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Complete List of Authors:	Nabergoj Makovec , Urska; Univerza v Ljubljani Fakulteta za farmacijo, Faculty of Pharmacy Goetzinger, Catherine ; Luxembourg Institute of Health, Deep Digital Phenotyping Research Unit, Department of Population Health; University of Luxembourg Faculty of Science Technology and Medicine Ribaut, Janette; University of Basel Faculty of Medicine, Institute of Nursing Science, Department Public Health; University Hospital Basel, Department of Theragnostic, Hematology Barnestein-Fonseca, Pilar; CUDECA Institute for Training and Research in Palliative Care, CUDECA Hospice Foundation, Málaga; Instituto de Investigación Biomédica de Málaga-IBIMA , Group C08: Pharma economy: Clinical and economic evaluation of medication and Palliative Care Haupenthal, Frederik; Medical University of Vienna Department of Medicine II, Division of Nephrology and Dialysis Herdeiro, Maria; University of Aveiro, Institute of Biomedicine, Medical Sciences Department Grant, Sean; Indiana University Richard M Fairbanks School of Public Health, Department of Social & Behavioral Sciences, Jácome, Cristina; University of Porto Faculty of Medicine, Department of Community Medicine, Information and Health Decision Sciences (MEDCIDS); University of Porto Faculty of Medicine, Center for Health Technology and Services Research (CINTESIS) Marques Roque, Fatima; Polytechnic Institute of Guarda Research Unit for Inland Development, Research Unit for Inland Development Smits, Dins; Riga Stradins University, Faculty of Public Health and Social Welfare, Department of Public Health and Epidemiology Tadic, Ivana; University of Belgrade Faculty of Pharmacy, Department of Social Pharmacy and Pharmaceutical Legislation Dima, Alexandra; Université Claude Bernard Lyon 1, , Research on Healthcare Performance (RESHAPE), INSERM U1290 ENABLE, Collaborators; COST Action ENABLE (CA19132)
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Developing a medication adherence technologies repository: proposed structure and protocol for an online real-time Delphi study

Urska Nabergoj Makovec (*ORCID ID: 0000-0001-5194-3314*)
University of Ljubljana, Faculty of Pharmacy, Department of Social Pharmacy, Ljubljana, Slovenia
urska.nabergoj.makovec@ffa.uni-lj.si
Catherine Goetzinger *(ORCID ID :0000-0002-6377-1078)*
Deep Digital Phenotyping Research Unit, Department of Population Health, Luxembourg Institute of Health, Strassen, Luxembourg.
University of Luxembourg, Faculty of Science, Technology and Medicine, Luxembourg
catherine.goetzinger@lih.lu
Janette Ribaut (*ORCID ID:* 0000-0003-0654-4052)
Institute of Nursing Science, Department Public Health, Faculty of Medicine, University of Basel, Switzerland & Department of Theragnostic, Hematology, University Hospital of Basel, Switzerland
janette.ribaut@unibas.ch
Pilar Barnestein-Fonseca *(ORCID ID 0000-0003-2767-8017)*
CUDECA Institute for Training and Research in Palliative Care, CUDECA Hospice Foundation, Málaga, Spain.
Instituto de Investigación Biomédica de Málaga-IBIMA Group C08: Pharma economy: Clinical and economic evaluation of medication and Palliative Care, Málaga, Spain.
pilar.barnestein@ibima.eu
Frederik Haupenthal (*ORCID ID:* 0000-0002-7708-9045)
Division of Nephrology and Dialysis, Department of Medicine II, Medical University of Vienna, Austria
frederik.haupenthal@meduniwien.ac.at
Maria Teresa Herdeiro *(ORCID ID: 0000-0002-0500-4049)*
Institute of Biomedicine, Medical Sciences Department, University of Aveiro, Aveiro, Portugal.
teresaherdeiro@ua.pt
Sean Patrick Grant *(ORCID: 0000-0002-7775-3022)*
Department of Social & Behavioral Sciences, Richard M. Fairbanks School of Public Health, Indiana University, Indianapolis, United States of America
spgrant@iu.edu
Cristina Jácome (*ORCID ID:* 0000-0002-1151-8791)
Department of Community Medicine, Information and Health Decision Sciences (MEDCIDS), Faculty of Medicine, University of Porto, Porto, Portugal
Center for Health Technology and Services Research (CINTESIS), Faculty of Medicine, University of Porto, Porto, Portugal
cristinajacome.ft@gmail.com
Fátima Roque (*ORCID ID:* 0000-0003-0169-3788)
Research Unit for Inland Development, Polytechnic of Guarda, Guarda, Portugal.
froque@ipg.pt
Dins Smits (*ORCID: 0000-0001-5514-7374)*
Faculty of Public Health and Social Welfare, Department of Public Health and Epidemiology, Riga Stradins University, Riga, Latvia
dins.smits@rsu.lv
Ivana Tadic (*ORCID: 0000-0001-5488-9261)*
University of Belgrade, Faculty of Pharmacy, Department of Social Pharmacy and Pharmaceutical Legislation, Belgrade, Serbia
ivana.tadic@pharmacy.bg.ac.rs
Alexandra Lelia Dima (*ORCID: 0000-0002-3106-2242)*

Université Claude Bernard Lyon 1, Research on Healthcare Performance (RESHAPE), INSERM U1290, Lyon, France
alexandra.dima@univ-lyon1.fr

and **European Network to Advance Best Practices and Technology on Medication AdherencE (ENABLE)**

Corresponding author:

Urska Nabergoj Makovec
ORCID ID: 0000-0001-5194-3314
University of Ljubljana, Faculty of Pharmacy, Department of Social Pharmacy,
Askerceva 7
1000 Ljubljana, Slovenia
Telephone: +386 1 4769 565
urska.nabergoj.makovec@ffa.uni-lj.si

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Article Summary

Abstract

Introduction: An online interactive repository of available technologies may facilitate their selection and adoption by different stakeholders. Developing a repository is among the main objectives of the ENABLE COST Action (CA19132). However, meeting the needs of diverse stakeholders requires careful consideration of the repository structure.

Methods and analysis: A real-time online Delphi study by stakeholders from 39 countries with research, practice, policy, patient representation and technology development backgrounds will be conducted. Eleven ENABLE members from 9 European countries formed an interdisciplinary steering committee to develop the repository structure, prepare study protocol and perform it. Definitions of medication adherence technologies and their attributes were developed iteratively through literature review, discussions within the steering committee and ENABLE Action members, following ontology development recommendations. Three domains (*product and provider information (D1), medication adherence descriptors (D2) and evaluation and implementation (D3)*) branching in 13 attribute groups are proposed: *product and provider information, target use scenarios, target health conditions, medication regimen, medication adherence management components, monitoring/measurement methods and targets, intervention modes of delivery, target behaviour determinants, behaviour change techniques, intervention providers, intervention settings, quality indicators and implementation indicators.* Stakeholders will evaluate the proposed definition and attributes' relevance, clarity and completeness and have multiple opportunities to reconsider their evaluations based on aggregated feedback in real-time. Data collection will stop when the predetermined response rate will be achieved. We will quantify agreement and perform analyses of process indicators on the whole sample and per stakeholder group.

Ethics and dissemination: Ethical approval for the COST ENABLE activities was granted by the Malaga Regional Research Ethics Committee. The Delphi protocol was considered compliant regarding data protection and security by the Data Protection Officer from University of Basel. Findings from the Delphi study will form the basis for the ENABLE repository structure and related activities.

Strengths and limitations of this study

- The diverse expertise and geographical spread of the ENABLE COST Action members (39 European countries) and their wider professional network represents a unique and timely opportunity to develop a repository of medication adherence technologies that meets the needs of a diverse audience.
- The scope and content of the Delphi survey represent the work of extensive literature review combined with multidisciplinary expertise of the steering committee.
- The real-time Delphi approach provides improved efficiency of the process, shortens the time of study completion and is particularly suitable for managing larger groups and including people from different geographic locations.
- The Delphi protocol will use state of the art methodology to measure agreement and predetermine agreement/consensus criteria as well as stability of responses.
- The real-time approach requires specialized software, which limits the range of possible survey configurations and raw data availability for detailed process analyses and requires relatively elaborate instructions for participants, which may increase participation burden.

Introduction

Taking medication as prescribed often proves difficult for people when managing their health, particularly in the long term.[1] Medication adherence is suboptimal in numerous chronic conditions [2 3] and has a negative impact on chronic disease management, patient's general health status, quality of life, working ability and health care costs. [2 4 5] Research on medication adherence has expanded and contributed to raised awareness of the prevalence of suboptimal adherence and how it affects health outcomes. Digital technologies have increasingly gained interest as new interventions for supporting medication adherence have been developed. A diversity of technologies has been proposed, from electronic monitoring devices to mobile applications, to support medication adherence measurements and empower patients with their disease management. However, the rapidly expanding offer of medication adherence technologies (MATech) makes it increasingly difficult to access, evaluate, and compare different technologies to make informed decisions and select appropriate tools for specific clinical or research needs. In a 2018 review by Ahmed et al.[6], 5881 medication adherence apps were identified on Google Play and Apple App Stores. However, most of them lacked evidence of effectiveness and didn't involve healthcare professionals (HCPs) during their development.[6] Lack of collaboration between stakeholders results in a limited number of developed MATech actually being implemented into the healthcare systems and used daily by HCPs and/or patients.[7] Furthermore, due to differences in healthcare systems across countries, healthcare organisations and reimbursement processes, harmonization of implementation strategies are lagging behind, which further delays adoption of best practices across countries.[4 7]

The ENABLE COST Action ('European Network to Advance Best practices & technoLogy on medication adherencE', CA19132)[8] was initiated by experts in medication adherence and digital technologies to fill these gaps regarding evidence and implementation of MATech within healthcare systems. ENABLE aims to raise awareness of available technologies, expand multidisciplinary knowledge on medication adherence at multiple levels, accelerate knowledge translation to clinical practice, and collaborate towards economically viable implementation of best practices and technologies across European healthcare systems. These objectives are being pursued within a 4-year period (2020-2023), by three distinct and interrelated working groups (WGs) that map best practices available (WG1), identify and showcase adherence technologies (WG2), and identify suitable reimbursement strategies for implementation in healthcare systems (WG3), supported transversally by a WG4 coordinating communication and dissemination. At present, the ENABLE Action includes a large interdisciplinary network of experts in medication adherence from 39 European countries.[8]

Effective implementation of technology-supported healthcare has been facilitated by centralisation of information in public repositories or 'solution showrooms', where users can search for technologies that meet their specific requirements.[9] Several such repositories already exist in the field of digital health, including medication adherence (e.g. NHS app Library[10], MyHealthApps[11], InterventieNet[12], GGD AppStore[13], DIGA[14], Weisse Liste[15]), but are limited to single countries or types of technology and none represents a comprehensive resource to facilitate adoption of appropriate MATech across health systems. Therefore, ENABLE sets out to develop and maintain a public online repository of MATech where patients, HCPs, researchers, and healthcare managers would be able to access and select technologies for adoption in their adherence management activities.[8] To meet this goal, the ENABLE repository would need to represent a flexible knowledge management system that would include information relevant to the needs of different stakeholders in a user-friendly format. In medical informatics, knowledge management relies on standardized terminologies, classifications and ontologies to record, share and use data on healthcare research and practice. These standards specify the types of information to encode in the form of distinct 'entities' representing objects or phenomena in the real world and their properties ('attributes'), thus enabling knowledge generation through inference and learning.[16] Adoption of evidence-based health innovations is also facilitated by these common standards, as new technologies need to interact with existing ecosystems in terms of both data interoperability and communicating with potential users in appropriate domain-specific language.[17]

The field of medication adherence is highly interdisciplinary, therefore a useful repository would cross multiple knowledge domains and align with several standards, whether medical (e.g., World Health Organisation International Classification of Disease; WHO ICD[18]), behavioural (e.g., the Behaviour Change Intervention Ontology; BCIO[19 20]), or technical (e.g., WHO Classification of Digital Health Interventions; WHO DHIs[21]). Moreover, stakeholder involvement would need to be at the core of this development process, to ensure its content is relevant, clear and complete, and meets community needs.[22] The diverse and geographically spread ENABLE membership and their wider professional network represents a unique and timely opportunity to conduct this work. Considering these quality standards and following methodological recommendations,[22-24] the initial version of the repository structure was prepared and a stakeholder consultation process is proposed to explore their views and level of agreement on the relevance, clarity and completeness of the initial version.[22 23] The resulting improved version would represent the structure of the ENABLE repository, which will be tested and populated in subsequent steps with users and developers of available technologies.

Methods and analysis

Steering committee

A steering committee (SC) was established within the COST ENABLE WG2 to coordinate and perform the work. The committee includes 11 ENABLE members from 9 countries in the following areas of expertise: adherence research and education, clinical practice, policy making and technology development. Members are responsible for: (i) determination of the repository scope and framework of attributes defining repository structure, (ii) preparation of the Delphi protocol, (ii) configuration and piloting the Delphi survey, (iv) selection and invitation of stakeholders to participate in the study, (v) moderating study performance via the online tool and (vi) analysis and interpretation of results.

Determining the repository scope and framework of attributes defining its structure

The determination of scope and development of the attributes' labels with definitions aimed to align with ontology development procedures as described by Wright et al.[24] and follow a stakeholder engagement methodology as described by Norris et al[22] and Khodyakov et al[25]. The principles of ontology development, actions taken when generating the framework of attributes and examples of how these principles are applied in the ENABLE project are presented in Table 1. Stakeholder engagement is primarily achieved through the proposed real-time Delphi study, which is described in more detail in the next sections.

Table 1. Principles of ontology development after Wright et al.[24] and actions taken in the ENABLE project.

Principles	How they have been applied in the ENABLE project
Have specified scope and scientifically sound and relevant content	Selection of established definitions for delimiting the scope, consultation of stakeholders, piloting for data input and platform search.
Meet the needs of community of users	Consultation of stakeholders, steering committee and Action members sampled from the user community and including diverse areas of expertise.
Enabling users to understand the meaning of entities	Naming examples of existing ontologies, piloting Delphi survey, technology description form, user form and platform use.
Be logically consistent	Using the methodology recommended for attribute description, checking consistency via Ontology Web Language (OWL).
Be interoperable with existing ontologies	Adopting attributes and labels available in existing ontologies and classifications, expert input on additional attributes and recommendations for interoperability.
Reflect changes in scientific consensus	Repository in open access, sustainability plan developed

and remain accurate over time	with Action members and stakeholders.

Scope and definition of MATech

Four established definitions were used to define the scope of repository and set the framework of attributes: (i) *WHO definition of health technologies* [26]; (ii) *the ABC definition of medication adherence*[1]; (iii) the *WHO definition of adherence to long-term therapies*[2] to highlight the importance of shared decision-making between the patient and the healthcare team and (iv) *the definition of best practice in healthcare proposed by the European Commission* to guide improvements in European health systems.[27] The information in this definition denotes evidence on safety, efficacy, effectiveness, cost-effectiveness, appropriateness, social and ethical values, and quality of the health care interventions.

Therefore, we propose to define ***Medication Adherence Technologies (MATech) as devices, procedures or systems developed based on evidence to support patients to take their medications as agreed with healthcare providers (i.e., to initiate, implement, and persist with the medication regimen).***

- **devices, procedures or systems** emphasize the inclusion of all technologies, irrespective of their mode of delivery (whether based on electronic or printed supports, delivered through human interaction, or a combination of these) with the aim to construct a comprehensive repository in which users can identify diverse technologies to fit their potentially diverse needs.
- **developed based on evidence** encompass the requirement of evidence/research that supports at least a potential contribution to either measurement or intervention on medication adherence (e.g., validation or pilot studies). Thus, technologies that are not (yet) supported by evidence (e.g., development and testing stages), or clinical practice protocols without an evidence base on at least one aspect (safety, efficacy, effectiveness, cost-effectiveness, appropriateness, social and ethical values or quality), will not be (yet) included in the repository until such evidence is produced and reported.
- **support patients to take their medications as agreed with the healthcare providers (i.e. to initiate, implement, and persist with the medication regimen)** encompass the contribution of the technology to medication adherence management – either directly in patients' self-management, or by supporting professionals to offer such services to patients through all phases of medication adherence. Thus, technologies that focus on other medication management goals, but do not target adherence specifically would be out of scope for this repository.

Furthermore, the technologies included would need to be described in terms of their technical characteristics and validation, their behaviour change content, format, and context, as well as the characteristics facilitating appropriate implementation in care processes. Hence, evidence from behaviour,[19 28] implementation[29 30] and computer sciences[18 21 31 32] informed the initial scope and attributes framework to ensure key features, such as user-centeredness, trustworthiness/credibility, accuracy & relevance of the presented information, tailoring to the needs of different users and interoperability with existing evidence and other sources of information on healthcare technologies.

Framework of attributes

An initial list of attributes was developed based on a literature review and knowledge from the ENABLE members activities such as (i) an ongoing systematic review of e-health interventions on medication adherence for chronic conditions,[33] (ii) a checklist of e-health quality criteria under development,[34] (iii) Interventienet.nl - platform showcasing evidence-based medication adherence interventions in the Netherlands[12] and (iv) the ABC taxonomy – consensus-based terminology and definitions of medication adherence[1].

The initial list was presented to the SC and discussed via several videoconferences to generate a more detailed list of attributes grouped on several themes. Each theme was further elaborated by a subgroup of 2 SC members following a standard format including labels and adherence-related definitions. We adopted the approach from BCIO[19], where related attributes were searched in topic relevant ontologies/taxonomies/classifications and original definitions and codes were added. The reasons for the choice of certain attributes and labels were detailed for each attribute group. The proposed framework of attributes is graphically presented in Figure 1, while rationale and sources used to define the labels for the MATech repository are presented in Table 2.

The final proposed framework consists of three domains (**i**) **product and provider information (D1)**, **(ii) medication adherence descriptors (D2)** and **(iii) evaluation and implementation (D3)** aligning with the three elements of the Donabedian health care model (i) structure, (ii) process and (iii) outcomes.[35] The domains branch in 13 attributes groups, which then branch further to up to four sublevels of attributes. Each attribute is described with a label and related definition.

Figure 1. The interactive graph showing framework of attributes for MATech ("the MATech Tree").

Table 2. The proposed framework of attributes used in the MATech repository. Each group is presented with the core question it is addressing, rationale and sources used to create labels within the group.

Domain and attribute group	Core question	Rationale	Existing ontology/ taxonomy/ classification used and adapted
D1 (D1.1) *Product and provider information*	***What product does the entry refer to, who provides it, who entered its description in the repository and when?***	Each entry in the ENABLE repository will refer to a unique product, which will be identified with a unique ID, provided by a unique organisation (manufacturer, developer) with its own unique ID and related metadata (e.g., date of entry, verification process, etc.) to present the identity of the described MATech and its provider.	• Ontology for medical technology innovation in healthcare centres by ITEMAS [36] – only concepts referring to products and their providers were used and adapted.
D2.1 *Target use scenario*	***What use scenarios and types of users is the technology intended for?***	We can distinguish two general categories of users and their characteristics that might influence the choice of technology: (i) *self-management use* (patients and caregivers) - labels describing patients' characteristics or their condition (age, functional status, (health) literacy, etc.); (ii) *adherence support use* by healthcare or social care providers and health system managers, who can initiate a search for MATech to integrate in their practice. The provider and the setting are also the focus of separate attribute groups.	• Systematized Nomenclature of Medicine, Clinical Terms (SNOMED-CT)[32], • WHO International Classification of Functioning, Disability and Health (ICF)[37] • The WHO DHI[21] • ABC Taxonomy[1]
D2.2 *Target health conditions*	***Which health conditions could the technology be used for as part of adherence support?***	MATech are usually developed and validated to be used in one or several clinical domains and potential users may search for technologies applicable to the health condition(s) they aim to manage. Since our stakeholders also include lay individuals, special focus was put on using simplified language to avoid misunderstandings and knowledge gaps.	• The International Classification of Disease (ICD-11)[18] • The Health Research Classification System (HRCS) from the UK clinical research association[38]
D2.3 *Medication regimen*	***What type of medication regimen(s) is the technology intended for?***	Medication regimen can take different schematic forms and be of varying complexity, which may influence the complexity and extent of medication adherence. MATech may be developed for medications with different characteristics, hence the repository users should be able to indicate the type of regimen to find a MATech that fits its specific characteristics.	• SNOMED-CT[32] • National Cancer Institute Thesaurus (NCIT)[39] • Medical Subject Headings (MeSH)[40]
D2.4 *Medication adherence management components*	***What adherence management types and phases does the technology target?***	Management of adherence entails two management type, e.g., monitoring/measurement (D2.4.2.**A**) and support/intervention (D2.4.2.**B**) by any stakeholder, including the patient himself. Both elements may require different approaches depending on the targeted phase of adherence (D2.4.1).	• ABC Taxonomy[1]

D2.4.2.A *Monitoring/measurement methods and targets*	***If measurement is a component, what measurement methods does the technology use and what do they measure?***	A broad range of measurement methods for adherence are available. In addition to adherence behaviours, measurement can also target adherence determinants, other self-management behaviours and outcome measures (e.g., HRQoL). Therefore, we have selected a range of measurement models as well as a selection of self-management behaviours to offer the possibility to describe technologies from a measurement perspective.	• SNOMED-CT[32] • extensive existing literature[2 3 41] and own (SC's) methodological know how • Train4Health (T4H) behaviour change competency framework [42] • BCIO[19]
D2.4.2.B.1 *Intervention modes of delivery*	***If intervention is a component, how is it delivered to its users?***	Mode of delivery is *'physical or informational medium through which a given behaviour change intervention is provided'*[19], can affect the intervention effectiveness. Although digitalization has entered in all aspects of everyday life, the analogue mode is still very relevant. This is especially true within the elderly, who on one hand require more support in medication adherence[43] and are on the other hand less digitally-literate.[44] Hence, the repository should encompass all modes.	• BCIO[19]; specifically a taxonomy of modes of delivery of BCI[45]
D2.4.2.B.2 *Target behaviour determinants*	***If intervention is a component, what reasons for non-adherence can the technology help address?***	The MATech can address different reasons for non-adherence, defined as determinants of behaviour, which can be non-modifiable or modifiable.[2 19 46] Individual-level and modifiable determinants are encompassed as capability (psychological and physical), opportunity (social and physical), and motivation (reflective and automatic), also known as the COM-B model.[47]	• Capability, Opportunity, Motivation and Behaviour (COM-B) model and Behaviour Change Wheel[47] • Theoretical Domains Framework (TDF)[48] • BCIO[19], specifically The Mechanisms of Action (MoA) Ontology[49 50] • International Classification of Health Interventions (ICHI)[31]
D2.4.2.B.3 *Behaviour change techniques*	***If intervention is a component, what are the 'active ingredients' present in the technology that may trigger change in the reasons for non-adherence targeted?***	To trigger/support change in a health behaviour interventions act by generating change in determinants of the targeted behaviour. The 'active ingredients' in these interventions are labelled *'behaviour change techniques'* (BCTs). We included only user-level BCTs (i.e., BCTs that provide support to medication users) and mapped them according to the COM-B model and across domains.[48] If considered relevant, HCPs level or system-level BCT can be included in the future	• Behaviour change technique (BCT) taxonomy[28 51] • Train4Health (T4H) behaviour change competency framework[42] • Cards for Change (C4C)[52 53]
D2.4.2.B.4 *Intervention providers*	***If intervention is a component, who delivers the intervention to users?***	The provider of intervention is a role played by a person, population or organization that provides/delivers an intervention. This includes their occupational role and type of relatedness. In medication adherence, the provider is often HCP, hence the quality of the *HCP-patient* relationships (communication skills, collaborative decision making, trust in the HCP,HCPs' cultural competences) correlate with patients' adherence.[54]	• BCIO[19], specifically Intervention Source Ontology[55] • Gender, Sex, and Sexual Orientation ontology (GSSO) [56]

D2.4.2.B.5 *Intervention settings*	***If intervention is a component, where is the service for improving adherence delivered?***	Setting is the social and physical environment in which the technology is used to manage medication adherence. Implementation[29] and behavioural[19] science emphasize the importance of understanding and describing the environment in which a certain intervention is delivered as it can significantly influence its outcomes. In addition, not every intervention is applicable or transferable to every setting. We can distinguish between physical and virtual settings as well as the possibility of applying the intervention in any setting.	• BCIO[19], specifically Intervention Setting Ontology[57] • Consolidated framework for advancing implementation science (CFIR)[29]
D3.1 *Quality indicators*	**How does the technology meet key quality indicators from different perspectives?**	Quality indicators (QI) are standardized, evidence-based, and measurable items for monitoring and evaluating the quality of healthcare performance.[58] They describe the structure, process and outcomes of care[35] and based on them the standards and review criteria are developed. The target audience of the repository is very diverse and with specific individual needs related to MATech. Thus, we decided to group quality indicators according to their different purposes of use (e.g., general, research, decision making, use).	• A checklist of e-health quality criteria (under development)[34] • Mobile Application Rating Scale (MARS)[59] • Consort-EHEALTH guideline[60] • Health Technology Assessment (HTA) Core Model, version 3.0 [61] • O'Rourke et al. The new definition of health technology assessment[62]
D3.2 *Implementation outcomes and strategies*	**What implementation outcomes and strategies are needed and available for adopting this technology in the intended setting?**	Implementation sciences provides knowledge on how to facilitate the adoption and use of technologies in real-world settings. The development of MATech often starts without considering the actual use in real-world setting, which prevents successful adoption and scaling up into clinical care.[63] Three implementation outcomes were selected for ENABLE repository: acceptability; feasibility and sustainability to target early, mid and late implementation phases. In addition, eight implementation strategies were selected and adapted to present information on training users for working with MATech, availability of education materials, expertise needed to use the MATech previous implementation experiences, financial, accreditation and other legal aspects of the use.	• Proctor et al. Outcomes for Implementation Research[64] • Consolidated framework for advancing implementation science (CFIR)[29] • The Expert Recommendations for Implementing Change (ERIC)[65] • Interventienet.nl[12]

Choice and description of the study design

We will perform an online real-time Delphi (RT-Delphi) survey to explore the level of agreement on the MATech definition and relevance, clarity and completeness of the proposed framework of attributes defining the repository structure and gain a deeper insight into stakeholders' distinct needs and requirements. The Delphi process is a flexible iterative process to consult and/or reach consensus among a group of people on a particular topic.[66 67] The key characteristics of a Delphi study are anonymity, iteration, controlled feedback, and statistical description of group response.[68] The RT-Delphi approach was developed by Gordon and Pease to improve efficiency of the process and shorten the time of performance.[69] Since then, several online tools have been developed to facilitate the RT-Delphi design[70] and literature describing the use of RT-Delphi and comparison with the traditional multi-round Delphi approach is growing.[23 71-74] In contrast to the traditional Delphi, the RT approach is round-less and offers a constant iteration by providing immediate (real-time) individual and aggregated feedback. Based on new information participants can re-think and modify their answers, which could lead to reconciliation of opinions and eventually to consensus. Participants are encouraged to re-visit and engage in the survey several times during the study period.[69 70 72 74] In comparison with the traditional approach, the RT approach encompasses all key Delphi features[73] and is similar from all key perspectives.[23 71 73 74] Furthermore, the RT approach is particularly suitable for managing larger groups, decreases moderators' workload, simplifies inclusion of people from different geographic locations and can be leaner in costs.[23 69 74] On the other hand, the approach requires specific software, which can sometimes be rigid in terms of survey configuration and analysis, contributes to increases study costs and requires specific instructions for participants.[70 74] Acknowledging the potential challenges, the advantages of the approach outweighed them and supported a decision to adopt the RT approach for our Delphi study.

