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# ISPOR MEDICATION ADHERENCE AND PERSISTENCE SPECIAL INTEREST GROUP & EUROPEAN NETWORK TO ADVANCE BEST PRACTICES & TECHNOLOGY ON MEDICATION ADHERENCE (ENABLE)

## Health Technology Assessment and Reimbursement of Medication Adherence Enhancing Interventions

Vienna, Austria  
November 8, 2022

## Speakers



**Andrew M. Peterson, PharmD, PhD, FCPP** Professor of Pharmacy and Philadelphia College of Pharmacy, Saint Joseph's University, Philadelphia, Pennsylvania, United States



**Przemyslaw Kardas, MD, PhD**, Professor of Family Medicine and Director, Medication Adherence Research Centre, Medical University of Lodz, Poland



**Tamás Ágh, MD, MSc, PhD** Principal Researcher, Center for HTA and Pharmacoeconomic Research, University of Pecs & Syreon Research Institute, Budapest, Hungary



**Bijan Borah, MSc, PhD** Professor of Health Services Research, Mayo Clinic College of Medicine and Science, Rochester, Minnesota, USA



**Mickaël Hiligsmann, MSc, PhD** Associate Professor in Health Economics and Health Technology Assessment, Maastricht University, Maastricht, Netherlands

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# Agenda

Item #	Time	Topic	Presenter
1	0-5min	Introduction	<i>Dr. Peterson</i>
2	6-15min	Terminology of medication adherence supporting activities (ENABLE)	<i>Dr. Kardas</i>
3	16-25min	Results of EUREcA study (ENABLE) - Overview of reimbursed MAEIs in Europe	<i>Dr. Agh</i>
4	26-35min	Preliminary results of ISPOR MAP SIG SLR on evaluation criteria of MAEIs	<i>Dr. Borah</i>
5	36-45min	Next steps of ISPOR MAP SIG research - Focus group	<i>Dr. Hiligsmann</i>
6	46-60min	Open Discussion	<i>Dr. Peterson</i>

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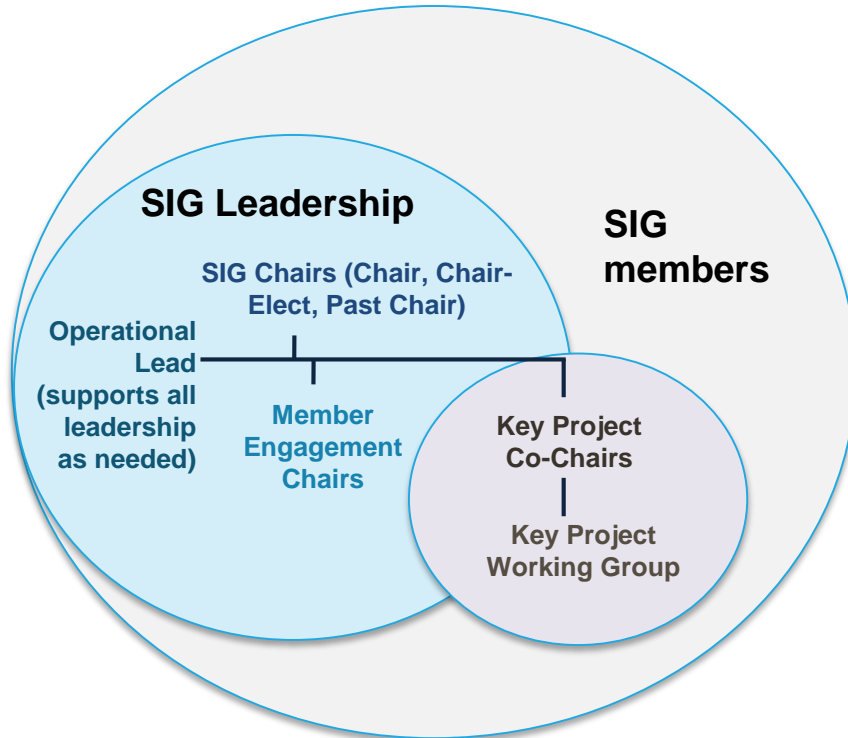
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# 1

## 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

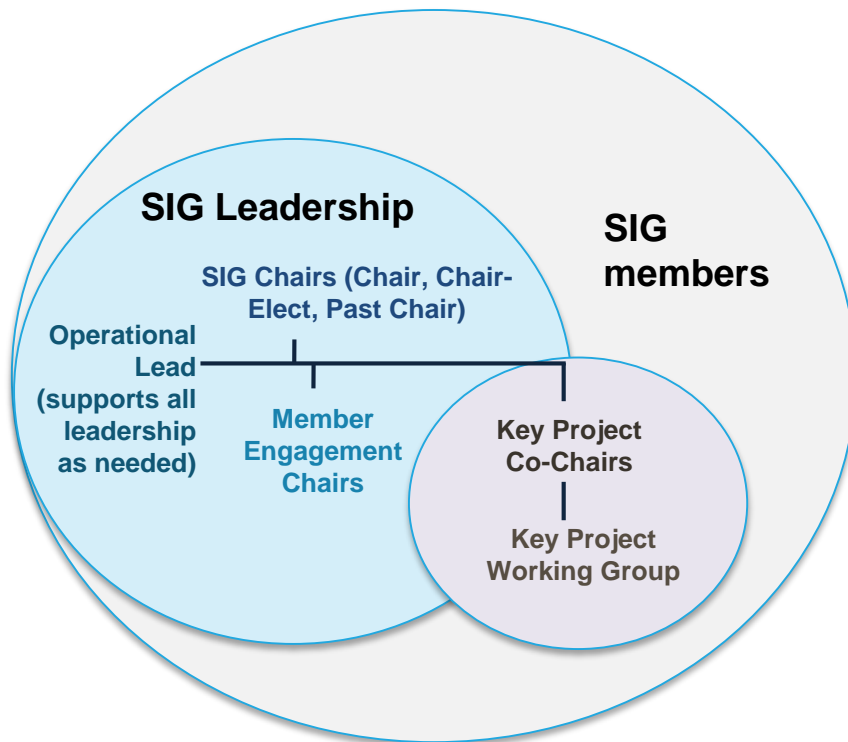
Adina Turcu-Stiolica, PhD, Prof.,  
University of Medicine and  
Pharmacy of Craiova, Romania

