"Impact of a pharmaceutical intervention to improve adherence of inhaled medication in asthma and COPD patients"

Baseline data from a randomized controlled trial

5th Swiss Health Services Research Symposium, 01.03.2017, Bern

Claudia Gregoriano, Eidg. dipl. pharm., PhD-Candidate
University Clinic of Medicine, Clinical Research
Ja ja, ich inhaliere ziemlich oft... aber keine Angst, ich mache keine Lungenzüge!!!
Clinical relevance of medication adherence

• On average, adherence to long-term therapy is estimated to be around 50%\(^1\)

• Poor adherence to long-term therapies may result in poor health outcomes and increased health care costs\(^2\)
  • Effectiveness of treatment is compromised
  • Negative effect on quality of life

• Despite the significant progress in pharmacological and non-pharmacological treatment in recent years, symptom control and management in asthma and COPD remain suboptimal

• Increased risk for recurrent exacerbations, which lead to massive costs for the health-care system (50-75% of the costs are caused by exacerbations\(^3\))

• Previous literature is limited to refill adherence and some retrospective studies based on pharmacy record databases

\(^2\) Hughes et al., The impact of non-adherence on the cost-effectiveness of pharmaceuticals: a review of the literature, Health Econ. (2001)
\(^3\) Celli et al., Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. The European respiratory journal (2004).
Aims

• To investigate the adherence of patients with asthma or COPD to prescribed long-term inhaled medication with specific electronic devices which provide data about the timing of inhaler action

• To assess the effects of an acoustic reminder and close supervision by a pharmacist on adherence with these medications and diseases outcomes
Study design

- On-going prospective single-blind randomized interventional trial

- Recruitment of at least 154 asthma and COPD patients
  - 70 subjects for each study group
  - +14 subjects for drop outs (+10%)

- Since January 2014, recruitment of in- and outpatients from several hospitals in the Basel region

- Inclusion criteria:
  - Clinical diagnosis of asthma or COPD
  - At least one exacerbation during the past 12 months
  - At least one inhaled medication, which is inhaled on a daily basis

- Exclusion criteria:
  - Severe comorbidities
  - Pregnant or lactating women

- Investigation of the adherence over the period of 6 months
  - 4 clinical visits (lung function tests, questionnaires and evaluation of inhalation techniques)
Intervention and control group

- Random assignment to either the intervention or control group
- Patients are not explicitly informed to which group they had been randomized
- Intervention group:
  - Monitoring of adherence with Audio-Reminder
  - Support calls when:
    - Use of rescue medication doubles
    - Inhaled medication is not taken as prescribed for more than 2 consecutive days
  - Feedback on adherence at each visit
- Control group:
  - Monitoring of adherence without Audio-Reminder
  - No support calls
  - No feedback on adherence
Adherence-Measurements

- Measurements of puff inhalers: Smartinhalers
  - Electronic monitor for MDI, Diskus, Turbohaler
  - Plastic casing into which a standard inhaler can be inserted
  - Each actuation (depression of the canister, turning off the device) is recorded with date and time

- Measurements of inhalation powder capsules: “Polymedication Electronic Monitoring System (POEMS)”
  - Electronic film technology for inhaled medication with capsule system
  - Self-adhesive polymer film with loop of conductive wires → Date and time are recorded when a loop is broken
Current status of the study

169 enrolled patients:

• 148 patients: completed the study
• 1 patient: ongoing

20 drop outs:
• 1 patient died after the 2nd visit
• 6 patients had to stop because of worsening health status
• 13 patients stopped for other reasons
Baseline data (n=149)

<table>
<thead>
<tr>
<th>Patients’ characteristics</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age [yrs]</td>
<td>68 ± 8 (range: 29-87)</td>
</tr>
<tr>
<td>Gender</td>
<td>Male: n=96 (64%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diagnoses</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>COPD</td>
<td>n=77 (52%)</td>
</tr>
<tr>
<td>Asthma</td>
<td>n=46 (31%)</td>
</tr>
<tr>
<td>Asthma-COPD overlap</td>
<td>n=26 (17%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>COPD Classification (n=103)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>GOLD I (FEV1 ≥ 80% predicted)</td>
<td>n=8 (7%)</td>
</tr>
<tr>
<td>GOLD II (50% ≤ FEV1 &lt; 80% predicted)</td>
<td>n=44 (43%)</td>
</tr>
<tr>
<td>GOLD III (30% ≤ FEV1 &lt; 50% predicted)</td>
<td>n=40 (39%)</td>
</tr>
<tr>
<td>GOLD IV (FEV1 &lt; 30 % predicted)</td>
<td>n=11 (11%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Smoking status:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-smokers</td>
<td>n=32 (22%)</td>
</tr>
<tr>
<td>Ex-smokers</td>
<td>n=87 (58%)</td>
</tr>
<tr>
<td>Current smokers</td>
<td>n=30 (20%)</td>
</tr>
</tbody>
</table>
# Baseline data (n=149)