Sampling and sample size

We aim to include stakeholders from the 39 countries, participating in the COST ENABLE covering 5 different backgrounds per country: (i) adherence and eHealth research (measurement, intervention development, implementation science, health economics), (ii) clinical care (specialist and primary care practitioners providing medication adherence support), (iii) patient representation (age > 18 years), (iv) policy making and (v) technology development. Hence the targeted sample size is at least 195 panellists to be invited in the study.

Purposive sampling will be applied to identify potential panellists. First, requests will be sent through the ENABLE Cost Action membership list to identify suitable candidates from all countries. ENABLE

members will provide the name, background, and e-mail for every potential candidate. Participants' e-mails will be entered in the online platform (eDelphi.org – Delphi method software[75]), which will enable anonymity in further steps, i.e., participant's activities and or/answers given on the platform will not be linked to personal data. All communication with the panellists (invitation, reminders, etc.) will be performed through the platform. If more candidates from the same background and country will be suggested, we will invite all candidates to increase the likelihood of achieving the planned sample size. If the expressed interest exceeds the planned sample size, purposeful sampling will be performed to ensure variation in expertise, country, and balance other characteristics (e.g., years of expertise, gender). To reach simple size and variation in sample characteristics, key international organizations from the field (e.g., ESPACOMP, PCNE, ESCP, WONCA, EMA, EPF, EARTO, EuroDURG etc.) will be contacted to fill any missing gaps, if needed.

Patient and Public Involvement

The goal of this Delphi consultation is to involve stakeholders (patient representatives among them) in decisions regarding the development of ENABLE repository and is part of the broader approach to Patient and Public Involvement followed in the ENABLE Action. Results will be communicated to all stakeholders and they will be listed and acknowledged among ENABLE collaborators.

Data collection

We will use an online platform, eDelphi.org (Metodix Ltd, Helsinki, Finland[75]), for data collection. All survey activities - distribution, reminders, communication with and between the panellists and interim analysis of the process will be performed through the tool. The survey will be conducted in autumn and winter 2021 in three stages:

1. **Pilot stage** - at least 10 members of the COST ENABLE Action, specifically members of the WG2, will be asked to test the survey (including instructions for participants) and to provide feedback on face validity as well as user experience.
2. **First stage phase** – invitation of 20 purposefully selected stakeholders (aiming for variation in expertise, geographical location, and gender) to create initial aggregated feedback of the RT-Delphi.
3. **Full scale RT-Delphi** - all remaining stakeholders will be invited to participate in the study.

Stakeholders will receive an email invitation via the eDelphi platform with personalized link to the survey. Detailed instructions describing survey aims, rules of engagement and how to use the platform will be available on the platform.

At the beginning of the survey, participants will be encouraged to think of a hypothetical situation in which they would search for MATech applicable to their own setting/role and to assess the proposed attributes from this perspective throughout the survey. First, panellists will be asked to familiarize with the proposed structure and provide general feedback on the completeness. Further, they will be asked to rate **agreement** with and **clarity** of the MATech definition and **relevance and clarity** of each proposed attribute group on a 9-points Likert scale, where 1 represents extremely irrelevant/unclear and 9 represents extremely relevant/clear. We will use the Live 2D format[75], where each outcome represents one of the two dimensions, i.e., the x axis stands for relevance and the y axis stands for clarity. Additionally, an open text field will be provided for panellists to comment on completeness of each attribute group, i.e., proposing additional attributes or revising definitions. We will moderate the discussion in the following ways: (i) address technical issues with the platform by responding to the comment when the issues will be solved or provide instructions how to manage the issue and (ii) outline the progress of the study and the most commented questions in bulletins send through the platform once a week. Delphi survey materials, including all attributes' labels and definitions as well as participant instructions, are shown in the *Supplementary Materials*.

For sample description purposes, participants will be requested to provide information on their expertise (profession, years of experience, relevant professional experiences) and demographic characteristics (age, gender, country of practice). These data will be presented in aggregated form and not linked to the individual's activity or answers. Re-visiting and re-rating will be encouraged by weekly reminders.

Data collection will be stopped upon reaching adequate sample size and characteristics to achieve sufficient representability and generalizability of the opinions gathered. Therefore, we propose stopping the Delphi, when 3 criteria will be met: (i) the total response rate to the survey is ≥ 30% (number of participants completing the survey, of the total number of stakeholders invited) [76]; (ii) a minimum of 10 panellists in each stakeholder group completed the survey; (iii) a minimum of 1 stakeholder from at least 2/3 of the COST ENABLE countries has completed the survey. We will operationalize survey completion as providing background data and answering at least 75% of the repository structure questions.

Data analysis

Descriptive statistics will be used to characterize the sample of panellists and each stakeholder subgroup regarding profession, years of experience, age, gender and country.

Several measures can be used to determine when consensus is reached, with the percentage of agreement being the most common. [77] Pre-specification of the consensus measure and criteria for consensus increases trustworthiness of findings.[78]

Level of agreement on relevance, clarity and completeness

Stakeholder agreement on the proposed definition and attributes will guide decisions on the repository structure. Therefore, we selected set of criteria representing different levels of agreement and consequently carrying different weights in these decisions. The level of agreement on every attribute for both outcomes (e.g., relevance and clarity) will be quantified using the Interpercentile Range Adjusted for Symmetry (IPRAS) analysis technique from the RAND/UCLA Appropriateness Method (RAM).[79] Firstly, the disagreement index (DI) will be calculated as a ratio between the Interpercentile Range (IPR) and IPRAS. A DI > 1 (i.e., IPR > IPRAS) indicates disagreement exist. IPR is calculated using the 30th to 70th percentile. IPRAS for the 9-points Likert scale is calculated according to the formula presented in the RAM User Manual.[79]

Secondly, the median and DI will define different levels of agreement and steer the decisions about the repository structure. For the relevance:

i. items with the median of 7-9 and no disagreement will be considered as *relevant and mandatory*.
ii. items with the median of 4-6 or disagreement will be considered as *optional*.
iii. items with the median of 1-3 and no disagreement, will be considered *not relevant* and candidates for *exclusion*.

For an even number of participants, median ratings of e.g., 6.5 or 3.5 will be assigned to the higher level.[79] Stakeholders' responses per question will be summarized using descriptive statistics.

For clarity ratings, the above criteria will be applied as (i) sufficiently clear to remain unchanged; (ii) optional changes and (iii) candidates for rephrasing.

Panellist comments in the open text fields will be analysed qualitatively, using content analysis. Findings will be used to rephrase and improve clarity of certain attributes or to add additional attributes proposed by stakeholders.

Subgroup analysis

Following the primary analysis on the whole sample, a subgroup analysis per stakeholder group will be conducted to examine variation in opinions and potential differences among subgroups. The same agreement criteria will be applied and descriptive statistics will be stratified by stakeholder group. In

addition, we will determine the reliability of ratings per question within stakeholder group by calculating the *intraclass correlation coefficient (ICC)*. The ICC calculation is based on the two-way random model, considering type (average measures) and definition of relationship (consistency) and is presented in Equation 1. ICC > 0.70 will indicate moderate to good reliability.[80 81]

Equation 1. Calculation of the intraclass correlation coefficient (ICC), expressed in %. MS_R stands for mean square for rows and MS_E stands for mean square for error.

$$ICC = \frac{MS_R - MS_E}{MS_R} x\ 100\ [\%]$$

Analysis of process indicators

By analysing process data from the online tool, we will describe in more detail how stakeholders responses evolved through iterations and how consensus or certain level of agreement has formed.[25 82]

Stability of response presents the consistency of responses within the study period and between respondent group stability, which is considered a necessary precondition for determining the level of agreement or if consensus was achieved.[83-85] Different measures of dispersion (e.g., median, interquartile range) and statistical approaches (e.g. descriptive, inferential) can be used[74 85] to measure stability, which can be calculated between rounds (traditional Delphi) or at the end of the study (RT-Delphi).[71 74]

We will use the c*oefficient of quartile variation (CQV)* as descriptive measure of response stability. CQV will be calculated over all participants (CQV_{total}) and within the same stakeholder group (CQV_{sub}) to account for expected higher variation in response between different stakeholder groups. A CQV_{total}< 30% and CQV_{sub} < 15% will be considered as stable response. CQV calculation is shown in *Equation 2.* [84 86]

Equation 2. Calculation of the coefficient of quartile variation (CQV), expressed in %. Q3 stands for value of the 3rd quartile and Q1 for 1st quartile.

$$CQV = \frac{Q3 - Q1}{Q3 + Q1} x\ 100\ [\%]$$

Final repository structure

After conducting the analyses described above, results suggesting modifications to the proposed structure will be considered for adoption by the Steering Committee in a subsequent version, which

will represent the final structure of the ENABLE repository implemented on the initial ENABLE repository version. Further work will be considered to address results that might suggest ongoing debates in the field about certain attribute groups or the need for more in-depth consultation and evidence generation. This work will accompany the iterative improvement of the repository during the ENABLE Action.

Ethics and dissemination

Ethical considerations and consent to publish

The study is designed to ensure participants' anonymity and to manage personal data in line with EU regulation. Before starting the survey, every participant will provide an informed consent electronically on the study entry page. Participants will be asked to carefully read through the statement regarding the study aim and nature as well as the data handling procedures and to mark their understanding and agreement. The results will only be published in an aggregated form and no personal details will be revealed.

An ethical approval for the activities of the COST ENABLE Action, including this Delphi study, was granted by the Malaga Regional Research Ethics Committee ("Comite de Etica de la Investigacion Provincial de Malaga") on 29th April 2021. In addition, a data protection assessment was carried out by the Data Protection Officer at the University of Basel. According to this instance the Delphi study protocol was determined as compliant regarding data protection and security. Both approvals are presented in the *Supplementary Materials*.

Dissemination

The proposed scope and framework of attributes together with findings from this Delphi study will represent the first steps on the pathway to create an evidence-based, interoperable and user-friendly MATech repository. Following the Delphi consultation and integration of the repository module on the ENABLE website[87], providers of MATech (public or private) would be invited to upload information on their products via a MATech description form based on the final repository structure. The accuracy of the information would be verified by an independent review panel through a procedure yet to be established. The repository will be publicly accessible for interested parties. Moreover, the use of the repository will be promoted and supported by dissemination meetings, workshops, and training schools. The findings of the study will be presented via publications (reports and manuscripts in open access peer-reviewed journals) and oral presentations to different stakeholders in conferences and meetings. The spirit of COST Actions is networking and dissemination of ideas; hence the action is open for anybody who would wish to join or would like to be informed about its activities.

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Contributorship statement

All authors contributed to the work and formation of this manuscript. The first draft was prepared by UNM, CG, JR and ALD. All other members of the steering committee (PBF, FH, MTH, CJ, FR, DS, and IT) reviewed and upgraded the first version. All steering committee members (CG, JR, PBF, FH, MTH, CJ, FR, DS, IT) worked on development of the scope and framework of the attribute groups, UNM and ALD coordinated the work. SPG was consulted as the expert in Delphi methodology, specifically the RAND/UCLA Appropriateness Method. The final version of the protocol was prepared by UNM and reviewed by all other authors (CG, JR, PBF, SPG, FH, MTH, CJ, FR, DS, IT, ALD). All authors have read and approve the final version of the manuscript.

Competing interests

SPG is a research team member for ExpertLens (an online platform and methodology for conducting modified-Delphi studies). SG's spouse is a salaried employee of, and owns stock in, Eli Lilly and Company.

All other authors declare no conflict of interests.

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Data sharing statement

Documents detailing the development of the present protocol and the data collection planned are shared as supplementary materials. The data, analyses and results of this study will be shared in open access according to the COST open access policy.

Supplementary materials

Delphi survey materials:

1. Medication Adherence Technology tree in Excel (outlining the whole proposed structure with corresponding labels and definitions).
2. Delphi information letter to participants
3. Instructions for Delphi participants
4. Summary of the Delphi survey
5. Ethical approval by Malaga Regional Research Ethics Committee
6. Data protection assessment by the Data Protection Officer at the University of Basel
7. General data protection statement

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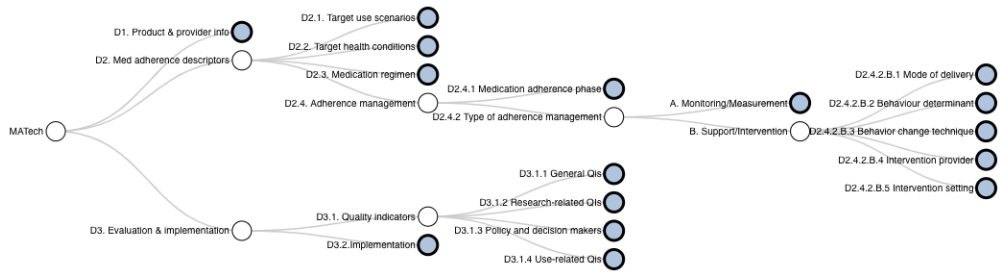


Figure 1. The interactive graph showing framework of attributes for MATech ("the MATech Tree").

945x263mm (28 x 28 DPI)

Presentation of the ENABLE repository framework of attributes

This document presents the framework of attributes developped for the ENABLE repository by the WG2 task force. ENABLE is a COST action aiming to enhance collaboration between stakeholders across Europe for adoption of best practice and technologies supporting medication adherence. To this end, ENABLE develops an online repository of medication adherence technologies. This repository will showcase a diverse range of technologies and describe them in detail so that repository users can search and select technologies that are most appropriate to their contexts and needs. Thus, the repository would need to include information relevant for this specific use.

Information about technologies can be coded/represented via a collection of various attributes. This coding is driven by a user perspective where a user (HCP, regulator, client/patient, researcher) will be willing to learn more about (or select) a technology based on their specific interests or needs, and therefore is looking for specific types of information where attributes of technologies correspond to attributes of the solutions envisaged by users. Attributes may apply to adherence-related goals, target user characteristics, health conditions, product characteristics, etc., each represented as distinct attribute groups. Such modular ("LEGO") approach allows describing a very diverse landscape of existing and future technologies.

The repository is supposed to include all potential attributes for all technologies so that they allow the descriptions of any medication adherence technology in detailed way to enable informed decision-making. The goal of the present work therefore is to create a framework of such attributes, each with their own unique labels (short names of attributes) and definitions (longer explanations of what the attributes refer to).

Once the repository is created using this framework of attributes, we will be able to describe and group available adherence technologies. If a new attribute is subsequently identified, it will be added to the list -as part of an existing attribute or by creating a new one- aiming to ensure the evolution of this repository with changes in the field, as well as backward compatibility.

Domain name		Attribute group name
D1 ***Product & provider information***	D1.1	*product and provider information*
D2 ***Medication adherence descriptors***	D2.1	*target use scenarios*
	D2.2	*target health conditions*
	D2.3	*medication regimen*
	D2.4	*medication adherence management components*
	D2.4.2.A	*Monitoring/measurement methods and tar*
	D2.4.2.B.1	*intervention modes of delivery*
	D2.4.2.B.2	*target behaviour determinants*
	D2.4.2.B.3	*behaviour change techniques*
	D2.4.2.B.4	*intervention providers*
	D2.4.2.B.5	*intervention settings*
D3 ***Evaluation & implementation***	D3.1	*quality indicators*
	D3.2	*implementation indicators*

Definition	*Core question*
Each entry in the ENABLE repository will refer to a unique product, which will be identified with a unique ID, provided by a unique organisation (manufacturer, developer) with its own unique ID and related metadata (e.g., date of entry, verification process, etc.) to present the identity of the described MATech and its provider.	What product does the entry refer to, who provides it, who entered its description in the repository and when?
The type of common adherence management activities that the technology is intended to be used for.	What use scenarios and types of users is the technology intended for?
The type of diseases or health problems the technology is intended for.	Which health conditions could the technology be used for as part of adherence support?
The prescribed schematic form/therapeutic plan of medication therapy that the technology is intended for.	What type of medication regimen(s) (treatment intention, route of administration, number of medications, and recommended dosing) is the technology intended for?
The type of procedures and time periods the technology facilitates to achieve the best use by patients of appropriately prescribed medicines.	What adherence management types and phases does the technology target?
What measurement methods are used and what is being measured (measurement targets).	If measurement is a component, what measurement methods does the technology use and what do they measure?
The modes used to deliver the medication adherence intervention	If intervention is a component, how is it delivered to its users?
Causal influences on medication adherence that can be modifiable (amenable to intervention with a medication adherence technology).	If intervention is a component, what reasons for non-adherence can the technology help address?
Options/activities included in the technology that aim to influence barriers and facilitators of medication adherence	If intervention is a component, what are the 'active ingredients' present in the technology that may trigger change in the reasons for non-adherence targeted?
A role played by a person who uses the technology to assist the patients in their self-management of medication adherence	If intervention is a component, who delivers the intervention to users?
The social and physical environment in which the technology is used to manage adherence to medication	If intervention is a component, where is the service for improving adherence delivered?
Quality indicators are standardized, evidence-based, and measurable items for monitoring and evaluating the quality of healthcare performance.	How does the technology meet key quality indicators from different perspectives?
Outcomes and strategies that help implement medication adherence measurement / intervention within its target setting	What implementation outcomes and strategies are needed and available for adopting this technology in the intended setting?

Upper Level	Sub-Level 1	Sub-level 2
Product		
	Product ID	
	Product Name	
	Brief product description	
	Date of release	
	Date of most recent update	
	Product type	
		Hardware
		Software
		Service
		Material
	Product Brand	
	Product integration	
		stand-alone
		component
	Language(s)	
	Country(ies)	
	Terms & Conditions of use	
	Cost	
Provider Organisation		
	Provider ID	
	Provider Name	
	Provider type	
		Privately-owned / for profit organisation
		Public / state-owned organisation
		Not-for-profit organisation
	Provider domain of activity	

		Technology
		Pharmaceutics
		Healthcare
		Research and Education
	Contact details	
Repository entry		
	Entry ID	
	Entry date	
	Date of last modification	
	External/peer verification of data accuracy	
Author of the product description		
	author ID	
	Author name	
	Date of account initiation	
	Author contact details	

Definition
health technology (device, procedure or system) that could be used to manage adherence to medication
random alphanumeric code given to the product at first entry in the database
name given by the technology provider to designate the product itself
text (max 500 characters including spaces) that provides a short summary of the main functionality and atributes of the technology
date when the technology first became available
date when the technology had the most recent update
type of support on which (components of) the product (are) is implemented
product (component) consisting of physical components of electronic systems
product (component) consisting of programs or other operating information for electronic systems
product (component) consisting of actions to support someone manage adherence to medication
product (component) consisting of physical substances or equipment other than electronic
name used by the technology provider to designate the group to which the product belongs
manner in which the product is intended to be integrated in an adherence support process
product integration in which the technology is intended to function unrelated to other products
product integration in which the technology is intended to link to other products as component of a wider system
languages in which the technology is available for use
name of country/countries where technology is in available
written rules which two or more parties engage to respect and meet to apply the technology in a setting; may include intelectual property, copyright.
amount paid, charged, or engaged to be paid, for purchasing the technology
organisation that produces and/or makes the product available for users
random alphanumeric code given at first entry of a product from a provider in the database
name of the provider organisation
administrative form in which the organisation is registered
organisation that operates to generate financial profit
organisation that is owned by a government
organisation not intended to make a profit but to provide or support a service that people need
general field in which the organisation is active

organisation performing activities related to the production of new machinery or equipment based on scientific knowledge or processes
organisation performing activities related to the production of medicines
organisation providing (medical) care services to individuals or/and communities
organisation providing services related to generation of new knowledge and teaching
contact name, email, phone number of the provider organisation
description of a health technology by a repository author account
random alphanumeric code given at entry registration
date of entry registration
date when the last modification of an entry was recorded
confirmation of whether the information recorded was checked for accuracy by an external/peer reviewer (group)
person or group of persons who enters information about at least one MAT in the ENABLE database
random alphanumeric code given at account opening
name of author given at account opening
date of account opening in the ENABLE platform
email address via which the author can be contacted

DEVELOPMENT AND JUSTIFICATION

A repository entry represents any contribution from an author describing a medication adherence technology using the ENABLE template, which they then upload on the platform. Each entry in the ENABLE repository will be stored individually. It will have a unique entry ID, and metadata such as the date of entry, date of most recent modification, and whether the information was verified by another manner (validation process to be developed). It will refer to a unique product, which will be identified with a unique ID, provided by a unique organisation (manufacturer, developer) with its own unique ID. Multiple entries can refer to the same product ID (the reconciliation of entries for the same product will be part of the validation procedures, i.e. by recency or merging of the entries), and an organisation may provide multiple products.

No ontology, taxonomy or classification could be identified in the BioPortal repository or in the literature that provides a formal description of product characteristics used for medication adherence technologies in particular. However, a related ontology was identified that refers to medical technology innovation in healthcare centers. This ontology, developed by members of the Platform for Innovation in Medical and Health Technologies (ITEMAS; a network of healthcare centers aiming to foster innovation in the Spanish healthcare system), includes relevant concepts on the development and adoption of technologies in healthcare and therefore it is an appropriate source of descriptors for the ENABLE repository. The ITEMAS concepts were consulted and concepts referring to products themselves and their providers were selected, since ENABLE aims to describe the technologies and not cover as well the process of developing and integrating them in healthcare systems. This choice of concepts makes the repository interoperable with organisations that would adopt ITEMAS for their activities. Additional constructs were generated after discussion with SC members.

upper level	Sub-level 1	Sub-level 2	Sub-level 3
adherence self-management use			
	Person in the healthcare environment		
		Patient	
		Caregiver	
	Patient age group		
		Adult	
			Older adult
		Adolescent	
		Child	
		Infant	
	Patient functional status		
		Mental functions	
			Memory functions
			Perceptual functions
		Sensory functions	
			Seeing functions
			Hearing functions
		Neuromusculoskeletal and movement-related functions	
	Patient literacy		
		Patient health literacy	
			Patient medication literacy
	Patient polypharmacy		
	Patient multimorbidity		
adherence support service use			

Professional health and social care providers

Health (system) manager

Definition
Scenario in which the technology is used for adherence self-management activities
Person who interacts with the technology within the process of self-management
Person who uses the technology for self-management of their own adherence
Person who uses the technology to assist the patient in their self-management of adherence
Age group of the person for which the medical technology is appropriate for use
Person aged over 18 years
Adult aged over 66 years
Person aged between 12 and 18 years
Person aged between 1 and 12 years
Person aged less than 1 year
The level of functioning of the person for which the technology is appropriate
Patient status regarding functions of the brain involved in adherence self-management
Functions regarding registering, storing, retrieving information for adherence self-management and/or using technology for this purpose
Functions regarding recognizing and interpreting sensory stimuli necessary for adherence self-management and/or using technology for this purpose
Functions regarding recognizing and interpreting visual stimuli (light, form, shape, size, color)
Functions regarding recognizing and interpreting auditive stimuli (presence, location, pitch, loudness and quality of sounds)
Functions regarding movement and mobility (of joints, bones, reflexes and muscles)
The patient's ability to read and write needed to manage adherence
The patient's capacity to obtain, process and understand basic health information and services needed to self-manage adherence
The patient's ability to understand and act on medication-related information
The use of multiple drugs (5+) administered to the same patient
complex interactions of several (2+) co-existing diseases occuring in the same patient
Scenario in which the technology is used for activities supporting taking medication in an health/social care provision setting

Members of the health and social care workforce who deliver adherence support services

Persons involved in the administration and oversight of public health systems delivering adherence support services

DEVELOPMENT AND JUSTIFICATION

Among the various use scenarios for medication adherence management, we can distinguish two general categories in what concerns the potential types of users and their characteristics that might influence the choice of technology: self-management use, and adherence support use. In the first scenario, it is either the patient or the caregiver who might be interested in searching the repository for technologies the patient can use themselves, or the couple patient-caregiver can use in the shared management of medication intake, for example at home. In the second scenario, a healthcare (or social care) provider may be interested in technologies they can use themselves to facilitate adherence support. A technology can apply to both use scenarios, for example when a monitoring technology is used by both patients/caregivers and the professionals who accompany them in their treatment and information can be transmitted from one to another (each having their own interface). Thus, the set of descriptors regarding target users operates this basic distinction.

The use of medication adherence technologies may be influenced by several characteristics of the patients, such as their age group, functional status regarding mental functions (e.g. memory and perception), sensory functions (e.g. vision and hearing), and movement-related functions, as well as characteristics of their health condition or treatment (e.g. multimorbidity and polypharmacy). Literacy and health literacy (and specifically medication literacy) are also central to the appropriateness and effectiveness of self-management support. Thus, descriptors related to these characteristics were identified in available ontologies (e.g. SNOMED-CT, WHO International Classification of Function) and included in the list of descriptors.

According to the WHO client classification (regarding DIgital Health Interventions; DHI), there are two categories of potential clients of digital health technologies in addition to patients and caregivers: healthcare providers and health system managers. These were included as sub-categories of the adherence support use scenario, since both types of professionals (including here social care organisations and providers) can initiate a search for technologies to integrate in their practice. No characteristics of these types of users/clients were considered relevant for the choice of the tool in this initial version of the list. The provider of an adherence support intervention and the setting in which this can be performed are the focus of separate descriptor sets, since they can be different from the user who initiates the search (who can perform this for an entire team, including the patient and their caregiver).