### 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

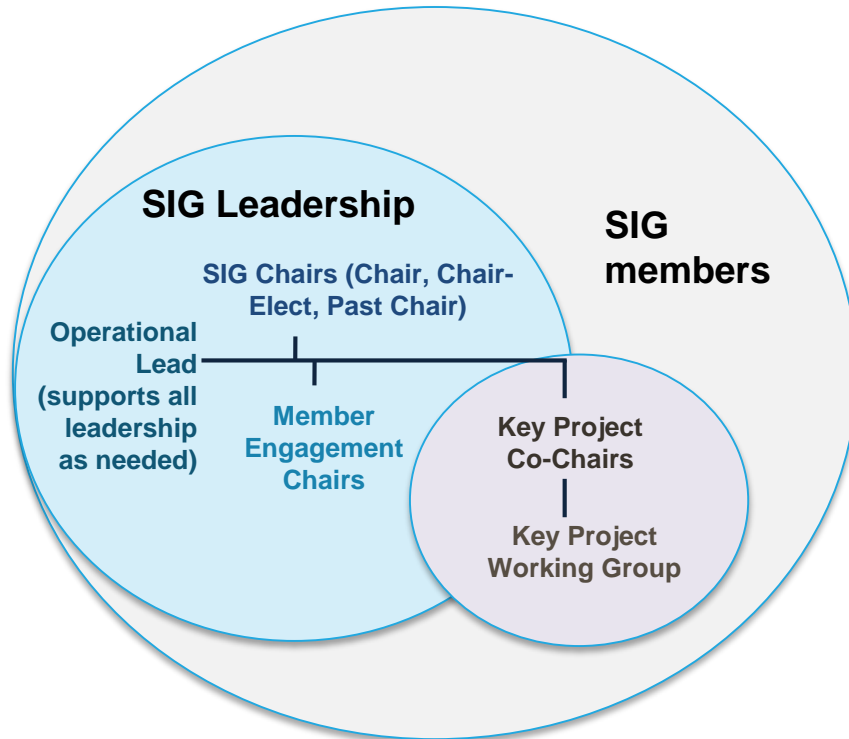
- 1-year term, renewable

**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

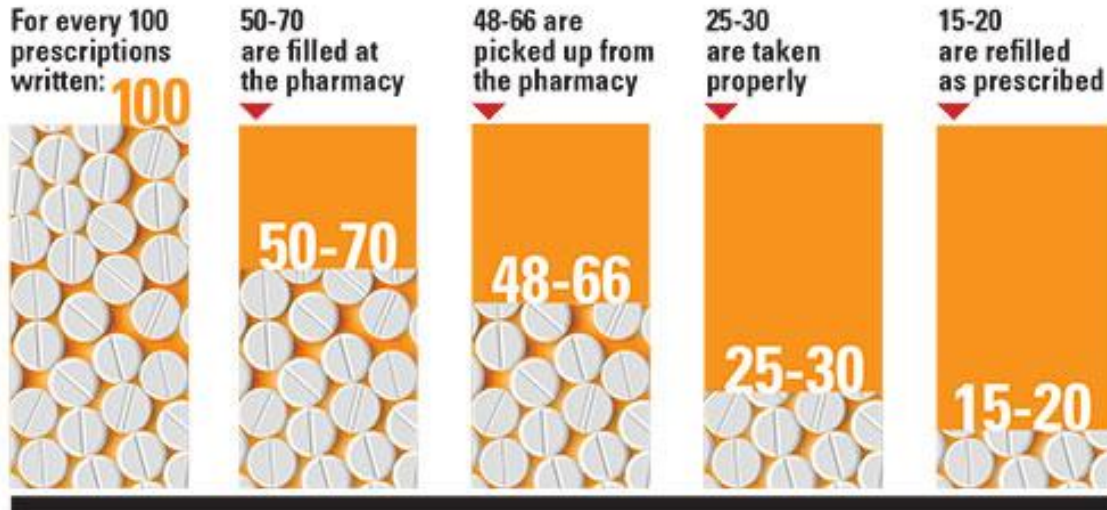
**Mickaël Hiligsmann**, PhD, Associate Professor, Maastricht University, Maastricht, Netherlands



## 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](mailto: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>

# What's the Issue?



# Consequences of medication non-adherence

- Increase the risk of hospitalization, number of emergency department visits, and rate of mortality<sup>1</sup>
- Total cost associated with medication non-adherence
  - In the United States: \$100 - \$300 billion/year <sup>2</sup>
  - In the European Union: €80 - €125 billion/year <sup>3</sup>

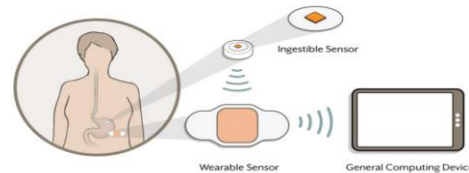
1 Ho PM, Rumsfeld JS, Masoudi FA. Effect of medication nonadherence on hospitalization and mortality among patients with diabetes mellitus. Arch Intern Med 2006;166:1836e41.

