Health Technology Assessment and Reimbursement of Medication Adherence Enhancing Interventions

Vienna, Austria
November 8, 2022
Speakers

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<td>0-5min</td>
<td>Introduction</td>
<td>Dr. Peterson</td>
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<td>2</td>
<td>6-15min</td>
<td>Terminology of medication adherence supporting activities (ENABLE)</td>
<td>Dr. Kardas</td>
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<td>Results of EUREcA study (ENABLE) - Overview of reimbursed MAEIs in Europe</td>
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<td>36-45min</td>
<td>Next steps of ISPOR MAP SIG research - Focus group</td>
<td>Dr. Hiligsmann</td>
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<td>6</td>
<td>46-60min</td>
<td>Open Discussion</td>
<td>Dr. Peterson</td>
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Medication Adherence and Persistence
Special Interest Group

Presented by: Andrew M. Peterson, PharmD, PhD, FCPP
Structure of Special Interest Group (SIG)

- **Special Interest Group Leadership**
  - **Chair**
  Adina Turcu-Stiolica, PhD, Prof., University of Medicine and Pharmacy of Craiova, Romania
  - **Past Chair**
  Priti Pednekar, MS, BS, PhD, Senior Research Scientist, PRECISIONheor, Newark, CA, United States

- Each position is a 1-year term, resulting in a 3-year commitment
**Structure of Special Interest Group (SIG)**

**Member Engagement Co-Chairs**
- 1-year term, renewable

**Andrew Peterson**, PharmD, BS, PhD, Professor, Philadelphia College of Pharmacy, Saint Joseph’s University, Philadelphia, PA, United States

**Zahra Majd**, PhD student, University of Houston College of Pharmacy, Houston, TX, United States

**Elizabeth Unni**, MBA, PhD, Chair & Associate Professor, Touro College of Pharmacy, New York, NY, United States
Structure of Special Interest Group (SIG)

Key project
Criteria for the value assessment for medication adherence-enhancing interventions (MAEI)

Co-Chairs
Tamas Agh, MSc, PhD, MD, Principal Researcher, Center for HTA and Pharmacoeconomic Research, University of Pecs & Syreon Research Institute, Esztergom, Hungary
Bijan Borah, MSc, PhD, Professor, Health Services Research, Mayo Clinic College of Medicine, Rochester, MN, United States
Mickaël Hiligsmann, PhD, Associate Professor, Maastricht University, Maastricht, Netherlands
Medication Adherence and Persistence SIG

• **Mission:** To stimulate research and evaluation on issues related to medication adherence, treatment persistence, and implications for health outcomes

• **Members:** 224 (interested to join: email to MedAdherenceSiG@ispor.org)

• **Some work products**
  - Methods for Measuring Multiple Medication Adherence: A Systematic Review Report
  - Medication Compliance and Persistence: Terminology and Definitions
  - Methods for Integrating Medication Compliance and Persistence in Pharmacoeconomic Evaluations
  - For more studies and information see ISPOR Medication Adherence and Persistence Special Interest Group webpage [https://www.ispor.org/member-groups/special-interest-groups/medication-adherence-and-persistence](https://www.ispor.org/member-groups/special-interest-groups/medication-adherence-and-persistence)
What’s the Issue?

For every 100 prescriptions written: 100
50-70 are filled at the pharmacy
48-66 are picked up from the pharmacy
25-30 are taken properly
15-20 are refilled as prescribed

National Association of Chain Drug Stores, Pharmacies: improving health, reducing costs, July 2010. Based on IMS Health Data
Consequences of medication non-adherence

- Increase the risk of hospitalization, number of emergency department visits, and rate of mortality\(^1\)

- Total cost associated with medication non-adherence
  - In the United States: $100 - $300 billion/year\(^2\)
  - In the European Union: €80 - €125 billion/year\(^3\)

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1 Ho PM, Rumsfeld JS, Masoudi FA. Effect of medication nonadherence on hospitalization and mortality among patients with diabetes mellitus. Arch Intern Med 2006;166:1836e41.
Interventions to Improve Medication Adherence

- Behavioral Interventions
- Biosensors
- Educational Interventions
- Patient Adherence Tools
- Tailored Interventions
Assessment of medication adherence-enhancing interventions (MAEIs)

• Several MAEIs have been developed in recent years; nevertheless
  – limited evidence on how to evaluate these interventions in real-world settings
  – Recent review indicated that “the vast majority of primary studies … were of low or very low quality according to the accepted methodology for evidence grading” (Anderson, 2020)