Upper level	Definition
Blood	Health condition category that refers to haematological diseases, anaemia, clotting (including thromboses and venous embolisms)
Cancer and neoplasms	Health condition category that refers to all types of neoplasms, including benign, potentially malignant, or malignant (cancer) cancer growths (including leukaemia and mesothelioma).
Cardiovascular	Health condition category that refers to coronary heart disease, diseases of the vasculature and circulation including the lymphatic system
Congenital disorder	Health condition category that refers to physical abnormalities and syndromes that are not associated with a single type of disease or condition, including Down's syndrome and cystic fibrosis
Ear	Health condition category that refers to diseases of the ear, such as deafness
Eye	Health condition category that refers to diseases of the eye
Infection	Health condition category that refers to diseases caused by pathogens, acquired immune deficiency syndrome, sexually transmitted infections
Inflammatory and immune system	Health condition category that refers to rheumatoid arthritis, connective tissue diseases, autoimmune diseases, allergies. (includes transplants)
Injuries and accidents	Fractures, poisoning and burns.
Mental health	Health condition category that refers to depression, schizophrenia, psychosis and personality disorders, addiction, suicide, anxiety, eating disorders, learning disabilities, autistic spectrum disorders
Metabolic and endocrine	Health condition category that refers to metabolic disorders (including diabetes, and diseases of the pineal, thyroid, parathyroid, pituitary and adrenal glands).
Musculoskeletal	Health condition category that refers to osteoporosis, osteoarthritis, muscular and skeletal disorders

Neurological	Health condition category that refers to dementias, transmissible spongiform encephalopathies, Parkinson's disease, neurodegenerative diseases, Alzheimer's disease, epilepsy, multiple sclerosis
Oral and gastrointestinal	Health condition category that refers to inflammatory bowel disease, Crohn's disease, diseases of the mouth, teeth, oesophagus, digestive system including liver and colon
Renal and urogenital	Health condition category that refers to kidney disease, pelvic inflammatory disease, renal and genital disorders
Reproductive health and childbirth	Health condition category that refers to fertility, contraception, abortion, in vitro fertilisation, pregnancy, mammary gland development, menstruation and menopause, breast feeding, antenatal care, childbirth and complications of newborns
Respiratory	Health condition category that refers to asthma, chronic obstructive pulmonary disease, and other respiratory diseases
Skin	Health condition category that refers to dermatological conditions
Stroke	Health condition category that refers to ischaemic stroke (caused by blood clots) and haemorrhagic stroke (caused by cerebral/intercranial haemorrhage).
Generic health relevance	Health condition category that refers to technologies applicable to all diseases and conditions

DEVELOPMENT AND JUSTIFICATION

Depending on the health conditions for which medication is prescribed, adherence behaviours may be influenced by different factors and therefore require condition-specific interventions. Adherence technologies are therefore usually developed and validated to be used in one or several clinical domains and potential users may search for technologies applicable to the health condition(s) they aim to manage.

The International Classification of Disease (ICD-11) is a global standard for diagnostic purposes, and groups diseases in over 17000 categories (icd.who.int). In ICD-11, 21 groups of codes (chapters) are proposed to describe health conditions, among other groups of codes for related diagnostic purposes. While ICD-11 is an elaborate classification used for clinical documentation and monitoring globally, a simpler classification has been developed by the UK Clinical Research Collaboration for research purposes: the Health Research Classification System (HRCS) (https://hrcsonline.net/health-categories). The HRCS is inspired by ICD and includes 21 separate disease categories, 19 of which are disease specific whereas the other 2 have a broader focus (e.g. general health and epidemiology, conditions of unknown aetiology). Of the 20 HRCS categories, 18 correspond broadly to ICD-11 chapters (merging 3 chapters into one category for reproductive health and childbirth, and omitting sleep-wake disorders), while the 19th refers to stroke as a distinct group of conditions. For the purpose of the present repository, we have therefore selected HRCS as 1) it is likely that research on adherence technologies will increasingly use these codes to record the type of health conditions studies are performed on and thus would map easier on these categories, and 2) the labels and descriptions used are relatively less technical and therefore easier to understand by stakeholders with diverse backgrounds. We considered that the last category ('Disputed aetiology and other') is less relevant for medication adherence and thus we excluded it from our descriptors list. The HRCS classification system, based on the ICD classification, would allow repository users to quickly and efficiently identify the type of health condition of their interest.

Upper level	Sub-level 1	Definition
type of intention		The purpose for which the medication is prescribed.
	preventive	Medication are prescribed as prevention/prophylaxis against the occurence of diseases or disease-related adverse events (e.g. excerbations, organ rejections etc.)
	therapeutic	Medication is prescribed as treatment of a disease and its associated symptoms.
duration of treatment		The duration of treatment presents the intended interval of treatment and relates to the clinical course and disease conditions.
	short-term	treatment is prescribed over a limited time-period, mostly to treat an acute disease of sudden-onset and predictable end.
	long-term	treatment is prescribed as a prolonged and peristently indicated therapy as it is the case in chronic, latent-progressive disease conditions.
route of administration		path by which medication is brought into contact with the body to unfold pharmacological effects.
	oral	Medications are administered as oral froms (tablets etc.) for drug reception via the mouth or gastro-intestinal tract.
	inhaled	Medications are administered as inhalation of aerosols, powders or gas via the respiratory tract.
	injections/subcutaneous	Medications are administered as injection in subcutanous layer for a relative slow drug release.
	infusion/parenteral	Medications are administered as parenteral infusion for direct intra-venous application.
	patches	Medications are administered as a dermal layer (e.g. patch) to achieve systemic drug-concentration and -efficacy.
	topical	Medications are administered as topical forms for local effects on dermal or mucous surfaces/layers.
number of monitored medications		how many distinct medications are monitored by the technology, if applicable
	single medication	Only treatment of a single medication is monitored.
	multiple medication	A combination therapy of two or more medications is monitored.

prescribed dosing frequency		dose-taking patterns recommended for medicines administration, in which doses should be taken at defined time intervals over a defined time period
	once-daily dosing	Only one dose is prescribed at a certain time during the day.
	multiple daily dosing at fixed intervals	Multiple doses are prescibed in a certain interval during the day.
	once per week dosing	Only one dose is prescribed at a certain day during the week.
	multiple dosing per week in fixed intervals	Mutliple doses are prescibed in a certain interval during the week.
	dose adjustment recommendations	The frequency or amount of a certain dose is adjusted to the newly prescribed treatment regimen.

DEVELOPMENT AND JUSTIFICATION

Factors related to the medication regimen are among the 5 main groups of determinants influencing medication adherence (WHO, 2003). The medication regimen for which adherence is to be managed can take different schematic forms and be of varying complexity, which may influence the complexity and extent of medication adherence. Medication adherence technologies may be developed for medications with different attributes, therefore ENABLE repository users should be able to indicate what type of medication regimen they are aiming to manage and how a technology fits these specific attributes.

We distinguished five descriptors relevant for medication adherence that refer to properties of medication regimens. The type of intention refers to the purpose of treatment as prevention or therapy, while the duration of treatment is related to the clinical course (e.g., acute/sudden-onset or chronic /latent-progressive course). Both depend on disease conditions and determine the purpose and duration of adherence management. The route of administration, the number of medications and the prescribed dosing frequency are the main components of the variability and complexity of prescribed regimens. Thus, descriptors related to these medication regimen attributes were identified in available ontologies (e.g., NCIT, MeSH and SNOMED-CT) and included in the list of descriptors.

It is important to note that we have selected, from among a broader range of routes of administration and types of dosing frequency, the ones we considered relevant for adherence to medication; for example, we have excluded ‘as needed’ dosing as it cannot be subject to a comparison between actual and prescribed dosing histories (the definition of adherence), and routes of administration likely to require a healthcare professional and thus be less influenced by adherence as a patient behavior.

Upper Level	Sub-Level 1	Definition
D2.4.1 Medication adherence phase		Time interval between the prescription start and end dates that is behaviorally distinct (i.e. linked with specific determinants
	Initiation	Phase of adherence that covers the start of a prescribed treatment, i.e. the period from when the prescription is issues to the first dose taken (i.e. the initiation event)
	Implementation	Phase of adherence from the initiation until the last dose taken during which one can estimate the extent to which the patient's dose taking and timing are linked to the prescribed dosing
	Discontinuation (Persistence)	Phase of adherence that refers to the end of treatment execution and covers the period until last dose is taken, e.g. end of therapy or termination by patient. Persistence is the period between initiation and discontinuation.
D2.4.2 Type of adherence management		The goal of adherence management that the technology is designed to address.
	Monitoring/Measurement	Type of adherence management that refers to estimating (repeatedly) medication adherence behaviours, determinants, and/or outcomes
	Support/Intervention	Type of adherence management that refers to generating change in medication adherence determinants and thus behaviours and outcomes.

DEVELOPMENT AND JUSTIFICATION

Technologies described in the ENABLE repository will be used either for self-management use by patients themselves or for supporting this process by health and social care providers within healthcare institutions or systems. The general term that describes both these use scenarios, according to the ABC taxonomy (Vrijens 2012), is “management of adherence”, i.e., “the process of monitoring and supporting patients' adherence to medications by health care systems, providers, patients, and or their social networks”. Thus, in this definition, a distinction is made between ‘monitoring’ (or measuring, which can target the behaviors themselves, their determinants, and/or their relevant outcomes), and ‘supporting’ adherence (or intervening to achieve best use of appropriately prescribed medicines by patients). As technologies may focus on one or both these goals, we have given the possibility for users to search for each goal/type of management (for example in situations when they would like to combine technologies into a broader adherence management solution). As both metrics and intervention may require different approaches depending on what phase of adherence is of concern, we have also given the possibility for users (and technologies) to specify which adherence phase they target, i.e.:

1) initiation, which “occurs when the patient takes the first dose of a prescribed medication”

2) implementation, which “is the extent to which a patient's actual dosing corresponds to the prescribed dosing regimen, from initiation until the last dose”

3) discontinuation marks the end of the adherence process “when the next dose to be taken is omitted and

Upper Level	Sub-Level 1	Sub-level 2	Sub-level 3	Definition
measurement method				the way in which information is gathered and summarized by the technology about the patient's medication adherence
	direct observation method			measurement method consisting in observing medication intake directly
	pill count method			measurement method consisting in calculating left over pills in containers/blisters at a specific time point
	self report method			measurement method using data reported by patients or caregivers about themselves
		diary		self-report method in which the respondent records information about their current behaviors, determinants or outcomes at regular intervals
		questionnaire		self-report method in which the respondent answers a set of pre-designed questions about their behaviors, determinants or outcomes
		interview / consultation		self-report method in which the respondent answers questions, either pre-defined or spontaneous, from another individual as part of a structured conversation
	Electronic monitoring method			measurement method using data from devices that record medication taking events electronically
		smart package		electronic monitoring method that uses data from a container/dispenser in which the medication is packaged
			smart box	smart package that includes a method to record the opening and closing of the box in which the medication is stored for use
			smart inhaler	smart package that includes a method to record the use of the inhaler device in which medication is stored for use
			smart tube	smart package that includes a method to record the use of the tube in which medication in ointment or liquid form is stored for use
			smart button	smart package that includes a device attached to private pillbox where medication is stored for use and includes a button on which the person can press to record a dose intake
		smart pill		electronic monitoring method that uses data from a mechanism integrated in the medication itself that records the ingestion of the medication

		digital event record system		digital technologies recording taking events (App, other devices)
	Electronic Healthcare Database method			measurement method using routinely collected data as part of a longitudinal healthcare process
		Electronic medical records		EHD method using data recorded in patients' medical records
		Claims / dispensing		EHD method using data recorded for insurance claims purposes based on medication dispensed as part of the patients' care process
		Record linkage system		EHD method using data recorded in several linked databases
	Laboratory method			measurement method based on clinical assessment through invasive procedure (e.g. body fluids samples)
		drug concentration		laboratory methods consisting in the detection of sufficient drug levels in blood
			intra patient variability	laboratory method indicating the fluctuation of drug concentration levels over a specific time period
		biomarker		laboratory method representing a surrogate for drug intake
		treatment response		laboratory method assessing clinical status as a proxy for adherence behaviours, e.g. habitus, lab results (blood glucose, Hba1c,) vital signs (blood pressure)
measurement target				the component of the adherence causal (logic) model measured by the technology
	determinant measure			measurement targeting causal influences on the behaviour that can be modifiable (amenable to intervention with a medication adherence technology)
	behaviour measure			measurement targeting a self-management behaviour
		adherence measure		behaviour measure assessing to the patient's medication intake as compared to the prescribed regimen
		alcohol intake measure		behaviour measure assessing the patient's intake of alcohol (frequency, type) on its own or in relation to treatment recommendations
		diet measure		behaviour measure assessing the patient's intake of food (frequency, type) on its own or in relation to treatment recommendations
		physical activity measure		behaviour measure assessing the patient's musculo-sceletal movements requiring energy expenditure (frequency, type) on its own or in relation to treatment recommendations
		tobacco use measure		behaviour measure assessing the patient's use of tobacco products

		symptom monitoring and management measure	behaviour measure assessing the patient's actions to assess symptoms regularly and/or reduce symptoms in relation to their daily goals and activities
	health outcome measure		measurement targeting the effects of the behaviour or change of behaviour on the patient's status
		clinical	outcome measure assessing clinical aspects of the patient's health status (e.g. morbidity, mortality,etc.)
		humanistic	outcome measure assessing aspects of the patient's health related quality of life, satisfaction,...
		economic	outcome measure assessing economic aspects, in particular direct, indirect and intangabile costs.

DEVELOPMENT AND JUSTIFICATION

Throughout the last decades of medication adherence research, the mode of medication adherence measurement has evolved.

If a technology aims to monitor or measure adherence as part of the adherence management process it aims to facilitate, a broad range of options opens in terms of the measurement methods it can adopt, and which elements it targets, among those included in the causal (logic) model at the 'scientific core' of this process. To measure medication adherence, numerous methods have been developed: observing patients' medication intake directly, counting the remaining medication after a period of treatment, as well as various methods using self-report, electronic monitoring, electronic healthcare databases or laboratory tests. Moreover, measurement can target not only adherence behaviours but also adherence determinants, other self-management behaviours common in chronic care interventions (as described by Train4Health, a recent competency framework for the management of chronic conditions), and outcome measures such as health and quality of life. Users of the ENABLE repository may be interested to search for technologies that implement one type of measurement method, depending on the specificities of the setting in which they work (resources, acceptability, local expertise), or of the medication (e.g., mode of administration, pre-packaging). They may also be interested not only in measuring adherence behaviours, but also in technologies that integrate other elements of the causal model of self-management specific to the health condition they need to manage. Therefore, we have selected a range of measurement models (some of them with corresponding codes in SNOMED-CT, some based on methodological work in relevant domains), and followed the BCIO ontology and the Train4Health selection of self-management behaviours to offer the possibility to describe technologies from a measurement perspective.

Upper level	Sub-level 1	Sub-level 2	Sub-level 3	Definition
Printed material				Mode of delivery that involves use of printed material
	Brochure			Printed material mode of delivery that involves use of a printed publication within a brochure
	Printed media			Printed material mode of delivery that uses formats of printed media to communicate and share information
		Poster		Printed media mode of delivery that involves display of a poster in a public location.
		Newspaper/leaflet		Printed media mode of delivery that involves use of a printed publication in a newspaper or leaflet.
Human interaction				Mode of delivery that involves a person as intervention source who interacts with an intervention recipient
	Face to face consultations			Human interactional mode of delivery that involves an intervention source and recipient being together in the same location and communicating directly.
	Networks/patient groups			are groups that meet in person to discuss their 'issues' or experiences related to their health condition and or medication
Electronic				Mode of delivery that involves electronic technology in the presentation of information or the mode of motivation to an intervention recipient
	Smart phone/tablet			Electronic mode of delivery that involves communication processes
		Call		Electronic mode of delivery that involves a communication process in which a signal is sent by a caller to a recipient to alert them of the communication intent, giving the recipient the opportunity to engage with the communication.
			interactive messaging or chat	Call mode of delivery that involves textual information in the communication through interactive messaging or chat
			sms -short text message	Call mode of delivery that involves textual information in the communication.
			audio	Call mode of delivery that involves only audio information in the communication
			video	Call mode of delivery that involves video and audio information in the communication
		email		Electronic mode of delivery that involves communication by email.
		application		Electronic mode of delivery that involves the intervention recipient interacting with a mobile application

			interactivity	Application mode of delivery that is interactive
			diary	Application mode of delivery that uses a diary to delivery a medication adherence intervention
			reminder system	Application mode of delivery that uses a reminder system to delivery a medication adherence intervention
			gaming	Application mode of delivery that uses gaming features to delivery a medication adherence intervention
	Wearable electronic device			Electronic mode of delivery that includes medication related devices to support users to adhere to their treatment
		smart box		smart package that records the opening and closing of the box in which the medication is stored for use
		smart inhaler		smart package that records the use of the inhaler device in which medication is stored for use
		smart tube		smart package that includes a method to record the use of the tube in which medication in ointment or liquid form is stored for use
		smart buttom		smart package that includes a device attached to private pillbox where medication is stored for use and includes a button on which the person can press to record a dose intake
	digital media			Electronic mode of delivery that includes the use of electronic devices commonly used for mass-media communication
		Internet		Electronic mode of delivery that involves presentation of information through the internet
			patient portals	Internet mode of delivery that allows patients to interact and communicate with other patients having the same health condition, treatment, and so on. these patient portals are not controlled on the quality of information shared and are available on the Internet at all hours.
			website	Electronic mode of delivery that involves the intervention recipient interacting with a website.
		social media		Electronic mode of delivery defined as online communication channels disseminate information to a huge audience world wide
		broadcast media		Electronic mode of delivery that involves presentation of information through different mediums of media through a radio, television or billboard receiver.
			Radio	Electronic mode of delivery that involves presentation of audio information that is broadcast and received by a radio receive

TV	Electronic mode of delivery that involves presentation of information that is broadcast and displayed by television
Billboard	Electronic mode of delivery that involves presentation of information by an electronic screen positioned in a public location.

DEVELOPMENT AND JUSTIFICATION

Effective behaviour change interventions depend on a thorough evaluation and thoughtful selection of the mode of delivery of that specific intervention. The mode of delivery is defined as the 'physical or informational medium through which a given behaviour change intervention is provided'. To date, no ontology or other classification systems exist, to our knowledge, that categorize the mode of delivery of a medication adherence interventions. The Human Behaviour Change project, a collaborative research project aiming to create a 'Knowledge System' for using existing behaviour change interventions, is in process of creating ontologies to generate new insights about behaviour change. Within this project, scientists develop the Behaviour Change Intervention Ontology (BCIO), which is 'a set of definitions for entities and relationships used to describe behaviour change interventions, their contexts, effects and evaluations'. The modes of delivery attributes for the present repository were inspired from BCIO.

Upper Level	Sub-level 1	Sub-level 2	Sub-level 3
individual-level behaviour determinant			
	Capability		
		psychological capability	
			knowledge
			psychological skills
			memory, attention, decision
			behavioral regulation
		physical capability/skills	
	Opportunity		
		social opportunity/influences	
		physical opportunity/ environmental context and resources	
	Motivation		
		reflective motivation	
			role & identity

beliefs about capabilities

optimism

beliefs about consequences

intentions

goals

automatic motivation

reinforcement

emotion

Definition
modifiable causal influences on medication adherence that reside within an individual person
behaviour determinant referring to what an individual can do themselves to take medication as agreed
behaviour determinant referring to the mental capabilities that help individuals themselves take medication as agreed
psychological capability referring to what an individual knows about taking medication as agreed for their condition
psychological capability referring to what an individual is good at doing to take medication as agreed
psychological capability referring to the individual's abilities to retain information, to focus on specific things, and to choose between different things that help individuals take medication as agreed
psychological capability referring to what an individual can do themselves to keep track of taking medication and change their habitual ways of doing this
behaviour determinant referring to the physical capabilities that help the individual take medication as agreed
behaviour determinant referring to the conditions in the individual's external environment that can facilitate medication adherence
behaviour determinant referring to the conditions in the social environment
behaviour determinant referring to the conditions in the physical environment
behaviour determinant referring to what extent the individual feels driven/willing/energised to take medication as agreed
behaviour determinant referring to the extent of feeling motivated to take medication as agreed by thinking about it
reflective motivation referring to how the individual perceives what they need to do and how they are in their social personal and/or professional environment

reflective motivation referring to how the individual thinks about whether they can take their medication as agreed in various situations

reflective motivation referring to the confidence that the individual will succeed in their efforts to take medication and manage their condition

reflective motivation referring to what the individual thinks about the effects of taking medication on their health and/or other life goals

reflective motivation referring to whether the individual has taken a conscious decision to take medication as agreed

reflective motivation referring to how the individual represents in their mind the fact of taking medication as agreed, or other life goals related to their treatment

behaviour determinant referring to the extent of feeling motivated to take medication as agreed by emotions and impulses occurring automatically

automatic motivation referring to how taking medication as agreed is associated repeatedly to external stimuli that make it more likely to happen

automatic motivation referring to how taking medication as agreed is associated to individual's reactions to cope with personally significant stimuli

DEVELOPMENT AND JUSTIFICATION

Numerous factors influencing medication adherence have been identified in the research literature. The term commonly employed in research is 'determinants of behaviour', and an important distinction is made between modifiable and non-modifiable determinants, depending on whether these are amenable to change by an intervention within the specific context. Modifiable determinants are also named 'mechanisms of action' when they are part of a behaviour change intervention scenario as a process through which change is affected on a behaviour. Among the determinants studied and targeted by adherence support interventions/technologies, most are patient-related, although several may be related to the therapy/medication, condition, socio-economic context, or the healthcare system. Patient-related adherence determinants include for example the individual's beliefs about the medication, their health condition, their habits and ways of coping with changes in routine.

A substantial body of research has been conducted using a diverse range of concepts, theories and frameworks from health psychology and behavioural medicine. This research resulted in a vast number of constructs, not all relevant for adherence. Therefore, a selection was necessary for the purposes of the ENABLE repository. Recently, these have been systematized via literature review and expert consensus in the Capability, Opportunity, Motivation and Behaviour (COM-B) model, Behaviour Change Wheel and the Theoretical Domains framework, a group of related tools aimed to facilitate the description and development of interventions and the synthesis of scientific evidence on behaviour change. These tools have been increasingly used in health research, including in supporting medication adherence. Three main categories of individual determinants are proposed in the COM-B model, each with two subcategories: Capability (psychological and physical), Opportunity (social and physical), and Motivation (reflective and automatic). For each subcategory, up to six theoretical domains of behaviour determinants have been identified by grouping similar constructs from different sources, resulting in a total of 14 distinct domains. The terminology of behaviour determinants is currently evolving. Recently, 12 new categories have been added to the 14 TDF domains resulting in 26 mechanisms of action mapped onto the current classification of behaviour change techniques for evidence synthesis purposes. The Mechanisms of Action (MoA) Ontology is currently under development. Some determinant categories are named and structured differently in the MoA ontology version 1 as compared with COM-B and TDF structures, and the terminology is likely to continue to evolve in the following years. Therefore, we have adopted the COM-B/TDF classification, as it has been in use for research for the last years. Some simplifications have been applied from the structure proposed by Cane et al. (2012) to avoid duplication (i.e., the categories of role and identity and optimism were considered only in the reflective motivation category, although they can pertain also to automatic motivation); we kept the distinction between psychological skills and physical skills, as these are likely to be targeted separately in adherence technologies.

Upper Level	Sub-Level 1	Sub-Level 2	Definition
Acting on Capability			Group of behaviour change techniques aiming to influence what an individual can do themselves to take medication as agreed with the healthcare provider
	Feedback and monitoring		The technology includes options to record medication intake and its effects, and feed this information back to the user
		Biofeedback	The technology includes an option/activity to record physiological/biochemical effects of taking medication as agreed with the healthcare provider.
		Feedback or self-monitoring on behaviour	The technology includes an option/activity to monitor and feedback on adherence behaviours (by the medication users themselves or other people who can relay the information to them)
		Feedback or self-monitoring on outcomes	The technology includes an option/activity to monitor and feedback on a positive outcome of adherence behaviours (by the medication users themselves or other people who can relay the information to them)
	Repetition & substitution		The technology includes options/activities to perform certain actions repeatedly and systematically in order to enforce medication adherence behaviours and replace other behaviours not beneficial for medication adherence
		habit formation	The technology includes ways to prompt rehearsal and repetition of medication intake in the same context repeatedly at the planned time for intake, so that the context elicits adherence
		behavioral practice/ rehearsal	The technology includes ways to prompt practice or rehearsal of medication intake in a context or at a time when it may not be necessary, in order to increase adherence habit and skill
		graded tasks	The technology includes options to set easy-to-perform tasks related to medication intake, making them increasingly difficult until adherence becomes achievable in all situations
	Shaping knowledge		The technology includes options for the user to learn about how to take medication as agreed with the healthcare provider, what they can do themselves to stick to the schedule in difficult situations, and test different ways of doing this

Acting on Opportunity			Group of behaviour change techniques aiming to influence the conditions in the individual's external environment that can facilitate medication adherence
	Demonstration of behaviour		The technology includes an observable sample of how to take medication as agreed, directly in person or indirectly (video, pictures, drawings)
	Prompts & cues		The technology includes ways to prompt medication intake at the agreed time
	Restructuring the physical environment & adding objects		The technology includes advice on how to change the environment to make it easier to take medication as agreed with the healthcare provider.
	Identity		The technology includes ways of strengthening a positive identity that includes taking medication as agreed with the healthcare provider.
Acting on Motivation			Group of behaviour change techniques aiming to influence to what extent the individual feels driven/willing/energised to take medication as agreed with the healthcare provider.
	Goals and planning		The technology includes options to encourage setting goals related to adherence and planning to achieve them
		Action planning	The technology includes an option/activity for the user to plan concretely how they will take the medication.
		Discrepancy between current behaviour and goals	The technology includes an option/activity to compare the user's adherence-related goals with their current adherence behaviour
		Goal setting & reviewing (behaviour)	The technology includes an option/activity to set or agree on a goal in terms of an adherence behaviour, and review this goal in light of achievement
		Goal setting & reviewing (outcome)	The technology includes an option/activity to set or agree on a goal in terms of an outcome of adherence, and review this goal in light of achievement
		Problem solving	The technology includes an option/activity to identify barriers & facilitators of their own adherence and propose solutions to overcome / increase them
	pros & cons		The technology includes ways to identify and compare reasons for wanting or not wanting to take medication as agreed with the healthcare provider.

	Regulation		The technology includes advice and/or options/activities aiming to keep motivation for medication adherence within a range favourable for performing adherence-related behaviours.
		conserving mental resources	The technology includes advice on how to make taking medication less demanding for the person
		reducing negative emotions	The technology includes ways of reducing negative emotions in relation to taking medication
	Self-belief		The technology includes ways of increasing the person's confidence they can take medication as agreed with the healthcare provider.
	Imaginary reward		The technology includes advice on how to imagine correct performance of medication intake
Acting across domains			Group of behaviour change techniques aiming to influence determinants from more than one determinant group (capability, opportunity, motivation)
	Social support (emotional and practical)		The technology includes options to advise, arrange or provide social support (practical, emotional, other), or praise/reward taking medication as agreed with the healthcare provider.
	Social reward		The technology includes verbal/non-verbal rewards when the patient shows effort and/or progress in taking medication as agreed with the healthcare provider.
	Information about consequences		The technology includes information about consequences (health-related, emotional, social, environmental) of medication adherence (or non-adherence), and emphasise their relevance for the person

DEVELOPMENT AND JUSTIFICATION

To trigger/support change in a health behaviour like medication adherence, interventions (whether mediated by technologies or not) act by generating change in determinants of the target behaviour. They do so in the same way that medications act on improving health outcomes by triggering changes in pathophysiological mechanisms of the health condition they aim to treat. The 'active ingredients' for behavioural health interventions have been labelled behaviour change techniques (BCT). For example, a reminder set within a medication adherence app on the user's smartphone to prompt medication intake at the agreed time is an application of a BCT in the category 'Prompts & cues', that acts on the 'Opportunity' group of determinants as it modifies the conditions in the user's environment that can facilitate medication adherence.