2 Benjamin RM. Medication adherence: helping patients take their medication as directed. Public Health Rep 2012;127:2e3.

3 European Commission/MEDI-VOICE. MEDI-VOICE Report Summary. Project ID: 17893. European Union/European Commission, 2011

# Interventions to Improve Medication Adherence

- Behavioral Interventions
- Biosensors
- Educational Interventions
- Patient Adherence Tools
- Tailored Interventions



*The ingestible sensor and the compatible medical device*



# 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)

Anderson LJ, et al. Am J Health-Syst Pharm. 2020; 77:138-147

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# 2

## ENABLE Agreed Terminology of Activities Improving Medication Adherence

Presented by: Przemyslaw Kardas, MD, PhD



# ENABLE COST Action

COST Action CA19132 ENABLE –  
“**E**uropean **N**etwork to **A**dvance **B**est  
practices & techno**L**ogy on medication  
adherence**E**”

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

No. of participating countries: 40

No. of participating researchers: > 100

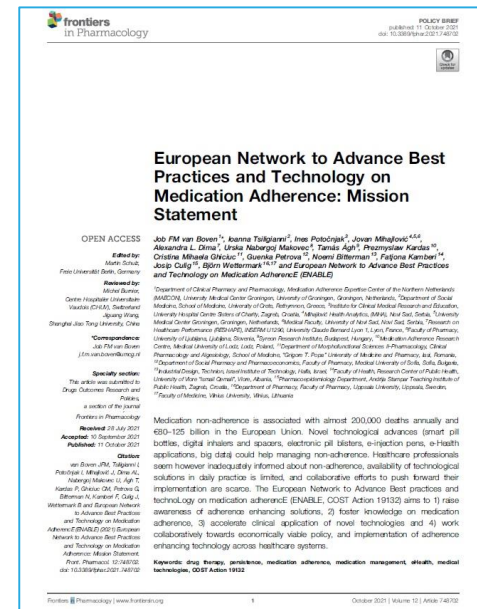
[www.ENABLEadherence.eu](http://www.ENABLEadherence.eu)





# Aims of ENABLE

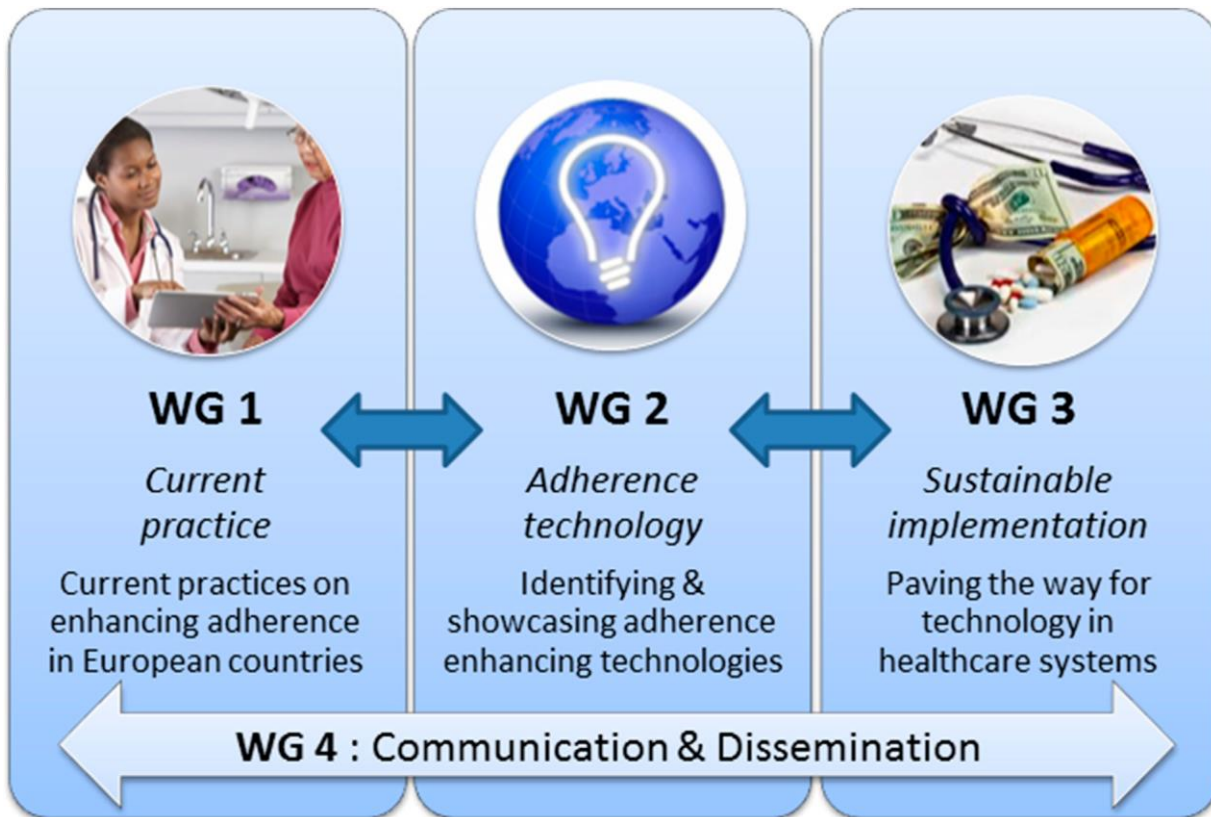
- To evaluate **current practices** related to medication adherence
- To establish a network to raise awareness of **adherence enhancing solutions**
- To accelerate translation of **adherence innovations into practice**
- To work collaboratively towards **economically viable policy and implementation** of adherence enhancing technology across healthcare systems







