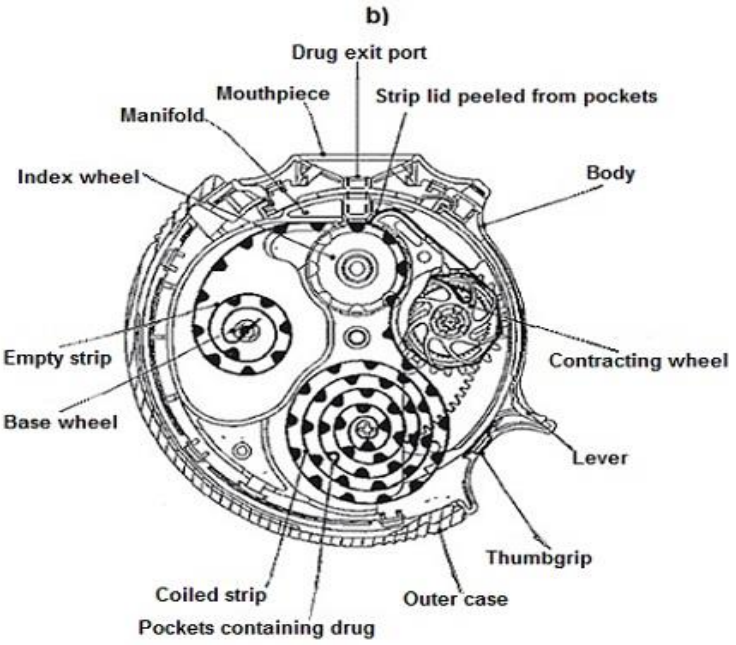


Figure 5a and 5b: Figure a) shows the structure and design of the Diskus inhaler. The blue arrows depict the airflow that occurs during inhalation. Figure b) shows a cross-sectional schematic design of the inhaler (Chrystyn 2007).

The fine particle fraction of the active ingredients used in a dose delivered by Diskus is considered to be low, approximately 20 %. Fine particle fraction is defined as the fine particle dose divided by the dose that is actually delivered (Derom & Thorsson 2001). The fine particle dose is defined as the dose which is delivered in particles that are smaller than 5 μm in diameter

4.12.4 Ellipta

The Ellipta is a handheld multi-unit dry powder inhaler that is relatively new on the Finnish market. Relvar, which is the only medicinal product using the Ellipta inhaler on the Finish market has a formulation that contains flutikasonfuroate and vilanterol as active ingredients and lactose monohydrate and magnesium stearate as excipients. Like in most DPI formulations lactose monohydrate acts as a carrier. Magnesium stearate is increasingly being used as an excipient in dry powder formulations in an attempt to reduce the inter-particulate bonds between carrier and drug particles (Begat et al. 2009; Traini et al. 2012; Hoppentoch et al. 2014). This is accomplished with the use of dispersion agents, or

so-called force control agents (FCAs), such as magnesium stearate (Begat et al. 2009; Traini et al. 2012; Zhou et al. 2013).

Scichilone et al. (2014) suggests that Ellipta belongs to a category of novel inhaler devices designed to be more intuitive than its older counterparts. These inhalers have been designed to operate according to a simple open–inhale–close operation that ensuring ease of use for the patient. The main scope of these new devices is to meet the needs of the patient, by simplifying the inhalation maneuvers and thereby improving adherence to treatment due to fewer mistakes during loading (Scichilone et al. 2014). Ellipta is activated with a single step action featuring a cover that is opened by the patient to uncover the mouthpiece, thereby activating the dose in the inhaler (Svedsater et al. 2014).

A recent exploratory study, suggests that many of Ellipta's attributes are viewed as positive by asthma and COPD patients (Svedsater et al. 2013). The attributes found to be positively viewed by patients included simplicity of operation, ease of use, the visibility and ease of interpretation of the dose counter, the design ergonomics as well as the feel and fit of the inhalation mouthpiece. Figure 6 shows the design and structure of Ellipta and how it is supposed to be operated by patients.

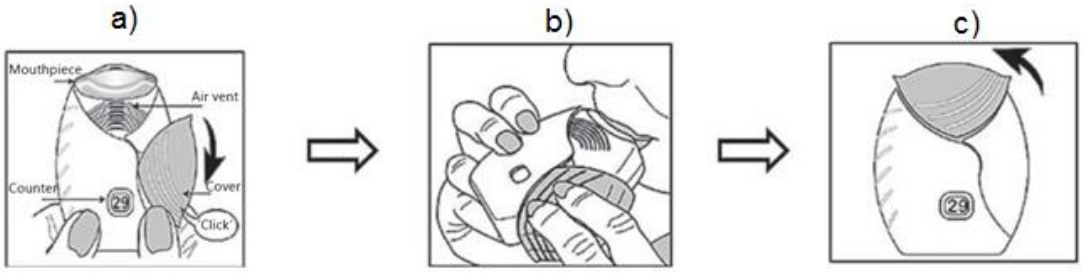


Figure 6: The three-step process for operating the Ellipta inhaler. Picture a) shows the different components of the inhaler, picture b) demonstrates the use of the inhaler and picture c) shows that the inhaler when the cover is on the inhaler and the inhaler is not being used (Lavorini et al. 2014).

4.13 Research gap

Many studies have addressed improper inhaler technique. Despite of this it remains a wide spread problem among asthma patients (Crompton et al. 2006; Lavorini et al. 2008). Most of the studies on the matter have measured the technique of asthma or COPD patients with prior inhaler experience. This study targets healthy inhaler naïve individuals and aims to investigate how easily they learn to use the inhalers in this study. The study measures the frequency of inhaler errors after receiving a video demonstration of the correct inhaler technique. Comparing how the four inhalers are used and perceived by inhaler naïve individuals may help prescribers better understand the needs of asthma patients with no prior inhaler experience.

Due to the fact that Ellipta is relatively new on the market, few studies regarding the inhaler technique have been conducted. The ones performed have mainly addressed inhaler technique in a clinical environment. In other cases the target population has been much older than that of this study. Hence this study may provide valuable information on the perception of Ellipta and the inhaler technique for it in the age group 24-35 years old.

The foundation for this thesis is the idea that easily accessible education in combination with a patient friendly and intuitive inhaler device that leave little room for mistakes could be a step towards reduced inhaler error frequency and increased adherence among asthma patients. Video instructions have been used as an easily accessible teaching method through which patients can get correct standardized instructions whenever they need to. Even though video instructions are commonly used for providing inhaler education, little research regarding the efficiency of this educational method exists. As a result, this study aims to evaluate video instructions as a teaching tool and investigate whether this educational method could be further developed in the future. Addressing the issue of incorrect inhaler use among patients is important as decreasing the amount of inhaler errors could not only contribute to a higher quality of life, but also reduced costs from a healthcare and societal point of view (Sullivan 2005).

5. Method

5.1Data collection and analysis

This study used a *triangular method* for data collection. Methodological triangulation implies a method that combines different methods of data collection (Hämeen-Anttila & Katajavuori 2008a). Quantitative data was collected through semi-structured interviews using the questionnaire frameworks that can be found in Appendix 1 and 2. All of the participants were asked to fill in a total of 5 questionnaires, including one for each device. In addition, observational qualitative data was collected through videotaping of the participants and note taking during the inhalation process. The data collection plan, including questionnaires as well all other material distributed to the participants, was reviewed and approved by the Ethical Review Board in the Humanities, Social and Behavioral Sciences at the university of Helsinki.

The questionnaires used for this study was built up as a *structured interview* and contained both open ended and closed questions. The participants were able to ask clarifying questions while filling in the questionnaires. This was considered to possibly eliminate the risk of misunderstandings among participants.

First the participant filled in a questionnaire containing closed, multiple choice questions. The purpose of this questionnaire was to collect information in the form of control variables and make sure that all participants fulfill the criteria for participating in the study. The purpose of the second questionnaire was to measure the participants' perception of each inhaler's different properties, their user experience and perception of the educational material. An identical questionnaire was completed for each device. The subjects' responses to questions assessing their perception of different aspects of the devices were elicited using a five-point Likert scale (strongly disagree, disagree, neutral, agree and strongly agree). In addition the questionnaire contained some open questions. The purpose of these questions were to give participants the opportunity to elaborate more freely on their opinions regarding the devices.

Before starting the process of data collection, the process was piloted. One individual acted as pilot for this study. After completing all four inhaler demonstrations the participant remembered he might have been prescribed one of the inhalers for a cough. Furthermore, the piloted individual did not receive the same instructions as the rest of the participants of the study. Due to these two factors the results may not have been comparable and the pilot was excluded from the results. As a result of the piloting, the procedure of additionally asking, if the participants had been prescribed any of the inhalers for any other purposes than asthma/COPD was added. In the pilot some issues regarding the instructions given to the participants arose. After the pilot testing of the data collection process, a checklist for information that were to be given to each participant was constructed. This checklist was created in order to assure the repeatability and generalizability of the study and it was used for all of the participants throughout the data collection process.

The order in which the participants handled the inhalers was randomized by lottery. The order in which the inhalers were to be used was determined before the process started. Then participants received video instructions for each inhaler. In order to simulate a situation in which the participants would have been watching the video at home, all participants were told that they were allowed to pause and go back in the videos, if they chose to do this, they were asked to write it down on their questionnaire paper.

