Adherence to inhalation technique and drugs in general in asthma- and COPD-patients.

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Abstract

Introduction: Asthma and chronic obstructive pulmonary disease (COPD) are chronic inflammatory diseases that affect the airways. Both metered dose inhalers (MDIs) and dry powder inhalers (DPIs) are being used for treatment of the diseases. There are multiple steps for each inhaler to get a dose, and some steps are more important than others. These are called critical factors i.e. steps that needs to be done in order for the drugs to reach the lungs. Inhalation technique is important for patients with asthma and/or COPD because poor inhalation technique can lead to worse prognosis and hospitalization. Despite this, errors in inhalation technique are common. Non-adherence that the patients not are aware of, such as for example poor inhalation technique, is called unintentional non-adherence. Intentional non-adherent on the other hand, is when patients actively choose not to follow the recommendations for prescribed treatments.

Aim: The aim with this study was to investigate the inhalation technique and adherence to drugs in general in patients with asthma and COPD.

Method: To measure unintentional adherence, inhalation technique observations with placebo-inhalers were conducted. If one or more critical steps according to a developed checklist were not performed correctly, the patient was considered unintentional non-adherent. The observations were made together with interviews, which consisted of two parts, questions about how the patients’ handle their general medications and the measurement of intentional adherence using MARS-5.

Results: Of 23 people included in the study, 26.1% were considered unintentional non-adherent and 30.4% were considered intentional non-adherent. It was more common to have COPD (p=0.008) and a higher number of medications (p=0.022) in the unintentional non-adherent group than in the unintentional adherent group. The most common mistakes patients did was to not check how many doses there were left in the inhalers with counters. Of the in total 34 observations, 20.7% of the DPI-observations had at least one critical error while the corresponding number in the MDI-observations was 60.0%.

Discussion: The prevalence (26.1%) of unintentional non-adherent patients are in line with other studies and it seems to be a problem in a lot of countries. Regarding intentional non-adherent patients, the number 30.4% is a bit low in comparison with other studies but still, it is a relative high value. It is probably even higher because of the fact that overestimating is a problem with self-reported measurements. Unfortunately the DPI and MDI observations were not comparable due to few observations with MDI, but the study indicates that it is more incorrect use in inhalation technique with MDIs than with DPIs. Regarding which step that patients missed the most, checking for doses remaining, this is suggested to be a critical step because if there are no doses left in the inhaler, the prognosis become worse for the patient. Finally, the result found in this study, that unintentional non-adherent patients have COPD to a greater extent and more medications, is similar to other studies. One explanation can be that patients with more medications have more instructions to keep in order and a greater chance of making mistakes.

Conclusion: This study indicates that both unintentional non-adherence and intentional non-adherence among people with asthma and COPD is a problem in Sweden.

Keywords: COPD, asthma, inhalation technique, adherence, MARS-5.
Introduction

Asthma, COPD and prevalence

Asthma and chronic obstructive pulmonary disease (COPD) are chronic inflammatory diseases that affect the airways. The difference between them is that asthma can be asymptomatic and stable with the right treatment while COPD is a progressive disease regardless of treatment. The main risk factors for developing asthma and COPD are inhaling of different particles and/or substances and smoking respectively. Asthma is common in all ages while COPD is more common in older people (1-3). The prevalence worldwide for asthma was 235 millions in 2017 and 251 millions for COPD in 2016 according to WHO (1, 2). In Sweden the reported prevalence for asthma is 800 000 patients and for COPD between 40 000 – 70 000 patients in 2017 (3).

Inhalers – MDI and DPI

Inhalers are the main device for treatment in asthma- and COPD-patients. There are two main types of inhalers, metered dose inhalers and dry powder inhalers. Throughout this paper, the term MDI will refer to metered dose inhalers and the term DPI to dry powder inhalers.

MDI’s are driven by an aerosol and DPI’s are driven by the patient’s inhalation and breath. There are some exceptions regarding MDI’s, autohaler for instance releases the aerosol when the patient is breathing in. Ordinary MDI’s works like a “spray” where the patient needs to coordinate their breathing while firing the aerosol. DPI works in such way that the patients charge a dose and then take a deep and often a quick breath to get the dose (4). Examples of MDIs are spray, respimat, autohaler and evohaler, and examples of DPIs are easyhaler, turbuhaler, diskus, breezhaler, handihaler, genuair and ellipta. However, all inhalers require several steps for the drugs to reach the lungs. Some inhalers require five steps while others ten, usually there are more steps required with DPIs then MDIs. Some common steps for both MDIs and DPIs are to remove the cap, breath out and empty the lungs before inhalation and to hold the breath after inhalation. Some steps seem to be more important than others, so called critical factors. Examples of critical factors are how to charge a dose and to place the inhaler between the lips. If the critical factors are not performed correctly, some or all drug substances will not reach the lungs and their active site (4, 5).

The importance of inhalation technique

Inhalation technique is important since incorrect technique can lead to worse prognosis of both asthma and COPD and increased risk of hospitalization (4, 6, 7). Extensive research has shown that it is common with mistakes in inhalation technique (7-10). A selection of them is these two studies. The first study was conducted in Uppsala, Sweden in 2016 and included 53 patients with a mean age of 79±7.5 years and with an average of 2.5±0.9 inhalers. That study found that 64% of the observations contained an error in critical factors. A reason for the high percentage might be that the patients in the study were recently hospitalized. The study also found that higher age resulted in more errors in inhalation technique (8). The second study by Siriam et al. was also performed in 2016 and included 150 people with the mean age 70±8.9. The study found that it is common with mistakes during inhalation with inhalers. At least one fault was made in the most of the inhalation demonstrations. The inhaler that gave most faults (more than one) in inhalation technique was turbuhaler and the one that gave the least was handihaler (9).

Associations with inhalation technique

As previously mentioned, a higher age was associated with more errors in inhalation technique in a Swedish study (8). Another associated factor to inhalation technique is education in inhalation technique. For example, one study from Italy by Melani et al. found that approximately 1/3 of 1664 patients had not received any instructions of how the inhalers work. Some of the other patients had received instructions verbally and some had received demonstrations with placebo-inhalers. The study found that absence of
instructions and older age led to more faults in critical factors (p<0.001 and p=0.008) (7).

Another study conducted by Göris et al. compared one intervention group with 34 patients that received education in inhalation technique with one control group with 35 patients that did not received any education. After three months they followed-up the two groups to see how many errors there were in each. 82.4% in the intervention group did not make any faults in inhalation technique while all the subjects in the control group made errors in inhalation technique. The same study presented significant results accord to fewer exacerbations in the intervention group than in the control group (p<0.001) during the three months. The intervention group also got less hospitalization and emergency care than the control group, this result were not statistically significant though (10).

Measuring of adherence
Adherence can both be if a patient takes the medicines according to ordination but also if the patient is using the inhalation device right. Non-adherence can be divided in two types, unintentional and intentional. Unintentional is when the patients don’t know that they perform incorrectly in either inhalation technique or in dosage and intentional is when the patients decide to perform incorrectly (6).

Intentional adherence can be measured by direct methods, for example through concentration of drugs in the blood, and by indirect methods, for example by using interviews/self-reported scales. Self-reported scales are cheaper than direct methods and more timesaving. Self-reported scales aim to measure intentional adherence and some example of scales that can be used are Medication Adherence Questionnaire (MAQ), Brief Medication Questionnaire (BMQ) (11) and Medication Adherence Report Scale (MARS)-5 (12). Both MAQ and BMQ have been used for measuring adherence in for example arterial hypertension and AIDS/HIV. MAQ has also been used in smoking cessation and BMQ for measuring adherence in people with diabetes mellitus (11).