# Structure of ENABLE





# Need for agreed terminology

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

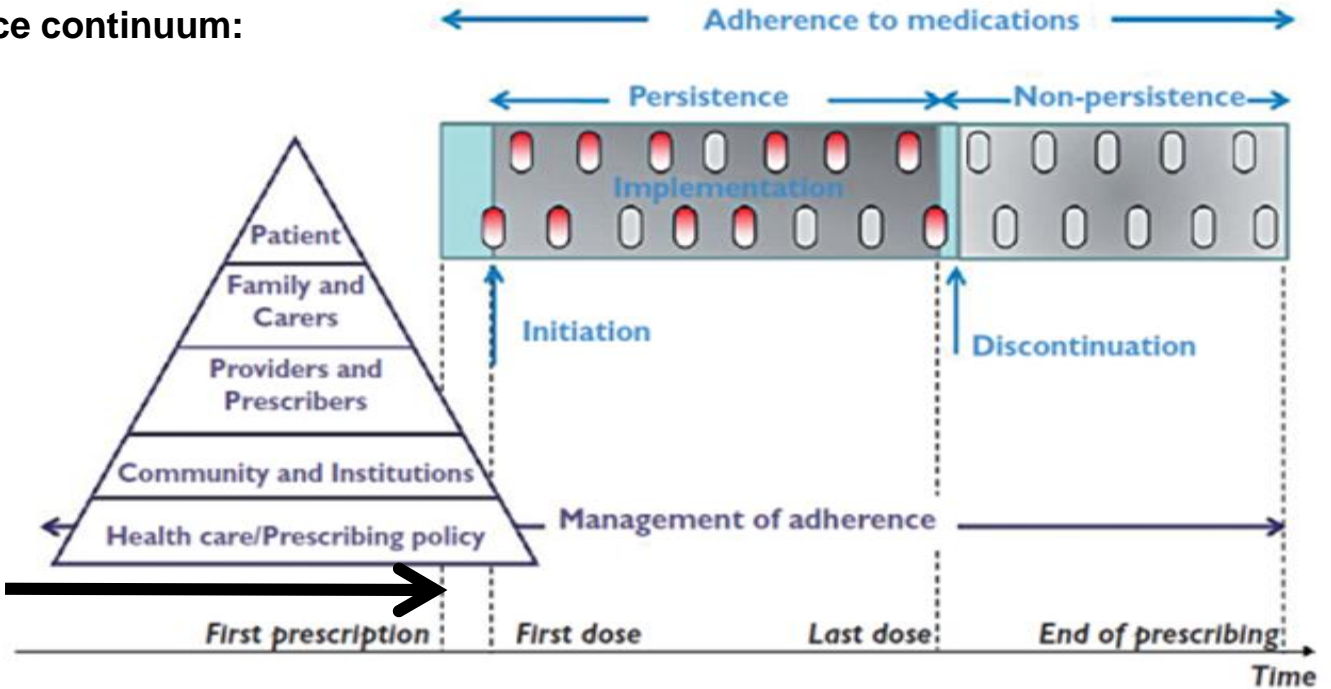


# ABC Taxonomy

## 3 Phases of adherence continuum:

- A. Initiation
- B. Implementation
- C. Discontinuation

**Primary Adherence / Initial Adherence**





# 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**

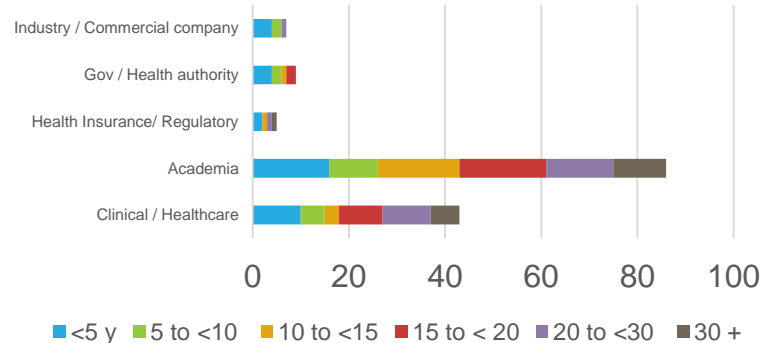


# On-line Delphi-like survey results

## Sample characteristics

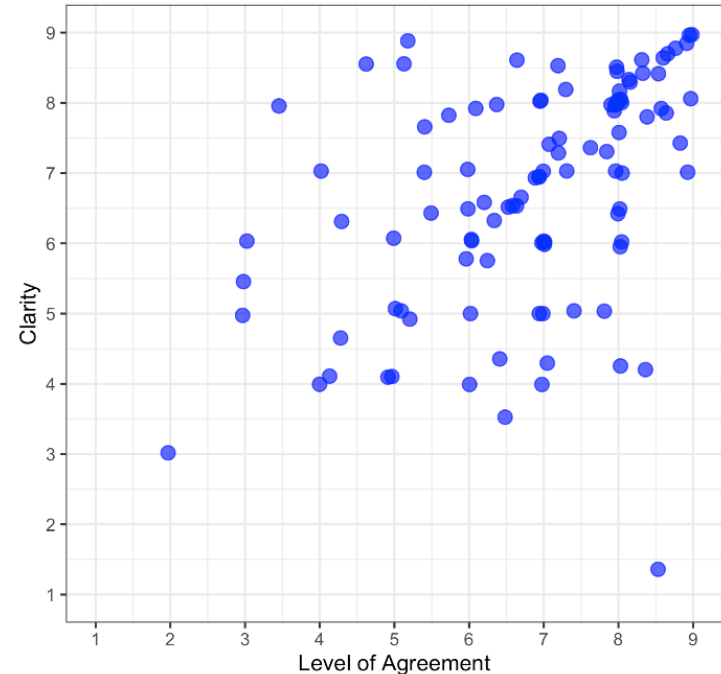
- 109 participants
- 68% women
- 65% ENABLE members
- 98 from 35 EU countries & 11 non-EU participants

## Expertise area



## 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

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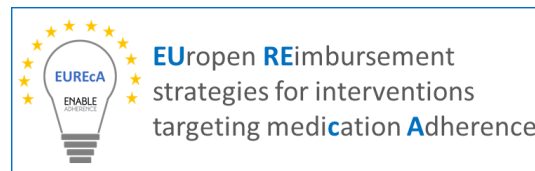
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# 3