ENABLE Agreed Terminology of Activities Improving Medication Adherence

Presented by: Przemyslaw Kardas, MD, PhD
ENABLE COST Action

COST Action CA19132 ENABLE – “European Network to Advance Best practices & technology on medication adherence”

Action duration - 20/10/2020 - 19/10/2024

No. of participating countries: 40

No. of participating researchers: > 100

www.ENABLEadherence.eu
Aims of ENABLE

• To evaluate **current practices** related to medication adherence

• To establish a network to raise awareness of adherence enhancing solutions

• To accelerate translation of **adherence innovations** into practice

• To work collaboratively towards **economically viable policy and implementation** of adherence enhancing technology across healthcare systems

Structure of ENABLE

WG 1: Current practice
Current practices on enhancing adherence in European countries

WG 2: Adherence technology
Identifying & showcasing adherence enhancing technologies

WG 3: Sustainable implementation
Paving the way for technology in healthcare systems

WG 4: Communication & Dissemination
In the last five decades of adherence research has not resulted in consensus in the terminology used to describe activities improving medication adherence. Consensus terminology not found in:

- MESH
- COCHRANE
- ISPOR (International Society for Pharmacoeconomics and Outcomes Research)
- ESPACOMP (International Society for medication adherence), ESCP (European Society of Clinical Pharmacists)
- PCNE (Pharmaceutical Care Network Europe)

There is a need for adherence-related terminology to allow:

- Comparison of research in this area
- Benchmarking of current interventions
- Implementation of adherence enhancing technology
ABC Taxonomy

3 Phases of adherence continuum:
A. Initiation
B. Implementation
C. Discontinuation
Methodology of obtaining agreed terminology

**Step 1:** Need definition - ENABLE WG3 meeting in Lodz, Poland (16-17 September 2021) focused on review of current medication adherence reimbursement scenarios in ENBLE member countries, and defined the **urgent need for agreed terminology**

**Step 2:** ENABLE meeting in Malaga, Spain (May 2-4, 2022) was the forum of presentation of **provisionally proposed definitions**

**Step 3:** **On-line Delphi-like survey** to assess level of agreement and clarity of proposed definitions

**Step 4:** **Further fine-tuning** of definitions during dedicated ENABLE workshop in Oslo (June 25, 2022)

**Step 5 (ongoing):** Final analysis of feedback obtained and **publication of agreed terminology**
On-line Delphi-like survey results

Sample characteristics

- 109 participants
- 68% women
- 65% ENABLE members
- 98 from 35 EU countries & 11 non-EU participants

Expertise area

- Industry / Commercial company
- Gov / Health authority
- Health Insurance/ Regulatory
- Academia
- Clinical / Healthcare

Example of ratings

What is a Medication Adherence Technology?
Current vision of agreed ENABLE terminology of activities enabling medication adherence

- **Medication Adherence Technologies (MATech)** are evidence-based health technologies (i.e., devices, techniques, procedures/services, or systems) used in management of medication adherence by diverse stakeholders (i.e., patients, caregivers, health care professionals, etc.).

- **Medication Adherence Enhancing Intervention (MAEI)** is any formalized activity taking place within, or in association with the healthcare system, that in any way could positively affect medication adherence at individual patient level.

- **Reimbursement** relates to public or private insurers’ payment to providers for covering the costs of delivering MATechs and/or MAEIs.

- **Best practice** is the most successful adherence interventions in the country among the interventions known to individual
Results of EUREcA study (ENABLE) - Overview of Reimbursed MAEIs in Europe

Presented by: Tamás Ágh, MD, MSc, PhD
EUREcA study - Aim

• To get a snapshot on the current European reimbursement landscape of MAEIs
  – To provide an in-depth overview and critical assessment of reimbursed MAEIs in European countries at national and regional levels
  – To pave the way for further MAEIs to be implemented in the future

EUREcA study - Methods

Desk review
- To investigate what evidence exists on MAEIs reimbursement policy
- Published evidence on evaluations of MAEI reimbursement policies in Europe is expected to be limited

Cross-sectional study
- On-line survey
- Target countries: all 39 ENABLE countries
- Target stakeholder groups (ENABLE collaborators)
  - Healthcare providers (i.e., physicians, pharmacists)
  - HTA experts / payers
- CHERRIES guideline
- SurveyMonkey: June 22 – July 20, 2021

EUREcA study - Questionnaire

• Structure of the questionnaire:
  – Demographic data on the responder (3 multiple choice questions)
  – Information on reimbursed MAEIs (≤3 interventions, 9 multiple choice questions per each intervention)