Evidence on effects of these BCTs on different behaviours has been accumulating and has been recently systematized based on the BCT taxonomy, a consensus classification of 93 BCTs that organizes theoretical constructs in this field (ref). The BCT taxonomy is currently part of the Human Behaviour Change Project and interoperable with the models and ontologies used in the other descriptor groups. It has been used extensively in the last decade in intervention description, development, validation and implementation, as well as in evidence synthesis and training of healthcare professionals. However, not all techniques included in this taxonomy are relevant for medication adherence support. The ENABLE repository would need to include only BCTs relevant for adherence support technologies and be compatible with other tools used for behaviour change training and practice in healthcare systems.

Two applications of the BCT taxonomy to healthcare professional training on behaviour change simplify the structure and provide solutions for the ENABLE repository. The first, Cards for Change, is a simplified version of the taxonomy for development of training content for HCP behaviour change that has been used already in several countries as part of the Change Exchange Initiative (ref). It builds on a tool developed for coding training sessions in healthcare professional continuous education (ref) and includes the most used techniques in healthcare settings with examples of possible training activities. The second is the Train4health competency framework, a consensus-based framework for professionals who support self-management of chronic conditions in Europe developed by the Train4Health project, funded via the Erasmus+ programme (ref). The framework identified a set of 12 foundational competencies and 14 behaviour change competencies, including knowledge and abilities to identify relevant behaviours, intervention models, BCTs and apply these collaboratively to develop and implement self-management programmes. A panel of experts selected the most relevant BCTs for the 5 priority behaviours, including medication adherence support, physical activity, diet, smoking cessation and symptom monitoring and management.

We have therefore selected 24 categories of BCTs consistent with the selections operated by the Train4Health consortium and the Cards for Change team, to align the terminology with healthcare professionals training programmes that are currently using or will be developed in the future using these tools. Some BCT categories were merged due to common co-occurrence (e.g., feedback and monitoring; shaping knowledge techniques), and some BCTs are present in C4C but not in T4H since the former is more comprehensive than the latter. The initial ENABLE descriptor list includes only user-level BCTs (i.e., BCTs that can be included in technologies that provide support to medication users); if considered relevant, future versions can include HCP-level interventions (e.g., training programmes) or organisation/system-level BCTs. To align this set of descriptors with the ones referring to adherence determinants, we have grouped the 24 categories into 4 dimensions (i.e., acting on Capability, Opportunity, Motivation, cross domains), using the theoretical mapping described by Cane et al. and previously applied in evidence synthesis in health behaviour change. Mapping work is ongoing and likely to be updated with further iterations of these ontologies. We have therefore chosen the terms most used currently and expect back-compatibility in future versions.

It is important to note that a new classification by WHO is currently under development for health interventions which includes terminology for behavioural interventions: International Classification of Health Interventions (ICHI). Currently, ICHI is designed to be interoperable with the COM-B model via a series of extension codes. However, for describing categories of health interventions, the ICHI classification uses over 20 terms, different from the behaviour change literature, that cover measurement (Assessment, Testing), several broader categories on individual-level intervention

from the behaviour change literature, that cover measurement (Assessment, Testing), several broader categories on individual-level intervention (Training, Education, Advising, Counselling, Emotional support, Provision of products to support, Provision of peer support), as well as health system and societal level interventions (Providing opportunities for participation, Advocacy, Building partnerships, Public facilities, Environment modification, Capacity building, Awareness raising, Public health surveillance, Health alerts, Enactment and enforcement of legislation, Economic and non-economic incentives, Policy change, Other). Ensuring interoperability between ICHI and the BCIO ontologies is under discussion.

Upper level	Sub-level 1	Sub-level 2
health care professional		
	medical doctor	
		generalist medical practitioner
		specialist medical practitioner
	nursing professional	
	midwifery professional	
	pharmacist	
		community pharmacist
		hospital/clinical pharmacist
	dentist	
	associated health professional	
		community healthcare worker

health care assistant

psychosocial care professional

psychologist

Personal care worker

Personal provider

family member

parent or guardian

spouse or partner

other

carer

friend

peer

Definition
An intervention provider that applies scientific knowledge in medicine, nursing, midwifery, pharmacy, dentistry and/or health promotion to support patients in
A health professional that studies, diagnoses, treats and prevents illness, disease, injury and other physical and mental impairments.
A medical doctor that does not limit their practice to certain disease categories or methods of treatment, and may assume responsibility for the provision of continuing and comprehensive medical care to individuals, families and communities
A medical doctor that specializes in certain disease categories, types of patients or methods of treatment and may conduct medical education and research in their chosen areas of specialization.
A health professional that provides treatment, support and care services for people who are in need of nursing care due to theeffects of ageing, injury, illness or other physical or mental impairment, or potential risks to health.
A health professional that plans, manages, provides and evaluates midwifery care services before, during and after pregnancy and childbirth.
A health professional that stores, preserves, compounds and dispenses medicinal products and counsel on the proper use and adverse effects of drugs and medicines following prescriptions issued by medical doctors and other health professionals.
A pharmacist that practices in primary care/ community settings.
A pharmacist that practices in secondary care / hospital settings.
A health professional that diagnoses treats and prevents diseases, injuries and abnormalities of the teeth, mouth, jaws and associated tissues.
A health professional that performs technical and practical tasks to support diagnosis and treatment of illness, disease, injuries and impairments, and supports the implementation of health care usually established by medical, nursing and other health professionals
Associated health professional that provides health education, referral and follow-up, case management, basic preventive health care and home visiting services to specific communities.

Associated health professional that provides basic care services for the prevention and treatment of diseases and disorders, according to care plans and procedures established by medical, nursing or other health professionals.

An intervention provider that applies scientific knowledge in psychology, sociology and other social sciences to support individuals and families in a community in their well-being and life goals

A social professional that studies the mental processes and behaviourof human beings as individuals or in groups, and applies this knowledge to promote personal, social, educational or occupational adjustment and development

An intervention provider that delivers care, supervision and assistance for children, patients and elderly, convalescent or disabled persons in institutional and residential settings.

an intervention provider that is related to the person to whom the intervention is targeted through aspects of their personal lives.

A personal provider who is related to another person as they are descended from a common progenitor, related by marriage or other legal tie, or by a feeling of closeness.

A family member that is a mother, father or legal carer of the person to whom the intervention is targeted

A family member that is an individual who is married or in a committed relationship with the person to whom the intervention is targeted

A family member that is a child, sibling or in the extended family (e.g. uncle, aunt, nephew) with the person to whom the intervention is targeted

A personal provider who is an individual who cares, unpaid, for a friend or family member who is the person to whom the intervention is targeted

A personal provider who is an individual who is known, liked and trusted by the person to whom the intervention is targeted, typically exclusive of sexual or family relations

A personal provider who is described as similar to the person to whom the intervention is targeted on the basis of similarities in age, social status, gender, experience, health status

DEVELOPMENT AND JUSTIFICATION

The provider or source of intervention is a role played by a person, population or organization that provides/delivers a given intervention. This includes their occupational role, education, sociodemographic, knowledge, skills and any relatedness between them and the target population. In terms of medication adherence, the provider is often HCP. The quality of the HCP-patient relationships, especially communication skills, collaborative decision making, trust in the HCP and HCPs' cultural competences, are in correlation with patients' adherence. Several different professions of intervention providers were recognized as the most influential OR relevant in relation to medication adherence of patients using the Intervention Source Ontology Coding Guidelines and Gender, Sex, and Sexual Orientation (GSSO) ontology.

Upper level	Sub-level 1	Sub-level 2	Sub-level 3	Definition
Physical setting				Intervention setting that consists in a physical environment where the medication adherence technology is used.
	Residential facility			A physical setting that has at least one housing unit as part in which a person to whom the intervention is targeted lives.
		Household residence		Residential facility where a person to whom the intervention is targeted lives alone or with one or more persons.
			Residential care or assisted living	Household residence where many vulnerable persons live.
			Student residence	Household residence where many students live.
	Healthcare facility			A physical setting that is administered by a health care organisation for the purpose of providing health care to a patient population.
		Hospital facility		healthcare facility that is run by a hospital organisation and is the bearer of a hospital function.
		Doctor-led primary care facility		A healthcare facility led by doctors
		Care home facility		A healthcare facility that is run by a care home organization and is the bearer of a care home function
		Hospice facility		A healthcare facility that bears a function to provide healthcare to the sick or terminally ill
		Pharmacy facility		A healthcare facility whose function is to store, prepare, dispense and monitor the usage of pharmaceutical drugs among patients in a given area or encountered in a given healthcare provider organization
		Psychiatric facility		A healthcare facility designed and staffed to house and treat individuals that need assistance with mental health
		Community healthcare facility		A healthcare faclity providing healthcare services to people in a certain area.
		Dentist facility		A healthcare facility where dental healthcare is provided
	Educational facility			A physical setting in which formal education is provided to a student population

	Community facility		A physical setting used by a group of people living in the same area or having a particular characteristic in common
		Social centre or Community Hall facility	A community facility used for socialising by those living in a given area.
Virtual setting			Intervention setting that consists in a virtual environment where the medication adherence technology is used.
	Telemedicine		Virtual setting through which healthcare services are delivered by medical doctors
	Telepharmacy		Virtual setting through which healthcare services are delivered by pharmacists

DEVELOPMENT AND JUSTIFICATION

Implementation and behavioral science emphasize the importance of understanding and describing the environment in which a certain intervention is delivered as it can significantly influence its outcomes. In addition, not every intervention is applicable or transferable to every setting. Similar to the mode of delivery, we can distinguish between physical and virtual settings. Healthcare services may be provided in different healthcare facilities using different technologies and adherence intervention models. Thus, the efficacy of direct in-person models of adherence intervention may be different than indirect interventions such as electronic strategies. Some interventions may be applicable in both types of settings, or require a combination of physical and virtual settings in order to be performed. The classification was made using the Intervention Setting Ontology, which is a component of the Behaviour Change Interventions Ontology (BCIO).

Upper Level	Sub-Level 1	Sub-Level 2
D3.1.1 General quality indicators		
	ISO certification	
	Evidence from scientific evaluation	
		Research base on development
		Research base on effectiveness
		Ethical and legal aspects
	Development standards	
		Development process
		User-centered design process
		Conflict of Interest
		Updating of information sources
	Technological standards	
		Performance
		Data protection

		System integration testing
		Inter-device portability
D3.1.2 Research-related quality indicators		
	Theory base	
	Measurement validity	
		content validity
	Intervention validity	
		coherence of the intervention model
	Measurement reliability	
		Internal consistency
		Inter-rater reliability
		Test-retest reliability
D3.1.3 Policy-related quality indicators		
	Cost and economic evaluation	
		Cost-effectiveness

			Cost-utility
			Cost-consequence
			Cost-benefit
			Cost-minimisation
			Budget impact
			Country(ies) where evaluation performed
		Current use of the technology	
			Regulatory status
D3.1.4 Use-related quality indicators			
		Usability	
			Simplicity
			Cleanliness
			Intuitiveness
			Reliability

Satisfaction	
	Satisfaction test
Customisation	
	Customisation of language
Aesthetics	
Readability	

Sub-Level 3	Sub-Level 4
Quality of evidence on development	
Quality of evidence on effectiveness	
Usability tests	
Reliability of interactive components	
Design scalability of the technology	

Data encryption

Antivirus with supported maintenance

Data storage place

Data storage capacity

Protection against theft or physical attacks

face validity

language validation

target population validation

vs no intervention

vs other interventions

Authorisation status

Country(ies) where approved

Approval body(ies)

Indication(s) approved

Reimbursement status

Country(ies) where

Indication(s) reimbursed

Definition
Quality indicators that that evaluate MATech characteristics relevant for all stages of the technology development, adoption and use.
General QI referring to whether the MATech has obtained one or more ISO certification labels relevant for its content and purpose.
General QI referring to whether the MATech has been evaluated through the systematic, rigorous, and meticulous application of scientific methods, and the evidence obtained.
Evidence from scientific evaluation is available to support the design of the MATech.
Attribute of the research base on development referring to the "grade (or strength) of recommendation", decided based on levels of evidence (sometimes called hierarchy of evidence) assigned to studies based on the methodological quality of their design, validity, and applicability to patient care.
Evidence from scientific evaluation is available to support the effectiveness of the MATech (excluding cost-effectiveness, outlined in section D2.1.3 and implementation outcomes, outlined in section D3.2).
Attribute of the research base on effectiveness referring to the "grade (or strength) of recommendation", decided based on levels of evidence (sometimes called hierarchy of evidence) assigned to studies based on the methodological quality of their design, validity, and applicability to patient care.
Attribute of the scientific evaluation of the MATech referring to whether the research has ethical approval, has considered and addressed any risks for the target population, complies with the current laws on research on humans and data privacy and safety, and has shared information about how it meets these requirements.
General QI referring to whether the MATech has been developed according to standards established in the development of health technologies.
All development activities undertaken with respect to MATech are clearly described, such as activities related to preparation, development and optimization of product components as well as the manufacturing, validation and distribution process.
The MATech was developed in an iterative design process in which designers involved the target users and their needs in each phase of the design process. The users's requirements, objectives, and feedback were taken into account during the development process.
Usability tests were performed and the results are available (e.g., described or available on a link) with a statement, how the findings influenced the MATech.
The provider's conflicts of interest are clearly described, if any, to ensure trust and transparency.
Information sources are periodically verified (proven to still be correct and accurate) and updated (new information added or design changed).
General QI referring to whether a MATech corresponds to criteria commonly used to assess the technical functioning of electronic components, if applicable.
The MATech works fast and accurately without bugs or errors.
The interactive components (e.g. alarm system) are secure and these characteristics are maintained even when the system grows.
The MATech shows efficiency even with a large volume of users / data.
Collected data are properly protected to prevent sensible data leakage.

Encrypting takes a part of the data and translates it into a new form so that only people with access to the key can read it, in order to protect the confidentiality of digital data.

The MATech has software installed for data protection against online theft and attacks, and regularly revised to fulfil the function of acting against malicious code or programs.

Data storage on MATech devices is not connected to network to further ensure data safety against network attacks.

How much storage space is provided by the MATech to contain data.

The MATech has measures in place for protection against burglary, theft, vandalism and terrorism.

The developed MATech conforms to the requirements in terms of technical, privacy and security requirements of health care systems.

The MATech can be connected with several other devices.

Quality indicators that evaluate if the research on the MATech has been performed according to standards established in measurement and intervention research.

The MATech is developed based on theory, evidence, and/or theoretical frameworks.

The MATech measurement components measure exactly what they propose to measure (the used measure represents the intended variable)

Type of validity referring to the extent to which a measure in the MATech “covers” the construct of interest

Type of content validity referring to the extent to which a measurement method in the MATech appears “on its face” to measure the construct of interest.

Type of content validity referring to whether the MATech and corresponding materials were validated for the available languages.

Type of content validity referring to the whether the MATech was tested and validated for the target population.

The MATech intervention components have the potential to influence the behaviour determinants they target.

The use of behaviour change techniques in the intervention components of the MATech is evidence based, i.e. there is scientific evidence that the chosen techniques are likely to be effective in influencing the chosen behaviour determinants.

The MATech measurement components reproduce a measurement result consistently in time and space.

Type of measurement reliability referring to the consistency across items or indicators of the same construct

Type of measurement reliability referring to consistency across different researchers

Type of measurement reliability referring to the consistency over time

Quality indicators related to Health Technology Assessment (HTA) procedures and concepts that inform decision-making regarding implementation and use of health technologies.

an economic analysis has been performed to inform value-for-money judgements about the MATech with information about costs, health-related outcomes and economic efficiency

CEE that examines the costs and health outcomes of one or more interventions, to estimate how much it costs to gain a unit of a health outcome, like a life year gained or a death prevented.

Cost-effectiveness analysis where the control group is represented by a population receiving no intervention (treatment as usual)

Cost-effectiveness analysis where the control group is represented by a population receiving other interventions.

CEE in which the incremental cost of a technology from a particular point of view is compared to the incremental health improvement expressed in the unit of quality adjusted life years (QALYs)

CEE in which a wide range of costs and consequences (effects) of the technology is assessed and reported separately. It includes all types of effects, including health, non-health, negative and positive effects, both to patients and other parties (e.g., caregivers).

CEE consisting of a systematic process to sum the potential rewards expected from the technology and then subtract the total costs associated with that technology; some analysts also build models to assign a monetary value on intangible items.

CEE consisting of applying basic rules to determine what mix of labor and capital produces output at the lowest cost, i.e., what the most cost-effective method of delivering goods and services would be while maintaining a desired level of quality.

CEE that estimates the financial consequences of adopting a new technology which is usually performed in addition to a cost-effectiveness analysis; it evaluates whether the high-value intervention is affordable.

Healthcare system or country where the economic evaluation has been performed

Specifies the regulatory status (authorization and reimbursement) of the technology. These information are country or system specific, thus the repository also needs to specify where these indicators apply.

The stage in which the MATech is in the process of obtaining necessary authorisations and being considered for reimbursement by authorities in order to be adopted in routine practice in a health system or country.

HTA CUR indicator specifying whether the technology is approved for clinical use by an appropriate local regulator via marketing authorisation and/or CE marking.

Healthcare system or country where the technology has received authorization.

Name of the body which has issued the technology approval for clinical use in the respective country (eg., NICE)

Diagnoses, clinical conditions or social conditions for which the MATech has been approved for clinical use

HTA CUR indicator specifying whether the technology cost is fully or partially covered for the patient by a reimbursement authority (eg., NHS, insurance company)

Healthcare system or country where the technology is reimbursed.

Diagnoses, clinical conditions or social conditions for which the technology is reimbursed

Quality indicators that evaluate if the MATech meets users expectations and provides a pleasurable experience of interaction with the technology.

The MATech is easy to use, and easy to learn or understand, as assessed in objective ways (as opposed to user-friendliness, which is subjective).

The interface is not overly complex, but instead is straightforward, providing quick access to common features or commands.

The interface is well-organized, making it easy to locate different tools and options.

The interface makes sense to the average user, requires minimal explanation for use, and provides clear explanations for how to use it.

The MATech is reliable and does not malfunction or crash.

The level of satisfaction of the end user with the MATech has been explored and found appropriate.

The manner in which the level of satisfaction from the patient with the MATech was assessed, e.g. online or telephone survey about satisfaction made by research staff.

The MATech or some parts of it can be customized to the needs of the individual user.

The MATech gives the option to customize language to adapt to different users.

The MATech has been evaluated as aesthetic (size, layout, graphic, font size etc. support the use of MATech) in a research project or external review.

The text included in the MATech is written in a style easy to understand, i.e. readers are able to recognize (decode) the words as well as comprehend the meaning of the text.

DEVELOPMENT AND JUSTIFICATION

Quality indicators are standardized, evidence-based, and measurable items for monitoring and evaluating the quality of healthcare performance. With their statement about the structure, process, or outcomes of care, review criteria and standards can be developed to help operationalize quality indicators.

No classification or list of criteria could be identified in the literature that provides a formal description of quality indicators specific to medication adherence technologies. However, several related sets of criteria refer to ehealth applications in general -such as the Mobile Application Rating Scale (MARS)- or guide reporting of research on ehealth applications -such as the Consort-EHEALTH guideline. These checklists and guidelines include relevant concepts of technology quality but are neither comprehensive nor specific to medication adherence technologies. MATech represent an important type of health technology and therefore should adopt HTA procedures and concepts to inform decision-making regarding their implementation and use. Two HTA domains were considered relevant for MATech: (i) Cost and economic evaluation (ECO) informs value-for-money appraisal with information about costs, health-related outcomes and economic efficiency; (ii) Current use of technology (CUR), specifies the authorization and reimbursement status of the technology. The indicators in both domains are often country or system specific, thus the repository also needs to specify where these indicators apply. Other HTA domains include assessment elements that are either captured in other attribute groups or not applicable to MATech.

Therefore, we decided to develop a checklist for assessing the quality of ehealth applications, building on the work of an ongoing project involving a systematic review of existing items and criteria in the literature. We synthesized the quality indicators identified in this work into a comprehensive list and adapted the items to be appropriate for medication adherence technologies for the ENABLE repository. This new list of items was discussed, adjusted, concretized, and refined in several rounds with SC members, and additional constructs were generated until consensus was reached.

As MATech follow different stages of development and implementation and need to meet quality standards specific or common to all stages, from research to adoption by decision-makers to routine use in specific settings, we decided to group quality indicators according to their relevance to these stages. We considered some indicators relevant to all stages, while others would be likely to be more research-related, policy-related, or use-related.

Upper Level	Sub-Level 1	Definition
implementation outcome		characteristic of the techology regarding its implementability in clinical practice, as supported by evidence
	Acceptability	Implementation outcome referring to whether stakeholders reported satisfaction with various features of the technology and the experience of using it to support medication adherence
	Feasibility	Implementation outcome referring to whether stakeholders perceived the technology as practical and fit for use in supporting medication adherence
	Sustainability	Implementation outcome referring to whether stakeholders perceived the technology as appropriate for routine sustained use in supporting medication adherence
implementation strategy		characteristic of the technology that facilitate implementation and maitenance of the technology in a setting
	training	Implementation strategy referring to activities to teach stakeholders about the technology and how to use it and integrate in the medication adherence support processes
	educational materials	Implementation strategy referring to materials stakeholders may consult to learn about the technology and how to use it and integrate in the medication adherence support processes
	funding	Implementation strategy referring to financial strategies and/or additional costs to facilitate adoption of the technology into medication adherence support practice
	expertise sharing	Implementation strategy referring to information from previous implementations on what helped adopt the technology into medication adherence support practice
	technical assistance	Implementation strategy referring to systems to support implementation of the technology into medication support practice
	consultation	Implementation strategy referring to accessing direct support from experts for the implementation of the technology into medication support practice

accreditation & legal approvals	Implementation strategy referring to credentials and/or licensing to acquire or prove to be able to use the technology in a setting in the conditions necessary for optimal safety and effectiveness
collaborations	Implementation strategy referring to involving multiple institutions in delivering the medication adherence support solution that uses the technology
access to additional resources	Implementation strategy referring to access to data, space, laboratory facilities

DEVELOPMENT AND JUSTIFICATION

Medication adherence support technologies (as medications themselves) work only if they are adopted by individual users or by a group of healthcare providers and users in a healthcare setting, if their use is maintained for the duration in which they are designed to be used to bring about the expected benefits, and if they are used as intended for this duration. Evidence in implementation sciences is accumulating in recent years on how to facilitate the adoption and use of technologies (or interventions) in real-world settings. This question needs to be addressed separately, as most interventions are developed in contexts not representative for real-world situations and many additional challenges occur, particularly when scaling-up such interventions within care delivery. To move from research/development settings into clinical care, researchers need to consider implementation challenges already from the technology development stage.

The field of implementation sciences is relatively new, and only recently efforts have been made to structure terminology and propose concepts to be used in a standardized way. To ascertain whether the implementation of an intervention has been successful, specific consideration needs to be given to implementation outcomes, i.e., "the effects of deliberate and purposive actions to implement new treatments, practices, and services", which are intermediary to the service and client outcomes envisaged by an intervention. Among the 8 outcomes proposed in the taxonomy of Proctor et al (2011) following literature review and expert panel discussions, some refer primarily to the process of implementation and use (e.g. adoption, penetration, fidelity) and to the application of the technology is a specific setting (appropriateness, implementation cost), others can be construed as mostly referring to the technology itself across settings and were selected for the ENABLE repository. The Expert Recommendations for Implementing Change (ERIC) project has compiled a list of 73 implementation strategies, i.e., "methods or techniques used to enhance the adoption, implementation, and sustainability of a clinical program or practice". This taxonomy, the result of a Delphi expert consensus process with input from numerous stakeholders, achieves a similar goal of aligning language and provides a comprehensive range of options from which implementers may choose strategies to boost the scaling-up of their innovation in a clinical setting. As for implementation outcomes, many of these strategies refer to the process of implementation itself and are highly dependent on the setting; thus, an implementation team may decide to start with assessing local needs, to conduct iterative tests of change, to create new clinical teams, to develop and implement tools for quality monitoring, etc. in response to barriers or facilitators identified during project planning, However, some implementation strategies are also dependent on the technology itself and can be addressed at least partly in the development and implementation of the technology across settings; we have therefore examined the ERIC compilation and selected strategies that could be technology-specific and addressed across settings. The conceptual structuring of this field is in constant evolution; however, these two classifications have already gained notoriety and are likely to be used by stakeholders to generate and use evidence on medication adherence technologies.

Following this preliminary work on the ENABLE repository, three implementation outcomes were selected and adapted from the taxonomy of implementation outcomes to target early-, mid-, and late-implementation phases. They refer to whether stakeholders are satisfied with the technology and using it (acceptability), whether they perceive it as practical and fit for use (feasibility) and appropriate for routine use on the long term (sustainability).

Eight implementation strategies were selected and adapted from the ERIC compilation of implementation strategies, following the interventienet.nl format. Thus, the ENABLE repository will aim to collect information on whether there is any information available, any benefit/need, and any support already provided for the following topics: training stakeholders and users for working with the technology, accessing education materials about the technology, any financial strategies or additional costs applicable, any expertise to share from previous implementations, any consultation to access for support in implementation/use, any accreditation or legal approvals necessary, and whether the involvement of multiple institutions is needed for implementing the technology into clinical care.

ENABLE Repository Delphi survey - study information letter

What is this study about?

Adherence to medication has been found to be suboptimal in numerous chronic conditions and to have a negative impact on chronic disease management, patient's general health status, quality of life and working abilities as well as health care costs and waste. Numerous technologies exist to support medication adherence, yet few are implemented into practice. An online interactive repository of available technologies may facilitate their selection and adoption by different stakeholders. Developing such repository is among the main tasks of the ENABLE COST Action (CA19132), within the remit of Working Group 2. To meet this challenge the ENABLE Action includes a large interdisciplinary network of experts in medication adherence from 39 European countries and has initiated several activities towards these goals. A definition of medication adherence technologies and a framework of attributes were developed. The framework was structured into three domains (product and provider information, medication adherence descriptors and evaluation and implementation) branching in attribute groups, which branch further into sublevels with related labels and definitions.

What to expect from study participation?

The proposed definition and framework will be evaluated in a real-time online Delphi study by stakeholders from 39 countries with research, practice, policy, patient representation and technology development backgrounds. It is expected that you and other invited stakeholders evaluate the proposed the relevance, clarity and completeness of the definition and repository attributes. All participants have multiple opportunities to reconsider their evaluations based on aggregated feedback updated in real-time.