After watching the educational video for a particular inhaler, the participants were asked to demonstrate the use of this inhaler. This demonstration was videotaped. Participants received no additional verbal or demonstrative instructions during the video demonstration. They were asked to demonstrate their first attempt of using the inhaler. Subjects then crossed over to the other inhalers in a random order. Preference was assessed using a self-completed questionnaire containing both open and closed questions. All comments made by the participants related to the inhalers or the video material were written down and used to complement the answers in the open-ended questions. The participants' inhaler demonstrations were filmed and assessed both during the demonstration and afterwards from a videotape using an inhaler specific checklist. The participants did not inhale any medication in the study, therefore efficacy and safety were not measured. As no PEF

meter was used during the study air flow resistance and strength of inhalation were not assessed.

The collected data was of both a qualitative and quantitative nature. The quantitative data, such as the scores for inhaler handling were put in tables and quantified. After putting the quantified collected data in tables it was easy to compare the participants' answers for the different inhalers to one another.

The results from the structured interview were themed into different categories and repeated answers and phenomenon's were observed and noted. The notes made based on the participants comments during and after the inhaler testing were also included in these themed comments from the structured interviews. The scoring methods for inhaler frequency and preference will be described in further detail in this chapter.

5.2 Video-taping and questionnaires

The participants started the data collection process by filling in a questionnaire with multiple choice questions. The questionnaire included general information about the participants' gender, age, educational level and home town. These questions act as control variables. The first questionnaire also contains questions designed to assure that the participants are considered inhaler naïve by the definition of this study. The questionnaires and educational videos used in this study were provided in Finnish and the outline of the questionnaires can be found in Appendix 1 and 2. A small number of the participants recruited indicated that their mother tongue was Swedish. In an attempt to eliminate any misunderstanding that might have arisen from answering the questions in a language other than their mother tongue, Swedish speaking participants were encouraged to answer the questions in Swedish.

After filling in the first questionnaire, participants were shown a demonstrational video of one of the inhalers produced by the Association of Finnish Pharmacies (Apteekkariliitto). After this the participants were asked to demonstrate the use of a particular inhaler and this demonstration was videotaped. After demonstrating how they would use

the inhaler for which they had just received video instructions, they were asked to fill in a questionnaires containing questions regarding the inhaler experience, their perception of the inhaler and its properties, as well as, their perception of the educational video. This process was be repeated for each inhaler until the patient had seen, and demonstrated the use of all four inhalers. The fact that demonstrations were provided via video was a conscious attempt to guarantee that the presented instructions were the same each time and subsequently avoid that the inhaler demonstration itself would give cause to possible biases towards any particular inhaler. In order to further avoid biases towards one particular inhaler any visible company logos on the placebo-inhalers used were covered with tape.

Previous studies have concluded that it is difficult to observe, measure, and judge inhalation technique, primarily due to the speed in which direct observed inhalation takes place. Most studies examining inhalation technique are subjective by design as instructors often assess the technique themselves (Rootmensen et al. 2010). Furthermore, investigators are often not blinded and little or no information is given about the kind of training received. This form of study design raises the prospect of observer bias and the likelihood of poor intra-observer repeatability (Rootmensen et al. 2010). Therefore, the videotaped demonstrations were judged using a predefined checklist specific for each inhaler. When all demonstrations had been judged, random checks were carried out in order to ensure that no mistakes were made in the judging. The judging of the inhalation videos and the random checks were conducted by the same individual several days apart in an attempt to create distance between the scoring of one videos.

After completing the video tape demonstration the participants were asked to fill in a form with questions regarding their opinions of the inhaler, the instructions given as well as a self-evaluation of their own performance.

5.3 Population and sample

People without asthma and no experience of handling asthma inhalers were recruited from the general public. The chosen population consisted of 25- 34 year old males and females as statistics provided by the National Institute for Health and Welfare (THL) showed that

asthma is most prevalent for this age group in the adult population in Finland; this can be observed in Table 5 (Borodulin et al. 2013). The distribution of asthma in different age groups varies between the sexes. In Helsinki and Vantaa, the age group in which asthma seems to occur most appears to be 25-34 years old for both sexes, this can be seen in Table 6 (Borodulin et al. 2013). A prerequisite for participation was that all subjects had to be entirely inexperienced in inhaler use.

Table 5: Prevalence of asthma in different age groups (Borodulin et al. 2013).

Finland (weighed average)					
Age group (years)	25–34	35–44	45–54	55–64	65–74
Percentage (%)	12.2	9.0	9.5	8.3	11.5
Number of participants	1036	1187	1294	1383	1475
Helsinki and Vantaa					
Age group (years)	25–34	35–44	45–54	55–64	65–74
Percentage (%)	13.5	7.9	10.3	9.9	9.9
Number of participants	193	215	251	263	292

Table 6: Prevalence of asthma for men and women between different age groups (Borodulin et al. 2013).

Finland (weighed average)										
	Men					**Women**				
Age group (years)	25–34	35–44	45–54	55–64	65–74	25–34	35–44	45–54	55–64	65–74
Percentage (%)	11.5	9.7	9.4	8.0	8.1	12.7	8.4	9.6	12.7	15.0
Number of participants	444	544	605	661	757	592	643	689	722	718
Helsinki and Vantaa										
	Men					**Women**				
Age group (years)	25–34	35–44	45–54	55–64	65–74	25–34	35–44	45–54	55–64	65–74
Percentage (%)	11.8	11.8	8.7	5.4	9.0	14.8	4.4	12.0	11.9	11.0
Number of participants	85	102	126	129	156	108	113	125	134	136

The individuals who belonged to the selected population were made aware of the study through fliers posted in a number of relevant locations, such as educational institutions, libraries, grocery stores and public places. Individuals who did not belong to the chosen age group were excluded from the study. The chosen participants were all individuals

living or working in the Helsinki Metropolitan area, as research has shown that asthma is more prevalent in larger city populations (Wisnivesky et al. 2005). After this the people who had been made aware of the study were themselves able to choose whether or not they wanted to participate in the research project. This form of sampling technique is called self-selection sampling (Saunders et al. 2012).

Purposive sampling was also used in the recruiting of candidates for this study. When using *purposive sampling* all participants have to fulfill certain predetermined criteria in order to be eligible to participate in the study (Hämeen-Anttila & Katajavuori 2008b). For example, this study only included participants within a predetermined age group who were classified as being inhaler naïve. For the purpose of this study subjects were considered inhaler naïve if they did not have asthma, nor any experience in using any type of inhaler devices. Subjects who indicated that they had worked within the pharmaceutical industry, at a pharmacy, or had family members who suffered from asthma, were excluded from the study as it was considered that their prior experience with a certain asthma inhaler could lead to a bias towards a particular inhaler in the study. The data was collected during the span of 1.5 months. The long period for data collection stemmed from a difficulty in finding volunteers.

At the beginning of the study an aim of reaching a sample size of at least 30 participants was set. In the end 31 people ended up participating in the study. The Central Limit Theorem (CLT)[3] determines that when the sample size is 30 or more, the sample size is large enough according to the Central Limit Theorem. With this sample size the average could be considered to be normal even if the sample does not come from a normal distribution. Consequently, when sample size is 30 or more, there is no need to check whether the sample originates from a Normal Distribution (Hays 1981).

In the end a total of 31 people participated in this study. The average age of the participants was 28 years, 17 participants were men and 14 were women. A large majority of

[3] According to Merriam Webster's dictionary CLT is a theorem which states that the distribution of a mean of a sample from a population with finite variance is approximated by the normal distribution as the number in the sample becomes large

participants in this study had an academic education (23/31), 5 participants had attended a university for applied sciences and 3 participants had completed secondary education. All participants lived or worked in the Helsinki Metropolitan Area. Two people who had announced they were willing to participate had to be excluded from the study. The pilot was excluded from the study due to the fact that this person did not receive the same instructions as the rest of the participants and had been prescribed one of the inhalers for a severe cough. Due to this indiscretion there was a fear that the results would not be comparable.

5.4 Scoring method

5.4.1 Scoring inhaler errors

The frequency of error for each inhaler was determined by scoring the participants' performance and errors were recorded against a predefined list of steps for each inhaler. Educational videos produced by the Association of Finnish Pharmacies were used to determine the check lists for each inhaler. Only errors that could influence the efficacy of treatment were noted. For the purpose of this study critical errors were defined as errors, displays of flawed technique or lack of knowledge in regards to the usage of the inhaler device that is likely to impair the delivery of adequate medication on all occasions of drug administration (Price et al. 2013). Tables 7-10 show the inhaler instructions patients received for each inhaler in the educational videos as well as the errors deemed critical for each inhaler.

The assessment form for correct use included six items for all inhalers in this study. The assessments vary somewhat from each other depending on the instructions given to participants. For example ‘‘Holding one's breath after the inhalation’’ was assessed for Diskus, Easyhaler and Ellipta, but not for Turbuhaler, because this instruction was not included in the video instructions.

Table 7: The instructions column describes the instructions given in the educational video for Turbuhaler. The second column describes the inhaler errors measured for Turbuhaler in this study.