• MAEI was defined as “any structured intervention, aiming to help patients to make optimal use of his/her pharmacotherapy”

• 4 external experts were involved in the validation process

EUREcA study – Results

- There is scarcity of publications targeting the reimbursement of MAEIs
- 54 participants covering all 39 ENABLE countries
- 13 reimbursed MAEIs from 9 countries were identified
EUREcA study –
No. of reimbursed MAEIs per country

EUREcA study – Conclusions

- Despite of the significant burden of medication non-adherence, reimbursement of MAEIs remain on a low priority on the health policy agenda
- Lack of common terminology made it difficult to identify reimbursed MAEIs
- Country income may influence the implementation and reimbursement of MAEIs
- Recommendation on reimbursement pathways for the different types of MAEIs would be warranted
- HTA guidelines involving multiple value indicators would allow the comprehensive assessment of MAEIs


Preliminary results of ISPOR MAP SIG SLR on evaluation criteria of MAEIs

Presented by: Bijan J. Borah, PhD
Study Aims

• One of the sub-studies of the key project for this SIG

• Parts of the results presented as a poster in this conference as well

• Aims: Conduct systematic literature review to identify outcome measures used for value assessments of Medication Adherence-Enhancing Interventions (MAEIs)

• The specific research questions to address the above aim are:
  – Which outcomes are considered for the assessment of MAEIs in clinical trials, prospective observational studies, and economic evaluations?
  – Which domains or criteria of published value frameworks can be considered for the assessment of MAEIs?
Methods

- Data Source: MEDLINE and PsycINFO (via OVID), Scopus, and CINAHL and Academic Search Complete (via EBSCO).
- Years: 2018-2020
- Registered in PROSPERO (# CRD42021242934)
- PRISMA guidelines followed
- The screening was conducted in two steps:
  - Abstract and title screening by two independent reviewers
  - Full text screening of relevant articles by two independent reviewers
  - Disagreements between reviewers were resolved by consensus
Methods (Continued)

• Exclusion criteria
  • No abstract
  • Article not reporting original data
  • Not evaluating an MAEI, or not presenting a value framework for pharmaceuticals or healthcare intervention programs
  • Not reporting relevant data

• Data extracted included
  • General characteristics of the study (e.g., study type, study population, country)
  • Data on the applied MAEI
  • Data on value framework
  • Relevant value domains and elements with a definition and measurement method where available

• Data were categorized by type of outcome and/or intervention
Results – Literature screening

Records identified through OVID Medline (n = 8,511)
Records identified through PsycInfo (n = 968)
Records identified through Scopus (n = 7,776)
Records identified through EBSCO CINAHL (n = 1,925)
Records identified through EBSCO Academic Search Complete (n = 3,204)

Duplicates (identified by EndNote & Rayyan) (n = 7,699)

Records for title and abstract screening (n = 14,685)

Records excluded in the "title-abstract screening" phase (n = 12,903)
Results – Literature screening

Full text screening
(n = 1,782)

Records excluded in the “full-text screening” phase, by reasons
(n = 799)
- Duplicate (n = 5)
- No English text (n = 14)
- Not original data (n = 27)
- Study protocol (n = 102)
- Not clinical trial, prospective observational study, economic evaluation or value framework (n = 78)
- Not evaluating a MAEI or not a value framework related to medication adherence (n = 306)
- SLR/Meta-analysis (n = 267)

Studies included in SLR
(n = 983)
Published 2018-2020 (n = 308)
Published 2010-2017 (n = 675)
## Results: Study Characteristics

*Literature search was conducted in September 2020

<table>
<thead>
<tr>
<th>Total number of included studies</th>
<th>N of studies (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>308</td>
<td>(100%)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Year of publication</th>
<th>N of studies (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2018</td>
<td>107 (35%)</td>
</tr>
<tr>
<td>2019</td>
<td>123 (40%)</td>
</tr>
<tr>
<td>2020*</td>
<td>78 (25%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Disease category (ICD-10)</th>
<th>N of studies (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease of the circulatory system</td>
<td>67 (22%)</td>
</tr>
<tr>
<td>Certain infectious or parasitic disease</td>
<td>58 (19%)</td>
</tr>
<tr>
<td>Endocrine, nutritional or metabolic disease</td>
<td>32 (10%)</td>
</tr>
<tr>
<td>Disease of the respiratory system</td>
<td>27 (9%)</td>
</tr>
<tr>
<td>Mental or behavioural disorder</td>
<td>23 (7%)</td>
</tr>
<tr>
<td>Other</td>
<td>101 (33%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Number of assessed MAEIs per study</th>
<th>N of studies (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 intervention</td>
<td>291 (94.5%)</td>
</tr>
<tr>
<td>2 interventions</td>
<td>16 (5.2%)</td>
</tr>
<tr>
<td>3 interventions</td>
<td>1 (0.3%)</td>
</tr>
</tbody>
</table>
### Results (Continued)