Participants are invited to rate the degree of relevance and clarity of the proposed definition of medication adherence technologies, and of each attribute group, by placing a dot on a 2D-grid; the position of the dot on the vertical axis indicates clarity (low to high = bottom to top), and its position on the horizontal axis indicates relevance (low to high = left to right). Participants are encouraged to provide their comments and suggestions (anonymously) on the comments section and engage with other participants' comments.

We will stop the survey when a predefined number of participants will respond, and when stability of responses will be reached. We will summarize the results descriptively and compare evaluations across stakeholder groups and countries. We will quantify agreement among stakeholders on proposed attribute groups using the IPRAS analysis technique from RAND/UCLA Appropriateness Method.

COST is supported by the European Commission Framework Programme of the European Union

How to participate?

Firstly, by this email we extended our invitation to you and are asking for authorization to use your email within the scope of this study. If after considering this information you agree to participate, please access directly the link provided in the email sent from the eDelphi.org. You will be formally asked about your consent to participate when you will access the survey after a brief introduction, and the questions will appear only once you will consent to this study.

How are data collected and stored?

For this study it is necessary to collect some personal data. This includes your name and email address, as well as your age, gender, field of work/expertise, country, education level and the role of your participation with years of experience in it (researcher/academic; healthcare practitioner; policy/decision maker; patient representation; eHealth/IT specialist). Your name and email address are not linked to other data you provide by answering the survey. The personal data will not be visible to other respondents. The personal data used for conducting this study will be stored until the end of the COST Action ENABLE (October 2024) and then erased.

Ethical and data protection approvals

This study obtained ethics approval from Malaga Regional Research Ethics Committee in April 2021. In addition, the Delphi protocol was determined as compliant regarding data protection and security by Data Protection Officer from University of Basel.

For more information about your rights on data processing, and further questions about the project please contact the ENABLE-R Delphi at wg2enablecost@gmail.com.

On behalf of the ENABLE WG2 Steering Committee,

Alex Dima and Urska Nabergoj Makovec

COST is supported by the European Union Framework Programme of the European Union

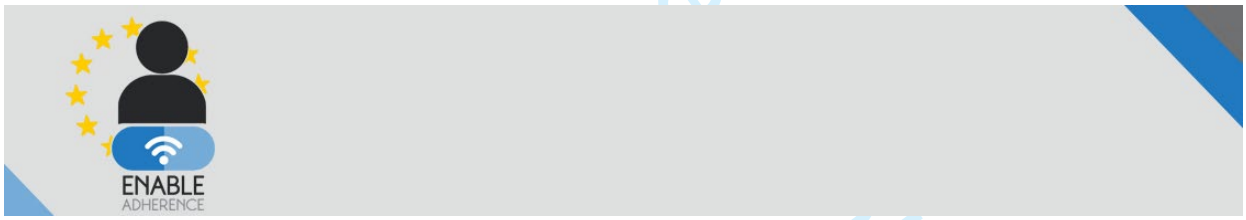
Welcome to the ENABLE-R real time Delphi survey!

ENABLE is a European Cooperation In Science and Technology (COST) project ("CA19132 - European Network to Advance Best practices & technoLogy on medication adherencE") that aims to raise awareness of medication adherence technologies and best practices, and to foster and extend multidisciplinary knowledge on medication adherence at patient, treatment and system levels. COST is supported by the EU Framework Programme Horizon 2020. ENABLE currently has members from 39 European countries.

ENABLE-R will be **an online repository of medication adherence technologies (ENABLE-R)**, which will describe a wide range of technologies relevant for different potential users: patients, healthcare professionals, managers of healthcare organisations, policy makers, researchers. The aim is to develop a user-firendly repository, where users will be able to search technologies with specific attributes, that would fit their context and needs.

This Delphi survey aims to explore the level of agreement with the proposed scope and structure of the repository. A steering committee has been working since October 2020 to define medication adherence technologies and propose a repository structure that considers many aspects of such technologies and their use in different settings. To ensure that the scope and structure is in line with stakeholders' needs and expectations, we created this Delphi survey to consult with stakeholders across Europe on several key elements of the proposed scope and structure. The study obtained ethical approval and positive data protection assessment. Please consult the survey information letter or contact us at wg2costenable@gmail.com f you have any questions.

You were recognized as a stakeholder in the area of medication adherence and are invited to participate in this Delphi survey. Thank you for taking time to complete this survey. We value your contribution.



Instruction for the Delphi survey

The content and structure of the survey

The survey includes **23 questions** related to repository structure, each presented on a separate page. Before starting the survey, we request some **basic information** about you and your experience in medication adherence.

- We present the proposed **definition of the medication adherence technologies (MATech)** for your consideration.
- We invite you to take some time **to explore the full framework of attributes**. It consists of **three domains** (D1. Product & provider information; D2. Medication adherence descriptors; D3. Evaluation & implementation) with underlying attribute groups. Each attribute group branches further in sublevels with related labels and definitions and is labeled with domain number and consecutive number according to the level it represents (e.g. D2.1 or D2.1.1). The complete framework is presented in an interactive graph and in a Excel document detailing proposed structure, labels, definitions and justifications; you may open these documents in separate windows so that you can consult them throughout the survey. After familiarizing yourself with the framework, we ask you to **provide general comments about any missing attributes** relevant for a future MATech repository.
- We describe each domain on one page and present each attribute group and respective sublevels for your consideration on separate pages and ask you to rate **their overall relevance and clarity** and provide **comments or suggestions for improvement** of attribute labels or definitions, and any specific thoughts about any missing attributes in this particular group.

The real time Delphi approach

This survey uses **a real-time approach**, which means that, once you answer a question, you will immediately see other's responses and comments and aggregated feedback on your screen. The strength of the Delphi approach lies in participants having the opportunity to revisit their answers based on other's answers and comments. Hence, it is very important that you **visit the survey two or more times during the study period and reconsider your answers based on the aggregated results and discussions in the comments section**. You are also encouraged to engage in the discussion by explaining the reasons for your responses and making suggestions for improvement. These will also appear in real-time and allow (anonymous) exchanges among stakeholders.

We will regulary check the platform, send updates on the study progress and reminders to (re)visit the survey.

Completing the survey

It should take you **45 to 60 minutes** to complete the survey the first time, and approximately **30 to 60 minutes** for revisiting your answers at a later moment (depending on the level of engagement in discussions you prefer).

You can **navigate across pages** in the survey by clicking on the **blue arrow above the page number**. An index window opens and you can choose which questions you would like to answer. For the first

visit to the survey, we recommend following the order provided. You can **log in and out of the survey** and upon return continue answering where you stopped the last time.

Format of the questions

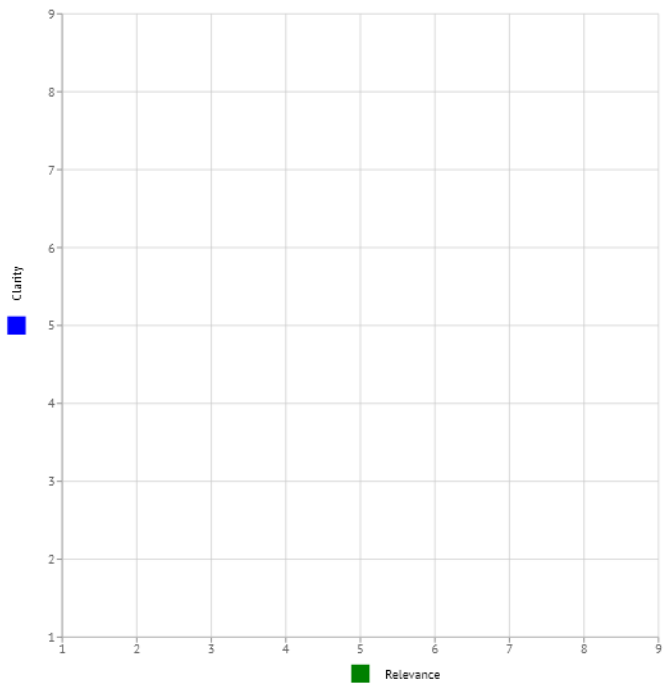
For each attribute, an **interactive 2D grid with two axes** (*see below*) will appear:

- the **horizontal (X) axis** represents **RELEVANCE** of the proposed attribute group for the repository structure on a scale from **1-9 (left-right)**, where 1 indicates extremely not relevant (*far left*) and 9 indicates extremely relevant (*far right*). By relevance, we mean **the extent to which these attributes are important in order to make informed choices regarding their adoption and use.**
- **the vertical (Y) axis** represents **CLARITY** of the attribute group labels and definitions on a scale from **1-9 (bottom-top)**, where 1 indicates extremely not clear (*bottom*) and 9 indicates extremely clear (*top*). By clarity, we mean **the extent to which the labels and definitions of these attributes are easy to understand and apply by repository users.**
- after deciding on your rating on both axes, you can mark your answer in the grid and **a blinking dot** will appear representing both your ratings. **One dot for two ratings: left-right RELEVANCE, bottom-up CLARITY.**
- the scale is continuous, which means you can click anywhere in the grid and thus rate using decimal values (e.g. 4.7)
- after providing your answer, you will be able **to see other participants' ratings represented as dots on the same grid**, and aggregated feedback on the right side of the 2D grid.
- You can change your ratings any time during the study period, by **moving the blinking dot on the grid**. Moreover, you are **encouraged to revisit your answers** on multiple occasions in light of other participants' answers.

Each attribute page also contains **a comments section**. Below the 2D grid you can find open text fields to provide comments or suggestions on the attribute and related sublevels. All comments are displayed anonymously. Please provide your comments in the relevant pre-defined category:

- revisions of attribute labels and definitions
- missing attributes in this group

There you can also see other participants' comments and suggestions and respond to them. Please remember to **save your comments** before leaving a page so that they can be recorded and displayed.



Distribution of answers

X-axis

Answer count	23.00
Lower quartile (Q1)	4.01
Median (Q2)	4.50
Upper quartile (Q3)	6.00

Y-axis

Answer count	23.00
Lower quartile (Q1)	4.33
Median (Q2)	5.01
Upper quartile (Q3)	6.40

Revisions of attribute labels and definitions | Missing attributes in this group

REVISIONS OF ATTRIBUTE LABELS AND DEFINITIONS

SAVE

COMMENTS Select the amount of shown comments 10 Newest first Oldest first

Summary of the Delphi survey

Welcome

Instructions for the Delphi survey (2 pages)

Agreement with the GDPR statement

Demographic information (gender, age, country, education, professional field)

Through which perspective are you answering today?

	Research/education professional	Healthcare practitioner	Policy/decision makers	Patient perspective	eHealth/ IT specialist
Less than 5 years experience					
10 to <15 years experience					
15 to <20 years experience					
20 to <30 years experience					
More than 30 years experience					

What is a "medication adherence technology"?

For the purpose of this repository, we propose the following definition: **"Medication Adherence Technologies (MATech) are devices, procedures or systems developed based on evidence to support patients to take their medications as agreed with the healthcare providers (i.e. to initiate, implement, and persist with the medication regimen)."**

1) Please rate your level of agreement with the proposed MATech definition (X axis).
2) Please rate the CLARITY of the MATech definition (Y axis).

Detailed explanation of the definition and repository scope:

- **devices, procedures or systems** emphasize the inclusion of all technologies, irrespective of their mode of delivery (whether based on electronic or printed supports, delivered through human interaction, or a combination of these) with the aim to construct a comprehensive repository in which users can identify diverse technologies to fit their potentially diverse needs.
- **developed based on evidence** encompass the requirement of evidence/research that supports at least a potential contribution to either measurement or intervention on medication adherence (e.g., validation study on measurement of medication adherence, or pilot study with medication adherence among outcomes). Thus, technologies that are not (yet) supported by evidence (e.g., are in earlier stages of development and testing), or clinical practice protocols without an evidence base on at least one aspect (safety, efficacy, effectiveness, cost-effectiveness, appropriateness, social and ethical values or quality), will not be (yet) included in the repository until such evidence is produced and reported.
- **support patients to take their medications as agreed with the healthcare providers (i.e., to initiate, implement, and persist with the medication regimen)** encompass the contribution of the technology to medication adherence management – either directly in patients' self-management, or by supporting professionals to offer such services to patients through all phases of medication adherence. Thus, technologies that focus on other medication management goals, but do not target adherence specifically would be out of scope for this repository.

The MATech definition and scope of the repository is based on the WHO definition of health technologies, the WHO publication "Adherence to long-term therapies: evidence for action", the ABC taxonomy and the European Commission definition of best practice.

D1.1 Product and provider information

The product and provider domain entails basic information about the product and provider organization as well as the description of the repository entry and source of information.

1) Please rate the RELEVANCE of this attribute group (X axis).
2) Please rate the CLARITY of this attribute group (Y axis).

Further explanation:
Domain 1 consists of one attribute group and includes the attributes for the description of basic product and manufacturer/developer information, as follows:

1. **Product** is a device, procedure or system, that could be used to manage adherence to medication described by its name, brand, type, release date, ...
2. **Provider organization** is the organization that produces and/or makes the product available for users described by its name, type, domain activity, contact details...
3. **Repository entry** is a description of a health technology by a repository author account (ID, date of entry, update, verification).
4. **Author of the product description** is a person or group of persons who enters information about at least one MATech in the ENABLE-R database (ID, name, date, contact details).

The definitions of domain 1 are based on the ITEMAS ontology. For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

Table of contents for Domain 2 – medication adherence descriptors

D2.1 Target use scenario

Target use scenario is the type of common adherence management activities that the technology is intended to be used for (i.e., for self-management of adherence or support service use).

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation:

Target use scenario entails:

1. **Adherence self-management** is the scenario in which the technology is used for adherence self-management activities and can be further defined by:
    - Person in the healthcare environment (*patient or caregiver*)
    - Patient age group (*adult, adolescent, child, infant*)
    - Patient functional status (*mental functions, sensory functions, movement-related functions*)
    - Patient literacy (health literacy, including medication literacy)
    - Patient polypharmacy
    - Patient multimorbidity

2. **Adherence support use** is the scenario in which the technology is used for activities supporting taking medication in a health/social care provision setting and can be further specified by the following user types:
    - Professional health and social care provider
    - Health (system) manager

The definitions of target use scenarios are based on several taxonomies -SNOMED-CT, and WHO International Classification of Functioning, Disability and Health (ICF), and Digital Health Interventions (DHI)- and research literature sources. For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

D2.2 Target health conditions

Target health conditions are the type of diseases or health problems the technology is intended for.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation:

Target health conditions entail:

1. Blood
2. Cancer and neoplasms
3. Cardiovascular
4. Congenital disorder
5. Ear
6. Eye
7. Infection

8. Inflammatory and immune system
9. Injuries and accidents
10. Mental health
11. Metabolic and endocrine
12. Musculoskeletal
13. Neurological
14. Oral and gastrointestinal
15. Renal and urogenital
16. Reproductive health and childbirth
17. Respiratory
18. Skin
19. Stroke
20. Generic health relevance

The definitions of target health conditions are based on The International Classification of Disease (ICD-11) and The Health Research Classification System (HRCS) from the UK clinical research association. For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

D2.3. Medication regimen

Medication regimen attributes are the prescribed schematic form/therapeutic plan of medication therapy that the technology is intended for.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation:

Medication regimen attributes entail:

1. **Type of intention** as the purpose for which the medication is prescribed (*e.g., preventive or therapeutic*).
2. **Duration of treatment** presents the intended interval of treatment and relates to the clinical course and disease conditions (*e.g., short or long-term*).
3. **Route of administration** is the route in which medications/doses are administered to unfold pharmacological effects (*e.g., oral, inhaled, injections/subcutaneous, infusion/parenteral, patches, topical*).
4. **Number of monitored medications** defines how many distinct medications are monitored by the technology, if applicable (*e.g., single medication, multiple medication*).
5. **Prescribed dosing frequency** defines the dose-taking patterns recommended for medicines administration, in which doses should be taken at defined time intervals over a defined time period (*e.g., once-daily, multiple daily dosing at fixed intervals, once per week dosing, multiple dosing per week in fixed intervals, dose adjustment recommendations*).

The definitions of medication regimen attributes are based on several taxonomies: SNOMED-CT; National Cancer Institute Thesaurus (NCIT) and Medical Subject Headings (MeSH). For a more detailed view of the respective sub-levels with lables and definitions please check the interactive graph or the Excel file under supporting information.

D2.4.1. Phase of medication adherence

A medication adherence phase is a time interval between the prescription start and end dates that is behaviourally (i.e., linked with specific determinants and outcomes) and metrically (i.e., requires specific estimation methods) distinct.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation

Medication adherence phases include

1. **Initiation** is the phase of adherence that covers the start of a prescribed treatment, i.e., the period from when the prescription is issues to the first dose taken (i.e., the initiation event)
2. **Implementation** is the phase of adherence from the initiation until the last dose taken during which one can estimate the extent to which the patient's dose taking and timing are linked to the prescribed dosing regimen.
3. **Discontinuation (Persistence)** is the phase of adherence that refers to the end of treatment execution and covers the period until last dose is taken, e.g. end of therapy or termination by patient. Persistence is the period between initiation and discontinuation.

The definitions of adherence management are based on the ABC Taxonomy. For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

D2.4.2.A Monitoring/measurement type of management

Medication adherence monitoring, or measurement, is type of adherence management that refers to estimating (repeatedly) medication adherence behaviours, determinants, and/or outcomes.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation

Medication adherence monitoring/measurement entails:

1. **Measurement method** is a way in which information is gathered and summarized by the technology about the patient's medication adherence. It is further specified into the following:
   - **Direct observation method** is a measurement method consisting in observing medication intake directly.
   - **Pill count method** is a measurement method consisting in calculating left over pills in containers/blisters at a specific time point.
   - **Self-report method** is a measurement method using data reported by patients or caregivers about themselves (*e.g., diary, questionnaire, interview/consultation*).
   - **Electronic monitoring method** is a measurement method using data from devices that record medication taking events electronically (*e.g., smart packages, smart pill, digital event record system*).
   - **Electronic healthcare database method** is a measurement method using routinely collected data as part of a longitudinal healthcare process (*e.g., electronic medical records, claims/dispensing, record linkage system*).
   - **Laboratory method** is a measurement method based on clinical assessment through invasive procedure (*e.g., measuring drug concentration, biomarker or treatment response in samples from body fluids*).

2. **Measurement target** is a component of the adherence causal (logic) model measured by the technology. It is further defined by:
   - **Determinant measure** is measurement targeting causal influences on the behaviour that can be modifiable (amenable to intervention with a medication adherence technology).

- **Behaviour measure** is measurement targeting a self-management behaviour (*e.g., adherence, diet, physical activity, tobacco use, symptom monitoring and management*).
- **Outcome measure** is the measurement targeting the effects of the behaviour or change of behaviour on the patient's status (*e.g., health outcome, quality of life*).

The definition of adherence monitoring/measurement is based on the ABC Taxonomy. The definitions of measurement methods and targets are based on several taxonomies -SNOMED-CT, the Train4Health (T4H) behaviour change competency framework and the behaviour change intervention ontology (BCIO)-, as well as scientific literature and the methodological expertise of the repository Steering Committee. For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

D2.4.2.B Support/intervention type of management

Medication adherence support and/or intervention is a type of adherence management that refers to generating change in medication adherence determinants and thus behaviours and outcomes.

1. **Please rate the RELEVANCE of this attribute (X axis).**
2. **Please rate the CLARITY of this attribute (Y axis).**

Attribute groups further describing medication adherence support/intervention type of management are presented for your review in the next pages.

The definitions of adherence management types are based on the ABC Taxonomy.

D2.4.2.B.1 Intervention modes of delivery

Intervention modes of delivery are the ways used to deliver a medication adherence intervention.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation

Intervention modes of delivery entails:

1. **Printed material** is the mode of delivery involving use of printed material (e.*g., brochure or printed media such as poster, newspaper/leaflet*)
2. **Human interaction** is the mode of delivery involving a person as intervention source who interacts with an intervention recipient (*e.g., face to face consultations or network/patient groups*)
3. **Electronic mode** is the mode involving electronic technology in the presentation of information or the mode of motivation to an intervention recipient (*e.g., smartphone/tablet, wearable electronic device like smart box, smart inhaler, smart tube, smart button or digital media like internet, social media, broadcast media, billboard*).

The definitions of intervention modes of delivery are based on the Behaviour Change Intervention Ontology (BCIO), specifically a taxonomy of mode of delivery of behaviour change interventions (BCI). For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

D2.4.2.B.2 Target behaviour determinants

Target behaviour determinants are causal influences on medication adherence that can be modifiable (amenable to intervention with a medication adherence technology).

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation

Target behaviour determinants entails:

1. **Capability** is a group of determinants referring to what an individual can do themselves to take medication as agreed with the healthcare provider (*e.g., psychological/cognitive capability or physical capability/skills*)
2. **Opportunity** is a group of determinants referring to the conditions in the individual's external environment that can facilitate medication adherence (*e.g., social opportunity/influences or physical opportunity/environmental context and resources*)
3. **Motivation** is a group of determinants referring to what extent the individual feels driven/willing/energized to take medication as agreed with the healthcare provider (*e.g., reflective motivation or automatic motivation*)

The definitions of target behaviour determinants are based on the Capability, Opportunity, Motivation and Behaviour (COM-B) model, the Theoretical Domains Framework (TDF) and the Behaviour Change Intervention Ontology (BCIO), specifically The Mechanisms of Action (MoA) Ontology currently in development. For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

D2.4.2.B.3 Behaviour change techniques

Behaviour change techniques (BCTs) are options/activities included in the technology that aim to influence determinants (barriers and facilitators) of medication adherence behaviours.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation

BCTs entails:

1. **BCTs acting on capability:**
    - **feedback and monitoring** means the technology includes options to record medication intake and its effects and feed this info back to the user (*e.g., biofeedback, feedback or self-monitoring on behaviour, feedback or self-monitoring on outcomes*).
    - **repetition and substitution** means the technology includes options/activities to perform certain actions repeatedly and systematically in order to enforce medication adherence behaviours and replace other behaviours not beneficial for medication adherence (*e.g., habit formation, behavioural practice, graded tasks*).
    - **shaping knowledge** means the technology includes options for the user to learn about how to take medication as agreed with the healthcare provider, what they can do themselves to stick to the schedule in difficult situations, and test different ways of doing this.

2. **BCTs acting on opportunity:**
   - **demonstration of behaviour** means the technology includes an observable sample of how to take medication as agreed with the healthcare provider, directly in person or indirectly (video, pictures, drawings).
   - **prompts & cues** means the technology includes ways to prompt medication intake at the agreed time. restructuring the physical environment & adding objects means the technology includes advice on how to change the environment to make it easier to take medication as agreed with the healthcare provider.
   - **identity** means the technology includes ways of strengthening a positive identity that includes taking medications agreed with the healthcare provider.

3. **BCTs acting on motivation:**
   - **goals and planning** means the technology includes options to encourage setting goals related to adherence and planning to achieve them (*e.g., action planning, discrepancy between behaviour and goals, goals setting and reviewing, problem solving).*
   - **pros & cons** means the technology includes ways to identify and compare reasons for wanting or not wanting to take medication as agreed with the healthcare provider.
   - **regulation** means the technology includes advice and/or options/activities aiming to keep motivation for medication adherence within a range favourable for performing adherence-related behaviours (*e.g., conserving mental resources, reducing negative emotions*).
   - **self-belief means** the technology includes ways of increasing the person's confidence they can take medication as agreed with the healthcare provider.
   - **imaginary reward** means the technology includes advice on how to imagine correct performance of medication intake.

4. **BCTs acting across all three determinant groups:**
   - **social support** means the technology includes options to advise, arrange or provide social support (practical, emotional, other), or praise/reward taking medication as agreed with the healthcare provider. social reward means the technology includes verbal/non-verbal rewards when the patient shows effort and/or progress in taking medication as agreed with the healthcare provider.
   - **information about consequences** means the technology includes information about consequences (health-related, emotional, social, environmental) of medication adherence (or non-adherence) and emphasize their relevance for the person.

The definitions of behaviour change techniques are based on the Capability, Opportunity, Motivation and Behaviour (COM-B) model, the Theoretical Domains Framework (TDF), the Behaviour Change Techniques (BCT) taxonomy v1, and the Behaviour Change Intervention Ontology (BCIO). For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

D2.4.2.B.4 Intervention provider

Intervention provider is a role played by a person who uses the technology to assist the patient in their self-management of medication adherence.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation

Intervention provider entails:

1. **Health care professional** is an intervention provider that applies scientific knowledge in medicine, nursing, midwifery, pharmacy, dentistry and/or health promotion to support patients in managing their health (*e.g., medical doctor, nursing professional, pharmacist, dentist, associated health professional*).
2. **Psychosocial care professional** is an intervention provider that applies scientific knowledge in psychology, sociology and other social sciences to support individual and families in a community in their well-being and life goals (*e.g., psychologist*).
3. **Personal care worker** is an intervention provider that delivers care, supervision and assistance for children, patients and elderly, convalescent or disabled persons in institutional and residential settings.
4. **Personal provider** is an intervention provider that is related to the person to whom the intervention is targeted through aspects of their personal lives (*e.g., family member, carer, friend, peer*).

The definitions of the intervention provider attributes are based on several taxonomies: BCIO, in particular the Intervention Source Ontology, and Gender, Sex and Sexual Orientation Ontology (GSSO). For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

D2.4.2.B.5 Intervention setting

Intervention setting is the social and physical environment in which the technology is or can be used to manage medication adherence.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation

Intervention setting entails:

Physical setting is an intervention setting that consists in a physical environment where the medication adherence technology is used (*e.g., residential facility, healthcare facility, educational facility, community facility*).

Virtual setting is an intervention setting that consists in a virtual environment where the medication adherence technology is used (*e.g., telemedicine, telepharmacy*).

An intervention can be applied or applicable to one type of settings, or to both.

The definitions of the intervention setting attributes group are based on the BCIO, in particular the Intervention Setting Ontology. For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

Table of contents for Domain 3 – evaluation and implementation

D3.1.1.A ISO certification

ISO certification is a general quality indicator referring to whether the MATech has obtained one or more ISO certification labels relevant for its content and purpose.

1. **Please rate the RELEVANCE of this attribute (X axis).**
2. **Please rate the CLARITY of this attribute (Y axis).**

The definitions of quality indicators are based on a checklist of e-health quality criteria (under development), Mobile Application Rating Scale (MARS), and the Consort-EHEALTH guideline.