Inhaler	**Instructions**	**Errors measured**
Turbuha- ler	1. Unscrew the cap and take it off. Hold the inhaler upright 2. Twist the grip of your Turbuhaler as far as it will go. Then twist it all the way back. When twisting you will hear a "click" 3. Breathe out deeply away from the device 4. Put the mouthpiece between your teeth, and close your lips around it. 5. Breathe in forcefully and deeply through your mouth 6. Remove the Turbuhaler from your mouth and calmly breathe out through the nose. 7. Replace the cap	1. Failure to open device 2. Failure to hold device in right position 3. Failure to emptying lungs before inhalation 4. Failure to load device 5. Failure to breathe out through the nose after inhalation 6. Exhalation into the mouth piece

Source: Price et al. (2012); Association of Finnish Pharmacies (2015); van der Palen et al. (1995); Melani et al. (2004); Khassawneh et al. (2008)

For Turbuhaler "breathe out through nose after inhalation" was assessed instead of "holding ones breathe" (see Table 7). The period for which participants were to hold their breath varied depending on the instructions given to them (see Tables 8, 9 and 10).

Table 8: The instructions column describes the instructions given in the educational video for Easyhaler. The second column describes the inhaler errors measured for Easyhaler in this study.

Inhaler	**Instructions**	**Errors measured**
Easyhaler	1. Open the protective cover 2. Insert the inhaler in a protective case. Make sure that the cover is on the mouthpiece. 3. Remove the mouthpiece cover 4. Shake the inhaler vigorously up and down 3-5 times. Do not trigger the inhaler when shaking it! 5. Hold the inhaler upright 6. Trigger the inhaler once until you hear a click and let the inhaler return to its original position. 7. Keep holding the inhaler in an upright position 8. Breathe out normally 9. Place the mouthpiece in your mouth between your teeth and close your lips tightly around the mouthpiece 10. Breathe in through your mouth in forcefully and deeply. Take the mouthpiece out of your mouth. 11. Hold your breath for at least 5 seconds and then breathe out through your nose. 12. Close the protective cover	1. Failure to open device 2. Failure to hold device in right position 3. Failure to emptying lungs before inhalation 4. Failure to load device - Failure to shake device - Failure to press button - Loading in wrong order - Triggering inhaler when shaking it 5. Failure to hold breath at least 5 seconds after inhalation 6. Exhalation into the mouth piece

Source: Price et al. (2012); Association of Finnish Pharmacies (2015); van der Palen et al. (1995); Melani et al. (2004); Khassawneh et al. (2008)

Table 9: The instructions column describes the instructions given in the educational video for Diskus. The second column describes the inhaler errors measured for Diskus in this study.

Inhaler	Instructions	Errors measured
Diskus	1. Open your Diskus: Hold it in the palm of your hand, put the thumb of your other hand on the thumb grip and push the thumb grip until it "clicks" into place 2. Load the Diskus by holding the device with the mouthpiece towards you. Slide the lever away from you as far as it will go to get your medication ready 3. Adjust your posture. Keep your shoulders down and head held high. 4. Breathe out away from the device for as long as you feel comfortable. 5. Place the mouthpiece gently in your mouth and close your lips around it 6. Breathe in deeply and evenly though the Diskus. 7. Remove the device from your mouth 8. Hold your breath for 5-10 seconds 9. Calmly breath out through your nose 10. Close the Diskus by sliding the thumb grip towards you until you hear a click	1. Failure to open device 2. Failure to hold device in right position 3. Failure to emptying lungs before inhalation 4. Failure to load device 5. Failure to hold breath at least 5-10 seconds after inhalation 6. Exhalation into the mouth piece

Source: Price et al. (2012); Association of Finnish Pharmacies (2015); van der Palen et al. (1995); Melani et al. (2004); Khassawneh et al. (2008)

For Ellipta the device is loaded when opening the device, therefore one step was eliminated for this inhaler. For this inhaler it is however very important that the air vents on the device are not blocked. Therefore an additional error to be measured was added (see Table 10).

Table 10: The instructions column describes the instructions given in the educational video for Ellipta. The second column describes the inhaler errors measured for Ellipta in this study.

Inhaler	Instructions	Errors measured
Ellipta	1. Wait to open the cover until you are ready to take your dose. Do not shake the inhaler 2. Slide the cover down to expose the mouthpiece. You should hear a click. 3. Breathe out away from the device for as long as you feel comfortable. Hold the inhaler away from your mouth - do not breathe out into the mouthpiece. 4. Put the mouthpiece between your lips, and close your lips firmly around it. Do not block the air vent with your fingers. 5. Take one long, steady, deep breath in through your mouth. 6. Hold your breath for at least 3-4 seconds 7. Remove the inhaler from your mouth. Breathe out slowly and gently. 8. Slide the cover upwards as far as it will go, to cover the mouthpiece.	1. Failure to open/load device 2. Failure to hold device in right position 3. Failure to emptying lungs before inhalation 4. Failure to hold breath at least 3-4 seconds after inhalation 5. Holding fingers on air vents 6. Exhalation into the mouth piece

Source: Price et al. (2012); Association of Finnish Pharmacies (2015); van der Palen et al. (1995); Melani et al. (2004); Khassawneh et al. (2008)

In addition to the errors measured, mentioned in Tables 7-10 there are other errors that may affect the inhaler efficacy. This mainly concerns not achieving a forceful enough inhalation. Since this was hard to measure based on observations only, it was excluded from this study. For readers it is however important to note that these factors also affect correct inhaler use.

5.4.2 Scoring the preference of the participants

Preference was assessed using a self-completed questionnaire containing both open and closed questions. After trying all four inhalers the participants were asked to rank the inhalers from 1-4, one being the best score and four being the worst. The distribution of the participants' rankings were counted and presented. This was done by calculating how many percent of participants had chosen each inhaler as first, second third and fourth.

After this the average preference score for each inhaler was calculated. The average preference score represents the average score assigned to each inhaler (scale from 1 to 4) when observing the whole sample (n=31). The lower the average score, the more highly the inhaler was on average ranked by participants. The statistical significance of the differences between the average preference-scores were assessed through running a paired samples t-test in Excel.

In order to gain a deeper understanding of why an inhaler was preferred each participant was asked to motivate why they had chosen their scores for the inhalers. This qualitative information was themed into different categories and the results were used to make comparisons between the inhalers. These motivations were also used to explain, which characteristics were deemed important by participants.

In addition to the open question regarding preference, all participants were asked closed questions regarding inhaler properties such as size, ease of use and ability to carry the inhaler with you if necessary were evaluated using structured questions and a Likert scale ranking. The purpose of these questions was to enable comparisons between different characteristics of the inhaler.

5.5 Statistical tests

5.5.1 T-test

In order to assess the significance of the obtained results from the study t-tests were performed. As the participants using the different inhalers remained constant, a *paired samples t-test* was found to be most suitable.

Shortly summarized the paired samples t-test tests for the probability that the observed difference between the means of two related samples can be explained by sampling error. The paired samples t-tests for frequency of error and preference scoring were calculated for each possible inhaler pairing.

The obtained p values from the t-tests were then observed in order to determine the significance of the differences between the sample means. A p value of 0.05 was used in this study. The differences between inhalers regarding error frequency and preference were therefore deemed significant, if the calculated p value was equal to or less than 0.05. If the calculated value was higher than 0.05, it was assumed that there was no statistically significant difference between the inhalers. The paired samples t-tests were performed using Microsoft Excel 2013 (Maciocha 2012).

6. Results and discussion

6.1 Inhaler error frequency

When observing the frequency of error amongst participants, it was found that only 41 out of 124 inhaler performances, or 33 %, were completed without any mistakes that could compromise the efficacy of the inhaled medication. The results of this study are comparable to other studies of handling error frequency for asthma inhalers. The frequency of error in other studies have varied based on inhaler types and study methodology. Crompton et al. (2006) and Lavorini et al. (2008) found that error frequency could concern as much as 50-94 % of asthma patients depending on the inhaler used.

The percentage of self-evaluated correct use and actual correct use varied greatly. The differences can be observed in Table 11. When examining the participants' use of the inhalers, Ellipta proved to be the one that was most often used correctly. Out of the participants 84 % thought they had used the inhaler without making any mistakes. The actual number of participants who were able to use the inhaler was 55 %. During self-evaluation for Diskus the same amount (84 %) reported that they had used the inhaler correctly. The actual amount who was able to use the inhaler without making any mistakes was 48 % of participants.

Easyhaler was evidently perceived to be more difficult to use than the two previously mentioned inhalers. The number of participants who thought they had handled the inhaler

correctly was 74 % of participants. The number of participants who actually used the inhaler correctly was much lower than the results obtained through the self-evaluation. The percentage of participants, who were actually able to use Easyhaler without making any mistakes, was 19 %.

Out of all four inhalers Turbuhaler was clearly perceived to be the hardest to use with 65 % of participants stating that they had used the inhaler correctly. The actual number of participants who were able to use the inhaler correctly without making any mistakes was 16 %.

Table 11: The percentages for self-evaluated correct use and actual correct use for each inhaler type.