## 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





EUropean REimbursement  
strategies for interventions  
targeting medication Adherence

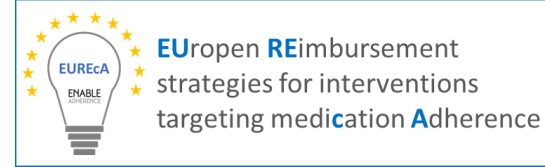
## EUREcA study - Methods

### 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

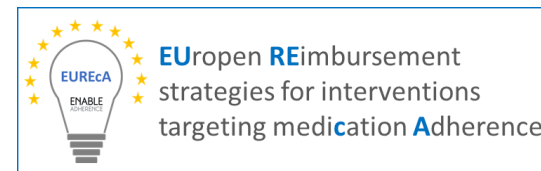
### Cross-sectional study

- 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



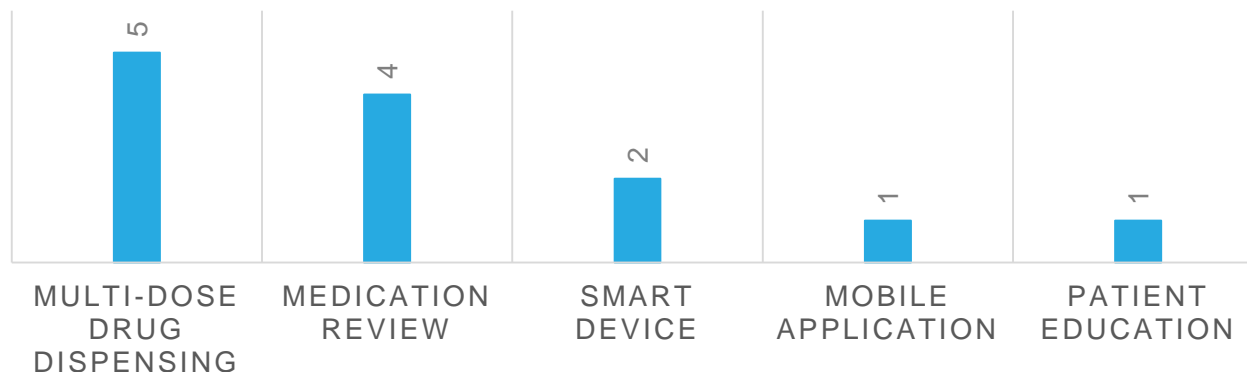
## EUREcA study - Questionnaire

- 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

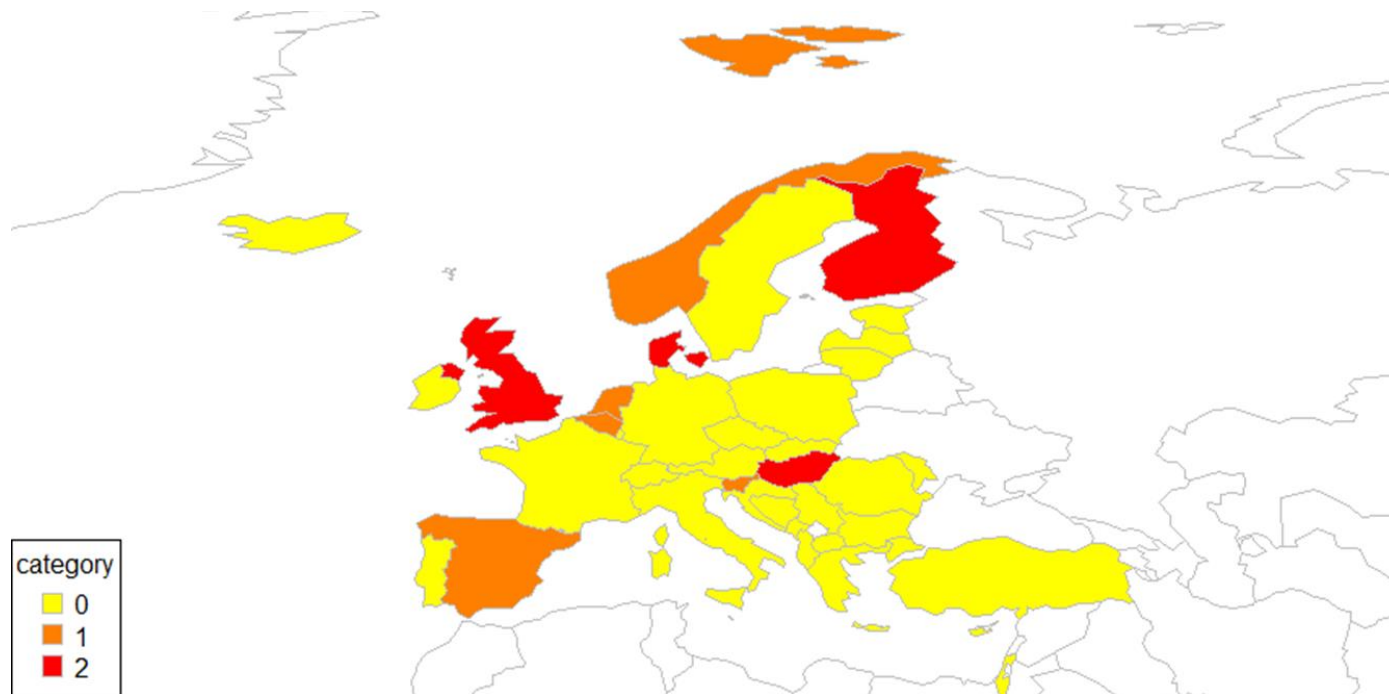
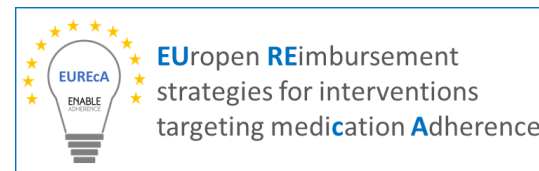