In this study, MARS-5 is used to measure general intentional adherence. MARS consists of five statements about adherence; M1 - I forget to take my medicines, M2 - I alter the dose of my medicines, M3 - I stop taking my medicines for a while, M4 - I decide to miss out a dose, M5 - I take less then instructed. These statements can then be answered by a likert scale (always, often, sometimes, rarely and never) where always gives 1 points, often 2 points, sometimes 3 points, rarely 4 points and never 5 points. The scale gives a maximum of 25 points and a minimum of 5 points. People that receive 23-25 points are considered adherent, while people that receive 5-22 points are considered non-adherent. MARS-5 is a validated scale that have been translated to Swedish and approved by the person who developed the original scale (12, 13).

One reason to choose MARS-5 was that it has been used for measuring adherence in different kinds of diseases like COPD (9), stroke (14), secondary prevention of coronary heart disease (15), asthma (16), epilepsy (17) and chronic pain (18). Another reason to choose MARS-5 to measure adherence is that a study on patients with schizophrenia and bipolar disease has presented a correlation (0.52) between serum concentrations and MARS-5 which indicates that MARS-5 is a reliable method for measuring adherence (19).

Adherence among people with COPD
According to a review of Sanduzzi et al. the frequency for unintentional adherence is as much as 20-50 % and for intentional adherence 15 % among people with COPD. They also mention that adherence to treatment of COPD is lower than to other diseases and that real life adherence is lower (10-40 %) than mentioned in literature (40-60 %) (20).

Sanduzzi et al. also indicate that there are three factors that affect adherence to inhalers among people with COPD: frequency of administration, rapid onset of action and the role of the device. Frequency of administration is how often the medicines are taken, one dose daily leads to higher adherence while three and four doses daily leads to a lower adherence. Rapid onset of action indicates that medicines that act rapidly generate a higher adherence and role of device is important since an easy device also encourage to a higher adherence
(20). Hopefully, this research will contribute to a deeper understanding of general intentional adherence and inhalation technique (unintentional adherence) in both COPD and asthma patients. A lot of studies have been done on this matter but much less is known about the relationship between general intentional adherence, gender, age, influence of other drugs and inhalation technique (unintentional adherence) - which we hope this study will contribute to.

Objective
The aim with this study is to investigate the inhalation technique and adherence to drugs in general in patients with asthma and COPD. The questions of interest are the following:

- What is the prevalence of incorrect use of the inhaler devices (unintentional non-adherence)?
- Does more errors appear when using DPI than MDI?
- Which are the most common mistakes when using an inhaler?
- Are there any differences between people with and without errors in inhalation technique?
- What is the prevalence of intentional non-adherence regarding general use of medications?
Method

Study design
This study was performed at Umeå University Hospital at the orthopedic-, geriatric- and medical department in October, November and December 2018. In order to answer the aim and the questions of this study both interviews and observations regarding inhalation technique were performed.

Definition of adherence to inhalation technique
Based on literature and discussions with a COPD-nurse, checklists for the inhalers were developed (appendix 1). The checklists include critical and non-critical factors for each inhaler. A patient was defined as non-adherent if one or more critical factor was not correctly performed. Only inhalers approved for use in Sweden received a checklist. Placebo-inhalers were used in the observations. No instructions were given beforehand. The observations were held by the bedside.

Interviews
The interviews aimed to investigate the general intentional adherence to medications. The interviews consisted of two parts, MARS-5 and questions about how the patients’ handle their medications. The questions in the interview had approximately four alternatives or were answered by yes or no to more easily sum up the data. Background information about the patients was included such as gender, age, diagnosis and living situation. This information was collected from the medical journal. The interview and background information sheet can be found in appendix 2.

Study population
Invited to participate were patients admitted to the orthopedic-, geriatric- and medical department in October, November and December 2018, with at least one inhaler prescribed before admission. Patients with dementia were excluded from the study.

Approach of the study
Patients with inhalators were identified by clinical pharmacists or by nurses working at the different wards. The patients were then asked if they wanted to participate in the study. If the patients agreed to participate, background information about the patient and about the inhalator type were collected from the electronic journal. The observations regarding inhalations technique and the interviews were performed at the wards, at the patients’ bedside.

Statistics
Tables were used to summarize data from both interviews and observations. Different factors related to adherence and non-adherence regarding inhalation technique, were investigated using t-test and chi-square-test. All analyses were carried out using SPSS, version 25. Statistic significant level (p-value) was 0.05.

Ethical approval and informed consent
The regional Ethics Review Board in Umeå approved the study, number 2018/165-31. An informed consent was collected from the patients that approved to participate in the study, see appendix 3. Information about the study and contact details to the researchers were also provided to the patients, see appendix 4.
Results
A total of 38 patients were asked to participate in the study. Of these, seven women and five men declined to participate in the study, while three patients were excluded because the ability to talk and understand was impaired due to disease. Of the 23 patients included, 78.3 % were women and the mean age were 65 (±16.2), range 22 to 86 years old. Asthma was the most common reason for using an inhaler. Only four of the 23 patients thought inhalers were difficult to handle. The average number of medications was 7.2 (±4.2), range 1 to 17, while 69.6 % of the patients had more than five medications. The mean years of having inhalators were 9 (±11.1), range between 0 to 48 years. For more background data, see Table 1.

Table 1. Background information

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>Total n (%)</th>
<th>23 (100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Woman n (%)</td>
<td>18 (78.3)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>Mean (±SD)</td>
<td>65.0 (±16.2)</td>
</tr>
<tr>
<td>Living situation*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Living alone n (%)</td>
<td>11 (47.8)</td>
<td></td>
</tr>
<tr>
<td>Living at home with a relative n (%)</td>
<td>11 (47.8)</td>
<td></td>
</tr>
<tr>
<td>Smoker</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes n (%)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>No n (%)</td>
<td>23 (100)</td>
<td></td>
</tr>
<tr>
<td>Diagnoses related to inhaler</td>
<td></td>
<td></td>
</tr>
<tr>
<td>COPD n (%)</td>
<td>6 (26.1)</td>
<td></td>
</tr>
<tr>
<td>Asthma n (%)</td>
<td>17 (73.9)</td>
<td></td>
</tr>
<tr>
<td>Other diagnoses</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart failure n (%)</td>
<td>3 (13.0)</td>
<td></td>
</tr>
<tr>
<td>Hypertension n (%)</td>
<td>9 (39.1)</td>
<td></td>
</tr>
<tr>
<td>Atrial Fibrillation n (%)</td>
<td>3 (13.0)</td>
<td></td>
</tr>
<tr>
<td>Diabetes Mellitus n (%)</td>
<td>3 (13.0)</td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td>4 (17.4)</td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction, past n (%)</td>
<td>2 (8.7)</td>
<td></td>
</tr>
<tr>
<td>Stroke, past % n (%)</td>
<td>1 (4.3)</td>
<td></td>
</tr>
<tr>
<td>Number of medications</td>
<td>Mean (±SD)</td>
<td>7.2 (±4.2)</td>
</tr>
<tr>
<td>More than five medications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes n (%)</td>
<td>16 (69.6)</td>
<td></td>
</tr>
<tr>
<td>No n (%)</td>
<td>7 (30.4)</td>
<td></td>
</tr>
<tr>
<td>Years of having inhalators</td>
<td>Mean (±SD)</td>
<td>9 (±11.1)</td>
</tr>
<tr>
<td>Patients who has someone who help them with their medicines</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes n (%)</td>
<td>1 (4.4)</td>
<td></td>
</tr>
<tr>
<td>No n (%)</td>
<td>22 (95.6)</td>
<td></td>
</tr>
<tr>
<td>Patients who get their medicines packaged in sachets</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes n (%)</td>
<td>1 (4.4)</td>
<td></td>
</tr>
<tr>
<td>No n (%)</td>
<td>22 (95.6)</td>
<td></td>
</tr>
</tbody>
</table>

SD = standard deviation
*data is missing for one person

There were six (26.1%) unintentional non-adherent patients in this study according to inhalation technique. There were in total 34 observations in this study, 29 observations regarding DPI and five for MDI. Of the 29 observations for DPI, six (20.7%) observations
included at least one critical error and of the five observations for MDI, three (60.0%) observations included at least one critical error. In the 29 observations with DPI there were a total of twelve critical errors and in the five observations with MDI there were four critical errors. The other results obtained in the observations are shown in table 2. The most frequent error in most of the inhalers was that the patients did not check for doses remaining. The step that almost every patient accomplished right was to remove the cap and place the inhaler between lips and teeth. Regarding the distribution of critical factors, there was no clear pattern (see table 2).