Number of participants who believed they had used inhaled correctly				**Number of participants who actually used the inhaler correctly**			
Diskus	Easyhaler	Ellipta	Turbu-haler	Diskus	Easyhaler	Ellipta	Turbu-haler
84 %	74 %	84 %	65 %	48%	19 %	55%	16 %

When comparing the frequency of error for the different inhaler types, not all differences were deemed statistically significant. The difference between average frequency of error for Ellipta and Diskus was statistically insignificant ($p = 0.103$). So was the difference between Turbuhaler and Easyhaler ($p = 0.655$). When examining the average error frequency for Ellipta in comparison to the Easyhaler and Turbuhaler the differences were statistically significant ($p = 8.4 \times 10^{-5}$ and $p = 3.6 \times 10^{-6}$). The average frequency of error was also deemed statistically significant between Diskus and Easyhaler as well as the Turbuhaler ($p = 0.001$ and $p = 0.005$). Table 12 shows the average frequency of error for each inhaler, as well as the p values from the paired samples t-tests.

Table 12: Average frequency of error for each inhaler and the p values from the paired samples t-tests. The average frequency of error represents the average number of mistakes made for each inhaler when observing the whole sample (n=31). P values equal to or less than 0.05 are indicated by *.

	Easyhaler (1.42)	**Ellipta** (0.52)	**Turbuhaler** (1.32)
Diskus (0.77)	**p=0.001***	p=0.103	**p=0.005***
Easyhaler (1.42)	-	**$p=8.4 \times 10^{-5}$ ***	p=0.655
Ellipta (0.52)	-	-	**$p=3.6 \times 10^{-6}$***

Based on the distinct difference between the participants' self-assed frequency of error in comparison to the actual one, it is clear that participants often thought they were using the inhaler correctly when they in fact were making mistakes. This is consistent with research from other studies regarding inhaler technique of asthma patients, which have found that many patients might not be aware of the fact that they are using their inhalers incorrectly (Erickson et al. 1998; Hämmerlein et al. 2011). Furthermore, it has been found that asthma patients often overestimate their own abilities and inhaler technique (Erickson et al. 1998; Hämmerlein et al. 2011). Studies regarding asthma patients' adherence to therapy have also shown that the self-reported adherence often is higher than the actual adherence to prescribed therapy (Bae et al. 2009).

The phenomenon described above should be taken into careful consideration by prescribers and pharmacists when refilling prescriptions and dispensing inhaler medication to asthma patients. Many asthma patients may be under the impression that they have perfect inhaler technique and that they are not in the need of additional instructions. Based on this study, and further supported by others, patients may very well need help in correcting their inhalation technique as they may not be aware of their mistakes.

Fink and Rubin (2005), among others, have suggested that inhalers represent technology that is considered to be so intuitive and easy to use that a large part of patients and prescribers do not receive sufficient training. This type of attitude towards asthma inhalers

and inhaler education is supported by some documented comments from the participants in this study. A few participants declared that they could not understand how these inhalers could be misused. This may have resulted in them paying less attention to the instructions given. After completing all four inhaler demonstrations and filling in all the questionnaires for the study a number of participants wanted to know, whether they had used the inhalers correctly. Many participants were shocked to learn that they had made mistakes. This supports the claim by Fink and Rubin (2005). The perception of inhalers as very intuitive and easy to use may lead to the importance of instructions being overlooked.

Table 13 presents a short summary of the most common mistakes detected for each inhaler type. The different types of inhaler errors and their frequency will be presented in further detail later on in this chapter.

Table 13: A short summary of the most common mistakes for each inhaler.

Inhalers	**Most common mistake ***	**Second most common mistake ***
Diskus	Insufficient emptying of the lungs before inhalation (42 %)	Insufficient holding of breath (29 %)
Easyhaler	Insufficient emptying of the lungs before inhalation (65 %)	Insufficient holding of breath (39 %)
Ellipta	Insufficient emptying of the lungs before inhalation (26 %)	Insufficient holding of breath (23 %)
Turbuhaler	Insufficient emptying of the lungs before inhalation (48 %) / Failure to load the device (48 %)	The inhaler is not held in the correct position (19 %)

* Percentage of participants who made the mistakes

6.2 Ease of use

In the questionnaires participants were asked to evaluate ease of use for each inhaler. Results show that ease of use was rated highest for Ellipta, with 26 out of 31 participants strongly agreeing with the statement that the inhaler was easy to use. Diskus was perceived as the second easiest to use with 17 out of 31 strongly agreeing with the statement. Easyhaler came in close to Diskus with 15 out 31 participants strongly agreeing that the inhaler was easy to use. Turbuhaler was perceived as the hardest to use with only 8 out of 31 participants strongly agreeing that the inhaler was easy to use.

The perception of ease of use in this study correlates well with the actual correct use observed among participants (see Table 11). As can be observed from the error frequencies found in the previous section, Ellipta emerged as the most frequently correct used inhaler out of all the inhalers in this study. Thereafter came the Diskus, Easyhaler was third and most handling errors was displayed with the Turbuhaler. There was no statistical difference between Ellipta and Diskus.

No other studies comparing the ease of use for Ellipta, Diskus, Easyhaler and Turbuhaler has been found. The order of easiest to hardest to use does, however, appear be to be supported by some studies. On the other hand, other studies contradict the findings of this study. One study assessing the competence of inhaler-naïve subjects in handling the Ellipta in comparison to the Diskus and the Turbuhaler and found that an overwhelming majority of users were able to use the Ellipta correctly on their first attempt after reading the inhaler handling leaflet (Sharma et al. 2014). These findings are not fully supported by this study as only a very small majority was able to successfully perform the inhalation process for Ellipta on their first attempt.

The results by Sharma et al. (2014) indicated that 38.2 % of users exhibited one or more mistakes when using Diskus for the first time. The participants of this study did, however, display a much higher incidence of errors using the Diskus with 62 % of participants making one or more mistakes. Sharma et al. (2014) found that 83 % of participants exhibited one or more mistakes upon inhalation when demonstrating the use of Turbuhaler for the first time. The frequency of for the Turbuhaler in this study was 87.1 %. There are some variations between the percentages of error frequencies of the study conducted by Sharma et al. (2014) and the results of this study. The order of easiest to use, to hardest to use is, however, consistent with the findings of this study.

Results by Clay (1994) also seem to support some of the findings of this study. Clay (1994) found that 74 % of patients were able to use the Diskus correctly after a single demonstration in comparison with just 32 % of patients who were able to use the Tur-

buhaler (Clay 1994). The fact that the Diskus is more often used correctly than the Turbuhaler is supported by the findings of this study. Clinical studies tend to exclude patients who exhibit suboptimal inhaler technique (Haughney et al. 2010). This may create a distorted perception of inhaler use and handling errors patients face in everyday life. The frequencies of correct inhaler technique for both Diskus and Turbuhaler appeared to be much higher in the study by Clay (1994) in comparison with results from this study. The findings that the Diskus appeared to be easier to use correctly than the Turbuhaler is, however, supported by the results of this study.

Not all previous research is in line with the findings of this study. A randomized multicenter parallel group trial compared correct use and acceptability of Diskus, Turbuhaler, and Easyhaler among 326 inhaler naive asthmatics/symptomatics (Rönmark et al. 2005). The differences between the inhalers in Rönmark's study were not significant. In this study, the difference in frequency of error was not significant between Easyhaler and Turbuhaler. The frequency of error for both inhalers in comparison to Diskus, was however significant.

After receiving the first demonstration in the trial by Rönmark et al. (2005) the following proportion of subjects were able to use the device correctly: Turbuhaler, 51 %, Easyhaler, 45 %; Diskus, 43 %. During the end of the four week trial, during which additional training was given, the corresponding figures were 89 % for the Diskus, 84 % for the Easyhaler and 81% for the Turbuhaler. Ellipta had not yet been launched at the time of which the study was conducted. The difference between the results of this study in comparison with Rönmark et al. (2005) is rather surprising. Much like this study, Rönmark et al. used inhaler naïve individuals and a validated scoring method using videotaped demonstrations of the inhaler performances. The most significant difference between the studies is the use of the product leaflet as an educational method. It is unclear whether the leaflet could be read during the actual inhalation demonstration. This may have promoted better recall of the process and led to lower error frequencies than those observed in this study. The leaflet for Easyhaler was reported to be easier to understand than those for Diskus and Turbuhaler (Rönmark et al. 2005). This may have led to better results for Easyhaler, than those observed in this study. Some difference in the difficulty to understand the video

instructions provided in this study were also reported. The videos for Ellipta and Easyhaler were often described as two fast to follow. This may have given these two inhalers in an unfair disadvantage.

The participants of this study were all young adults and a majority had an academic education. Higher educational level has been shown to significantly correlate with scores of correct handling of inhaler devices (Molimard et al. 2003). Furthermore it has been suggested that older people may find it difficult to operate inhalers as poor manual dexterity, weakness, and visual limitations present potential problems affecting inhaler use amongst elderly (Jarvis et al. 2007).The participants of this study should therefore, at least in theory, find it easier to learn how to use the inhalers correctly than many asthma and COPD in the real world. This may be considered alarming as the frequency of error was high (67 %) in the sample population of this study.