#### Distribution of Study Types (n=308)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>N of studies (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication adherence/persistence</td>
<td>286 (93%)</td>
</tr>
<tr>
<td>Clinical outcome</td>
<td>155 (50%)</td>
</tr>
<tr>
<td>Quality of life</td>
<td>57 (19%)</td>
</tr>
<tr>
<td>Resource use</td>
<td>43 (14%)</td>
</tr>
<tr>
<td>Patient satisfaction</td>
<td>31 (10%)</td>
</tr>
<tr>
<td>Economic outcome</td>
<td>18 (6%)</td>
</tr>
<tr>
<td>Other outcome</td>
<td>76 (25%)</td>
</tr>
</tbody>
</table>

#### Study Countries

- **USA**: 105 (34%)
- **China**: 17 (6%)
- **Netherlands**: 16 (5%)
- **Iran**: 11 (4%)
- **India**: 10 (3%)
- **Other**: 149 (48%)

#### Type of MAEIs per intervention category

<table>
<thead>
<tr>
<th>Type of MAEI</th>
<th>N of MAEIs (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Behavioral intervention</td>
<td>143 (44%)</td>
</tr>
<tr>
<td>Reminders (e.g., mail, telephone, email)</td>
<td>48 (35%)</td>
</tr>
<tr>
<td>Adherence monitoring with or without feedback</td>
<td>18 (13%)</td>
</tr>
<tr>
<td>Follow-up (e.g., home visit, scheduled clinic visit)</td>
<td>12 (8%)</td>
</tr>
<tr>
<td>Tailoring (routinization)</td>
<td>19 (7%)</td>
</tr>
<tr>
<td>Skill building (supervised, group)</td>
<td>8 (6%)</td>
</tr>
<tr>
<td>Multi-compartment pillbox/calendar pack/compliance aid</td>
<td>5 (3%)</td>
</tr>
<tr>
<td>Reminder chart/medication list</td>
<td>5 (3%)</td>
</tr>
<tr>
<td>Other</td>
<td>37 (26%)</td>
</tr>
<tr>
<td>Educational intervention</td>
<td>110 (34%)</td>
</tr>
<tr>
<td>Mixed behavioral &amp; educational intervention</td>
<td>73 (22%)</td>
</tr>
</tbody>
</table>
### Results (Continued)

#### Number of outcomes per outcome category

<table>
<thead>
<tr>
<th>Total number of identified outcomes</th>
<th>N of outcomes (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication adherence/persistence</td>
<td>983 (100%)</td>
</tr>
<tr>
<td>Clinical outcome</td>
<td>377 (38%)</td>
</tr>
<tr>
<td>Quality of life</td>
<td>306 (31%)</td>
</tr>
<tr>
<td>Resource use</td>
<td>65 (7%)</td>
</tr>
<tr>
<td>Patient satisfaction</td>
<td>54 (5%)</td>
</tr>
<tr>
<td>Economic outcome</td>
<td>36 (4%)</td>
</tr>
<tr>
<td>Other outcome</td>
<td>25 (3%)</td>
</tr>
<tr>
<td></td>
<td>120 (12%)</td>
</tr>
</tbody>
</table>

#### Number of outcomes per outcome sub-category

<table>
<thead>
<tr>
<th>Medication adherence/persistence</th>
<th>N of outcomes (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-report method</td>
<td>203 (54%)</td>
</tr>
<tr>
<td>Electronic medication monitoring</td>
<td>64 (17%)</td>
</tr>
<tr>
<td>Medical/pharmacy claims or prescription refills data</td>
<td>61 (16%)</td>
</tr>
<tr>
<td>Pill count</td>
<td>26 (7%)</td>
</tr>
<tr>
<td>Clinical measures</td>
<td>9 (2%)</td>
</tr>
<tr>
<td>Caregiver-report adherence</td>
<td>3 (1%)</td>
</tr>
<tr>
<td>Physician-report method</td>
<td>3 (1%)</td>
</tr>
<tr>
<td>Direct observation</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Method not reported</td>
<td>7 (2%)</td>
</tr>
</tbody>
</table>