<table>
<thead>
<tr>
<th>Medication</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short-acting β2-agonists (SABA)</td>
<td>63</td>
<td>22%</td>
</tr>
<tr>
<td>Long-acting β2-agonists (LABA)</td>
<td>18</td>
<td>6%</td>
</tr>
<tr>
<td>Long-acting anticholinergics (LAMA)</td>
<td>69</td>
<td>24%</td>
</tr>
<tr>
<td>Inhaled corticosteroids (ICS)</td>
<td>13</td>
<td>4%</td>
</tr>
<tr>
<td>Combination of LAMA+SABA/LABA</td>
<td>20</td>
<td>7%</td>
</tr>
<tr>
<td>Combination of LABA+ICS</td>
<td>106</td>
<td>37%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Asthma Control Test (ACT) (n=72)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Sum score</td>
<td>19.5±4.3</td>
</tr>
<tr>
<td>Well-controlled (20-25)</td>
<td>45 (63%)</td>
</tr>
<tr>
<td>Not well-controlled (16-19)</td>
<td>13 (18%)</td>
</tr>
<tr>
<td>Poorly controlled (5-15)</td>
<td>14 (19%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>COPD Assessment Test (CAT) (n=103)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Sum score</td>
<td>16.0±6.9</td>
</tr>
<tr>
<td>Low impact (0-10)</td>
<td>21 (20%)</td>
</tr>
<tr>
<td>Medium impact (11-20)</td>
<td>54 (53%)</td>
</tr>
<tr>
<td>High impact (21-30)</td>
<td>25 (24%)</td>
</tr>
<tr>
<td>Very high impact (31-40)</td>
<td>3 (3%)</td>
</tr>
</tbody>
</table>
Taking adherence over the first 30 days

### Taking adherence for puff inhalers

<table>
<thead>
<tr>
<th></th>
<th>Intervention group (n=56)*</th>
<th>Control group (n=58)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correct dosing days</td>
<td>24.0±5.5 (range:9-30)</td>
<td>19.4±8.5 (range:0-30)</td>
</tr>
</tbody>
</table>

* p<0.01 intervention vs. control group

### Taking adherence for inhalation powder capsules

<table>
<thead>
<tr>
<th></th>
<th>Intervention group (n=38)</th>
<th>Control group (n=46)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correct dosing days</td>
<td>27.8±4.6 (range:4-30)</td>
<td>26.2±5.9 (range:5-30)</td>
</tr>
</tbody>
</table>

### Taking adherence for powder capsules vs. puff inhalers

<table>
<thead>
<tr>
<th></th>
<th>Powder capsules (n=84)*</th>
<th>Puff inhalers (n=53)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correct dosing days</td>
<td>26.9±5.4 (range:4-30)</td>
<td>20.7±7.4 (range:1-30)</td>
</tr>
</tbody>
</table>

* p<0.001 intervention vs. control group

### Taking adherence for once daily dosage vs multiple doses per day

<table>
<thead>
<tr>
<th></th>
<th>Once daily dosage (n=105)*</th>
<th>Multiple doses per day (n=93)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correct dosing days</td>
<td>26.6±5.4 (range:4-30)</td>
<td>20.8±7.7 (range:0-30)</td>
</tr>
</tbody>
</table>

* p<0.001 intervention vs. control group
Conclusions

• The results of our study suggest a beneficial effect of a regular reminder on adherence to long-term medication for treatment of asthma or COPD

• Adherence appears to be better when devices allowing the administration of predefined dose regimens (capsule inhalers) are used compared to devices that have to be loaded by the patient (puff inhalers)

• Adherence with once-daily dosage regimens appears to be higher than adherence observed in treatment plans urging the inhalation of multiple doses per day
Samwassm
Schweizerische Akademie der Medizinischen Wissenschaften
Académie Suisse des Sciences Médicales
Academia Svizzera delle Scienze Mediche
Swiss Academy of Medical Sciences

Gottfried & Julia Bangerter-Rhyner Stiftung

AstraZeneca

Mundi Pharma

Boehringer Ingelheim

Kantonsspital
Baselland
THANKS FOR YOUR ATTENTION
Backup Slides
## Overview of the study structure