D3.1.1.B Evidence from scientific evaluation

Evidence from scientific evaluation is a group of general quality indicators referring to whether the evaluation of MATech has been performed through the systematic, rigorous, and meticulous application of scientific methods, and the evidence obtained.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation

The evidence from scientific evaluation entails:

1. **Research on development** means evidence from scientific evaluation is available to support the design of the MATech. This also encompasses the classification of quality of the presented evidence.
2. **Research on effectiveness** means evidence from scientific evaluation is available to support the effectiveness of the MATech (excluding cost-effectiveness, outlined in section D2.1.3 and implementation outcomes, outlined in section D3.2). This also encompasses the classification of quality of the presented evidence.
3. **Ethical and legal aspects** means the MATech research has ethical approval, has considered and addressed any risks for the target population, complies with the current laws on research on humans and data privacy and safety, and has shared information about how it meets these requirements.

The definitions of quality indicators are based on a checklist of e-health quality criteria (under development), the Mobile Application Rating Scale (MARS), and the Consort-EHEALTH guidelines. For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

D3.1.1.C Development standards

Development standards are a group of general quality indicators referring to whether the MATech has been developed according to standards established in the development of health technologies.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation

The development standards entail:

1. **Development process** means all development activities undertaken with respect to MATech are clearly described, such as activities related to preparation, development and optimization of product components as well as the manufacturing, validation and distribution process of the MATech.
2. **User-centred design process** means the MATech was developed in an iterative design process in which designers involved the target users and their needs in each phase of the design process. The users' requirements, objectives, and feedback were taken into account during the development process.
3. **Conflict of interest** means the provider's conflict of interests are clearly described to assure trust and transparency.
4. **Updates of information sources** means information sources are periodically verified (proven to still be correct and accurate) and updated (new information added or design changed).

The definitions of quality indicators are based on a checklist of e-health quality criteria (under development), Mobile Application Rating Scale (MARS), Consort-EHEALTH guideline. For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

D3.1.1.D Technological standards

Technological standards are a group of general quality indicators referring to whether a MATech corresponds to criteria commonly used to assess the technical functioning of electronic/digital components, if applicable.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation

The technological standards entail:

1. **Performance** - the MATech works fast and accurately without bugs or errors (*e.g., reliability of the interactive components, design scalability*).
2. **Data protection** - collected data is properly protected to prevent sensible data leakage (*e.g., data encryptions, antivirus supported maintenance, data storage place and capacity and protection against theft or physical attacks*).
3. **System integration** - evidence of MATech meeting the technical, privacy and security requirements of health care systems.
4. **Inter-devices portability** - the MATech can be connected with several devices.

The definitions of quality indicators are based on a checklist of e-health quality criteria (under development), Mobile Application Rating Scale (MARS), Consort-EHEALTH guideline. For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

D3.1.2 Research-related quality indicators

Quality indicators that evaluate if the research on the MATech has been performed according to standards established in measurement and intervention research.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation

The research-related quality indicators entail:

1. **Theory base** means the MATech is developed based on theory, evidence, theoretical framework.
2. **Validity of measurement** means the MATech is valid for certain conditions, populations, etc. (content validity)
3. **Validity of intervention** means the use of BCTs in the MATech is evidence based, i.e., there is scientific evidence that the chosen BCTs are likely to be effective in influencing the chosen behaviour determinants.
4. **Reliability of measurement** means the MATech shows a high test-retest reliability, internal consistency, and inter-rater reliability.

The definitions of quality indicators are based on a checklist of e-health quality criteria (under development), Mobile Application Rating Scale (MARS), Consort-EHEALTH guideline. For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

D3.1.3 Policy-related quality indicators

Quality indicators related to Health Technology Assessment (HTA) procedures and concepts that inform decision-making regarding implementation and use of health technologies.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation

The policy-related quality indicators entail:

1. **Economic and cost evaluation (ECO**) means an economic analysis has been performed to inform value-for-money judgements about the MATech with information about costs, health-related outcomes and economic efficiency. It entails several types of analysis (e.g., cost-effectiveness, cost-utility, cost-benefit, budget impact), which can be country or system specific, thus the repository also needs to specify where these indicators apply.
2. **Current use of technology (CUR)** specifies the regulatory status (authorization and reimbursement) of the technology. These information are country or system specific, thus the repository also needs to specify where these indicators apply.

The definitions of policy-related quality indicators are based on Health Technology Assessment (HTA) Core Model, version 3.0 and O'Rourke et al. (2020). "The new definition of health technology assessment". For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

D3.1.4 Use-related quality indicators

Quality indicators that evaluate if the MATech use meets users' expectations and provides a pleasurable experience of interaction with the technology.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation

The use-related quality indicators entail:

1. **Usability** means MATech qualities such as simplicity, organization, intuitiveness and reliability. High usability is indicated when MATech is simple, well organized, intuitive and reliable.
2. **Satisfaction** means satisfaction with MATech assesments were performed to control the level of satisfaction of the end user.
3. **Customization** means the MATech or some parts of it can be customized to the needs of the individual user.
4. **Aesthetics** is the perception of the product, which can be described as aesthetic (size, layout, graphic, font size etc.) as this was evaluated in a research project or external review.
5. **Readability** means the ease of understanding or comprehension achieved by the style of writing. The reader must be able to recognize (decode) the words in the medical device patient labelling as well as comprehend the meaning of the text.

The definitions of quality indicators are based on a checklist of e-health quality criteria (under development), the Mobile Application Rating Scale (MARS), and the Consort-EHEALTH guideline. For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

D3.2.1 Implementation outcomes

Implementation outcomes are characteristics of the technology regarding its implementability in clinical practice, as supported by evidence.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation

Implementation outcomes entail:

Acceptability means whether stakeholders reported satisfaction with various features of the technology and the experience of using it to support medication adherence

Feasibility means whether stakeholders perceived the technology as practical and fit for use in supporting medication adherence

Sustainability means whether stakeholders perceived the technology as appropriate for routine sustained use in supporting medication adherence

Definitions of implementation outcomes and strategies are based on Proctor et al. (2011) "Outcomes for Implementation Research: Conceptual Distinctions, Measurement Challenges, and Research Agenda", the Consolidated framework for advancing implementation science (CFIR), the Expert Recommendations for Implementing Change (ERIC) and the Interventienet.nl website. For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

D3.2.2 Implementation strategies

Implementation strategies are characteristics of the technology that facilitate implementation and maintenance of the technology in a setting.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation

Implementation strategies entail:

1. **Training** are activities to teach stakeholders about the technology and how to use it and integrate in the medication adherence support processes.
2. **Educational materials** are materials stakeholders may consult to learn about the technology and how to use it and integrate in the medication adherence support processes.
3. **Funding** are financial strategies and/or additional costs to facilitate adoption of the technology into medication adherence support practice.
4. **Expertise sharing** are information from previous implementations on what helped adopt the technology into medication adherence support practice.
5. **Technical assistance** are systems to support implementation of the technology into medication support practice
6. **Consultation** means accessing direct support from experts for the implementation of the technology into medication support practice.
7. **Accreditation & legal approvals** are credentials and/or licensing to acquire or prove to be able to use the technology in a setting in the conditions necessary for optimal safety and effectiveness.
8. **Collaborations** means involving multiple institutions in delivering the medication adherence support solution that uses the technology.
9. **Access to additional resources** means access to data, space, laboratory facilities.

Definitions of implementation outcomes and strategies are based on Proctor et al. (2011) "Outcomes for Implementation Research: Conceptual Distinctions, Measurement Challenges, and Research Agenda", the Consolidated framework for advancing implementation science (CFIR), the Expert Recommendations for Implementing Change (ERIC) and the Interventienet.nl website. For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

Thank you and see you soon!

Dear panellist,

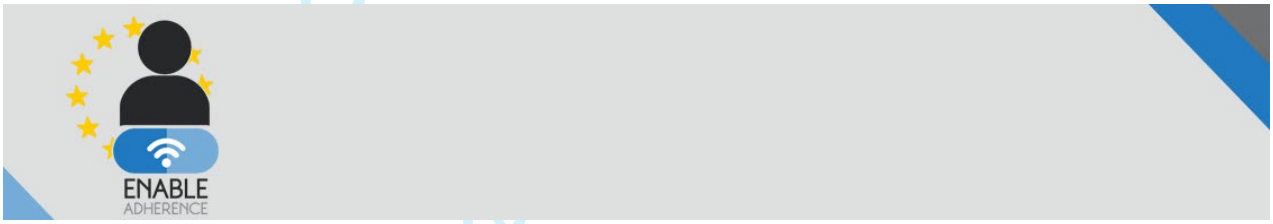
you have made it to the end of the survey. We appreciate your effort and valuable contribution to development of the ENABLE repository of medication adherence technologies.

Please remember to visit the survey several times during the study period to reconsider your answers based on the aggregated feedback and discussions with the other anonymous panellists. Reminders will be sent every 2 weeks to remind you to log in and participate again.

Please don't hesitate to contact us on wg2costenable@gmail.com in case of any questions.

Best wishes,

The ENABLE WG2 Steering Committee



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CONSEJERÍA DE SALUD

Dra. Dña. Gloria Luque Fernández, Secretaria del CEI Provincial de Málaga

CERTICA:

Que en la sesión de CEI de fecha: 29/04/2021 ha evaluado la propuesta de D/Dña.: Pilar Barnestein Fonseca, referido a la MS1 del Proyecto de Investigación: "COST Action "European Network to Advance Best practices & technoLogy on medication adherencE" (ENABLE) ".

Este Comité lo considera ética y metodológicamente correcto.

La composición del CEI en esta sesión es la siguiente:

Dra. Ana Alonso Torres (UGC Neurociencias)
Dra. Encarncación Blanco Reina (Farmacología Clínica)
Dra. Begoña Jiménez Rodríguez (UGC Oncología)
Dra. Marta Blasco Alonso (Obst. y Ginecología)
Dr. Rafael Carvia Ponsaille (Anatomía Patológica)
Dª. Ana Díaz Ruíz (Licenciada en Derecho)
Dr. José C. Fernández García (UGC Endocrinología y Nutrición)
Dr. Manuel Herrera Gutiérrez (UGC UCI)
Dra. Mª Victoria de la Torre Prados (UMA)
Dr. José Leiva Fernández (Médico Familia)
Dra. Mª Dolores López Carmona (Medicina Interna)
Dr. Jesús López del Peral (Esp.Protec.Datos)
Dña. Carmen López Gálvez del Postigo (Miembro Lego)
Dª. Inmaculada Doña Díaz (Alergología)
Dra. Gloria Luque Fernández (Investigación)
Dra. Cristobalina Mayorga Mayorga (Laboratorio)
Dra. Mª Angeles Rosado Souvirón (UGC Farmacia)
Dra. Leonor Ruíz Sicilia (UGC Salud Menta.)
Dra. Elena Sánchez Yáñez
Dr. Antonio López Téllez (Médico de Familia)

Lo que firmo en Málaga, a 29 de abril de 2021

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C.I.F.: Q-9150013-B

Fdo.: Dra. Gloria Luque Fernández
Secretaria del CEI

Universität Basel

Verwaltungsdirektion

Universität Basel, Verwaltungsdirektion, Postfach, 4001 Basel

Mrs Janette Ribaut
Bernoullistrasse 28
4056 Basel

Basel, 25. Mai 2021

Data Protection Assessment of your project "Developing a medication adherence technologies repository: an online real-time Delphi survey protocol"

Dear Ms. Ribaut

I would like to confirm, that we have reviewed your project with regard to data protection and data security. Based on the documents provided to us, we can confirm that data protection is complied with in your project. In particular, since you collect the survey responses exclusively anonymously and no conclusions can be drawn about individual persons.

Yours sincerely,

Danielle Kaufmann
Data Protection Officer

Seite 1/2

Universität Basel
Verwaltungsdirektion
Petersgraben 35, Postfach 2148
4001 Basel, Switzerland

Danielle Kaufmann, lic. iur.
Datenschutzbeauftragte
T +41 61 207 30 22
M +41 79 381 20 72
Danielle.kaufmann@unibas.ch

Universität Basel

Verwaltungsdirektion

General data protection statement (GDPR)

By continuing the survey, you declare that you have read, understood and agreed with the following statements:

1. *This Delphi survey is performed by the COST Action ENABLE (CA19132) Working group 2 with principal investigators Alexandra Lelia Dima and Urska Nabergoj Makovec.*
2. *The aim of the study is to explore the level of agreement on the proposed structure for a repository of medication adherence technologies*
3. *Participation in the survey is voluntary and the study is designed to ensure participants' anonymity as one of the key features of the Delphi approach.*
4. *The collected personal data will be used exclusively for conducting the study and analysing and reporting results in an aggregated form.*
5. *In order to illustrate some study findings, we might quote statements provided by individual respondents in open text fields; however, the Delphi platform ensures that no personal data can linked to such statements.*
6. *A data protection assessment was carried out by the Data Protection Officer at the University of Basel. According to this instance the Delphi study protocol was determined as compliant with data protection and security standards.*
7. *The personal data used for conducting this study will be stored until the end of the COST Action ENABLE (October 2024). You can address your rights regarding access to, correction of or limitation of use of your personal data through the email wg2enablecost@gmail.com anytime during that time period.*

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BMJ Open

Developing a medication adherence technologies repository: proposed structure and protocol for an online real-time Delphi study

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Complete List of Authors:	Nabergoj Makovec , Urska; Univerza v Ljubljani Fakulteta za farmacijo, Faculty of Pharmacy Goetzinger, Catherine ; Luxembourg Institute of Health, Deep Digital Phenotyping Research Unit, Department of Population Health; University of Luxembourg Faculty of Science Technology and Medicine Ribaut, Janette; University of Basel Faculty of Medicine, Institute of Nursing Science, Department Public Health; University Hospital Basel, Department of Theragnostic, Hematology Barnestein-Fonseca, Pilar; CUDECA Institute for Training and Research in Palliative Care, CUDECA Hospice Foundation, Málaga; Instituto de Investigación Biomédica de Málaga-IBIMA , Group C08: Pharma economy: Clinical and economic evaluation of medication and Palliative Care Haupenthal, Frederik; Medical University of Vienna Department of Medicine II, Division of Nephrology and Dialysis Herdeiro, Maria; University of Aveiro, Institute of Biomedicine, Medical Sciences Department Grant, Sean; Indiana University Richard M Fairbanks School of Public Health, Department of Social & Behavioral Sciences, Jácome, Cristina; University of Porto Faculty of Medicine, Department of Community Medicine, Information and Health Decision Sciences (MEDCIDS); University of Porto Faculty of Medicine, Center for Health Technology and Services Research (CINTESIS) Marques Roque, Fatima; Polytechnic Institute of Guarda Research Unit for Inland Development, Research Unit for Inland Development Smits, Dins; Riga Stradins University, Faculty of Public Health and Social Welfare, Department of Public Health and Epidemiology Tadic, Ivana; University of Belgrade Faculty of Pharmacy, Department of Social Pharmacy and Pharmaceutical Legislation Dima, Alexandra; Université Claude Bernard Lyon 1, , Research on Healthcare Performance (RESHAPE), INSERM U1290 ENABLE, Collaborators; COST Action ENABLE (CA19132)
Primary Subject Heading:	Global health
Secondary Subject Heading:	Health informatics, Patient-centred medicine, Public health
Keywords:	Health informatics < BIOTECHNOLOGY & BIOINFORMATICS, PUBLIC HEALTH, SOCIAL MEDICINE

Note: The following files were submitted by the author for peer review, but cannot be converted to PDF. You must view these files (e.g. movies) online.
Fig 1.tiff

Developing a medication adherence technologies repository: proposed structure and protocol for an online real-time Delphi study

Urska Nabergoj Makovec (*ORCID ID: 0000-0001-5194-3314*)
University of Ljubljana, Faculty of Pharmacy, Department of Social Pharmacy, Ljubljana, Slovenia
urska.nabergoj.makovec@ffa.uni-lj.si
Catherine Goetzinger *(ORCID ID :0000-0002-6377-1078)*
Deep Digital Phenotyping Research Unit, Department of Precision Health, Luxembourg Institute of Health, Strassen, Luxembourg.
University of Luxembourg, Faculty of Science, Technology and Medicine, Luxembourg
catherine.goetzinger@lih.lu
Janette Ribaut (*ORCID ID:* 0000-0003-0654-4052)
Institute of Nursing Science, Department Public Health, Faculty of Medicine, University of Basel, Switzerland & Department of Theragnostic, Hematology, University Hospital of Basel, Switzerland
janette.ribaut@unibas.ch
Pilar Barnestein-Fonseca *(ORCID ID 0000-0003-2767-8017)*
CUDECA Institute for Training and Research in Palliative Care, CUDECA Hospice Foundation, Málaga, Spain.
Instituto de Investigación Biomédica de Málaga-IBIMA Group C08: Pharma economy: Clinical and economic evaluation of medication and Palliative Care, Málaga, Spain
pilar.barnestein@ibima.eu
Frederik Haupenthal (*ORCID ID:* 0000-0002-7708-9045)
Division of Nephrology and Dialysis, Department of Medicine II, Medical University of Vienna, Austria
frederik.haupenthal@meduniwien.ac.at
Maria Teresa Herdeiro *(ORCID ID: 0000-0002-0500-4049)*
Institute of Biomedicine, Medical Sciences Department, University of Aveiro, Aveiro, Portugal
teresaherdeiro@ua.pt
Sean Patrick Grant *(ORCID: 0000-0002-7775-3022)*
Department of Social & Behavioral Sciences, Richard M. Fairbanks School of Public Health, Indiana University, Indianapolis, United States of America
spgrant@iu.edu
Cristina Jácome (*ORCID ID:* 0000-0002-1151-8791)
Department of Community Medicine, Information and Health Decision Sciences (MEDCIDS), Faculty of Medicine, University of Porto, Porto, Portugal
Center for Health Technology and Services Research (CINTESIS), Faculty of Medicine, University of Porto, Porto, Portugal
cristinajacome.ft@gmail.com
Fátima Roque (*ORCID ID:* 0000-0003-0169-3788)
Research Unit for Inland Development, Polytechnic of Guarda, Guarda, Portugal
froque@ipg.pt
Dins Smits (*ORCID: 0000-0001-5514-7374)*
Faculty of Public Health and Social Welfare, Department of Public Health and Epidemiology, Riga Stradins University, Riga, Latvia
dins.smits@rsu.lv
Ivana Tadic (*ORCID: 0000-0001-5488-9261)*
University of Belgrade, Faculty of Pharmacy, Department of Social Pharmacy and Pharmaceutical Legislation, Belgrade, Serbia
ivana.tadic@pharmacy.bg.ac.rs

Alexandra Lelia Dima (*ORCID: 0000-0002-3106-2242)*
Université Claude Bernard Lyon 1, Research on Healthcare Performance (RESHAPE), INSERM U1290, Lyon, France
alexandra.dima@univ-lyon1.fr

and **European Network to Advance Best Practices and Technology on Medication AdherencE (ENABLE)**

Corresponding author:
Urska Nabergoj Makovec
ORCID ID: 0000-0001-5194-3314
University of Ljubljana, Faculty of Pharmacy, Department of Social Pharmacy,
Askerceva 7
1000 Ljubljana, Slovenia
Telephone: +386 1 4769 565
urska.nabergoj.makovec@ffa.uni-lj.si

Key words: health technology, medication adherence, Delphi study, stakeholder engagement, digital health, behavioural science, implementation science

Word count:
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Abstract: 297
Strengths and limitations: 158

Article Summary

Abstract

Introduction: An online interactive repository of available medication adherence technologies may facilitate their selection and adoption by different stakeholders. Developing a repository is among the main objectives of the ENABLE COST Action (CA19132). However, meeting the needs of diverse stakeholders requires careful consideration of the repository structure.

Methods and analysis: A real-time online Delphi study by stakeholders from 39 countries with research, practice, policy, patient representation and technology development backgrounds will be conducted. Eleven ENABLE members from 9 European countries formed an interdisciplinary steering committee to develop the repository structure, prepare study protocol and perform it. Definitions of medication adherence technologies and their attributes were developed iteratively through literature review, discussions within the steering committee and ENABLE Action members, following ontology development recommendations. Three domains (*product and provider information (D1), medication adherence descriptors (D2) and evaluation and implementation (D3)*) branching in 13 attribute groups are proposed: *product and provider information, target use scenarios, target health conditions, medication regimen, medication adherence management components, monitoring/measurement methods and targets, intervention modes of delivery, target behaviour determinants, behaviour change techniques, intervention providers, intervention settings, quality indicators and implementation indicators.* Stakeholders will evaluate the proposed definition and attributes' relevance, clarity and completeness and have multiple opportunities to reconsider their evaluations based on aggregated feedback in real-time. Data collection will stop when the predetermined response rate will be achieved. We will quantify agreement and perform analyses of process indicators on the whole sample and per stakeholder group.

Ethics and dissemination: Ethical approval for the COST ENABLE activities was granted by the Malaga Regional Research Ethics Committee. The Delphi protocol was considered compliant regarding data protection and security by the Data Protection Officer from University of Basel. Findings from the Delphi study will form the basis for the ENABLE repository structure and related activities.

Strengths and limitations of this study

- The diverse expertise and geographical spread of the ENABLE COST Action members (39 European countries) and their wider professional network represents a unique and timely opportunity to develop a repository of medication adherence technologies that meets the needs of a diverse audience.
- The scope and content of the Delphi survey represent the work of extensive literature review combined with multidisciplinary expertise of the steering committee.
- The real-time Delphi approach provides improved efficiency of the process, shortens the time of study completion and is particularly suitable for managing larger groups and including people from different geographic locations.
- The Delphi protocol will use state of the art methodology to measure agreement and predetermine agreement/consensus criteria as well as stability of responses.
- The real-time approach requires specialized software, which limits the range of possible survey configurations and raw data availability for detailed process analyses and requires relatively elaborate instructions for participants, which may increase participation burden.

Introduction

Taking medication as prescribed often proves difficult for people when managing their health, particularly in the long term.[1] Medication adherence is suboptimal in numerous chronic conditions [2 3] and has a negative impact on chronic disease management, patient's general health status, quality of life, working ability and health care costs. [2 4 5] Research on medication adherence has expanded and contributed to raised awareness of the prevalence of suboptimal adherence and how it affects health outcomes. Digital technologies have increasingly gained interest as new interventions for supporting medication adherence have been developed. A diversity of technologies has been proposed, from electronic monitoring devices to mobile applications, to support medication adherence measurements and empower patients with their disease management. However, the rapidly expanding offer of medication adherence technologies (MATech) makes it increasingly difficult to access, evaluate, and compare different technologies to make informed decisions and select appropriate tools for specific clinical or research needs. In a 2018 review by Ahmed et al.[6], 5881 medication adherence apps were identified on Google Play and Apple App Stores. However, most of them lacked evidence of effectiveness and didn't involve healthcare professionals (HCPs) during their development.[6] Lack of collaboration between stakeholders results in a limited number of developed MATech actually being implemented into the healthcare systems and used daily by HCPs and/or patients.[7] Furthermore, due to differences in healthcare systems across countries, healthcare organisations and reimbursement processes, harmonization of implementation strategies are lagging behind, which further delays adoption of best practices across countries.[4 7]

The ENABLE COST Action ('**E**uropean **N**etwork to **A**dvance **B**est practices & techno**L**ogy on medication adheren**E**', CA19132)[8] was initiated by experts in medication adherence and digital technologies to fill these gaps regarding evidence and implementation of MATech within healthcare systems. ENABLE aims to raise awareness of available technologies, expand multidisciplinary knowledge on medication adherence at multiple levels, accelerate knowledge translation to clinical practice, and collaborate towards economically viable implementation of best practices and technologies across European healthcare systems. These objectives are being pursued within a 4-year period (2020-2023), by three distinct and interrelated working groups (WGs) that map best practices available (WG1), identify and showcase adherence technologies (WG2), and identify suitable reimbursement strategies for implementation in healthcare systems (WG3), supported transversally by a WG4 coordinating communication and dissemination. At present, the ENABLE Action includes a large interdisciplinary network of experts in medication adherence from 39 European countries.[8]

Effective implementation of technology-supported healthcare has been facilitated by centralisation of information in public repositories or 'solution showrooms', where users can search for technologies that meet their specific requirements.[9] Several such repositories already exist in the field of digital health, including medication adherence (e.g. NHS app Library[10], MyHealthApps[11], InterventieNet[12], GGD AppStore[13], DIGA[14], Weisse Liste[15]), but are limited to single countries or types of technology and none represents a comprehensive resource to facilitate adoption of appropriate MATech across health systems. Therefore, ENABLE sets out to develop and maintain a public online repository of MATech where patients, HCPs, researchers, and healthcare managers would be able to access and select technologies for adoption in their adherence management activities.[8] For example, a patient may be interested more in the practical benefits of using a MATech in their daily lives, while a researcher may be keen to examine in detail the methodology theory and evidence base behind the MATech development. To meet this goal, the ENABLE repository would need to represent a flexible knowledge management system that would include information relevant to the needs of different stakeholders in a user-friendly format. In medical informatics, knowledge management relies on standardized terminologies, classifications and ontologies to record, share and use data on healthcare research and practice. These standards specify the types of information to encode in the form of distinct 'entities' representing objects or phenomena in the real world and their properties ('attributes'), thus enabling knowledge generation through inference and learning.[16] Adoption of evidence-based health innovations is also facilitated by these common standards, as new technologies need to interact with existing ecosystems in terms of both data interoperability and communicating with potential users in appropriate domain-specific language.[17]

The field of medication adherence is highly interdisciplinary, therefore a useful repository would cross multiple knowledge domains and align with several standards, whether medical (e.g., World Health Organisation International Classification of Disease; WHO ICD[18]), behavioural (e.g., the Behaviour Change Intervention Ontology; BCIO[19 20]), or technical (e.g., WHO Classification of Digital Health Interventions; WHO DHIs[21]). Stakeholder involvement would need to be at the core of this development process, to ensure its content is relevant, clear and complete, and meets community needs.[22] The diverse and geographically spread ENABLE membership and their wider professional network represents a unique and timely opportunity to conduct this work. Considering these quality standards and following methodological recommendations,[22-24] the initial version of the repository structure was prepared. A stakeholder consultation process is proposed to explore their views and level of agreement on the relevance, clarity and completeness of the initial version.[22 23] The resulting

improved version would represent the structure of the ENABLE repository, which will be tested and populated in subsequent steps with users and developers of available technologies.

The present manuscript describes two elements:

1) The proposed structure for the repository
2) The protocol of the real time Delphi study to explore stakeholder views on this structure

Methods and analysis

Steering committee

A steering committee (SC) was established within the COST ENABLE WG2 to coordinate and perform the work. The committee includes 11 ENABLE members from 9 countries in the following areas of expertise: adherence research and education, clinical practice, policy making and technology development. Members are responsible for: (i) determination of the repository scope and framework of attributes defining repository structure, (ii) preparation of the Delphi protocol, (ii) configuration and piloting the Delphi survey, (iv) selection and invitation of stakeholders to participate in the study, (v) moderating study performance via the online tool and (vi) analysis and interpretation of results.