Autohaler, evohaler, zonda, forspiro, spiromax and twisthaler were not included in the study because there were no patients with these kinds of inhalers. In this study, 34 observations with different inhalers occurred among the 23 participants. However, the total number of inhalers was 39 for the reason that some patients had two turbuhalers, i.e one Bricanyl® and one Pulmicort®, but only one observation was performed. Patient one had two turbuhalers, patient three had two easyhalers and one ellipta, patient five had two easyhalers and patient 21 had two turbuhalers.

Table 2. Checklists and number of errors in inhalation technique.

<table>
<thead>
<tr>
<th>Type of inhalers - DPI (n)</th>
<th>Checklist (steps in italics are considered as critical factors)*</th>
<th>Number of errors (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Turbuhaler (13)</strong></td>
<td>Check for doses remaining</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td><em>Remove the cap</em></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td><em>Charge the dose</em></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td><em>Breath out and empty the lungs of air</em></td>
<td>8</td>
</tr>
<tr>
<td></td>
<td><em>Don’t breath out in the inhaler</em></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>*Place the inhaler between lips and teeth while standing/sitting</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td><em>Inhale deep and vigorously through the inhaler</em></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>*Hold the breath, if indication of holding breath exists it’s OK</td>
<td>5</td>
</tr>
<tr>
<td><strong>Easyhaler (10)</strong></td>
<td>Check for doses remaining</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td><em>Remove the cap</em></td>
<td>0</td>
</tr>
<tr>
<td></td>
<td><em>Shake the inhaler forcefully a couple of times (3-5 times)</em></td>
<td>3</td>
</tr>
<tr>
<td></td>
<td><em>Charge the dose</em></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td><em>Breath out and empty the lungs of air</em></td>
<td>5</td>
</tr>
<tr>
<td></td>
<td><em>Place the inhaler between lips and teeth and end tight.</em></td>
<td>0</td>
</tr>
<tr>
<td></td>
<td><em>Inhale deep and vigorously through the inhaler</em></td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>*Hold the breath, if indication of holding breath exists it’s OK</td>
<td>2</td>
</tr>
<tr>
<td><strong>HandiHalier (1)</strong></td>
<td><em>Open the grey lid by pressing the green button</em></td>
<td>0</td>
</tr>
<tr>
<td></td>
<td><em>Charge a dose (includes placing the capsule right and puncture it) – actually 3 critical errors</em></td>
<td>0</td>
</tr>
<tr>
<td></td>
<td><em>Breath out and empty the lungs of air</em></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td><em>Place the inhaler between lips and teeth</em></td>
<td>0</td>
</tr>
<tr>
<td></td>
<td><em>Take a deep but even breath through the inhaler (hear the capsule vibrate)</em></td>
<td>0</td>
</tr>
<tr>
<td>Inhaler</td>
<td>Instructions</td>
<td>Step</td>
</tr>
<tr>
<td>------------------</td>
<td>-------------------------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td><strong>Ellipta (1)</strong></td>
<td>Hold the breath, if indication of holding breath exists it’s OK</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Do everything one more time from step 2 to ensure that the capsule gets emptied</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Check for doses remaining</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Charge the dose</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Breath out and empty the lungs of air (don’t breath out in the inhaler)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Place the inhaler between lips and teeth</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Take a deep, long but even breath through the inhaler</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Hold the breath, if indication of holding breath exists it’s OK</td>
<td>0</td>
</tr>
<tr>
<td><strong>Diskus (2)</strong></td>
<td>Check for doses remaining</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Keep the diskus horizontal</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Open the diskus</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Charge the dose</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Breath out and empty the lungs of air (don’t breath out in the inhaler)</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Place the inhaler between lips and teeth</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Inhale deep and vigorously through the inhaler</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Hold the breath, if indication of holding breath exists it’s OK</td>
<td>0</td>
</tr>
<tr>
<td><strong>Breezhaler (1)</strong></td>
<td>Open the lid</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Charge a dose (includes placing the capsule right and puncture it)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Breath out and empty the lungs of air (don’t breath out in the inhaler)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Place the inhaler between lips and teeth</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Take a deep and vigorously breath through the inhaler (hear the capsule vibrate)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Hold the breath, if indication of holding breath exists it’s OK</td>
<td>0</td>
</tr>
<tr>
<td><strong>Novolizer/Genuair (1)</strong></td>
<td>Check for doses remaining</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Remove the cap</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Charge the dose</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Breath out and empty the lungs of air (don’t breath out in the inhaler)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Place the inhaler between lips and teeth</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Take a deep and vigorously breath through the inhaler, keep inhaling after the “klick”</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Hold the breath, if indication of holding breath exists it’s OK</td>
<td>1</td>
</tr>
<tr>
<td>Type of inhalers - MDI (n)</td>
<td>Checklist (steps in italics are considered as critical factors)*</td>
<td>Number of errors (n)</td>
</tr>
<tr>
<td>---------------------------</td>
<td>---------------------------------------------------------------</td>
<td>----------------------</td>
</tr>
<tr>
<td><strong>Spacer + MDI (1)</strong></td>
<td><em>Shake the MDI/evohaler or prepare a dose of Respimat as usual</em></td>
<td>0</td>
</tr>
<tr>
<td></td>
<td><em>Attach the inhaler to the spacer</em></td>
<td>0</td>
</tr>
<tr>
<td></td>
<td><em>Place the mask to the mouth</em></td>
<td>0</td>
</tr>
<tr>
<td></td>
<td><em>Release a dose from the MDI/evohaler/Respimat</em></td>
<td>0</td>
</tr>
<tr>
<td></td>
<td><em>Breath as usual for five breath to get the whole dose</em></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td><em>Remove the spacer and hold the breath, if indication of holding breath exists it’s OK</em></td>
<td>0</td>
</tr>
<tr>
<td><strong>Respimat (1)</strong></td>
<td>Check for doses remaining</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td><em>Charge the dose</em></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td><em>Remove the cap</em></td>
<td>0</td>
</tr>
<tr>
<td></td>
<td><em>Breath out and empty the lungs of air</em></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td><em>Place the inhaler between lips and teeth and end tight</em></td>
<td>0</td>
</tr>
<tr>
<td></td>
<td><em>Take a deep and slow breath through the inhaler, just at the beginning of the breath – press the top of the inhaler so the aerosol is sprayed out. Keep breath in after the pressure</em></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td><em>Hold the breath, if indication of holding breath exists it’s OK</em></td>
<td>0</td>
</tr>
<tr>
<td></td>
<td><em>It requires two inhalations for a dose, repeat step 1-7</em></td>
<td>1</td>
</tr>
<tr>
<td><strong>MDI/Evohaler (3)</strong></td>
<td><em>Remove the cap</em></td>
<td>0</td>
</tr>
<tr>
<td></td>
<td><em>Shake the inhaler a couple of times (4-5 times)</em></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td><em>Breath out and empty the lungs of air (don’t breath out in the inhaler)</em></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td><em>Place the inhaler between lips and teeth and end tight</em></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td><em>Take a deep and slow breath through the inhaler, just at the beginning of the breath – press the top of the inhaler so the aerosol is sprayed out. Keep breath in after the pressure</em></td>
<td>0</td>
</tr>
<tr>
<td></td>
<td><em>Hold the breath, if indication of holding breath exists it’s OK</em></td>
<td>1</td>
</tr>
</tbody>
</table>

*Appendix 1

When comparing patients judged as adherent with patients judged as non-adherent to inhalation technique, there was no significant difference between the groups except for two factors. It was more common to have COPD among patients judged as non-adherent (p=0.008), and the number of regularly prescribed drugs was significantly higher among patients judged as non-adherent to inhalation technique (p=0.022) (Table 3).
Table 3. Statistical analysis with t-test and chi-square-test regarding the comparison between people with and without errors in inhalation technique.