<table>
<thead>
<tr>
<th>Schulung</th>
<th>Tag 1 (Erste Visite)</th>
<th>Tag 2-59 (zweite Visite)</th>
<th>Tag 60-119 (dritte Visite)</th>
<th>Tag 120-179 (vierte Visite)</th>
<th>Day 180</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primäres Ziel:</strong></td>
<td>Eintrittsgespräch **</td>
<td>Gespräch **</td>
<td>Gespräch **</td>
<td>Gespräch **</td>
<td>Abschluss-gespräch **</td>
</tr>
<tr>
<td>Korrekte Anwendung der Inhalationsgeräte mit dem Ziel, dass alle Teilnehmer bei Studienbeginn auf demselben Wissensstand sind und dass sie alle wissen wie sie ihre Inhalationsgeräte richtig anwenden</td>
<td>Schwangerschafts-test bei gebärfähigen Frauen **</td>
<td>Lungenfunktion-Messungen **</td>
<td>Lungenfunktion-Messungen **</td>
<td>Lungenfunktion-Messungen **</td>
<td></td>
</tr>
<tr>
<td>**</td>
<td>Lungenfunktion-Messungen **</td>
<td>Beurteilung der Inhalations-technik **</td>
<td>Beurteilung der Inhalations-technik **</td>
<td>Beurteilung der Inhalations-technik **</td>
<td></td>
</tr>
<tr>
<td>**</td>
<td>Fragebögen **</td>
<td>Teilauswertung der registrierten Daten</td>
<td>Fragebögen **</td>
<td>Fragebögen **</td>
<td></td>
</tr>
<tr>
<td>**</td>
<td>Abgabe und Erklärung der Geräte</td>
<td></td>
<td>Teilauswertung der registrierten Daten</td>
<td>Auswertung der registrierten Daten</td>
<td></td>
</tr>
</tbody>
</table>
Smartinhaler ➔ Datatransfer

Patient 1
SmartTurbo
Smartphone
Nexus6 Cellular Data

Patient 2
SmartTurbo
Smartphone
Nexus6 Cellular Data

Patient 3
SmartTurbo
Smartphone
Nexus6 Cellular Data

Nexus6 SmartinhalerLive.com

Investigator 1
Investigator 2
Smartinhaler output

![Graph showing daily usage and peak flow over a period of time.](image)
POEMS output
Stepwise approach for asthma treatment

<table>
<thead>
<tr>
<th>Stufe 1</th>
<th>Stufe 2</th>
<th>Stufe 3</th>
<th>Stufe 4</th>
<th>Stufe 5: zusätzlich zu 4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Patientenschulung, Kontrolle von Risiko- und Umweltfaktoren**

**Bedarfsmedikation (Reliever):**

- **SABA**
- **SABA ODER Low-dose ICS + Formoterol**

**Langzeitmedikation (Controller):**

**Primäre Therapiewahl**

- Low-dose ICS
- Low-dose ICS + LABA
- Medium oder High-dose ICS + LABA
- Anti-IgE bei IgE induziertem Asthma

**ODER**

**Alternative Therapiewahl**

- **LRA**
- Medium oder High-dose ICS
- High-dose ICS + LRA
- Low-dose ICS

**ODER**

**Alternative Therapiewahlen**

- Low-dose ICS + LRA
- Theophyllin

**ODER**

**SABA**: short acting B2-agonist; **ICS**: inhaled corticosteroid; **LABA**: Long-acting beta2-agonist; **LRA**: Leukotrien-rezeptor-Antagonist

Modified according to GINA-Guidelines (www.ginasthma.org)
# COPD Treatment Guidelines

<table>
<thead>
<tr>
<th>Risikogruppe</th>
<th>Primäre Therapiewahl</th>
<th>Alternative Therapiewahl</th>
<th>Weitere Therapiemöglichkeiten</th>
</tr>
</thead>
</table>
| A           | SAAC
**oder**
SABA        | LAAC **oder**
LABA **oder**
SABA + SAAC | Theophyllin            |
| B           | LAAC **oder**
LABA        | LAAC + LABA             | Theophyllin +
**oder** SABA +/oder SAAC |
| C           | ICS +
LABA **oder**
LAAC         | LAAC + LABA **oder**
LAAC + PDE-4 Inhibitor | Theophyllin +
**oder** SABA +/oder SAAC |
| D           | ICS +
LABA +/oder LAAC | ICS + LABA + LAAC **oder**
ICS + LABA + PDE-4 Inhib. | Theophyllin +
Carbocystein +
**oder** SABA +/oder SAAC |

**SABA**: short acting B2-agonist; **LABA**: long acting B2-agonist;
**SAAC**: short acting anticholinergic; **LAAC**: long acting anticholinergic;
**ICS**: inhaled corticosteroids; **PDE-4**: Phosphodiesterase-4

Modified according to GOLD-Guidelines (www.goldcopd.org)
Classification of COPD patients into risk groups A-D

Modified according GOLD-Guidelines (www.goldcopd.org)