6.3 Defining the most common inhaler errors

When analyzing the videos of the participants' inhaler technique some patterns regarding the errors made started emerging. Table 14 lists the inhaler handling errors deemed critical for the inhaler to work properly, and the frequency of the mistakes for each inhaler. In addition to these errors the inspiratory flow rate of the inhalation is deemed a critical step in order for the used DPIs to work properly. Due to the fact that no meter of inspiratory flow rate was available for this study, this critical error was left out. It is, however, important to point out that frequency of error may have been higher, had the strength of the participants inhalations been measured.

Table 14: Most common mistakes made by participants of this study (n=31). Error frequency expressed in percentage within parentheses.

Error	**Diskus**	**Easy-haler**	**Ellipta**	**Turbu-haler**
The inhaler is not held in the correct position	0	2 (6.5 %)	0	6 (19 %)
Insufficient emptying of the lungs before inhalation	13 (42 %)	20 (65 %)	8 (26 %)	15 (48 %)
Insufficient holding of breath	9 (29 %)	12 (39 %)	7 (23 %)	-
Breathing out through mouth after inhalation (Turbuhaler only)	-	-	-	2 (6.5 %)
Exhalation into the mouth piece	2 (6.5 %)	0	0	0
Holding fingers on air vents (Ellipta only)	-	-	0	-
Loading the device	1 (3 %)	7 (23 %)	0	15 (48 %)
Failure to open device	0	0	0	0

n = number of participants.

As observed in Table 14, the most frequent mistakes made by participants were related to the breathing technique that should have been used during inhalation. When analyzing the videos, insufficient emptying of the lungs emerged as the most frequently made mistake for all four inhalers. These results are consistent with the results from a literature review carried out by Lavorini et al. (2008), which indicated that the most frequently observed error was failure to exhale before inhaling through their DPI device; this error was made by 12–77 % participants depending on the inhalers used and with results varying between different studies.

The second most common mistake observed in this study was insufficient holding of breath after the inhalation. This too was consistent with the results by Lavorini et al. (2008). The breathing technique required for Turbuhaler differs slightly from the breathing technique for the other three inhalers in this study. For Diskus, Easyhaler and Ellipta the participants are required to hold their breath for 3-10 seconds depending on the inhaler. For the Turbuhaler no holding of breath is required, instead the participants were asked to breathe out slowly through their nose after completing the inhalation. As seen in Table 14, much fewer mistakes were made for the post inhalation breathing technique for Turbuhaler than for the other three inhalers.

Other errors commonly found in previous research included incorrect positioning of the inhaler, incorrect rotation sequence during loading, and failure to execute a forceful and deep enough inhalation (Lavorini et al. 2008). The results from previous studies appear to be consistent with the findings of this study.

6.4 Preference

After trying all four inhalers the participants were asked to rank the inhalers from 1-4, one being the best score and four being the worst. Table 15 shows the distribution of the participants' preferences and how often each inhaler was ranked first, second, third and fourth.

Table 15: Distribution of the participants' inhaler rankings.

Ranking	Diskus	Easyhaler	Ellipta	Turbuhaler
1st	9.7 % (3/31)	12.9 % (4/31)	51.6 % (16/31)	25.8 % (8/31)
2nd	45.1 % (14/31)	19.4 % (6/31)	9.7 % (3/31)	25.8 % (8/31)
3rd	22.6 % (7/31)	25.8 % (8/31)	25.8 % (8/31)	25.8 % (8/31)
4th	22.6 % (7/31)	41.9 % (13/31)	12.9 % (4/31)	22.6 % (7/31)

The final rankings, based on the calculated average score given to each inhaler, can be observed in Table 16. The lower the average score, the more highly the inhaler was ranked by participants. The average score was obtained by adding the scores given for each inhaler type and dividing the results by the number of participants. The average preference scores were compared to each other using a paired sample t-test. The results from the t-test can be observed in table 17.

Table 16: The order of preference of the inhalation devices.

Ranking	Inhaler	Average score
1st	Ellipta	2.0
2nd	Turbuhaler	2.5
3rd	Diskus	2.6
4th	Easyhaler	3.0

Ellipta received the lowest average score and was thereby found to be most preferred by participants (see table 16). Ellipta was also chosen as a favorite by most participants with 51.6 % (16/31) of participants stating that Ellipta was their favorite out of the four inhalers. Turbuhaler was the second most preferred inhaler based on the average score. As observed in Table 15 the distribution of preference in the four categories was most even for Turbuhaler with the inhaler receiving almost equal distribution in all categories.

Diskus came in third when measuring the participants' average score. The inhaler was, however, chosen as a favorite the fewest times. As seen in Table 15, only 9.7 % (3/31) chose the inhaler as their favorite. The reason for Diskus receiving a more preferable average score than Easyhaler comes down to the fact that the largest percentage of participants scored it as their second most preferred inhaler. In fact 45.1 % (14/31) of participants chose the inhaler as their second most preferred device.

Based on the average score Easyhaler was the least preferred inhaler amongst the participants of this study. The inhaler was also the one that was chosen to be the least favorite by the largest number of participants. Thirteen out of 31 participants, or 41.9 %, stated that the inhaler was their least preferred out of the four. The inhaler was chosen as a favorite by 12.9 % (4/31) of participants. This is more than the number of individuals who declared Diskus to be their favorite.

When comparing the average preference scores, only the difference between the inhaler that received the highest score (Ellipta) and the inhaler that received the lowest score (Easyhaler) was deemed statistically significant ($p=0.010$). Table 17 presents the p values for each inhaler combination when comparing their average preference scores.

Table 17: The table shows the average preference score for each inhaler, as well as the p values from paired samples t-tests. P values equal to or less than 0.05 are indicated by *.

	Easyhaler (3.0)	**Ellipta** (2.0)	**Turbuhaler** (2.5)
Diskus (2.6)	p=0.178	p=0.059	p=0.690
Easyhaler (3.0)	-	**p=0.010***	p=0.111
Ellipta (2.0)	-	-	p=0.186

The most frequently occurring answer for why Ellipta had been ranked high was the fact that it was easy to use, had few steps and that it was easy to get a grip of and hold correctly. Many participants (6/31) did, however, note that the inhaler looked somewhat boring and some suggested including color to brighten up the device and make it more fun and approachable. Even some (3/32) who ranked Ellipta first in the preference category criticized the design for being boring or colorless and, as one participant put it, "not suitable for young people". Overall 14/31 participants made comments that could be classified as negative, or slightly negative regarding the look and size of Ellipta. Others (8/31) liked the modest design of the inhaler stating that is was neutral and suitable for a medicine.

Turbuhaler received the second best average preference score and received high praises for its size. Many people mentioned that it would be easy to carry around and the design of the device was liked by many participants. The fact that no holding of breath was required after inhalation was also mentioned as a positive aspect of the inhaler. The device was perceived as hard to use by many participants. This was repeatedly mentioned as a negative aspect. It was also commented that the text on the dose counter was written with very small print, and that it would be hard to keep track of the doses, if the inhaler was used in real life.

The Diskus was, like Ellipta, perceived to be easy to use by participants. Those who gave it a high ranking mentioned that because the inhaler had only a few steps to complete during the inhalation process it was easy to operate. The design of the Diskus was, by many, considered modern and appealing. The negative comments of those who rated

Diskus with a low ranking were related to the design of the inhaler and the size, which many thought would make it harder to carry the inhaler around.

The least preferred inhaler was the Easyhaler. The size of the inhaler was by many (12/31) considered to be a big plus and several participants stated that the inhaler would be easy to carry around. Participants stated that the inhaler had many steps that were to be completed before the inhaler was ready to use. This gave participants the perception of Easyhaler being complicated to use. This appeared to be one of the most often recurring motivations as to why the inhaler was given a low ranking.

No other preference studies comparing all four inhalers were found during the literature review. Comparisons between some of the inhalers were, however, found. In a preference study van der Palen et al. (1998) found that the Turbuhaler was preferred over the Diskus regarding factors related to size and the number of available dosages. The dose counter of the Diskus was preferred over the Turbuhalers. These results appear to be in line with the findings of this study which also show a preference for the Turbuhaler over the Diskus. In accordance with the results by van der Palen et al. (1998) the size of Turbuhaler appeared to be preferred over the size of Diskus.

A qualitative interview based study measuring patient satisfaction and preference among asthma and COPD patients for Diskus and Ellipta found Ellipta to be more often preferred than Diskus (Svedsatser et al. 2013) The fact that Ellipta was preferred over the Diskus seems to be supported by the findings of this study. The studies by van der Palen et al. (1998) and Svedsatser et al. (2013) were both sponsored by GSK.

Some research contradicting the findings of this study was also found. A patient preference study judging patient satisfaction for the Turbuhaler, Diskus/Accuhaler and the Easyhaler, found the Easyhaler to be the most satisfactory for patients (Giner 2004). When looking at these results it is important to note that all participants were asthmatics. Due to their existing asthma the patients had habitually used inhaled corticosteroids. Previous experience of inhalers may have created a bias towards some devices, or in other impacted the results of the study.

Researchers have proposed that patients who use their preferred inhaler might obtain a greater degree of satisfaction with therapy (Anderson 2015). If this were true, it would be an important advantage for both patients and caregivers with regards to the patient's therapy and achieving adherence. Based on the results of this study it is hard to argue a position on this claim. On one hand the inhaler that was most often chosen as a favorite amongst the participants also emerged as the easiest one to use, and fewer mistakes might in fact lead to greater adherence to therapy. It is possible that this is merely a coincidence and of no significance. On the other hand the second most preferred inhaler turned out to be the one that the participants' most often used incorrectly. In a real life situation if the inhalers were actually used incorrectly, this could lead to negative effects on the patient's therapy.