<table>
<thead>
<tr>
<th></th>
<th>Patients with no errors in inhalation technique (n=17)</th>
<th>Patients with errors in inhalation technique (n=6)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women n (%)</td>
<td>12 (70.6)</td>
<td>6 (100.0)</td>
<td>0.133</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (±SD)</td>
<td>62.1 (±17.0)</td>
<td>73.2 (±11.1)</td>
<td>0.153</td>
</tr>
<tr>
<td><strong>Living situation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Living alone n (%)</td>
<td>7 (41.2)</td>
<td>4 (66.7)</td>
<td>0.338</td>
</tr>
<tr>
<td>Living at home with a relative n (%)</td>
<td>9 (52.9)</td>
<td>2 (33.3)</td>
<td></td>
</tr>
<tr>
<td><strong>Diagnoses</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>COPD n (%)</td>
<td>2 (11.8)</td>
<td>4 (66.7)</td>
<td>0.008</td>
</tr>
<tr>
<td>Asthma n (%)</td>
<td>14 (82.4)</td>
<td>3 (50.5)</td>
<td>0.062</td>
</tr>
<tr>
<td><strong>Number of medications</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (±SD)</td>
<td>6.1 (±4.2)</td>
<td>10.5 (±1.9)</td>
<td>0.022</td>
</tr>
<tr>
<td><strong>Years of having inhalators</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (±SD)</td>
<td>8.7 (±11.7)</td>
<td>9.8 (±10.3)</td>
<td>0.828</td>
</tr>
<tr>
<td><strong>Have received an instruction about inhalers</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes n (%)</td>
<td>15 (88.2)</td>
<td>5 (83.3)</td>
<td>0.769</td>
</tr>
<tr>
<td>No n (%)</td>
<td>2 (11.8)</td>
<td>1 (16.7)</td>
<td></td>
</tr>
<tr>
<td><strong>MARS-5</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-adherent patients (5-23 p) n (%)</td>
<td>5 (29.4)</td>
<td>2 (0.3)</td>
<td>0.858</td>
</tr>
<tr>
<td>Adherent patients (24-25 p) n (%)</td>
<td>12 (70.6)</td>
<td>4 (66.7)</td>
<td></td>
</tr>
</tbody>
</table>

p=points, SD = standard deviation

*one patient had both asthma and COPD.

Table 4 presents the MARS-5 values. There were more intentionally adherent patients (69.6%) than intentionally non-adherent patients (30.4%) concerning the general use of medications, i.e. all drugs the participants had and not just the inhalers, according to MARS-5, see Table 4.

Table 4. Data about the MARS-5 prevalence.

<table>
<thead>
<tr>
<th><strong>MARS-5</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-adherent patients (5-23 p) n (%)</td>
<td>7 (30.4)</td>
</tr>
<tr>
<td>Adherent patients (24-25 p) n (%)</td>
<td>16 (69.6)</td>
</tr>
</tbody>
</table>
Discussion

In this study there were 26.1% unintentional non-adherent patients according to inhalation technique and 30.4% intentional non-adherent patients according to MARS-5. Two significant results were found when comparing unintentional non-adherent and adherent patients; it was more common to have COPD and more medications in the unintentional non-adherent group than the adherent group. Of the in total 34 observations, 20.7% of the DPI-observations had at least one critical error while the corresponding number was 60.0% in the MDI-observations.

The prevalence of patients that were unintentional non-adherent according to inhalation technique was 26.1%. This is in line with or lower compared to other studies that have investigated inhalation technique, where ranges from 24.2% to 64% have been found (8, 21, 22). In these studies, one or more critical factor not correctly performed is defined as non-adherence, the same as in the present study. In the study of Rootmensen et al. the prevalence (40.0%) were a summarized value of all inhalers included in the study (21), as in the present study. The same applies to the study of Salaneck (64%) (8) and Hesselink et al. (24.2%) (22). Studies that are measuring total errors in inhalation technique, and don’t make a distinction between critical and non-critical factors usually have a higher prevalence, ranging from 71.0%-82.3% (23-25). The prevalence of unintentional non-adherence in this study would increase if all errors should be included and not only the critical ones.

As mentioned, the prevalence in the present study is in line with one study (22) but lower compared with two other studies (8, 21). This can depend on the fact that the present study only had 23 patients while Rootmensen et al. included 156 patients, Salaneck et al. 53 patients and Hesselink et al. 558 participants (8, 21, 22). Typically, a higher number of participants usually indicate a more accurate result because of the fact that a larger sample reflects the true population (users of inhalers) better (26).

Older age is another factor that can affect the adherence negatively (20), in the study of Rootmensen et al. the mean age was 61±14 years, in the study of Salaneck it was 79±7.5 years, in Hesselink et al. it was 48.6±16.5 years and in the present study it was 65±16.2 years. According to the previous study, this is accurate, since there were less faults in the study of Hesselink et al. (24.2%) and more faults in the other two, 64.0% respectively 40.0% (8, 21, 22).

Nevertheless, the results from all these studies, including the present one, conclude that incorrect use of inhalers is a problem. How big of a problem there is, is debatable. Also studies from early 1990 conclude that there is problem with inhalation technique in patients with asthma and COPD (27, 28). This suggests that incorrect use of inhalers have been a problem for a long time, and it does not seem to have been resolved.

The mean value for intentional non-adherent (MARS-5) was 30.4%. This is lower than in other studies, were ranges between 35.3-58.0% have been found (9, 29, 30). A reason that the result in this study is lower can be because of the fact that the present study had a smaller number of participants. It must be said that the study of Sriram et al. is similar to the present study, while the studies of Tommelein et al. and Garcia-Marcos et al. compare the MARS-5 questionnaire with other direct adherence measuring methods (9, 29, 30). To overestimate intentional adherence with self-reported scales is known (13, 29, 31). Leading to that the value of the intentional non-adherent in the present study, 30.4%, actually may be a bit higher due to patients ability to overestimate their adherence, and possibly in the range as the other articles.

One of the questions to examine was if there were more errors using DPI than MDI. This study found that there were more incorrect observations regarding MDIs (60.0%) than DPIs (20.7%), the opposite of what the questions to examine was. This seems to be a result not in line with most other studies investigating which type of device that is associated with
the most correct use. A study of Molimard et al. have found that there were 28% critical errors with MDI while there were 11-32% with aerolizer, diskus, turbuhaler (DPIs) and autohaler (a kind of MDI)(32). The results from a study performed by Melani et al. indicated that there were more faults using DPI compared to MDI, the opposite to the results in the present study. But they are careful to point out that the study they did was not comparing DPI and MDI (7). Further, there are other studies that show that MDI are better than DPI, both in adherence aspect and in the fact that it lower exacerbations more than DPI (33, 34).