Determining the repository scope and framework of attributes defining its structure

The determination of scope and development of the attributes' labels with definitions aimed to align with ontology development procedures as described by Wright et al.[24] and follow a stakeholder engagement methodology as described by Norris et al[22] and Khodyakov et al[25]. The principles of ontology development, actions taken when generating the framework of attributes and examples of how these principles are applied in the ENABLE project are presented in Table 1. The stakeholder engagement is primarily achieved through the proposed real-time Delphi study, which is described in more detail in the next sections.

Table 1. Principles of ontology development after Wright et al.[24] and actions taken in the ENABLE project.

Principles	How they have been applied in the ENABLE project
Have specified scope and scientifically sound and relevant content	Selection of established definitions for delimiting the scope, consultation of stakeholders, piloting for data input and platform search.
Meet the needs of community of users	Consultation of stakeholders, steering committee and Action members sampled from the user community and including diverse areas of expertise.
Enabling users to understand the meaning of entities	Naming examples of existing ontologies, piloting Delphi survey, technology description form, user form and platform use.

Be logically consistent	Using the methodology recommended for attribute description, checking consistency via Ontology Web Language (OWL).
Be interoperable with existing ontologies	Adopting attributes and labels available in existing ontologies and classifications, expert input on additional attributes and recommendations for interoperability.
Reflect changes in scientific consensus and remain accurate over time	Repository in open access, sustainability plan developed with Action members and stakeholders.

Scope and definition of MATech

Four established definitions were used to define the scope of repository and set the framework of attributes: (i) *WHO definition of health technologies* [26]; (ii) *the ABC definition of medication adherence*[1]; (iii) the *WHO definition of adherence to long-term therapies*[2] to highlight the importance of shared decision-making between the patient and the healthcare team and (iv) *the definition of best practice in healthcare proposed by the European Commission* to guide improvements in European health systems.[27] The information in this definition denotes evidence on safety, efficacy, effectiveness, cost-effectiveness, appropriateness, social and ethical values, and quality of the health care interventions.

Therefore, we propose to define ***Medication Adherence Technologies (MATech) as devices, procedures or systems developed based on evidence to support patients to take their medications as agreed with healthcare providers (i.e., to initiate, implement, and persist with the medication regimen).***

- **devices, procedures or systems** emphasize the inclusion of all technologies, irrespective of their mode of delivery (whether based on electronic or printed supports, delivered through human interaction, or a combination of these) with the aim to construct a comprehensive repository in which users can identify diverse technologies to fit their potentially diverse needs.
- **developed based on evidence** encompass the requirement of evidence/research that supports at least a potential contribution to either measurement or intervention on medication adherence (e.g., validation or pilot studies). Thus, technologies that are not (yet) supported by evidence (e.g., development and testing stages), or clinical practice protocols without an evidence base on at least one aspect (safety, efficacy, effectiveness, cost-effectiveness, appropriateness, social and ethical values or quality), will not be (yet) included in the repository until such evidence is produced and reported.
- **support patients to take their medications as agreed with the healthcare providers (i.e. to initiate, implement, and persist with the medication regimen)** encompass the contribution of

the technology to medication adherence management – either directly in patients' self-management, or by supporting professionals to offer such services to patients through all phases of medication adherence. Thus, technologies that focus on other medication management goals, but do not target adherence specifically would be out of scope for this repository.

Furthermore, the technologies included would need to be described in terms of their technical characteristics and validation, their behaviour change content, format, and context, as well as the characteristics facilitating appropriate implementation in care processes. Hence, evidence from behaviour,[19 28] implementation[29 30] and computer sciences[18 21 31 32] informed the initial scope and attributes framework to ensure key features, such as user-centeredness, trustworthiness/credibility, accuracy & relevance of the presented information, tailoring to the needs of different users and interoperability with existing evidence and other sources of information on healthcare technologies.

Framework of attributes

An initial list of attributes was developed based on a literature review and knowledge from the ENABLE members activities such as (i) an ongoing systematic review of e-health interventions on medication adherence for chronic conditions,[33] (ii) a checklist of e-health quality criteria under development,[34] (iii) Interventienet.nl - platform showcasing evidence-based medication adherence interventions in the Netherlands[12] and (iv) the ABC taxonomy – consensus-based terminology and definitions of medication adherence[1].

The initial list was presented to the SC and discussed via several videoconferences to generate a more detailed list of attributes grouped on several themes. Each theme was further elaborated by a subgroup of 2 SC members following a standard format including labels and adherence-related definitions. We adopted the approach from BCIO[19], where related attributes were searched in topic relevant ontologies/taxonomies/classifications and original definitions and codes were added. The reasons for the choice of certain attributes and labels were detailed for each attribute group. The proposed framework of attributes is graphically presented in Figure 1 and Supplementary file 1, while rationale and sources used to define the labels for the MATech repository are presented in Table 2 and Supplementary file 2.

The final proposed framework consists of three domains (**i**) **product and provider information (D1)**, **(ii) medication adherence descriptors (D2)** and **(iii) evaluation and implementation (D3)** aligning with the three elements of the Donabedian health care model (i) structure, (ii) process and (iii) outcomes.[35]

The domains branch in 13 attributes groups, which then branch further to up to four sublevels of attributes. Each attribute is described with a label and related definition.

Figure 1. The interactive graph showing the framework of attributes for MATech ("the MATech Tree"). The MATech tree is available as interactive feature in the Supplementary file 1.

Table 2. The proposed framework of attributes used in the MATech repository. Each group is presented with the core question it is addressing, rationale and sources used to create labels within the group. A detailed description of all attribute groups with labels and definitions is also available in the Supplementary file 2.

Domain and attribute group	Core question	Rationale	Existing ontology/ taxonomy/ classification used and adapted
D1 (D1.1) *Product and provider information*	***What product does the entry refer to, who provides it, who entered its description in the repository and when?***	Each entry in the ENABLE repository will refer to a unique product, which will be identified with a unique ID, provided by a unique organisation (manufacturer, developer) with its own unique ID and related metadata (e.g., date of entry, verification process, etc.) to present the identity of the described MATech and its provider.	• Ontology for medical technology innovation in healthcare centres by ITEMAS [36] – only concepts referring to products and their providers were used and adapted.
D2.1 *Target use scenario*	***What use scenarios and types of users is the technology intended for?***	We can distinguish two general categories of users and their characteristics that might influence the choice of technology: (i) *self-management use* (patients and caregivers) - labels describing patients' characteristics or their condition (age, functional status, (health) literacy, etc.); (ii) *adherence support use* by healthcare or social care providers and health system managers, who can initiate a search for MATech to integrate in their practice. The provider and the setting are also the focus of separate attribute groups.	• Systematized Nomenclature of Medicine, Clinical Terms (SNOMED-CT)[32], • WHO International Classification of Functioning, Disability and Health (ICF)[37] • The WHO DHI[21] • ABC Taxonomy[1]
D2.2 *Target health conditions*	***Which health conditions could the technology be used for as part of adherence support?***	MATech are usually developed and validated to be used in one or several clinical domains and potential users may search for technologies applicable to the health condition(s) they aim to manage. Since our stakeholders also include lay individuals, special focus was put on using simplified language to avoid misunderstandings and knowledge gaps.	• The International Classification of Disease (ICD-11)[18] • The Health Research Classification System (HRCS) from the UK clinical research association[38]
D2.3 *Medication regimen*	***What type of medication regimen(s) is the technology intended for?***	Medication regimen can take different schematic forms and be of varying complexity, which may influence the complexity and extent of medication adherence. MATech may be developed for medications with different characteristics, hence the repository users should be able to indicate the type of regimen to find a MATech that fits its specific characteristics.	• SNOMED-CT[32] • National Cancer Institute Thesaurus (NCIT)[39] • Medical Subject Headings (MeSH)[40]

D2.4 *Medication adherence management components*	***What adherence management types and phases does the technology target?***	Management of adherence entails two management type, e.g., monitoring/measurement (D2.4.2.**A**) and support/intervention (D2.4.2.**B**) by any stakeholder, including the patient himself. Both elements may require different approaches depending on the targeted phase of adherence (D2.4.1).	• ABC Taxonomy[1]
D2.4.2.A *Monitoring/measurement methods and targets*	***If measurement is a component, what measurement methods does the technology use and what do they measure?***	A broad range of measurement methods for adherence are available. In addition to adherence behaviours, measurement can also target adherence determinants, other self-management behaviours and outcome measures (e.g., HRQoL). Therefore, we have selected a range of measurement models as well as a selection of self-management behaviours to offer the possibility to describe technologies from a measurement perspective.	• SNOMED-CT[32] • extensive existing literature[2 3 41] and own (SC's) methodological know how • Train4Health (T4H) behaviour change competency framework [42] • BCIO[19]
D2.4.2.B.1 *Intervention modes of delivery*	***If intervention is a component, how is it delivered to its users?***	Mode of delivery is *'physical or informational medium through which a given behaviour change intervention is provided'*[19], can affect the intervention effectiveness. Although digitalization has entered in all aspects of everyday life, the analogue mode is still very relevant. This is especially true within the elderly, who on one hand require more support in medication adherence[43] and are on the other hand less digitally-literate.[44] Hence, the repository should encompass all modes.	• BCIO[19]; specifically a taxonomy of modes of delivery of BCI[45]
D2.4.2.B.2 *Target behaviour determinants*	***If intervention is a component, what reasons for non-adherence can the technology help address?***	The MATech can address different reasons for non-adherence, defined as determinants of behaviour, which can be non-modifiable or modifiable.[2 19 46] Individual-level and modifiable determinants are encompassed as capability (psychological and physical), opportunity (social and physical), and motivation (reflective and automatic), also known as the COM-B model.[47]	• Capability, Opportunity, Motivation and Behaviour (COM-B) model and Behaviour Change Wheel[47] • Theoretical Domains Framework (TDF)[48] • BCIO[19], specifically The Mechanisms of Action (MoA) Ontology[49 50] • International Classification of Health Interventions (ICHI)[31]
D2.4.2.B.3 *Behaviour change techniques*	***If intervention is a component, what are the 'active ingredients' present in the technology that may trigger change in the reasons for non-adherence targeted?***	To trigger/support change in a health behaviour, interventions act by generating change in determinants of the targeted behaviour. The 'active ingredients' in these interventions are labelled *'behaviour change techniques'* (BCTs). We included only user-level BCTs (i.e., BCTs that provide support to medication users) and mapped them according to the COM-B model and across domains.[48] If considered relevant, HCPs level or system-level BCT can be included in the future	• Behaviour change technique (BCT) taxonomy[28 51] • Train4Health (T4H) behaviour change competency framework[42] • Cards for Change (C4C)[52 53]

D2.4.2.B.4 *Intervention providers*	***If intervention is a component, who delivers the intervention to users?***	The provider of intervention is a role played by a person, population or organization that provides/delivers an intervention. This includes their occupational role and type of relatedness. In medication adherence, the provider is often HCP, hence the quality of the *HCP-patient* relationships (communication skills, collaborative decision making, trust in the HCP, HCPs' cultural competences) correlate with patients' adherence.[54]	• BCIO[19], specifically Intervention Source Ontology[55] • Gender, Sex, and Sexual Orientation ontology (GSSO) [56]
D2.4.2.B.5 *Intervention settings*	***If intervention is a component, where is the service for improving adherence delivered?***	Setting is the social and physical environment in which the technology is used to manage medication adherence. Implementation[29] and behavioural[19] science emphasize the importance of understanding and describing the environment in which a certain intervention is delivered as it can significantly influence its outcomes. In addition, not every intervention is applicable or transferable to every setting. We can distinguish between physical and virtual settings as well as the possibility of applying the intervention in any setting.	• BCIO[19], specifically Intervention Setting Ontology[57] • Consolidated framework for advancing implementation science (CFIR)[29]
D3.1 *Quality indicators*	**How does the technology meet key quality indicators from different perspectives?**	Quality indicators (QI) are standardized, evidence-based, and measurable items for monitoring and evaluating the quality of healthcare performance.[58] They describe the structure, process and outcomes of care[35] and based on them the standards and review criteria are developed. The target audience of the repository is very diverse and with specific individual needs related to MATech. Thus, we decided to group quality indicators according to their different purposes of use (e.g., general, research, decision making, use).	• A checklist of e-health quality criteria (under development)[34] • Mobile Application Rating Scale (MARS)[59] • Consort-EHEALTH guideline[60] • Health Technology Assessment (HTA) Core Model, version 3.0 [61] • O'Rourke et al. The new definition of health technology assessment[62]
D3.2 *Implementation outcomes and strategies*	**What implementation outcomes and strategies are needed and available for adopting this technology in the intended setting?**	Implementation sciences provides knowledge on how to facilitate the adoption and use of technologies in real-world settings. The development of MATech often starts without considering the actual use in real-world setting, which prevents successful adoption and scaling up into clinical care.[63] Three implementation outcomes were selected for ENABLE repository: acceptability; feasibility and sustainability to target early, mid and late implementation phases. In addition, eight implementation strategies were selected and adapted to present information on training users for working with MATech, availability of education materials, expertise needed to use the MATech previous implementation experiences, financial, accreditation and other legal aspects of the use.	• Proctor et al. Outcomes for Implementation Research[64] • Consolidated framework for advancing implementation science (CFIR)[29] • The Expert Recommendations for Implementing Change (ERIC)[65] • Interventienet.nl[12]

Choice and description of the study design

We will perform an online real-time Delphi (RT-Delphi) survey to explore the level of agreement on the MATech definition and relevance, clarity and completeness of the proposed framework of attributes defining the repository structure and gain a deeper insight into stakeholders' distinct needs and requirements. The Delphi process is a flexible iterative process to consult and/or reach consensus among a group of people on a particular topic.[66 67] The key characteristics of a Delphi study are anonymity, iteration, controlled feedback, and statistical description of group response.[68] The RT-Delphi approach was developed by Gordon and Pease to improve efficiency of the process and shorten the time of performance.[69] Since then, several online tools have been developed to facilitate the RT-Delphi design[70] and literature describing the use of RT-Delphi and comparison with the traditional multi-round Delphi approach is growing.[23 71-74] In contrast to the traditional Delphi, the real time approach is round-less and offers a constant iteration by providing immediate (real-time) individual and aggregated feedback. Based on new information participants can re-think and modify their answers, which could lead to reconciliation of opinions and eventually to consensus. Participants are encouraged to re-visit and engage in the survey several times during the study period.[69 70 72 74] In comparison with the traditional approach, the real time approach encompasses all key Delphi features[73] and is similar from all key perspectives.[23 71 73 74] Furthermore, the real time approach is particularly suitable for managing larger groups, decreases moderators' workload, simplifies inclusion of people from different geographic locations and can be leaner in costs.[23 69 74] On the other hand, the approach requires specific software, which can sometimes be rigid in terms of survey configuration and analysis, contributes to increases study costs and requires specific instructions for participants.[70 74] Acknowledging the potential challenges, the advantages of the approach outweighed them and supported a decision to adopt the real time approach for our Delphi study.

Sampling and sample size

We aim to include stakeholders from all 39 countries, participating in the COST ENABLE, covering 5 different backgrounds per country: (i) adherence and eHealth research (measurement, intervention development, implementation science, health economics), (ii) clinical care (specialist and primary care practitioners providing medication adherence support), (iii) patient representation (age > 18 years, active representative in patient associations or health care facilities), (iv) policy making and (v) technology development. Hence, the targeted sample size is at least 195 panellists to be invited in the study (39 countries * 5 stakeholders).

Purposive sampling will be applied to identify potential panellists. First, requests will be sent through the ENABLE Cost Action membership list to representatives of all 39 countries, requesting them to identify suitable panellists from all five backgrounds. ENABLE members will provide the steering committee the name, background, and e-mail for every potential panellist. Participants' e-mails will be entered in the online platform (eDelphi.org – Delphi method software[75]), which will enable anonymity in further steps, i.e., individual's activity and or/answers will not be linked to personal data. All communication with the panellists (invitation, reminders, etc.) will be performed through the platform. If more candidates from the same background and country will be suggested, we will invite all candidates to increase the likelihood of achieving the planned sample size. If the expressed interest exceeds the planned sample size, purposeful sampling will be performed to ensure variation in expertise, country, and balance other characteristics (e.g., years of expertise, gender). To reach simple size and variation in sample characteristics, key international organizations from the field (e.g., ESPACOMP, PCNE, ESCP, WONCA, EMA, EPF, EARTO, EuroDURG etc.) will be contacted to fill any missing gaps, if needed.

Patient and Public Involvement

The goal of this Delphi consultation is to involve stakeholders (patient representatives among them) in decisions regarding the development of ENABLE repository and is part of the broader approach to Patient and Public Involvement followed in the ENABLE Action. Results will be communicated to all stakeholders, and they will be listed and acknowledged among ENABLE collaborators.

Data collection

We will use an online platform, eDelphi.org (Metodix Ltd, Helsinki, Finland[75]), for data collection. All survey activities - distribution, reminders, communication with and between the panellists and interim analysis of the process will be performed through the tool. The survey will be conducted from 1st October 2021 to 15th January 2022 in three stages:

1. **Pilot stage** - at least 10 members of the COST ENABLE Action, specifically members of the WG2, will be asked to test the survey (including instructions for participants) and to provide feedback on face validity as well as user experience.
2. **First stage phase** – invitation of 20 purposefully selected stakeholders (aiming for variation in expertise, geographical location, and gender) to create initial aggregated feedback of the RT-Delphi.
3. **Full scale RT-Delphi** - all remaining stakeholders will be invited to participate in the study.

Stakeholders will receive an email invitation via the eDelphi platform with a personalized link to the survey. Detailed instructions describing survey aims, rules of engagement and how to use the platform will be available on the platform.

At the beginning of the survey, participants will be encouraged to think of a hypothetical situation in which they would search for MATech applicable to their own setting/role and to assess the proposed attributes from this perspective throughout the survey. First, panellists will be asked to familiarize with the proposed structure and provide general feedback on the completeness. Further, they will be asked to rate **agreement** with and **clarity** of the MATech definition and **relevance and clarity** of each proposed attribute group on a 9-points Likert scale, where 1 represents extremely irrelevant/unclear and 9 represents extremely relevant/clear. We will use the Live 2D format[75], where each outcome represents one of the two dimensions; i.e., the x axis stands for relevance and the y axis stands for clarity. Additionally, an open text field will be provided for panellists to comment on completeness of each attribute group, i.e., proposing additional attributes or revising definitions. We will moderate the discussion in the following ways: (i) address technical issues with the platform by responding to the comment when the issues will be solved or provide instructions how to manage the issue and (ii) outline the progress of the study and the most commented questions in bulletins send through the platform once a week. We considered these strategies to encourage panellists to participate, taking into account the length of the survey and the complexity of the concepts they are rating. Delphi survey materials (Supplementary file 3. - Information letter, Supplementary file 4. - Summary of the Delphi survey and Supplementary file 5. – GDPR statement), including all attributes' labels and definitions (Supplementary file 1. and Supplementary file 2.) as well as participant instructions (Supplementary file 6.), are shown in the Supplementary Materials.

For sample description purposes, participants will be requested to provide information on their expertise (profession, years of experience, relevant professional experiences) and demographic characteristics (age, gender, country of practice). This information will also be used to examine differences in participants' ratings and comments depending on their background and location. These data will be presented in aggregated form and not linked to the individual's activity or answers. Re-visiting and re-rating will be encouraged by weekly reminders.

Data collection will be stopped upon reaching adequate sample size and characteristics to achieve sufficient representability and generalizability of the opinions gathered. Therefore, we propose stopping the Delphi, when 3 criteria will be met: (i) the total response rate to the survey is ≥ 30% (number of participants completing the survey, of the total number of stakeholders invited)[76]; (ii) a minimum of 10 panellists in each stakeholder group completed the survey; (iii) a minimum of 1

stakeholder from at least 2/3 of the COST ENABLE countries has completed the survey. We will operationalize survey completion as providing background data and answering at least 75% of the repository structure questions.

Data analysis

Descriptive statistics will be used to characterize the sample of panellists and each stakeholder subgroup regarding profession, years of experience, age, gender and country.

Several measures can be used to determine when consensus is reached, with the percentage of agreement being the most common. [77] Pre-specification of the consensus measure and criteria for consensus increases trustworthiness of findings.[78]

Level of agreement on relevance, clarity and completeness

Stakeholder agreement on the proposed definition and attributes will guide decisions on the repository structure. Therefore, we selected a set of criteria representing different levels of agreement and consequently carrying different weights in these decisions. The level of agreement on every attribute for both outcomes (e.g., relevance and clarity) will be quantified using the Interpercentile Range Adjusted for Symmetry (IPRAS) analysis technique from the RAND/UCLA Appropriateness Method (RAM).[79] Firstly, the disagreement index (DI) will be calculated as a ratio between the Interpercentile Range (IPR) and IPRAS. A DI > 1 (i.e., IPR > IPRAS) indicates disagreement exists. IPR is calculated using the 30th to 70th percentile. IPRAS for the 9-points Likert scale is calculated according to the formula presented in the RAM User Manual.[79]

Secondly, the median and DI will define different levels of agreement and steer the decisions about the repository structure. For the relevance:

i. items with the median of 7-9 and no disagreement will be considered as *relevant and mandatory*.
ii. items with the median of 4-6 or disagreement will be considered as *optional*.
iii. items with the median of 1-3 and no disagreement, will be considered *not relevant* and candidates for *exclusion*.

For an even number of participants, median ratings of e.g., 6.5 or 3.5 will be assigned to the higher level.[79] Stakeholders' responses per question will be summarized using descriptive statistics.

For clarity ratings, the above criteria will be applied as (i) sufficiently clear to remain unchanged; (ii) optional changes and (iii) candidates for rephrasing.

Panellist comments in the open text fields will be analysed qualitatively, using content analysis. Findings will be used to rephrase and improve clarity of certain attributes or to add additional attributes proposed by stakeholders.

Subgroup analysis

Following the primary analysis on the whole sample, a subgroup analysis per stakeholder group will be conducted to examine variation in opinions and potential differences among subgroups. The same agreement criteria will be applied and descriptive statistics will be stratified by stakeholder group. In addition, we will determine the reliability of ratings per question within stakeholder group by calculating the *intraclass correlation coefficient (ICC)*. The ICC calculation is based on the two-way random model, considering type (average measures) and definition of relationship (consistency) and is presented in Equation 1. ICC > 0.70 will indicate moderate to good reliability.[80 81]

Equation 1. Calculation of the intraclass correlation coefficient (ICC), expressed in %. MS_R stands for mean square for rows and MS_E stands for mean square for error.

$$ICC = \frac{MS_R - MS_E}{MS_R} x\ 100\ \ [\%]$$

Analysis of process indicators

By analysing process data from the online tool, we will describe in more detail how stakeholders' responses evolved through iterations and how consensus or certain level of agreement has formed.[25 82]

Stability of response presents the consistency of responses within the study period and between respondent group stability, which is considered a necessary precondition for determining the level of agreement or if consensus was achieved.[83-85] Different measures of dispersion (e.g., median, interquartile range) and statistical approaches (e.g. descriptive, inferential) can be used [74 85] to measure stability, which can be calculated between rounds (traditional Delphi) or at the end of the study (RT-Delphi).[71 74]

We will use the c*oefficient of quartile variation (CQV)* as a descriptive measure of response stability. CQV will be calculated over all participants (CQV_{total}) and within the same stakeholder group (CQV_{sub}) to account for expected higher variation in response between different stakeholder groups. A CQV_{total}< 30% and CQV_{sub} < 15% will be considered as stable response. CQV calculation is shown in *Equation 2.* [84 86]

Equation 2. Calculation of the coefficient of quartile variation (CQV), expressed in %. Q3 stands for value of the 3rd quartile and Q1 for 1st quartile.

$$CQV = \frac{Q3 - Q1}{Q3 + Q1} x\ 100\ \ [\%]$$

Final repository structure

After conducting the analyses described above (planned to be finalized at the end of April 2022), results suggesting modifications to the proposed structure will be considered for adoption by the Steering Committee in a subsequent version, which will represent the final structure of the ENABLE repository implemented on the initial ENABLE repository version. Further work will be considered to address results that might suggest ongoing debates in the field about certain attribute groups or the need for more in-depth consultation and evidence generation. This work will accompany the iterative improvement of the repository during the ENABLE Action.

Ethics and dissemination

Ethical considerations and consent to publish

The study is designed to ensure participants' anonymity and to manage personal data in line with EU regulation. Before starting the survey, every participant will provide an informed consent electronically on the study entry page. Participants will be asked to carefully read through the statement regarding the study aim and nature as well as the data handling procedures and to mark their understanding and agreement. The results will only be published in an aggregated form and no personal details will be revealed.

An ethical approval for the activities of the COST ENABLE Action, including this Delphi study, was granted by the Malaga Regional Research Ethics Committee ("Comite de Etica de la Investigacion Provincial de Malaga") on 29th April 2021 (Supplementary file 7.). In addition, a data protection assessment was carried out by the Data Protection Officer at the University of Basel. According to this instance the Delphi study protocol was determined as compliant regarding data protection and security (Supplementary file 8.).

Future implications and challenges

The proposed scope and framework of attributes together with findings from this Delphi study will represent the first steps on the pathway to create an evidence-based, interoperable and user-friendly MATech repository. Following the Delphi consultation and integration of the repository module on the ENABLE website[87], providers of MATech (public or private) would be invited to upload information on their products via a MATech description form based on the final repository structure. The accuracy of the information would be verified by an independent review panel through a procedure yet to be established. Important challenges lay ahead, such as how to select MATech for inclusion in the

repository given the broad scope of the definitions proposed, how to ensure accurate information about the technologies included, how to provide the information in other languages than English and in non-technical language accessible for all, and how to maintain a representative and varied offer of technologies in the long term. Nevertheless, the ENABLE repository promises to bring together stakeholders from different backgrounds to build a common language which can have an important positive impact on medication adherence research and practice.

Dissemination

The repository will be publicly accessible for interested parties. The use of the repository will be promoted and supported by dissemination meetings, workshops, and training schools. The findings of the study will be presented via publications (reports and manuscripts in open access peer-reviewed journals) and oral presentations to different stakeholders in conferences and meetings. The spirit of COST Actions is networking and dissemination of ideas; hence the action is open for anybody who would wish to join or would like to be informed about its activities.

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Authors contribution statement

All authors contributed to the work and formation of this manuscript. The first draft was prepared by UNM, CG, JR and ALD. All other members of the steering committee (PBF, FH, MTH, CJ, FR, DS, and IT) reviewed and upgraded the first version. All steering committee members (CG, JR, PBF, FH, MTH, CJ, FR, DS, IT) worked on development of the scope and framework of the attribute groups, UNM and ALD coordinated the work. SPG was consulted as the expert in Delphi methodology, specifically the RAND/UCLA Appropriateness Method. The final version of the protocol was prepared by UNM and reviewed by all other authors (CG, JR, PBF, SPG, FH, MTH, CJ, FR, DS, IT, ALD). All authors have read and approve the final version of the manuscript.