## EUREcA study – Results

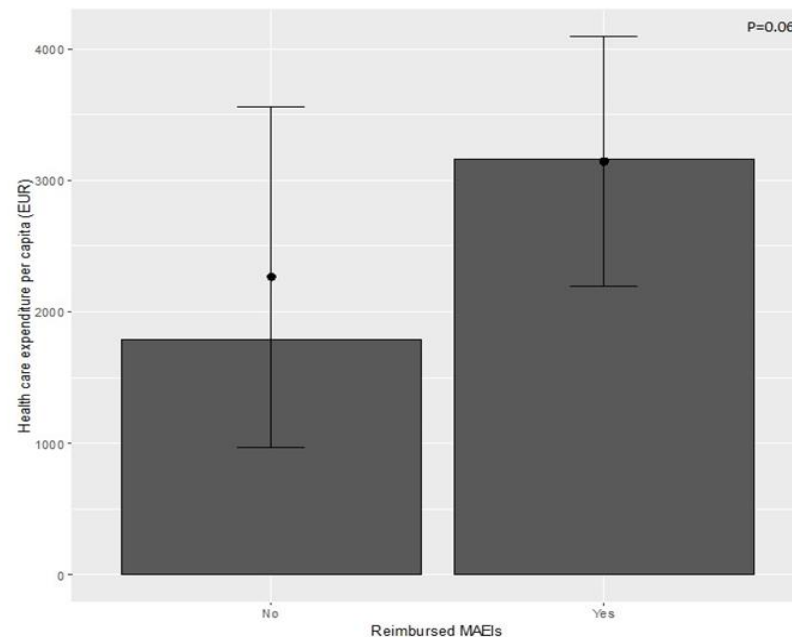
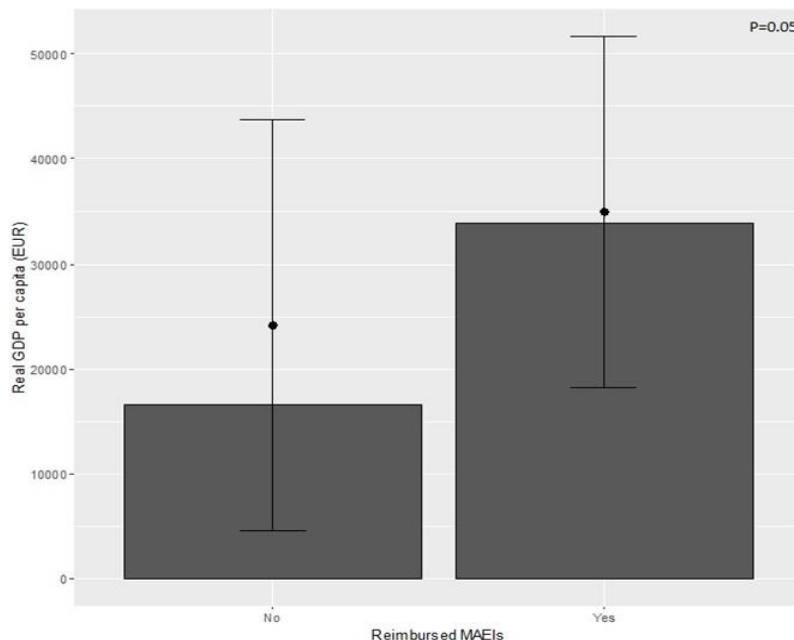
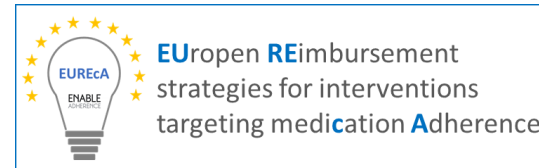
- There is scarcity of publications targeting the reimbursement of MAEIs
- 54 participants covering all 39 ENABLE countries
- 13 reimbursed MAEIs from 9 countries were identified



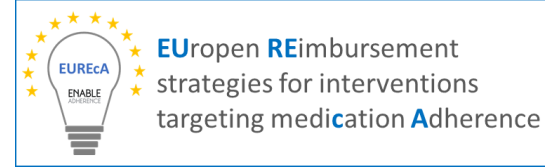
# EUREcA study – No. of reimbursed MAEIs per country



# EUREcA study – Country economy ↔ reimbursed MAEIs



■ median; ● mean; I : standard deviation



## 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

Ágh T, et al. Reimbursed Medication Adherence Enhancing Interventions in European Countries: Results of the EUREcA Study. *Front Pharmacol.* 2022; 13:892240.

30 Kardas P, et al. Reimbursed medication adherence enhancing interventions in 12 european countries: Current state of the art and future challenges. *Front Pharmacol.* 2022; 13:944829