Another study, an in vitro study, has shown that MDI benefits more than DPI according to where the substances end up in the airway system. The study showed that correct administration with MDIs provide more drugs to the tracheobronchial tree (8.1%) than administration with DPIs (4.2%), while DPIs (69.8%) provide more drugs to the mouth and throat than MDIs (40.0%) (35). This favor MDIs since the drugs come closer to their active site and can therefore give better effect. Further, this in vitro study also investigated differences between MDIs and DPIs when these are used incorrectly. The study found that MDI (5.8%) provides more drugs to the tracheobronchial tree than DPI (3.3%) with incorrect use (35), i.e. MDIs are considered better in this aspect as well. This in vitro study together with the results from previous mentioned studies (7, 32-34), supports the hypothesis of the present study, that it seems to appear more errors with DPI than MDI, i.e the opposite of what was found in the present study.

As mentioned in the introduction, DPIs work by the patient’s own breath and inhalation, and among very ill patients with low breathability this can be a severe problem since enough drugs do not reach the lungs. On the other hand, coordination while firing the aerosol (MDIs) can be hard for some patients (35). Regional Council Skåne recommends DPI before MDI (exception is respimat) due to not such a big price difference with MDIs and because no studies have, according to them, shown that there are any benefits to any type of inhaler (36). According to County Council of Västerbotten, patients try out their own inhaler according to adherence together with a COPD-nurse for best effect. If MDIs are used continuously, a spacer is recommended for best effect and to avoid the risk for fault in the coordination step. However, there is a larger proportion of DPIs than MDIs recommended in the therapy recommendations (37).

In conclusion, due to few observations this study can only indicate that there are more errors in incorrect technique with MDI than DPI even though previous studies indicate the opposite (7, 32-35). One thing that could have affected the result in the present study is that there was much more observations with DPI then MDI which makes the DPI and MDI not comparable.

Another question of interest were “which are the most common mistakes when using an inhaler?”, and a step that almost all of the patients missed was to check how many doses were left in the inhalers before using them. This result is similar to a previous study investigating turbuhaler and accuhaler (9). This step was not applied as a critical error in the checklists in the present study but since almost every patient missed it, it’s suggested that it should have been. This because if the patient never check the counter, they do not know if there is any doses left. This can indicate that patients could inhale from empty inhalers, which may result in deterioration of the disease due to lack of effect. However, the patients might have acted differently since they knew they were using placebo inhalers and therefore did not think they needed to check the dose counter.

When comparing the groups with and without error in inhalation technique, this study only found two significant results. Patients who were judged as unintentional non-adherent to inhalations technique suffered from COPD to a greater extent and were generally treated with a larger number of medications compared to those not judged adherent. The fact that patients judged as unintentional non-adherent have a larger number of medications is confirmed by the review of Sanduzzi et al. that mentioned that a higher number of medications and a greater number of doses (inhalations) can contribute to a lower general
adherence (20). A reason that there was a difference between people with and without errors in inhalation technique according to a larger number of medications can be due to the fact that the group with errors has more instructions to their larger number of medications to remember. They have therefore more to keep in order and a greater chance of making mistakes unlike the ones that have a smaller number of medications.

It has previously been found that COPD and asthma patients have a poor unintentional adherence according to inhalation technique (7-10). Though, it cannot be found in any of these articles that COPD is associated with unintentional non-adherence as presented in the present study. These articles only mentioned that asthma and/or COPD patients had errors in inhalation technique (7-10) and therefore indirect are non-adherent according to the studies’ definitions. A study of Plaza et al. found though, that COPD-patients are more non-adherent according to inhalation technique than asthma-patients (38). To actually see if the disease COPD affects the patient’s to be unintentional non-adherent according to inhalation technique a larger study of patients with both asthma and COPD must be performed.

One association that was investigated in the present study was if the intentional adherence (MARS-5 value) was associated with unintentional adherence (critical errors in inhalation technique), but no such association was found. This is however in line with another study that investigated intentional adherence and unintentional adherence (9). A reason that no association were found may depend, once again, on the low number of participants or simply because MARS-5 is not a good method for measuring adherence in patients with asthma and/or COPD, like other studies has shown (29, 30).

Other studies have found that absence of instructions, older age and no education in inhalation technique are associated with poor inhalation technique (7, 8, 10). None of these characteristics were found to be significant in the present study, perhaps according to the few number of participants. Even though no associations were found in the present study between unintentional non-adherent patients and patients that had received an instruction about inhalers, other studies have (10, 24). It is therefore suggested that all patients should get a thorough instruction of the inhalers and time to practice in the health care system to minimize the risk of being worse in the asthma and/or COPD or hospitalized, which can happen with poor inhalation technique (4, 6, 7).

Limitations of the study
A major advantage of using observations as a method to determine the patients’ inhalation technique is that it was a good way to judge how the patients are using their inhalers in their everyday-life. Along with interviews this was a suitable way to understand what contributed to their errors in inhalation technique. Confirmation bias may be relevant in this study since the observer could have missed some steps in the observations. It must also be said that the present study hasn’t investigated if the drugs in the inhalers actually reach the lungs, the study relies entirely on the fact the errors in critical factors are equal to non-adherence and that the drugs most likely don’t reach the lungs.

Another factor that wasn’t taking into consideration in this study was if the patients inhaled the DPIs with enough force. The reason to not include this factor was that only ellipta and diskus had whistles that marked if the force of the inhalation was good enough. This could be a bias in the step “inhale deep trough the inhaler” since the observer couldn’t actually see or decide if the inhalation was deep enough, but only if the patient tried to inhale. According to a previous study by Sulaiman et al with 103 participants and 5045 inhalations there were 1204 inhalations that had errors during one month, low inhalation force were the most common error in inhalation technique (27%) (39). Having said that, a lot of patients with DPI made the step “inhale deep through the inhaler” right. But since there is no indication if the inhalation was strong enough there were probably more patients who had error in the step “inhale deep trough the inhaler” than shown in this study. For that reason, it is not absolutely certain that the drug reach the lung and their active site.
Regarding intentional adherence, there is not much research done with MARS-5 to compare if it is a reliable method according to direct adherence measurement. But there is a few, for example the article about schizophrenia- and bipolar patients where both serum concentrations and MARS-5 value correspond to each other. According to this, MARS-5 is a trustworthy measurement of intentional adherence (19). However, other studies suggest that MARS-5 is not a trustworthy measurement of intentional adherence. One study of Garcia-Marcos et al. compared MARS-5 values with a direct method of measuring adherence, electronic monitoring, and found out that MARS-5 is not a trustworthy measurement for intentional adherence. However, the study was done in 133 children between 2-12 years old and it was their parents that answered the MARS-5 statements (30). Another study of Tommelein et al. compared MARS-5 with medication refill adherence, MRA, in 613 patients with COPD and found that MARS-5 not is a reliable method for measuring adherence. In this study MARS-5 overestimated the patients adherence. The MRA-ratio took both the days of supply, i.e. how much they took out from the pharmacy, and the days the patients were supposed to use their medications into account. Though, the study mentioned that MRA can be limited reference due to that MRA only measures how much medicines the patients are having from the pharmacy and it is then assumed that the patients are taking the medications as they should (29).

Another bias might be that some patients didn’t understand how to answer the MARS-5 scale and didn’t answer by always, often, sometimes, rarely and never but with mostly “no”. When this happened the interviewer repeated “rarely and never”, because these were the answers most closely to “no”, and almost every patient answered with “never” without second thoughts. To minimize the risk for bias, the interviewer should have repeated all the answer options instead. One other thing that can have affected the MARS-5 result, and can be a bias, was that a lot of the patients were laying in a medical consultation room with other patients. This can affect the patients in a way that they answered the statements with other patients. This can affect the patients in a way that they answered the statements with the answer that made them appear or sound better than they were. This can be a problem also towards the interviewer, but to decrease the risk, the patient should be in a room alone with the interviewer.