6.5 Overview of the results for each inhaler

6.5.1 Turbuhaler

Turbuhaler emerged as the second most preferred inhaler when participants were asked to rank the inhalers according to preference. The inhaler received the highest scores for suitable size and out of all four inhalers the largest amount of participants stated that they strongly agreed with the claim that the inhaler would be easy to carry around if needed. The design of the device also seemed to be appealing to most of the participants and the white and red color combination also received compliments. Furthermore 18 out of 31 participants declared that they strongly agreed with the statement that the inhaler was easy to hold in the hands during inhalation (see Table 18).

Despite of the fact that the inhaler received high preference and was widely liked by participants, Turbuhaler proved to be the hardest inhaler to use with only 16 % managing to complete the inhalation without making any mistakes. This was reflected in the participants' feedback on ease of use; only 9 out of 31 participants strongly agreed with the statement that the Turbuhaler had been easy to use. The distribution of the answers can be seen in Table 18. This is the lowest score for any of the inhalers present in this study. Almost half of the participants did however state that the different steps required for

achieving correct inhalation had been easy to memorize. This was more than for both Diskus and Easyhaler.

The most common mistake among participants when demonstrating the use of Turbuhaler was not remembering to exhale before inhalation. Just as many as many participants failed to load the device properly. Some people who made mistakes during loading only turned the circle once instead of twice, others turned the circle too many times and some did not manage to turn until a click was heard. Even though the click is designed to act as a reinforcement for the patient, indicating that the dose has been loaded, many participants still managed to make mistakes in the process of loading the device. The fact that the click was supposed to act as a reinforcement indicating that the circle had been correctly loaded, was not noted by any of the participants of this study.

Table 18: The distribution of answers to multiple choice questions regarding the properties of the inhaler. The response rate for the following questions was 100 %. n = 31.

	Strongly disagree	**Disagree**	**Neither agree nor disagree**	**Agree**	**Strongly agree**
The inhaler was easy to hold during the inhalation	1	1	0	11	18
The inhaler was easy to use	1	1	3	17	9
The different steps in the inhalation process were easy to remember	0	5	2	9	15
The size of the inhaler was suitable	0	0	0	10	21
The inhaler would be easy to carry around if needed	0	0	0	7	24

6.5.2 Easyhaler

Despite Easyhaler receiving a low preference rank, many of its properties were ranked favorably. High remarks were given for the size of the inhaler with 19 out of 31 participants stating that they strongly agreed that the size of the inhaler was suitable (see table 19). Furthermore, 21 out of 31 participants indicated that they strongly agreed with the

statement that the inhaler would be easy to carry around if needed. Only Turbuhaler received higher remarks in these categories. See Table 19 for the full distribution of the participants' answers for Easyhaler.

Few comments (2/31) were made regarding the dose counter in the open questions. The participants who commented did, however, say that they thought the counter was very small and that the small print might have made it hard to read how many doses were left. The same types of comments were made for the dose counters of Turbuhaler and Diskus (3/31 and 1/31).

When participants were asked what they thought of if the inhaler was easy to use, almost half of the participants stated that they strongly agreed with the claim. Yet, when demonstrating the use of the inhaler only 19 % were able to complete the inhalation without making any mistakes. Just like with Diskus and Ellipta, the most frequently recurring inhalation errors were related to the breathing technique such as not exhaling before the inhalation and not holding their breath long enough after the inhalation. These errors were, however, more frequent in Easyhaler than in the two above mentioned inhalers.

One of the factors that may contribute to the difficulties participants had using the Easyhaler is the many steps required in the inhalation process. Some participants stated that the large number of steps made it harder to remember all the things that needed to be done. The number of participants who thought the different inhalation steps were easy to remember were, however, slightly higher than those for Diskus, which had fewer steps to memorize.

When participants were asked to indicate preference, the Easyhaler emerged as the least preferred inhaler. Many participants stated that the inhaler had too many steps to complete before the inhaler was ready to use, this made it complicated. This factor appeared to be one of the most often recurring motivations for giving the inhaler a low ranking.

Table 19: The distribution of answers to multiple choice questions regarding the properties of the inhaler. The response rate for the following questions was 100 %. n=31.

	Strongly disagree	**Disagree**	**Neither agree nor disagree**	**Agree**	**Strongly agree**
The inhaler was easy to hold during the inhalation	0	1	3	10	17
The inhaler was easy to use	1	4	3	8	15
The different steps in the inhalation process were easy to remember	2	6	2	10	11
The size of the inhaler was suitable	0	1	3	8	19
The inhaler would be easy to carry around if needed	0	2	1	7	21

6.5.3 Diskus

Ease of use is an important characteristic of an inhaler. The results of this study showed that Diskus was the second easiest to use to use out of the inhalers studied. No significance between the average error frequency for Ellipta and Diskus was found. The average error frequency for Diskus in comparison to both Easyhaler and Turbuhaler was significantly lower. The inhaler required fewer steps for reconstitution than for example Easyhaler and Turbuhaler. The steps for Diskus were, however, more than those for Ellipta. According to previous studies on inhaler properties, an ideal inhaler should be ease to teach, as well as learn, how to use. When the participants were asked if they thought that Diskus had been easy to use, 17 out of 31 participants, or 55 %, strongly agreed with the statement. The distribution of the participants' answers to this question among other questions can be seen in Table 20.

Results of this study showed that 52 % of the participants failed to use the inhaler without making any mistakes when they were asked to demonstrate the use of it for the first time. Even though this is a good result in comparison with some of the other inhalers in this study there is still room for improvement. The most common mistake participants made when demonstrating how they would have used the Diskus was insufficient emptying of

the lungs before inhalation. The requirement for holding the breath for 5-10 seconds after the inhalation was another step that was often completed incorrectly amongst the participants' of this study.

Even though the Diskus had fewer steps in its inhalation process than Easyhaler and Turbuhaler, fewer participants stated that they strongly agreed with the statement that the steps in the inhalation process were easy to remember. This is an interesting phenomenon. No indications as to why participants thought so could be found from the structured interview or the comments of the participants that were written down.

Melani (2007) states that an ideal inhaler should be pocket sized, light weighed and easy to carry around. When participants of this study were asked whether they thought the size of the inhaler was suitable only 8 out of 31 participants stated that they strongly agreed with the argument. When asked if the inhaler would be easy to carry around, if needed, merely 6 participants stated that they strongly agreed with the claim. The satisfaction with regards to size was the lowest for all inhalers in this study and much lower than that for Easyhaler and Turbuhaler which are smaller in size. Even though the size did not please the participants of this study, Diskus was still, by many, considered to be the best looking out of all of the inhalers.

Only one participant commented on the dose counter of the Diskus, and this individual thought the small print in which it was stated made it hard to follow the remaining doses. When participants were asked whether it was easy to hold the Diskus in their hand during the inhalation just under half of the participants strongly agreed to the claim. The Diskus is loaded when the lever on the device is pushed down. This acts as a feedback mechanism for the patient, indicating that the dose has been loaded correctly. The feedback mechanism was not commented on by participants.

Table 20: The distribution of answers to multiple choice questions regarding the properties of the inhaler. The response rate for the following questions was 100 %. n= 31.

	Strongly disagree	**Disagree**	**Neither agree nor disagree**	**Agree**	**Strongly agree**
The inhaler was easy to hold during the inhalation	0	1	0	15	15
The inhaler was easy to use	0	2	4	8	17
The different steps in the inhalation process were easy to remember	0	3	5	13	10
The size of the inhaler was suitable	0	3	10	9	8
The inhaler would be easy to carry around if needed	0	5	6	14	6

6.5.4 Ellipta

Based on the results of this study, Ellipta was the inhaler that was most frequently used correctly with 55% of participants' completing the inhalation without making any mistakes. Based on the participants' answers regarding ease of use, the inhaler was also the one that was perceived to be the easiest to use out of all the four inhalers with 26 out of 31 participants strongly agreeing with the statement that the inhaler had been easy to use. Even though a very small majority learned how to use the inhaler properly on the first try, there were still almost as many participants who made at least one mistake when demonstrating the use of the Ellipta.

All of the mistakes participants made using the Ellipta were related to breathing technique. In the light of this information it is important to highlight these steps when teaching patients how to use the inhaler. The few number of steps needed to be completed during the inhalation process does seem to indicate that it makes it easier than some of the other inhalers to learn how to use, and this aspect may also make it easier to teach how to use. Ellipta was the inhaler for which participants stated that it had been easiest to remember all of the steps during the inhalation. The ergonomics of the inhaler were also appreciated and a clear majority of the participants (21/31) stated that they strongly agreed with the statement that the inhaler was easy to hold in the hand during the inhalation.