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# 4

## 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?



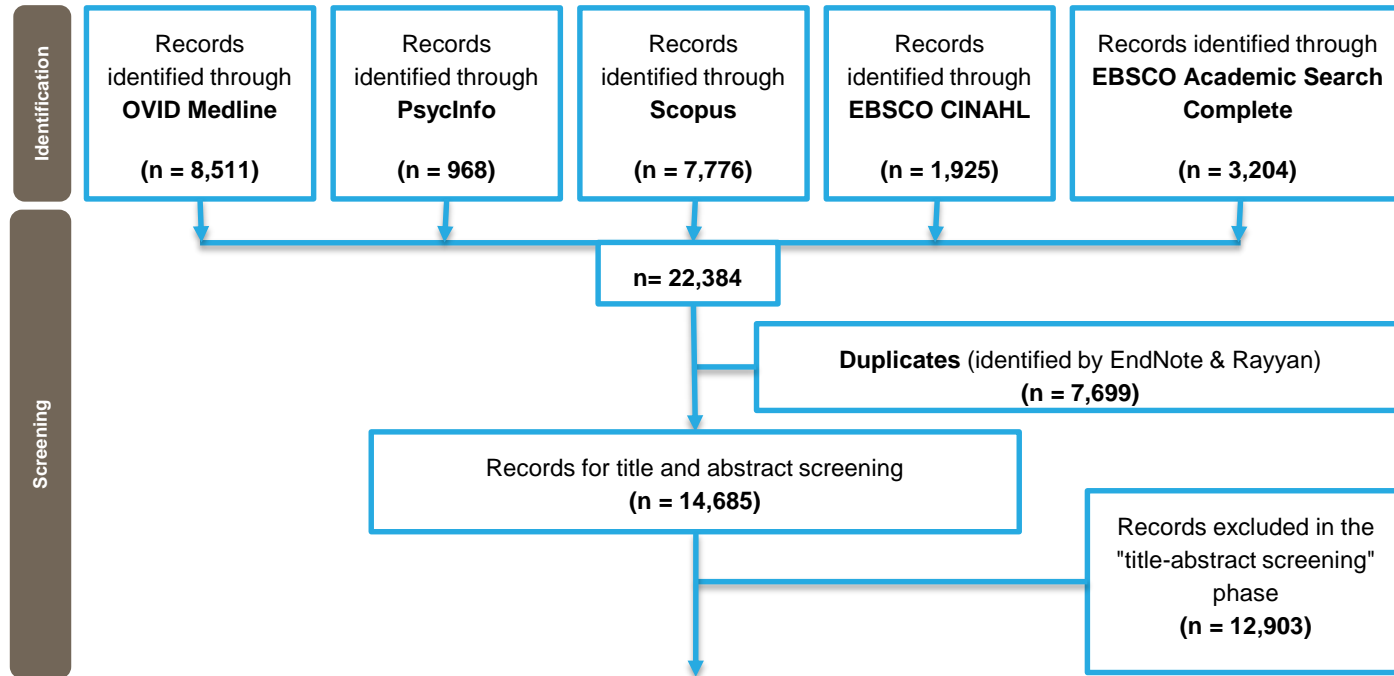
## Methods

- 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

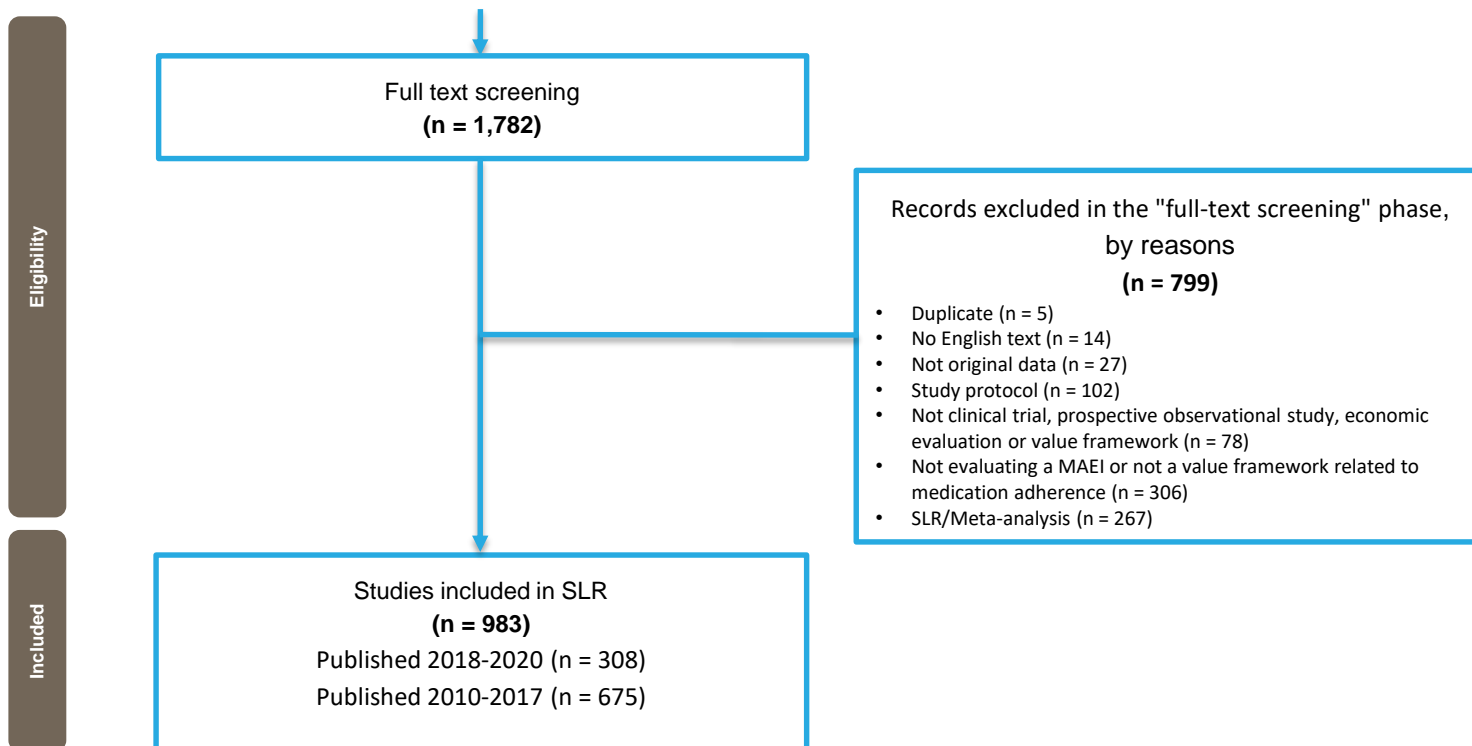
## Methods (Continued)