Since no reference has been used in this study to see if the MARS-5 value is correct or not, it can only be assumed that the MARS-5 value is correct or a bit overestimated due to previous studies (13, 29, 31). With this small number of patients and no reference there is difficult to conclude if the results are accurate or not.

Five men and 18 women were included in the study. That it was a greater proportion of women can depend on the fact that COPD is getting more and more common among women. Among people with COPD there are more women than men that are being hospitalized (40), which this study also indicates. One reason that women are being more affected than men from this disease can depend on the fact that women lungs are more sensitive to smoke (40, 41). A study from 2017 of Cephus et al. showed that women have more ILC2 than men, (ILCS2 = type 2 innate lymphoid cells) and ILC2 is associated with asthma. They came to the conclusion after much laboratory work in mice, that, in short, testosterone reduces ILC2 (42).

It was seven women and five men, a total of 12 patients that declined to participate in the study. One reason for the large proportion, in relation to the number of participates, can depend on the fact that they were hospitalized on the orthopedic, geriatric and medical departments. Patients that are laying at these kind of wards are often in bad shape and are very sick or have a lot of pain. The reason to exclude patients with dementia was that it is difficult to interview these patients according to inhalation technique. The reason for non-adherence in patients with dementia can be because of the illness or because they haven’t received any education and it is difficult to distinguish this.

The importance of this kind of studies
It’s important with these kind of studies because it is important to come to a conclusion regarding which kind of inhaler that is easiest to use and have least errors in critical factors.
Another reason why this kind of studies is important is that it has been showed in previous studies (7, 10) that training and adaption of the inhaler to the patient is required to avoid unintentional non-adherence. To save more lives in the middle- and low income countries, where the highest mortality in both asthma and COPD are observed (80% respectively 90%) (43, 44), it’s important to find out which inhaler that is the best according to both adherence and price, to make it so cost effective as possible. Nothing has, until this day, been found regarding which inhaler type is the best and/or most cost effective (36).

Conclusion
The conclusion that can be drawn from this study is that it indicates that both unintentional non-adherence (26.1%) and intentional non-adherence (30.4%) among people with asthma and COPD is a problem in Sweden. The most frequent errors among patients is not checking for doses remaining in the inhaler. Unintentional non-adherence patients have more medications and suffer from COPD to a greater extent. There are also indications that there are more critical errors using MDI than DPI. However, to determine this study’s result, a larger study with a greater number of participants is needed.

Acknowledgement
I would like to thank supervisor Maria Gustafsson for great cooperation, Bettina Pfister for helping with recruitment of patients, Eva Sunna for answer to all questions and information and finally to all the patients who participated in this study.
References
8. A S. Assessment of Inhaler Handling in Elderly Hospitalized Patients with Asthma or COPD. Uppsala University: Department of Pharmaceutical Life Sciences. Master’s program in clinical pharmacy; 2016.


Appendix 1

Checklista – Autohaler (Airomir, Aerobec)

Ta bort skyddshylsan.
Skaka inhalatorn lätt.
Håll inhalatorn upprätt och dra i den röda spaken rakt upp för att ladda en dos.
Andas ut och töm lungorna på luft, men inte ner i inhalatorn.
Placera munstycket mellan tänderna och läpparna och slut tätt.
Ta ett djupt och långsamt andetag genom inhalatorn. Sluta inte när klicket hörs.
Håll andan i ca 5-10 sekunder (om antydan att hålla andan finns är det OK).

Referenser:

Checklista – Breezhaler (Onbrez, Seebri och Ultibro)

Ta av locket på breezhalern (BH) och ta fram en kapsel från blistret.
Ta tag i munstycket och vik det bakåt, placera kapseln kapselbehållaren och vik tillbaka munstycket tills ett klick hörs.
Håll BH mellan tummen och pekfingret och tryck till från båda sidor för att göra hål på kapseln.
Andas ut och töm lungorna på luft, men inte ner i BH.
Placera munstycket mellan tänderna och munnen, slut tätt.
Inhalera kraftigt, djup och länge genom BH så att ett snurrande ljud hörs.
Efter inhaleringen så försök att hålla andan i ca 5-10 sek (om en antydan om att hålla andan så är det OK).
Ta tag i munstycket och vak det bakåt för att kontrollera att kapseln är tömd. Om den inte är tömd så repetera steg 4-7.
När kapseln är tömd så ta bort kapseln och släng den.
Skölj munnen om ICS.

Referenser:

Checklista – Diskus (Ventoline, Serevent, Flutide, Seretide)

Kontrollera att det finns doser kvar och håll diskusen horisontellt och öppna den.
Ladda en dos genom att dra ”spaken” så långt det går tills en klick hörs.
Andas ut och töm lungorna på luft, men inte ner i diskusen.
Slut läpparna och tändera runt munstycket.
Inhalera kraftigt och djupt genom diskusen.
Håll andan i ca 5-10 sekunder (om antydan till att hålla andan finns är det OK).
Skölj munnen om ICS.

Referenser:

Checklista – Easyhaler (Buventol, Giona, Beclomet, Bufomix)

Kontrollera hur många doser det finns kvar och ta bort skyddshylsan från easyhalern (EH).

Skaka EH kraftigt några gånger (3-5 ggr).

Håll EH upprätt och klicka på ”knappen” en gång, ett klick ska höras.

Andas ut normalt för att tömma lungorna på luft (inte ner i EH).

Placera munstycket mellan tänder och läppar, var noga med att sluta tätt.

Inhalera kraftigt och djupt via EH.

Efter inhalationen så försök att hålla andan minst 5 sekunder (om ett antydande finns för att hålla andan är det OK).

Skölj munnen med vatten om ICS.

Referenser:

Checklista – Ellipta (Anoro, Incruse, Relvar, Trelegy)

Kontrollera att det finns doser kvar och skjut skyddsslocket åt sidan tills ett klick hörs (dosen är framladdad).

Andas ut och töm lungorna på luft men inte ner i inhalatorn.

Slut läpparna och tänderna runt munstycket.

Andas in med ett djupt, långt och jämnt andetag via inhalatorn.

Håll andan ca 5-10 sekunder (om antydan att hålla andan finns så är det OK).

Skölj munnen med vatten om ICS.

Referenser:

Checklista – Evohaler (Ventoline, Serevent, Flutide, Seretide)

Ta bort skyddshylsan.

Skaka inhalatorn väl, ca 4-5 gånger.

Andas ut och töm lungorna på luft, men inte ner i inhalatorn.

Placera munstycket mellan tänderna och läpparna och slut tätt.
Ta ett djupt och långsamt andetag genom inhalatorn, precis vid andetagets början så tryck på toppen av inhalatorn så att aerosolen sprayas ut. Fortsätt att andas in efter trycket.
Håll andan i ca 5-10 sekunder (om antydan att hålla andan finns är det OK).
Skölj munnen med vatten om ICS.

Referenser:

Checklista – Forspiro (AirFluSal)
Kontrollera att det finns doser kvar och öppna skyddslocket så att munstycket syns. Luft därefter munstycket så långt det går tills ett klick hörs, vik tillbaka munstycket tills ett klick hörs.
Andas ut och töm lungorna på luft men inte i inhalatorn.
Slut läpparna och tänderna kring munstycket, skyddslocket ska då vara neråt.
Andas in djupt men jämt genom inhalatorn.
Håll andan i 5-10 sekunder (om antydan till att hålla andan finns så är det OK).
Skölj munnen efter om ICS.