Ellipta also emerged as the inhaler that was most often chosen as the favorite out of the four inhalers with 51.6 % of participants ranking it as their favorite. Despite of this Ellipta received frequent critique for its design and size by many of the participants in this study. Only nine out of 31 participants strongly agreed with the statements that size of the inhaler was suitable, and that it would be easy to carry around if needed. The exact distribution of answers can be seen in Table 21. The design of the inhaler was by many considered to be colorless and dull. Some did, however, state that the dull look did not matter because the purpose of the inhaler was not to look good, but to act as a medicine.

The dose counter received compliments for being very clear and visually easy to understand. When the cover of Ellipta is slid open there is a clicking sound that acts as reinforcement that the dose has been loaded correctly, this was, however, not commented on by any of the participants.

Table 21: The distribution of answers to multiple choice questions regarding the properties of the inhaler. The response rate for the following questions was 100 %. n = 31.

	Strongly disagree	**Disagree**	**Neither agree nor disagree**	**Agree**	**Strongly agree**
The inhaler was easy to hold during the inhalation	0	0	1	9	21
The inhaler was easy to use	0	1	1	3	26
The different steps in the inhalation process were easy to remember	1	2	0	5	23
The size of the inhaler was suitable	0	3	4	15	9
The inhaler would be easy to carry around if needed	0	6	2	14	9

6.6 Inhaler education and instructions

It has been claimed that patient education is a factor that plays one of the most important roles in the patients' use and misuse of asthma inhalers (Fink & Rubin 2005). Many studies regarding the efficiency of different training methods have been made to evaluate which one is optimal for achieving correct inhaler technique. There are several different approaches available for training in inhaler technique. In this study video instructions were used to give the participants standardized instructions on how to use the inhaler present in this study.

The participants of this were asked what kind of education they would have needed in order to properly learn how to use the inhalers present for this study. Many participants thought that a video was a good way of giving instructions for how to use an asthma inhaler. When asked what the instructions should be like, participants stated that they should be clear and simple steps that showed how the inhaler should be loaded, inhaled and the breathing technique that should be used. The videos used for the purpose of this study all contained the above mentioned steps.

Recurring feedback from participants for all of the videos was that they were so fast that the information didn't really have time to sink in. The educational video for Ellipta received the most negative comments with many participants stating that the tempo was too fast to follow the instructions properly. The distribution regarding the participants' statement of how easy the steps of the education were to understand can be found in Appendix 4. Some suggested that combining the video education with written instructions, or a checklist of the different steps, might have been a good reminder of how to use the inhaler.

Many participants (5/31) commented that they thought a video was a better way of teaching the use of an inhaler than just providing them with a written manual. The perception that a manual might not be enough if the object is to learn how to use the device is supported by previous research. A study by Roberts et al. (1982) suggested that provision of the manufacturer's instruction sheet alone was ineffective, partially due to the fact that

patients tended to overlook the information in it. Other studies have shown written instructions in the form of a leaflet to be inefficient, even for those patients who actually read the leaflet (Melani et al. 2004). Nimmo et al. (1993) as seen in Rönmark et al. (2005) found that only 6 % of participants in their study demonstrated a correct technique with Turbuhaler the first time after receiving written instructions on how to use the device.

In this study 67 % of the videotaped inhaler demonstrations by participants were done with the participants making at least one critical error. As a majority made mistakes when first demonstrating the use of the inhalers it could be argued that video instructions alone might not be enough when teaching patients how to use an asthma inhaler. The results may also be indicating that there is considerable room for improvement in video instructions for the purpose of teaching asthma patients to learn how to use the inhalers.

When the participants were asked what kind of education they would have needed in order to properly learn how to use the inhalers, a frequently recurring comment for each inhaler was that the participants' felt they needed feedback on their own performance. Participants often mentioned that a personal one on one meeting would have allowed them to clear up unclear issues and questions that may have arisen during the demonstration. Participants also seemed to have questions regarding the different steps presented in the videos. Questions people tried to ask included "why should I shake the inhaler" and "why shouldn't I shake the others inhaler?" etc. There were also many misconceptions regarding the inhalers. One participant explained that the instructions on how to adjust the dosage had been very unclear. In reality none of the inhalers asthma doses can be adjusted. During the videos this participant had been under the impression that the size of a dose of the medication could be adjusted by the patient themselves.

The questions that arise may vary greatly between different individuals. That was apparent in this study even though the participants all received identical instructions. In order for inhaler users to get an achieve correct inhaler technique it would be important that these individuals would have the opportunity to ask questions, get feedback and have someone correct the mistakes that were made. As it has been presented in the section "Inhaler error frequency" a significant number of participants believed that they had

learned how to use the inhaler correctly even though the results from the scored video demonstrations showed that mistakes had actually been made. One on one education with feedback on inhaler technique support the patients' treatment, by making them aware of their mistakes, and thereby giving them clear guidelines on what to improve on.

The participants' perception that one on one interactive sessions would have been a better way of making sure that they actually learned how to use the inhalers is backed up by previous studies. Van der Palen et al. (1997), among others, have found that individual and small group demonstrations of interactive nature be the most effective alternatives for providing inhaler education. Furthermore research has shown that periodic retraining is needed as inhaler technique declines over time. Inhaler handling must be repeated regularly in order to achieve and maintain the correct technique (Takemura et al. 2010; O'Bey et al. 1982).

Some who said that they would prefer a one on one instruction with feedback provided on their performance stated that they thought the video instructions would act as great reminders of how to use the inhaler. The idea of using videos was mentioned by two separate individuals on several different occasions. This perception is supported by previous research. Research by Wilson et al. (2010) among others indicates that the use of video and print interventions can promote recall on inhaler use in asthma patients.

Previous studies have shown that health care professionals play an important role in the achieving correct inhaler technique and maintaining it over time (Takemura et al. 2010). Many health care professionals, however, display some difficulties when asked to demonstrate the correct technique for asthma inhalers and according to Fink & Rubin (2005) between 39–67 % of nurses, respiratory therapists and doctors are unable to sufficiently describe, or perform, critical steps for inhaler use. Because of this, it was hypothesized that videos would be a good form of providing easily accessible standardized form of providing correct training for asthma patients.

The video instructions used for this study were very basic, non-interactive, instruction videos describing each step that the participants were to perform during inhalation. Research on the subject of instructional videos in e-learning have established that students who were provided interactive educational videos achieved significantly better learning performance and a higher level of learner satisfaction than those who were provided a non-interactive video, or no video at all (Zhang et al. 2006). These findings indicated that it may be important to integrate interactive instructional video into e-learning systems (Zhang et al. 2006). If video instructions were to be more widely used as a method of providing instructions to asthma patients it would be interesting to look into the possibility of developing interactive videos for this purpose.

Future research should look into if these types of videos would be suitable for giving inhaler education to patients, and how different types of interactive videos could assist in the goal of achieving and maintaining correct inhaler technique.

6.7 Limitations of the study

The first limitation that arose during the data collection process was the fact that the instruction video for Easyhaler included a protective cover which the inhaler could be placed in during the inhalation process and afterwards for protection from environmental factors. When the demonstrational placebo inhalers were ordered from Orion, the protective cases were not included in the delivery and therefore these covers were not accessed during the data collection process. All demonstrational inhalers were ordered through the same process that any other health care professionals would have ordered those inhalers. As such the situation simulates the reality many patients face when receiving instructions from health care professionals. Measures were taken to minimize the harm caused by this discrepancy as much as possible.

All participants were informed that the video would feature an “extra” cover for the inhaler, and the participants were told to disregard it. The fact that the participants were not able to fully follow the instructions of the video may have harmed their perception of the Easyhaler and its ease of use. The absence of the protective cover did, however, remove

an additional step in the inhaler handling process and it reduced the participants' perception of the inhaler size. These are again factors that based on the general comments of the participants were considered to be positive, and thereby they may have benefited the participants' perception of the Easyhaler.

Another possible limitation of this study lies in the educational distribution of the sample of this study. A clear majority of participants (23/31) were from an academic background. Previous research has shown that educational level significantly correlated with scores of correct handling of inhaler devices (Molimard et al. 2003). This may have influenced the results of this study. The sample size was too small to find any relationship between educational background and inhaler control. If the results were affected by the educational background one can assume that it would have affected the inhaler handling for all of the inhalers in this study, therefore, it should not have distorted the results of this study by creating a bias towards any inhaler in particular.

The final area that could possibly arise as a limitation of this study is the fact that the design of this study required participants to use all four inhalers right after one another. Previous research has shown that patients who used several different inhalers are at a higher risk of getting confused with the instructions and they usually require more time to learn how to use their devices correctly (Melani 2007).

Due to the fact that all the participants were inhaler naïve, and the steps for the DPIs used share some similarities, it was considered very likely that the subjects would actually learn how to use DPIs better later in the process. In this case the inhaler that was tried first would be at the greatest disadvantage. As the participant would watch the other videos and repeat the other process it was hypothesized that the participants' would learn to use DPIs better along the way due to the similar steps shared by the inhalers. The order of the inhaler performances was randomized by lottery in order to remove a bias towards any inhaler in particular. For the purpose of this study, it was important that the inhalers could be compared against each other. The benefits and disadvantages were weighed against each other and it was determined that the chosen method was the best way to go. In the end it was considered that the risks for bias were equally high for each inhaler due to the fact that the order was determined by lottery.