- 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



## Results – Literature screening



## Results: Study Characteristics

	N of studies (%)
<b>Total number of included studies</b>	308 (100%)
<b>Year of publication</b>	
2018	107 (35%)
2019	123 (40%)
2020*	78 (25%)
<b>Disease category (ICD-10)</b>	
Disease of the circulatory system	67 (22%)
Certain infectious or parasitic disease	58 (19%)
Endocrine, nutritional or metabolic disease	32 (10%)
Disease of the respiratory system	27 (9%)
Mental or behavioural disorder	23 (7%)
Other	101 (33%)
<b>Number of assessed MAEIs per study</b>	
1 intervention	291 (94.5%)
2 interventions	16 (5.2%)
3 interventions	1 (0.3%)

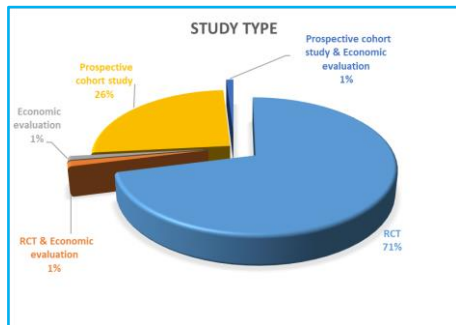
\*Literature search was conducted in September 2020

# Results (Continued)

Study Countries



Distribution of Study Types (n=308)



Distribution of Study Types (n=308)

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

Number of studies per outcome category

	N of studies (%)
Medication adherence/persistence	286 (93%)
Clinical outcome	155 (50%)
Quality of life	57 (19%)
Resource use	43 (14%)
Patient satisfaction	31 (10%)
Economic outcome	18 (6%)
Other outcome	76 (25%)

Type of MAEIs per intervention category

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

# Results (Continued)

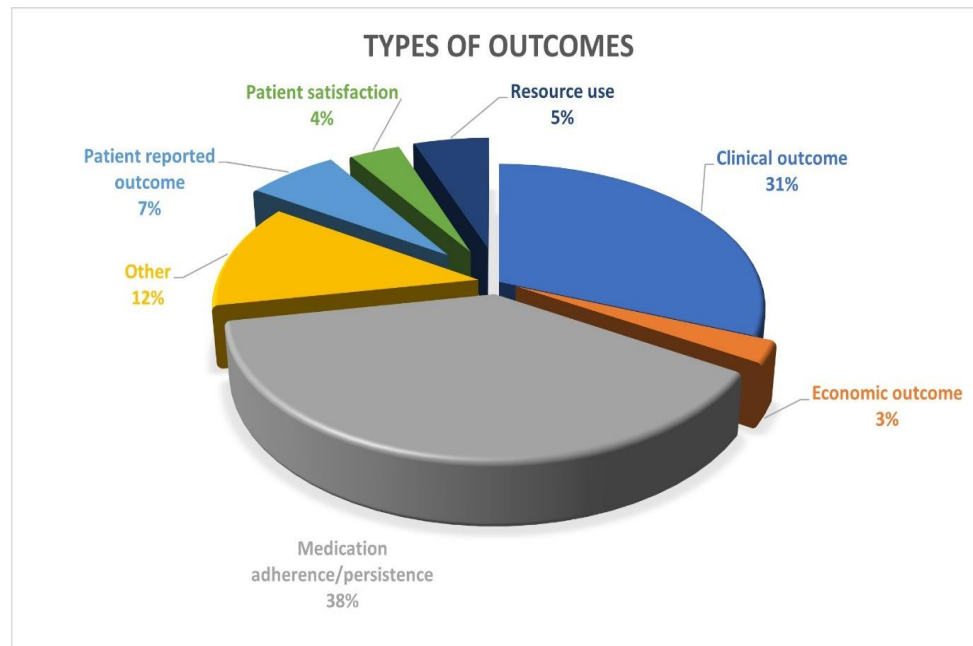
## Number of outcomes per outcome category

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

## Number of outcomes per outcome sub-category

	N of outcomes (%)
<b>Medication adherence/persistence</b>	377 (100%)
Self-report method	203 (54%)
Electronic medication monitoring	64 (17%)
Medical/pharmacy claims or prescription refills data	61 (16%)
Pill count	26 (7%)
Clinical measures	9 (2%)
Caregiver-report adherence	3 (1%)
Physician-report method	3 (1%)
Direct observation	1 (0.2%)
Method not reported	7 (2%)

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+educationa)
- 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



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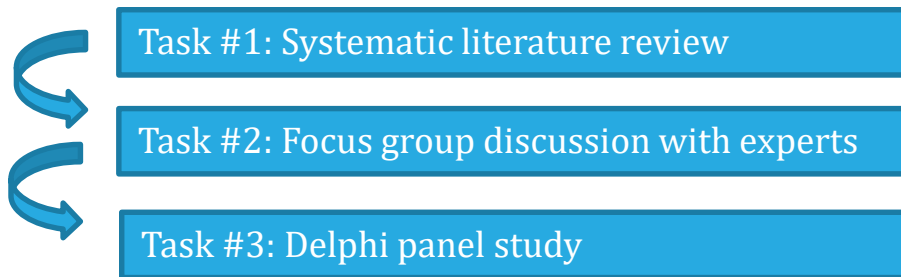
# 5

## 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:**



# KEY PROJECT OBJECTIVES

Identify relevant value criteria to assess MAEIs

Task #1: Systematic literature review

Measure the (relative) importance of the identified value criteria

Task #2: Focus group discussion with experts

Task #3: Delphi panel study

## 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](mailto: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](mailto:m.hiligsmann@maastrichtuniversity.nl)

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# 6

## 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 [MedAdherenceSiG@ispor.org](mailto:MedAdherenceSiG@ispor.org)



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# 7

**Backup slides**



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

# Extra Results

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

*Number of outcomes per outcome sub-category*