Referenser:

Checklista – HandiHaler (spiriva)
Öppna det gråa skyddslocket genom att trycka på den gröna knappen.
Vik bak det vita munstycket och lägg ner en kapsel från blistret i kapselhållaren.
Vik tillbaka det vita munstycket tills det hörs ett klick.
Gör hål på kapseln genom att klicka på den gröna kapseln hela vägen ner till botten
Andas ut och töm lungorna på luft, men andas inte ner i inhalatorn.
Slut läpparna och tänderna runt munstycket.
Andas in djupt men jämt genom inhalatorn (hör kapseln vibrera).
Håll andan i ca 5-10 sekunder (om antydan till att hålla andan finns så är det OK).
Gör om steg 5-8 för att försäkra sig om att allt innehåll i kapseln är tömt.

Referenser:

Checklista – Novolizer (Ventilastin, Formatris och Novopulmon) samt Genuair (Eklira och Duaklir).
Kontrollera att det finns doser kvar och ta bort skyddshylsan.
Ladda inhalatorn genom att klicka på knappen. Det röda fönstret ska då bli grönt, vilket indikerar att en dos har laddats fram.

Andas ut och töm lungorna på luft, men inte i inhalatorn.

**Slut läpparna och tänderna runt munstycket.**

**Inhalera kraftigt och djupt genom munstycket.** Ett klick kommer att höaras, fortsätt att inhalera efter klicket.

Håll andan i ca 5-10 sek (om en antydan om att hålla andan finns så OK).

Kolla så att fönstret har blivit rött igen, det bekräftar en godkänd inhalering.

Referenser:


Checklista – Respimat (Striverdi, Spiriva, Spiolto)

Kontrollera att det finns doser kvar medan det genomskinliga locket fortfarande är stängt, vrid den nedre delen av inhalatorn tills ett klick hörs (samma riktning som pilen visar).

Vik upp det genomskinliga locket.

Andas ut och töm lungorna på luft.

Placera munstycket mellan tänderna och läpparna och slut tätt.

Ta ett djupt och långsamt andetag genom inhalatorn, precis vid andetagets början så tryck på den gråa knappen på inhalatorn så att aerosolen sprayas ut. Fortsätt att andas in efter trycket.

Håll andan i ca 5-10 sekunder (om antydan att hålla andan finns är det OK).

**För en dos så krävs två inhalatorer → Upprepa steg 1-6.**

Referenser:


Checklista – Spacer (till MDI, evohaler, respimat)

Fäst MDI/evohaler/respimat på spacern och skaka MDI/evohaler eller förbered respimat genom att ladda en dos som vanligt.

Placera munstycket/masken till munnen.

Tryck en gång på MDI/evohaler/respimat.

Andas 5 andetag helt normalt för att få i hela dosen. Om optichamber diamond används så kan man se hur många andetag som tas samt att den ger ifrån sig ett ljud om patienten inhalerar för kraftigt.

Ta bort spacern från munnen och försök hålla andan i 5-10 sekunder (om antydan till att hålla andan finns är det OK).

Om fler doseringar har ordinerats eller om respimat används så görs proceduren om.

Referenser:

Checklista – Spiromax (Duoresp och aerivio)

Kontrollera att det finns doser och håll inhalatorn med locket neråt och vik ner skyddslocket helt tills ett klick hörs, en dos är då laddad.

Andas ut och töm lungorna på luft.

Slut läpparna och tänderna kring munstycket, håll inte fingrarna på luftventilen så att den blockeras.

Andas in kraftigt och djupt genom inhalatorn.

Håll andan i 5-10 sekunder (om antydan till att hålla andan finns så ok).

Skölj munnen efter om ICS.

Referenser:

Checklista – Spray/MDI (Airomir, Airsalb, AeroBec, Alvesco, Flutiform, Innovair, Atrovent, Symbicort)

Ta bort skyddshylsan.

Skaka inhalatorn väl, ca 4-5 gånger.

Andas ut och töm lungorna på luft, men inte ner i inhalatorn.

Placera munstycket mellan tänderna och läpparna och slut tätt.

Ta ett djupt och långsamt andetag genom inhalatorn, precis vid andetagets början så tryck på toppen av inhalatorn så att aerosolen sprayas ut. Fortsätt att andas in efter trycket.

Håll andan i ca 5-10 sekunder (om antydan att hålla andan finns är det OK).

Skölj munnen med vatten om ICS.

Referenser:
2. FASS. Airsalb. [Internet]. Läkemedelsföreningen, LIF. Hämtat från: http://www.fass.se/LIF/product?userType=2&nplId=20061206000076. [uppdaterad 2017-10-20, citerad 2018-06-15].
5. FASS. Flutiform. [Internet]. Läkemedelsföreningen, LIF. Hämtat från: http://www.fass.se/LIF/product?userType=2&nplId=2010033000130. [uppdaterad 2017-12-13, citerad 2018-06-15].

Checklista – Turbuhaler (Bricanyl, Oxis, Pulmicort, Symbicort)

Kontrollera att det finns doser kvar och ta bort locket.
Vrid den nedersta delen åt ett håll (det spelar ingen roll vilket) och sen tillbaka så att ett klick hörs medan turbuhalern (TBH) är stående (lutning på 45 grader är ok).
Andas ut fullständigt och töm lungorna på luft (dock inte ner i TBH).
Sätt munstycket mellan tänder och läppar sittande eller stående (fri luftstruppe).
Andas in djupt och kraftigt genom inhalatorn.
Försök hålla andan i max 10 sec (om antydan till att hålla andan finns är det OK). Skölj munnen om ICS.

Referenser:

Checklista – Twistrhaler (Asmanex)

Kontrollera att det finns doser kvar samt kolla så att räknaren och pilen på skyddshylsan står mitt för varandra.
Håll inhalatorn upprätt (rosa/rödbruna botten neråt) och öppna inhalatorn genom att ta bort skyddshylsan. När skyddshylsan tas bort kommer räknaren att minska ett steg (vid borttagandet av skyddshylsan laddas dosen).
Andas ut och töm lungorna på luft men inte ner i inhalatorn.
Slut läpparna och tänderna runt munstycket.
Ta ett djupt och snabbt andetag genom inhalatorn.
Håll andan i 5-10 sekunder (om antydan att hålla andan finns så är det OK). Skölj munnen med vatten.
Sätt tillbaka skyddshylsan ordentligt efter inhalationen, detta för att ladda dosen till nästan inhalation.

Referenser:
1. FASS. Asmanex, Twistrhaler. [Internet]. Läkemedelsföreningen, LIF. Hämtat från: http://www.fass.se/LIF/product?userType=2&nplId=20020208000286&docType=7&scrollPosition=493. [uppdaterad 2017-12-14, citerad 2018-06-15].

Checklista – Zonda (braltus)
Öppna skyddsocklet. Och öppna munstycket genom att lyfta det bakåt.
Lägg ner en kapsel från burken i kapselhållaren.
Vik tillbaka det munstycket tills det hör ett klick.
Gör hål på kapseln genom att klicka på den vita knappen hela vägen ner till botten.
Släpp därefter knappen.
Andas ut och töm lungorna på luft, men andas inte ner i inhalatorn.
Slut läpparna och tänderna runt munstycket.
Andas in djupt men jämnt genom inhalatorn (hör kapseln vibrera).
Håll andan i ca 5-10 sekunder (om antydan till att hålla andan finns så är det OK). Gör om steg 5-8 för att försäkra sig om att allt innehåll i kapseln är tömt.