Note: Only outcomes for subcategory of medication adherence shown. Outcomes for other subcategories such as clinical outcome, resource use are not shown.
## Overall summary of the Results

- There are many studies examining MAEIs, with nearly half of them being behavioral interventions alone
  - Most of the behavioral interventions were also reminder-based interventions
  - Approx. 22% used combined methods (behavioral+educational)
- Among the types of outcomes, medication adherence/persistence dominated followed by clinical outcomes
- Further studies would be warranted to select and rank the most relevant outcome measures for the value assessment of MAEIs
Next steps of ISPOR MAP SIG research - Focus group

Presented by: Mickaël Hiligsmann, MSc, PhD
ISPOR MAP SIG

• **Aim**: To systematically identify and prioritize relevant criteria for the value assessment of medication adherence enhancing interventions

• **Project structure:**

  - Task #1: Systematic literature review
  - Task #2: Focus group discussion with experts
  - Task #3: Delphi panel study
KEY PROJECT OBJECTIVES

Identify relevant value criteria to assess MAEIs

Task #1: Systematic literature review

Task #2: Focus group discussion with experts

Task #3: Delphi panel study

Measure the (relative) importance of the identified value criteria
Task #2: Focus groups

• **Aim**: To identify and prioritize relevant criteria for the value assessment of medication adherence enhancing interventions

• **Methods**: Nominal group technique
Nominal group technique

1. Literature-based criteria & silent generation of new criteria
2. Sharing ideas
3. Discussion of all criteria
4. Score importance
   
   Ten most important
   
   Rank five most important
Sample and setting

• 3 working groups (up to data saturation)
• Between 7 and 10 participants per focus group
• Experience in MAEI: payers, healthcare providers, industry, academia and patients
• Online (Zoom/Teams platform)
• Recruitment:
  • SIG members’ extensive professional network
  • ISPOR member’s database
  • Interested? send an email to m.hiligsmann@maastrichtuniversity.nl
Expected outcomes

• Value criteria to assess MAEIs

• Preliminary assessment of the importance of the criteria
Task #3: Delphi panel

• **Aim**: To prioritize relevant criteria for the value assessment of medication adherence enhancing interventions

• **Methods**: Delphi panel
Delphi panel

- A 3-round Delphi study
- About 100 experts: payers, healthcare providers, industry, academia and patients
- Online platform
- Recruitment:
  - SIG members’ extensive professional network
  - ISPOR member’s database
  - *Interested?* send an email to m.hiligsmann@maastrichtuniversity.nl
Open Discussion
Sign up to join our Special Interest Group

- Scan the code and select: **Select a Special Interest Group to Join**
- Login with your email and ISPOR password
- It should bring you to a page where you can select the Medication Adherence & Persistence SIG
- You must be an ISPOR member to join a SIG.
Sign up to join our Special Interest Group

- Question for the Medication Adherence and Persistence Special Interest Group email MedAherenceSiG@ispor.org