7. Conclusions

This study aimed to address how easily an individual with no inhaler experience can learn how to use an asthma inhaler through video education. The different properties affecting ease of use were also investigated. The results show that the overall frequency of error for participants' inhaler demonstrations was high. Out of 124 inhaler demonstrations, 67 % were completed with the participants displaying at least one mistake. The error frequency varied greatly between the inhalers. Based on the results, it could be proposed that it is rather difficult for individuals with no prior inhaler experience to learn how to use an asthma inhaler solely through video education. The level of difficulty varied between the inhalers and some proved to be either harder to use, or harder to teach through video instructions alone.

When participants were asked to evaluate their own inhaler technique it became clear that a large number of participants strongly overestimated their own performance. This phenomenon could be observed for all four inhalers. These results highlight the importance of providing feedback on inhaler use in order to assure that correct inhaler technique is achieved.

Few logical steps that were easy to memorize seemed to be something that participants most often associated with ease of use. The inhalers that required the fewest steps (Diskus and Ellipta) were also more often used correctly. The participants' own perception of which inhalers were easy, and which were hard, seemed to correlate fairly well with the actual results for correct use. In self-evaluation, participants most often perceived they had used Ellipta and Diskus correctly. These were also the two inhalers for which participants displayed the fewest amount of errors during handling.

When patients were asked to indicate preference, Ellipta emerged as the most frequently preferred inhaler followed by Turbuhaler. Those who preferred Ellipta seemed to value its ease of use, whereas those who gave the highest rank to Turbuhaler appreciated the design, as well as the size, of the inhaler. Diskus came in third and Easyhaler was the least preferred inhaler. For Easyhaler, many stated that the inhaler had too many steps to

complete before the inhaler was ready to use, this made it complicated. This factor was one of the most often recurring motivations for giving the inhaler a low ranking. Overall the preference rankings for each inhaler were quite close to one another. This is illustrated by the fact that only the difference between preference scores for Ellipta (most preferred) and Easyhaler (least preferred) was deemed statistically significant.

After evaluating the properties of all four inhalers, as well as the preferences of the participants of this study, it is fair to conclude that there still is no such thing as an ideal inhaler that would be suitable and liked by everyone. The differences in needs and preferences require careful weighing when prescribers choose a new inhaler for a patient. The significant difference in error frequency for the oldest inhaler (Turbuhaler) and the newest one (Ellipta) can been seen as an indication that inhalers have developed to be more intuitive and easier to use in the last 25 years. As many participants still made mistakes for all inhalers used in this study, it may be fair to conclude that none of the inhalers are easy and intuitive enough to use without careful inhaler education and clear instructions. Patient education plays a central role in asthma care and needs to be given proper attention even though the inhalers might be considered intuitive and easy to operate.

Finally, the goal of this study was to investigate educational videos as a method of providing inhaler education. According to the participants of this study, an educational video needs to explain all inhalation steps clearly in a slow enough pace. Only 33 % of the analyzed inhaler demonstrations were completed without any mistakes. Consequently it may be fair to conclude that video demonstrations are not an ideal way of providing inhaler education for first time users of inhalers. The most prominent problem with video instructions is that it provides no feedback to the user regarding their inhaler technique. This may present real problems as the results of this study also show that people tend to overestimate their own technique. Another problem arises from the fact that the users are unable to ask questions and clear up misunderstandings. E-learning and video education could play a part in providing successful inhaler instructions in the future, but if so more interactive approaches providing patients with feedback should be developed. Future research could therefore look into the use of interactive learning videos as a means of providing asthma patients with education on inhaler technique.

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Appendix 1

Täytä alla olevat kysymykset ennen kuin aloitat esittelyvideoiden katselua

□ Nainen □ Mies

Ikä ____

Asuinpaikkakunta:

□ Pääkaupunkiseutu (Helsinki, Espoo, Vantaa tai Kauniainen)

□ Muu:_____

Koulutustausta/ koulutusta jota parhaillaan suoritan

□ Yliopisto □Ammattikorkeakoulu □Ammattikoulu

Minulla on astma

□ Kyllä □ Ei

Perheenjäseneni kärsii astmasta

□ Kyllä □ Ei

Minulla on aiempaa kokemusta astmainhalaattoreiden käytöstä

□ Kyllä □ Ei

Työskentelen/ olen työskennellyt apteekissa/lääketeollisuudessa

□ Kyllä □ Ei

Appendix 2

□ Laite A □ Laite B □ Laite C □ Laite D

	Täysin eri mieltä	Jokseenkin eri mieltä	Ei samaa eikä eri mieltä	Jokseenkin samaa mieltä	Täysin samaa mieltä
Inhalaattori oli helppo pitää kädessä käytön aikana	□	□	□	□	□
Inhalaattorin käyttö oli helppoa	□	□	□	□	□
Käyttöohjeet koulutusvideossa olivat selkeät	□	□	□	□	□
Laitteen valmisteluvaiheet oli helposti ymmärrettäviä videokoulutuksessa	□	□	□	□	□
Inhalaation eri valmisteluvaiheet oli helppo muistaa	□	□	□	□	□
Inhalaattorin koko oli sopiva	□	□	□	□	□
Laite kulkisi helposti mukana tarvittaessa	□	□	□	□	□

Mitä mieltä olet astmalaitteen ulkonäöstä?

_____
_____
_____
_____
_____
_____

Millaista ohjeistusta tarvitsisit astmalaitteiden käytöstä?

Mitä mieltä olit laitteen käytettävyydestä?

Opitko videon perusteella käyttämään inhalaatiolaitetta?

Miksi/Miksi et?

_____
_____

Vastaa viimeiseen kysymykseen vasta sitten kun olet käyttänyt kaikki neljä inhalaattoria.

Järjestele laiteet preferenssi järjestykseen yhdestä neljään. (1- pidin laitteesta eniten 2- pidin laitteesta toiseksi eniten, 3 – pidin laitteesta toiseksi vähiten, 4 – pidin laitteesta vähiten).

____Laite A ____ Laite B ___ Laite C ____ Laite D

Perustele valintasi

_____
_____
_____
_____
_____
_____

Appendix 3

Answers provided to the multiple choice questions for each inhaler to the multiple choice questions

Diskus	Täysin eri mieltä	Jokseenkin eri mieltä	Ei samaa eikä eri mieltä	Jokseenkin samaa mieltä	Täysin samaa mieltä
Inhalaattori oli helppo pitää kädessä käytön aikana	0	1	0	15	15
Inhalaattorin käyttö oli helppoa	0	2	4	8	17
Käyttöohjeet koulutusvideossa olivat selkeät	0	1	1	12	17
Laitteen valmisteluvaiheet oli helposti ymmärrettäviä videokoulutuksessa	0	1	2	11	17
Inhalaation eri valmisteluvaiheet oli helppo muistaa	0	3	5	13	10
Inhalaattorin koko oli sopiva	0	3	10	9	8
Laite kulkisi helposti mukana tarvittaessa	0	5	6	14	6

Easyhaler	Täysin eri mieltä	Jokseenkin eri mieltä	Ei samaa eikä eri mieltä	Jokseenkin samaa mieltä	Täysin samaa mieltä
Inhalaattori oli helppo pitää kädessä käytön aikana	0	1	3	10	17
Inhalaattorin käyttö oli helppoa	1	4	3	8	15
Käyttöohjeet koulutusvideossa olivat selkeät	1	2	3	13	12
Laitteen valmisteluvaiheet oli helposti ymmärrettäviä videokoulutuksessa	1	2	2	14	12
Inhalaation eri valmisteluvaiheet oli helppo muistaa	2	6	2	10	11
Inhalaattorin koko oli sopiva	0	1	3	8	19
Laite kulkisi helposti mukana tarvittaessa	0	2	1	7	21

Ellipta	Täysin eri mieltä	Jokseenkin eri mieltä	Ei samaa eikä eri mieltä	Jokseenkin samaa mieltä	Täysin samaa mieltä
Inhalaattori oli helppo pitää kädessä käytön aikana	0	0	1	9	21
Inhalaattorin käyttö oli helppoa	0	1	1	3	26
Käyttöohjeet koulutusvideossa olivat selkeät	1	2	4	5	19
Laitteen valmisteluvaiheet oli helposti ymmärrettäviä videokoulutuksessa	0	2	2	2	25
Inhalaation eri valmisteluvaiheet oli helppo muistaa	1	2		5	23
Inhalaattorin koko oli sopiva	0	3	4	15	9
Laite kulkisi helposti mukana tarvittaessa	0	6	2	14	9

Turbuhaler	Täysin eri mieltä	Jokseenkin eri mieltä	Ei samaa eikä eri mieltä	Jokseenkin samaa mieltä	Täysin samaa mieltä
Inhalaattori oli helppo pitää kädessä käytön aikana	1	1	0	11	18
Inhalaattorin käyttö oli helppoa	1	1	3	17	9
Käyttöohjeet koulutusvideossa olivat selkeät	0	2	3	13	13
Laitteen valmisteluvaiheet oli helposti ymmärrettäviä videokoulutuksessa	0	3	2	14	12
Inhalaation eri valmisteluvaiheet oli helppo muistaa	0	5	2	9	15
Inhalaattorin koko oli sopiva	0	0	0	10	21
Laite kulkisi helposti mukana tarvittaessa	0	0	0	7	24