Referenser:
1. FASS. Braltus. [Internet]. Läkemedelsindustriföreningen, LIF. Hämtat från: http://www.fass.se/LIF/product?userType=2&nplId=20141028000031. [uppdaterad 2016-07-20, citerad 2018-06-15].
Appendix 2

Bakgrundsinformation (från journalen):
Datum: _________________

Identifikationsnummer: _________________

Kön: Man [ ] Kvinna [ ]

Ålder: _________________

Avdelning: _________________ Sängplats: _________________

Boendesituation: Ensamboende [ ] Sammanboende [ ]

Vikt: _________________ Längd: _________________ Kreatinin: _________________

Rökare: JA [ ] NEJ [ ] Övrigt: _________________

<table>
<thead>
<tr>
<th>Diagnoser förutom KOL/astma</th>
<th>Ja</th>
<th>Nej</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hjärtsvikt</td>
<td></td>
<td></td>
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<tr>
<td>Hypertoni</td>
<td></td>
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<tr>
<td>Förmaksflimmer</td>
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<td></td>
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<tr>
<td>Diabetes Mellitus</td>
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<td></td>
</tr>
<tr>
<td>Cancer, nuvarande eller tidigare</td>
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<td></td>
</tr>
<tr>
<td>Hjärtinfarkt, tidigare</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke, tidigare</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Läkemedel:

Antal stående läkemedel (boendet): __________

Antal vid behovs LM: ____________________

≥ 5 stående läkemedel: Ja [ ] Nej [ ]

Ej inräknat:

Korta kurer, ex antibiotika
Utvärtes LM, ex mjukgörande LM, Schampo

Hur länge har patienten haft aktuella inhalationsläkemedel _________________

<table>
<thead>
<tr>
<th>Typ av aktuella inhalatorer hemma</th>
<th>Styrka</th>
<th>Dos</th>
<th>Insatt (datum)</th>
<th>Med till sjukhuset</th>
</tr>
</thead>
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</tbody>
</table>
### Diagnoser för inhalatorer

<table>
<thead>
<tr>
<th></th>
<th>Ja</th>
<th>Nej</th>
</tr>
</thead>
<tbody>
<tr>
<td>KOL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Astma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Övrigt</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### På avdelning

Patienten lades in detta datum ______________________

<table>
<thead>
<tr>
<th>Inhalationsläkemedel på avdelning</th>
<th>Styrka</th>
<th>Dos</th>
<th>Insatt (datum)</th>
<th>Tas enligt patient</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>

### Frågor till patienten under läkemedelsamtalet

**A: Inhalationsläkemedel**

1. Har du med dina inhalationsläkemedel?

<table>
<thead>
<tr>
<th>JA</th>
<th>NEJ</th>
</tr>
</thead>
</table>

2. Har du någon gång fått en genomgång hur du hanterar dina inhalationsläkemedel?

<table>
<thead>
<tr>
<th>JA</th>
<th>NEJ</th>
</tr>
</thead>
</table>

**B: Hjälp med läkemedelshantering:**

1a. Har du någon som hjälper dig med dina läkemedel?

<table>
<thead>
<tr>
<th>JA</th>
<th>NEJ</th>
</tr>
</thead>
</table>

1b. Får du dina läkemedel förpackade i dospåsar?

<table>
<thead>
<tr>
<th>JA</th>
<th>NEJ</th>
</tr>
</thead>
</table>

1c. Om svaret är JA (1a), vem hjälper dig?

- [ ] Make/Maka
- [ ] Annan släktning
- [ ] Hemtjänsten
- [ ] Sjuksköterskan
- [ ] Någon annan, nämligen..............................

1d. Vad är det du får hjälp med?

- [ ] Inköp av läkemedel
- [ ] Fördelning till t ex dosett/mugg
- [ ] Administrering t ex med spruta, inhalator
- [ ] Delning/krossning av tabletter
- [ ] Annat, nämligen.................................
2. Hur vet du vilka läkemedel du ska ta och när du ska ta dem?
- Kommer ihåg ur minnet
- Burketiketterna
- Recepten
- Läkemedelslistan
- Annat sätt, nämligen..............................

3. Vad använder du för knep, rutiner eller sätt för att komma ihåg hur du skall ta dina läkemedel?
- Inget speciellt
- Med måltid
- Dosett
- Signal (klocka)
- TV, radio
- Annat, nämligen.....................................

4. Praktisk hantering
Svårt att svälja tabletter? Ja Nej
Krossar/delar du tabletter Ja Nej
Får du ut LM ur förpackningen? Ja Nej
Känner du igen LM/förpackningen? Ja Nej
Tycker du inhalationer är krångliga? Ja Nej
Andra problem...........................................

5. Har du några upplevda biverkningar?

C: Följsamhet till inhalationsläkemedel:

<table>
<thead>
<tr>
<th></th>
<th>Alltid</th>
<th>Ofta</th>
<th>Ibland</th>
<th>Sällan</th>
<th>Aldrig</th>
</tr>
</thead>
<tbody>
<tr>
<td>M1 Jag glömmer att ta mina mediciner</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M2 Jag ändrar på doseringen av mina mediciner</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M3 Jag gör uppehåll i min medicinering</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>M4 Jag bestämmer mig för att hoppa över en dos</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M5 Jag tar mindre än jag har blivit ordinerad</td>
<td></td>
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</tr>
</tbody>
</table>

1. Vad är anledningen till att du inte tar dina inhalationsläkemedel?
Appendix 3
INFORMERAT SAMTYCKE

Inhalationsteknik och läkemedelsföljksamhet hos personer med inhalationsläkemedel

Astrid Elander, Umeå Universität
astridelander@hotmail.com

Vänligen kryssa i rutan

1. Jag intygar att jag har läst och förstått informationsbrevet för ovanstående studie och att jag har haft möjlighet att ställa frågor.

2. Jag förstår att min medverkan är frivillig och att jag när som helt, utan att ange någon anledning, kan avsluta min medverkan.

3. Jag vill delta i ovanstående studie och jag tillåter att resultatet kan användas för att färdigställa detta projekt samt att det kan användas i framtida publikationer.

Jag samtycker till att delta i denna studie och att apotekarstudenten får ta del av min läkemedelslista och patientjournal.

Underskrift: ____________________________________________

Datum: ___________________________
Appendix 4

Information till patient angående ett vetenskapligt projekt om inhalationsteknik och följsamhet till behandling med inhalationsläkemedel

Följande brev ger bakgrundsinformation angående det projekt som du ombeds delta i. Projektet genomförs vid Institutionen för farmakologi och klinisk neurovetenskap vid Umeå universitet.


Alla uppgifter kommer att behandlas konfidentiellt, med samma sekretess som i övriga delar av sjukvården, och då resultaten presenteras kommer det att göras på ett sådant sätt att de inte kan kopplas till någon enskild person. För denna vetenskapliga studie är Umeå universitet personuppgiftsansvarig och ansvarar för att data behandlas enligt personuppgiftslagen (PUL). Om du deltar i studien har du rätt till ett kostnadsfritt registerutdrag en gång per år och rätt att få rättelse av eventuellt felaktiga uppgifter.

Studien är godkänd av en etikprövningsnämnd.

Du har tillfrågats om att vara med i detta projekt för att du lagts in på medicinavdelningen, geriatriken eller ortopedavdelningen i Umeå. Att vara med i studien förväntas inte innebära några risker för dig.

Om du inte vill delta i denna studie har du naturligtvis möjlighet att tacka nej, och du behöver inte ange något särskilt skäl till detta. Du kan också när som helst meddela att du vill avbryta ditt deltagande, även om du först sagt ja.

Om du har frågor angående studien vänligen kontakta:

Astrid Elander, apotekarstudent
Telefon: 076-8064883
astridelander@hotmail.com

Ansvarig för studien är:
Maria Gustafsson, apotekare
Klinisk farmakologi
Umeå Universitet