www.ispor.org
Backup slides
<table>
<thead>
<tr>
<th>Type of intervention</th>
<th>Country</th>
<th>Year of introduction</th>
<th>Target population</th>
<th>Who pays the reimbursement?</th>
<th>Who gets the reimbursement?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multi-dose drug dispensing</td>
<td>Belgium</td>
<td>2012</td>
<td>Elderly patients</td>
<td>Public insurance / Public healthcare system / Government</td>
<td>Pharmacy</td>
</tr>
<tr>
<td></td>
<td>Denmark</td>
<td>2001</td>
<td>Elderly patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Finland</td>
<td>2006</td>
<td>Reimbursed only for patients ≥75 years of age and using ≥6 drugs suitable for drug dispensing</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Norway</td>
<td>Early 2010s</td>
<td>Elderly patients</td>
<td>Public insurance / Public healthcare system / Government</td>
<td>Pharmacy</td>
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<tr>
<td></td>
<td>United Kingdom</td>
<td>2014</td>
<td>Elderly patients, or those otherwise struggling to cope with their medication</td>
<td></td>
<td></td>
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<tr>
<td>Medication review</td>
<td>Hungary</td>
<td>2019</td>
<td>40-65 years old patients with chronic disorders</td>
<td>Public insurance / Public healthcare system / Government</td>
<td>Primary care (GP)</td>
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<tr>
<td></td>
<td>Slovenia</td>
<td>2016</td>
<td>Patients with drug related problems; identified and referred by a GP</td>
<td>Public insurance / Public healthcare system / Government</td>
<td>Primary care (clinical pharmacist)</td>
</tr>
<tr>
<td></td>
<td>Spain</td>
<td>2012</td>
<td>Patients with chronic diseases and polypharmacy</td>
<td>Public insurance / Public healthcare system / Government</td>
<td>Primary care, Hospital &amp; Pharmacy</td>
</tr>
<tr>
<td></td>
<td>United Kingdom</td>
<td>Years ago</td>
<td>Patients on long-term medication</td>
<td></td>
<td>Pharmacy &amp; Hospital</td>
</tr>
<tr>
<td>Smart device</td>
<td>Finland</td>
<td>2019</td>
<td>Patients on rheumatoid arthritis medication</td>
<td>Pharma company</td>
<td>IT company</td>
</tr>
<tr>
<td></td>
<td>Netherlands</td>
<td>2020</td>
<td>Patients with asthma/COPD</td>
<td>Public insurance / Public healthcare system / Government &amp; Pharma company</td>
<td>Pharmacy</td>
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<td>Mobile application</td>
<td>Denmark</td>
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<td>Patients with mental disorder</td>
<td>No information</td>
<td>No information</td>
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<tr>
<td>Patient education</td>
<td>Hungary</td>
<td>2016</td>
<td>Newly transplanted patients</td>
<td>Patient organization</td>
<td>Healthcare provider</td>
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</table>
### Extra Results

<table>
<thead>
<tr>
<th>Metric</th>
<th>N of outcomes (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medication adherence/persistence</strong></td>
<td></td>
</tr>
<tr>
<td>Self-report method (e.g., MMAS-4/8, MARS)</td>
<td>377</td>
</tr>
<tr>
<td>Electronic medication monitoring (e.g., MEMS, smart inhaler)</td>
<td>203 (54%)</td>
</tr>
<tr>
<td>Medical/pharmacy claims or prescription refills data (e.g., MPR, PDC)</td>
<td>64 (17%)</td>
</tr>
<tr>
<td>Other</td>
<td>61 (16%)</td>
</tr>
<tr>
<td></td>
<td>49 (13%)</td>
</tr>
<tr>
<td><strong>Clinical outcome</strong></td>
<td></td>
</tr>
<tr>
<td>Disease control - Cardiovascular disorders (e.g., blood pressure, heart rate)</td>
<td>306</td>
</tr>
<tr>
<td>Disease control - Anxiety/depression/other mental health disorder (e.g., MADRS, MHI-5)</td>
<td>44 (14%)</td>
</tr>
<tr>
<td>Disease control – Other (e.g., McGill Pain Questionnaire; FSS)</td>
<td>42 (14%)</td>
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<tr>
<td>Other</td>
<td>40 (13%)</td>
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<tr>
<td></td>
<td>180 (59%)</td>
</tr>
<tr>
<td><strong>Quality of life (e.g., EQ-5D, FS-36)</strong></td>
<td>65</td>
</tr>
<tr>
<td><strong>Resource use</strong></td>
<td>54</td>
</tr>
<tr>
<td>In-patient, out-patient care, nurse visit and/or ER visit</td>
<td>37 (69%)</td>
</tr>
<tr>
<td>Use of intervention</td>
<td>13 (24%)</td>
</tr>
<tr>
<td>Medication utilization</td>
<td>4 (7%)</td>
</tr>
<tr>
<td><strong>Economic outcome</strong></td>
<td>25</td>
</tr>
<tr>
<td>Cost-effectiveness/utility</td>
<td>11 (44%)</td>
</tr>
<tr>
<td>Direct medical costs</td>
<td>9 (36%)</td>
</tr>
<tr>
<td>Healthcare utilization</td>
<td>2 (8%)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (12%)</td>
</tr>
<tr>
<td><strong>Patient satisfaction</strong></td>
<td>36</td>
</tr>
<tr>
<td><strong>Other outcome</strong></td>
<td>120</td>
</tr>
<tr>
<td>Disease knowledge</td>
<td>16 (13%)</td>
</tr>
<tr>
<td>Self-efficacy</td>
<td>15 (12%)</td>
</tr>
<tr>
<td>Beliefs about medicines</td>
<td>9 (8%)</td>
</tr>
<tr>
<td>Other</td>
<td>80 (67%)</td>
</tr>
</tbody>
</table>

**Number of outcomes per outcome sub-category**