Competing interests

SPG is a research team member for ExpertLens (an online platform and methodology for conducting modified-Delphi studies). SG's spouse is a salaried employee of, and owns stock in, Eli Lilly and Company.

All other authors declare no conflict of interests.

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Data sharing statement

Documents detailing the development of the present protocol and the data collection planned are shared as supplementary materials. The data, analyses and results of this study will be shared in open access according to the COST open access policy.

Supplementary materials

Supplementary file 1. Medication Adherence Technology tree as an interactive feature (graphical representation of the proposed structure).

Supplementary file 2. Medication Adherence Technology tree in Excel (outlining the whole proposed structure with corresponding labels and definitions).

Supplementary file 3. Delphi information letter to participants

Supplementary file 4. Summary of the Delphi survey

Supplementary file 5. General data protection statement used in the Delphi survey

Supplementary file 6. Instructions for Delphi participants

Supplementary file 7. Ethical approval by Malaga Regional Research Ethics Committee

Supplementary file 8. Data protection assessment by the Data Protection Officer at the University of Basel

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Presentation of the ENABLE repository framework of attributes

This document presents the framework of attributes developped for the ENABLE repository by the WG2 task force. ENABLE is a COST action aiming to enhance collaboration between stakeholders across Europe for adoption of best practice and technologies supporting medication adherence. To this end, ENABLE develops an online repository of medication adherence technologies. This repository will showcase a diverse range of technologies and describe them in detail so that repository users can search and select technologies that are most appropriate to their contexts and needs. Thus, the repository would need to include information relevant for this specific use.

Information about technologies can be coded/represented via a collection of various attributes. This coding is driven by a user perspective where a user (HCP, regulator, client/patient, researcher) will be willing to learn more about (or select) a technology based on their specific interests or needs, and therefore is looking for specific types of information where attributes of technologies correspond to attributes of the solutions envisaged by users. Attributes may apply to adherence-related goals, target user characteristics, health conditions, product characteristics, etc., each represented as distinct attribute groups. Such modular ("LEGO") approach allows describing a very diverse landscape of existing and future technologies.

The repository is supposed to include all potential attributes for all technologies so that they allow the descriptions of any medication adherence technology in detailed way to enable informed decision-making. The goal of the present work therefore is to create a framework of such attributes, each with their own unique labels (short names of attributes) and definitions (longer explanations of what the attributes refer to).

Once the repository is created using this framework of attributes, we will be able to describe and group available adherence technologies. If a new attribute is subsequently identified, it will be added to the list -as part of an existing attribute or by creating a new one- aiming to ensure the evolution of this repository with changes in the field, as well as backward compatibility.

Domain name		Attribute group name
D1 ***Product & provider information***	D1.1	*product and provider information*
D2 ***Medication adherence descriptors***	D2.1	*target use scenarios*
	D2.2	*target health conditions*
	D2.3	*medication regimen*
	D2.4	*medication adherence management components*
	D2.4.2.A	*Monitoring/measurement methods and tar*
	D2.4.2.B.1	*intervention modes of delivery*
	D2.4.2.B.2	*target behaviour determinants*
	D2.4.2.B.3	*behaviour change techniques*
	D2.4.2.B.4	*intervention providers*
	D2.4.2.B.5	*intervention settings*
D3 ***Evaluation & implementation***	D3.1	*quality indicators*
	D3.2	*implementation indicators*

Definition	*Core question*
Each entry in the ENABLE repository will refer to a unique product, which will be identified with a unique ID, provided by a unique organisation (manufacturer, developer) with its own unique ID and related metadata (e.g., date of entry, verification process, etc.) to present the identity of the described MATech and its provider.	What product does the entry refer to, who provides it, who entered its description in the repository and when?
The type of common adherence management activities that the technology is intended to be used for.	What use scenarios and types of users is the technology intended for?
The type of diseases or health problems the technology is intended for.	Which health conditions could the technology be used for as part of adherence support?
The prescribed schematic form/therapeutic plan of medication therapy that the technology is intended for.	What type of medication regimen(s) (treatment intention, route of administration, number of medications, and recommended dosing) is the technology intended for?
The type of procedures and time periods the technology facilitates to achieve the best use by patients of appropriately prescribed medicines.	What adherence management types and phases does the technology target?
What measurement methods are used and what is being measured (measurement targets).	If measurement is a component, what measurement methods does the technology use and what do they measure?
The modes used to deliver the medication adherence intervention	If intervention is a component, how is it delivered to its users?
Causal influences on medication adherence that can be modifiable (amenable to intervention with a medication adherence technology).	If intervention is a component, what reasons for non-adherence can the technology help address?
Options/activities included in the technology that aim to influence barriers and facilitators of medication adherence	If intervention is a component, what are the 'active ingredients' present in the technology that may trigger change in the reasons for non-adherence targeted?
A role played by a person who uses the technology to assist the patients in their self-management of medication adherence	If intervention is a component, who delivers the intervention to users?
The social and physical environment in which the technology is used to manage adherence to medication	If intervention is a component, where is the service for improving adherence delivered?
Quality indicators are standardized, evidence-based, and measurable items for monitoring and evaluating the quality of healthcare performance.	How does the technology meet key quality indicators from different perspectives?
Outcomes and strategies that help implement medication adherence measurement / intervention within its target setting	What implementation outcomes and strategies are needed and available for adopting this technology in the intended setting?

Upper Level	Sub-Level 1	Sub-level 2
Product		
	Product ID	
	Product Name	
	Brief product description	
	Date of release	
	Date of most recent update	
	Product type	
		Hardware
		Software
		Service
		Material
	Product Brand	
	Product integration	
		stand-alone
		component
	Language(s)	
	Country(ies)	
	Terms & Conditions of use	
	Cost	
Provider Organisation		
	Provider ID	
	Provider Name	
	Provider type	
		Privately-owned / for profit organisation
		Public / state-owned organisation
		Not-for-profit organisation
	Provider domain of activity	

		Technology
		Pharmaceutics
		Healthcare
		Research and Education
	Contact details	
Repository entry		
	Entry ID	
	Entry date	
	Date of last modification	
	External/peer verification of data accuracy	
Author of the product description		
	author ID	
	Author name	
	Date of account initiation	
	Author contact details	

Definition
health technology (device, procedure or system) that could be used to manage adherence to medication
random alphanumeric code given to the product at first entry in the database
name given by the technology provider to designate the product itself
text (max 500 characters including spaces) that provides a short summary of the main functionality and atributes of the technology
date when the technology first became available
date when the technology had the most recent update
type of support on which (components of) the product (are) is implemented
product (component) consisting of physical components of electronic systems
product (component) consisting of programs or other operating information for electronic systems
product (component) consisting of actions to support someone manage adherence to medication
product (component) consisting of physical substances or equipment other than electronic
name used by the technology provider to designate the group to which the product belongs
manner in which the product is intended to be integrated in an adherence support process
product integration in which the technology is intended to function unrelated to other products
product integration in which the technology is intended to link to other products as component of a wider system
languages in which the technology is available for use
name of country/countries where technology is in available
written rules which two or more parties engage to respect and meet to apply the technology in a setting; may include intelectual property, copyright.
amount paid, charged, or engaged to be paid, for purchasing the technology
organisation that produces and/or makes the product available for users
random alphanumeric code given at first entry of a product from a provider in the database
name of the provider organisation
administrative form in which the organisation is registered
organisation that operates to generate financial profit
organisation that is owned by a government
organisation not intended to make a profit but to provide or support a service that people need
general field in which the organisation is active

organisation performing activities related to the production of new machinery or equipment based on scientific knowledge or processes
organisation performing activities related to the production of medicines
organisation providing (medical) care services to individuals or/and communities
organisation providing services related to generation of new knowledge and teaching
contact name, email, phone number of the provider organisation
description of a health technology by a repository author account
random alphanumeric code given at entry registration
date of entry registration
date when the last modification of an entry was recorded
confirmation of whether the information recorded was checked for accuracy by an external/peer reviewer (group)
person or group of persons who enters information about at least one MAT in the ENABLE database
random alphanumeric code given at account opening
name of author given at account opening
date of account opening in the ENABLE platform
email address via which the author can be contacted

DEVELOPMENT AND JUSTIFICATION

A repository entry represents any contribution from an author describing a medication adherence technology using the ENABLE template, which they then upload on the platform. Each entry in the ENABLE repository will be stored individually. It will have a unique entry ID, and metadata such as the date of entry, date of most recent modification, and whether the information was verified by another manner (validation process to be developed). It will refer to a unique product, which will be identified with a unique ID, provided by a unique organisation (manufacturer, developer) with its own unique ID. Multiple entries can refer to the same product ID (the reconciliation of entries for the same product will be part of the validation procedures, i.e. by recency or merging of the entries), and an organisation may provide multiple products.

No ontology, taxonomy or classification could be identified in the BioPortal repository or in the literature that provides a formal description of product characteristics used for medication adherence technologies in particular. However, a related ontology was identified that refers to medical technology innovation in healthcare centers. This ontology, developed by members of the Platform for Innovation in Medical and Health Technologies (ITEMAS; a network of healthcare centers aiming to foster innovation in the Spanish healthcare system), includes relevant concepts on the development and adoption of technologies in healthcare and therefore it is an appropriate source of descriptors for the ENABLE repository. The ITEMAS concepts were consulted and concepts referring to products themselves and their providers were selected, since ENABLE aims to describe the technologies and not cover as well the process of developing and integrating them in healthcare systems. This choice of concepts makes the repository interoperable with organisations that would adopt ITEMAS for their activities. Additional constructs were generated after discussion with SC members.

upper level	Sub-level 1	Sub-level 2	Sub-level 3
adherence self-management use			
	Person in the healthcare environment		
		Patient	
		Caregiver	
	Patient age group		
		Adult	
			Older adult
		Adolescent	
		Child	
		Infant	
	Patient functional status		
		Mental functions	
			Memory functions
			Perceptual functions
		Sensory functions	
			Seeing functions
			Hearing functions
		Neuromusculoskeletal and movement-related functions	
	Patient literacy		
		Patient health literacy	
			Patient medication literacy
	Patient polypharmacy		
	Patient multimorbidity		
adherence support service use			

Professional health and social care providers

Health (system) manager

Definition
Scenario in which the technology is used for adherence self-management activities
Person who interacts with the technology within the process of self-management
Person who uses the technology for self-management of their own adherence
Person who uses the technology to assist the patient in their self-management of adherence
Age group of the person for which the medical technology is appropriate for use
Person aged over 18 years
Adult aged over 66 years
Person aged between 12 and 18 years
Person aged between 1 and 12 years
Person aged less than 1 year
The level of functioning of the person for which the technology is appropriate
Patient status regarding functions of the brain involved in adherence self-management
Functions regarding registering, storing, retrieving information for adherence self-management and/or using technology for this purpose
Functions regarding recognizing and interpreting sensory stimuli necessary for adherence self-management and/or using technology for this purpose
Functions regarding recognizing and interpreting visual stimuli (light, form, shape, size, color)
Functions regarding recognizing and interpreting auditive stimuli (presence, location, pitch, loudness and quality of sounds)
Functions regarding movement and mobility (of joints, bones, reflexes and muscles)
The patient's ability to read and write needed to manage adherence
The patient's capacity to obtain, process and understand basic health information and services needed to self-manage adherence
The patient's ability to understand and act on medication-related information
The use of multiple drugs (5+) administered to the same patient
complex interactions of several (2+) co-existing diseases occuring in the same patient
Scenario in which the technology is used for activities supporting taking medication in an health/social care provision setting

Members of the health and social care workforce who deliver adherence support services

Persons involved in the administration and oversight of public health systems delivering adherence support services

DEVELOPMENT AND JUSTIFICATION

Among the various use scenarios for medication adherence management, we can distinguish two general categories in what concerns the potential types of users and their characteristics that might influence the choice of technology: self-management use, and adherence support use. In the first scenario, it is either the patient or the caregiver who might be interested in searching the repository for technologies the patient can use themselves, or the couple patient-caregiver can use in the shared management of medication intake, for example at home. In the second scenario, a healthcare (or social care) provider may be interested in technologies they can use themselves to facilitate adherence support. A technology can apply to both use scenarios, for example when a monitoring technology is used by both patients/caregivers and the professionals who accompany them in their treatment and information can be transmitted from one to another (each having their own interface). Thus, the set of descriptors regarding target users operates this basic distinction.

The use of medication adherence technologies may be influenced by several characteristics of the patients, such as their age group, functional status regarding mental functions (e.g. memory and perception), sensory functions (e.g. vision and hearing), and movement-related functions, as well as characteristics of their health condition or treatment (e.g. multimorbidity and polypharmacy). Literacy and health literacy (and specifically medication literacy) are also central to the appropriateness and effectiveness of self-management support. Thus, descriptors related to these characteristics were identified in available ontologies (e.g. SNOMED-CT, WHO International Classification of Function) and included in the list of descriptors.

According to the WHO client classification (regarding DIgital Health Interventions; DHI), there are two categories of potential clients of digital health technologies in addition to patients and caregivers: healthcare providers and health system managers. These were included as sub-categories of the adherence support use scenario, since both types of professionals (including here social care organisations and providers) can initiate a search for technologies to integrate in their practice. No characteristics of these types of users/clients were considered relevant for the choice of the tool in this initial version of the list. The provider of an adherence support intervention and the setting in which this can be performed are the focus of separate descriptor sets, since they can be different from the user who initiates the search (who can perform this for an entire team, including the patient and their caregiver).

Upper level	Definition
Blood	Health condition category that refers to haematological diseases, anaemia, clotting (including thromboses and venous embolisms)
Cancer and neoplasms	Health condition category that refers to all types of neoplasms, including benign, potentially malignant, or malignant (cancer) cancer growths (including leukaemia and mesothelioma).
Cardiovascular	Health condition category that refers to coronary heart disease, diseases of the vasculature and circulation including the lymphatic system
Congenital disorder	Health condition category that refers to physical abnormalities and syndromes that are not associated with a single type of disease or condition, including Down's syndrome and cystic fibrosis
Ear	Health condition category that refers to diseases of the ear, such as deafness
Eye	Health condition category that refers to diseases of the eye
Infection	Health condition category that refers to diseases caused by pathogens, acquired immune deficiency syndrome, sexually transmitted infections
Inflammatory and immune system	Health condition category that refers to rheumatoid arthritis, connective tissue diseases, autoimmune diseases, allergies. (includes transplants)
Injuries and accidents	Fractures, poisoning and burns.
Mental health	Health condition category that refers to depression, schizophrenia, psychosis and personality disorders, addiction, suicide, anxiety, eating disorders, learning disabilities, autistic spectrum disorders
Metabolic and endocrine	Health condition category that refers to metabolic disorders (including diabetes, and diseases of the pineal, thyroid, parathyroid, pituitary and adrenal glands).
Musculoskeletal	Health condition category that refers to osteoporosis, osteoarthritis, muscular and skeletal disorders

Neurological	Health condition category that refers to dementias, transmissible spongiform encephalopathies, Parkinson's disease, neurodegenerative diseases, Alzheimer's disease, epilepsy, multiple sclerosis
Oral and gastrointestinal	Health condition category that refers to inflammatory bowel disease, Crohn's disease, diseases of the mouth, teeth, oesophagus, digestive system including liver and colon
Renal and urogenital	Health condition category that refers to kidney disease, pelvic inflammatory disease, renal and genital disorders
Reproductive health and childbirth	Health condition category that refers to fertility, contraception, abortion, in vitro fertilisation, pregnancy, mammary gland development, menstruation and menopause, breast feeding, antenatal care, childbirth and complications of newborns
Respiratory	Health condition category that refers to asthma, chronic obstructive pulmonary disease, and other respiratory diseases
Skin	Health condition category that refers to dermatological conditions
Stroke	Health condition category that refers to ischaemic stroke (caused by blood clots) and haemorrhagic stroke (caused by cerebral/intercranial haemorrhage).
Generic health relevance	Health condition category that refers to technologies applicable to all diseases and conditions

DEVELOPMENT AND JUSTIFICATION

Depending on the health conditions for which medication is prescribed, adherence behaviours may be influenced by different factors and therefore require condition-specific interventions. Adherence technologies are therefore usually developed and validated to be used in one or several clinical domains and potential users may search for technologies applicable to the health condition(s) they aim to manage.

The International Classification of Disease (ICD-11) is a global standard for diagnostic purposes, and groups diseases in over 17000 categories (icd.who.int). In ICD-11, 21 groups of codes (chapters) are proposed to describe health conditions, among other groups of codes for related diagnostic purposes. While ICD-11 is an elaborate classification used for clinical documentation and monitoring globally, a simpler classification has been developed by the UK Clinical Research Collaboration for research purposes: the Health Research Classification System (HRCS) (https://hrcsonline.net/health-categories). The HRCS is inspired by ICD and includes 21 separate disease categories, 19 of which are disease specific whereas the other 2 have a broader focus (e.g. general health and epidemiology, conditions of unknown aetiology). Of the 20 HRCS categories, 18 correspond broadly to ICD-11 chapters (merging 3 chapters into one category for reproductive health and childbirth, and omitting sleep-wake disorders), while the 19th refers to stroke as a distinct group of conditions. For the purpose of the present repository, we have therefore selected HRCS as 1) it is likely that research on adherence technologies will increasingly use these codes to record the type of health conditions studies are performed on and thus would map easier on these categories, and 2) the labels and descriptions used are relatively less technical and therefore easier to understand by stakeholders with diverse backgrounds. We considered that the last category ('Disputed aetiology and other') is less relevant for medication adherence and thus we excluded it from our descriptors list. The HRCS classification system, based on the ICD classification, would allow repository users to quickly and efficiently identify the type of health condition of their interest.

Upper level	Sub-level 1	Definition
type of intention		The purpose for which the medication is prescribed.
	preventive	Medication are prescribed as prevention/prophylaxis against the occurence of diseases or disease-related adverse events (e.g. excerbations, organ rejections etc.)
	therapeutic	Medication is prescribed as treatment of a disease and its associated symptoms.
duration of treatment		The duration of treatment presents the intended interval of treatment and relates to the clinical course and disease conditions.
	short-term	treatment is prescribed over a limited time-period, mostly to treat an acute disease of sudden-onset and predictable end.
	long-term	treatment is prescribed as a prolonged and peristently indicated therapy as it is the case in chronic, latent-progressive disease conditions.
route of administration		path by which medication is brought into contact with the body to unfold pharmacological effects.
	oral	Medications are administered as oral froms (tablets etc.) for drug reception via the mouth or gastro-intestinal tract.
	inhaled	Medications are administered as inhalation of aerosols, powders or gas via the respiratory tract.
	injections/subcutaneous	Medications are administered as injection in subcutanous layer for a relative slow drug release.
	infusion/parenteral	Medications are administered as parenteral infusion for direct intra-venous application.
	patches	Medications are administered as a dermal layer (e.g. patch) to achieve systemic drug-concentration and -efficacy.
	topical	Medications are administered as topical forms for local effects on dermal or mucous surfaces/layers.
number of monitored medications		how many distinct medications are monitored by the technology, if applicable
	single medication	Only treatment of a single medication is monitored.
	multiple medication	A combination therapy of two or more medications is monitored.

prescribed dosing frequency		dose-taking patterns recommended for medicines administration, in which doses should be taken at defined time intervals over a defined time period
	once-daily dosing	Only one dose is prescribed at a certain time during the day.
	multiple daily dosing at fixed intervals	Multiple doses are prescibed in a certain interval during the day.
	once per week dosing	Only one dose is prescribed at a certain day during the week.
	multiple dosing per week in fixed intervals	Mutliple doses are prescibed in a certain interval during the week.
	dose adjustment recommendations	The frequency or amount of a certain dose is adjusted to the newly prescribed treatment regimen.

DEVELOPMENT AND JUSTIFICATION

Factors related to the medication regimen are among the 5 main groups of determinants influencing medication adherence (WHO, 2003). The medication regimen for which adherence is to be managed can take different schematic forms and be of varying complexity, which may influence the complexity and extent of medication adherence. Medication adherence technologies may be developed for medications with different attributes, therefore ENABLE repository users should be able to indicate what type of medication regimen they are aiming to manage and how a technology fits these specific attributes.

We distinguished five descriptors relevant for medication adherence that refer to properties of medication regimens. The type of intention refers to the purpose of treatment as prevention or therapy, while the duration of treatment is related to the clinical course (e.g., acute/sudden-onset or chronic /latent-progressive course). Both depend on disease conditions and determine the purpose and duration of adherence management. The route of administration, the number of medications and the prescribed dosing frequency are the main components of the variability and complexity of prescribed regimens. Thus, descriptors related to these medication regimen attributes were identified in available ontologies (e.g., NCIT, MeSH and SNOMED-CT) and included in the list of descriptors.

It is important to note that we have selected, from among a broader range of routes of administration and types of dosing frequency, the ones we considered relevant for adherence to medication; for example, we have excluded ‘as needed’ dosing as it cannot be subject to a comparison between actual and prescribed dosing histories (the definition of adherence), and routes of administration likely to require a healthcare professional and thus be less influenced by adherence as a patient behavior.

Upper Level	Sub-Level 1	Definition
D2.4.1 Medication adherence phase		Time interval between the prescription start and end dates that is behaviorally distinct (i.e. linked with specific determinants
	Initiation	Phase of adherence that covers the start of a prescribed treatment, i.e. the period from when the prescription is issues to the first dose taken (i.e. the initiation event)
	Implementation	Phase of adherence from the initiation until the last dose taken during which one can estimate the extent to which the patient's dose taking and timing are linked to the prescribed dosing
	Discontinuation (Persistence)	Phase of adherence that refers to the end of treatment execution and covers the period until last dose is taken, e.g. end of therapy or termination by patient. Persistence is the period between initiation and discontinuation.
D2.4.2 Type of adherence management		The goal of adherence management that the technology is designed to address.
	Monitoring/Measurement	Type of adherence management that refers to estimating (repeatedly) medication adherence behaviours, determinants, and/or outcomes
	Support/Intervention	Type of adherence management that refers to generating change in medication adherence determinants and thus behaviours and outcomes.

DEVELOPMENT AND JUSTIFICATION

Technologies described in the ENABLE repository will be used either for self-management use by patients themselves or for supporting this process by health and social care providers within healthcare institutions or systems. The general term that describes both these use scenarios, according to the ABC taxonomy (Vrijens 2012), is “management of adherence”, i.e., “the process of monitoring and supporting patients' adherence to medications by health care systems, providers, patients, and or their social networks”. Thus, in this definition, a distinction is made between ‘monitoring’ (or measuring, which can target the behaviors themselves, their determinants, and/or their relevant outcomes), and ‘supporting’ adherence (or intervening to achieve best use of appropriately prescribed medicines by patients). As technologies may focus on one or both these goals, we have given the possibility for users to search for each goal/type of management (for example in situations when they would like to combine technologies into a broader adherence management solution). As both metrics and intervention may require different approaches depending on what phase of adherence is of concern, we have also given the possibility for users (and technologies) to specify which adherence phase they target, i.e.:

1) initiation, which “occurs when the patient takes the first dose of a prescribed medication”

2) implementation, which “is the extent to which a patient's actual dosing corresponds to the prescribed dosing regimen, from initiation until the last dose”

3) discontinuation marks the end of the adherence process “when the next dose to be taken is omitted and

Upper Level	Sub-Level 1	Sub-level 2	Sub-level 3	Definition
measurement method				the way in which information is gathered and summarized by the technology about the patient's medication adherence
	direct observation method			measurement method consisting in observing medication intake directly
	pill count method			measurement method consisting in calculating left over pills in containers/blisters at a specific time point
	self report method			measurement method using data reported by patients or caregivers about themselves
		diary		self-report method in which the respondent records information about their current behaviors, determinants or outcomes at regular intervals
		questionnaire		self-report method in which the respondent answers a set of pre-designed questions about their behaviors, determinants or outcomes
		interview / consultation		self-report method in which the respondent answers questions, either pre-defined or spontaneous, from another individual as part of a structured conversation
	Electronic monitoring method			measurement method using data from devices that record medication taking events electronically
		smart package		electronic monitoring method that uses data from a container/dispenser in which the medication is packaged
			smart box	smart package that includes a method to record the opening and closing of the box in which the medication is stored for use
			smart inhaler	smart package that includes a method to record the use of the inhaler device in which medication is stored for use
			smart tube	smart package that includes a method to record the use of the tube in which medication in ointment or liquid form is stored for use
			smart button	smart package that includes a device attached to private pillbox where medication is stored for use and includes a button on which the person can press to record a dose intake
		smart pill		electronic monitoring method that uses data from a mechanism integrated in the medication itself that records the ingestion of the medication

		digital event record system		digital technologies recording taking events (App, other devices)
	Electronic Healthcare Database method			measurement method using routinely collected data as part of a longitudinal healthcare process
		Electronic medical records		EHD method using data recorded in patients' medical records
		Claims / dispensing		EHD method using data recorded for insurance claims purposes based on medication dispensed as part of the patients' care process
		Record linkage system		EHD method using data recorded in several linked databases
	Laboratory method			measurement method based on clinical assessment through invasive procedure (e.g. body fluids samples)
		drug concentration		laboratory methods consisting in the detection of sufficient drug levels in blood
			intra patient variability	laboratory method indicating the fluctuation of drug concentration levels over a specific time period
		biomarker		laboratory method representing a surrogate for drug intake
		treatment response		laboratory method assessing clinical status as a proxy for adherence behaviours, e.g. habitus, lab results (blood glucose, Hba1c,) vital signs (blood pressure)
measurement target				the component of the adherence causal (logic) model measured by the technology
	determinant measure			measurement targeting causal influences on the behaviour that can be modifiable (amenable to intervention with a medication adherence technology)
	behaviour measure			measurement targeting a self-management behaviour
		adherence measure		behaviour measure assessing to the patient's medication intake as compared to the prescribed regimen
		alcohol intake measure		behaviour measure assessing the patient's intake of alcohol (frequency, type) on its own or in relation to treatment recommendations
		diet measure		behaviour measure assessing the patient's intake of food (frequency, type) on its own or in relation to treatment recommendations
		physical activity measure		behaviour measure assessing the patient's musculo-sceletal movements requiring energy expenditure (frequency, type) on its own or in relation to treatment recommendations
		tobacco use measure		behaviour measure assessing the patient's use of tobacco products

		symptom monitoring and management measure	behaviour measure assessing the patient's actions to assess symptoms regularly and/or reduce symptoms in relation to their daily goals and activities
	health outcome measure		measurement targeting the effects of the behaviour or change of behaviour on the patient's status
		clinical	outcome measure assessing clinical aspects of the patient's health status (e.g. morbidity, mortality,etc.)
		humanistic	outcome measure assessing aspects of the patient's health related quality of life, satisfaction,...
		economic	outcome measure assessing economic aspects, in particular direct, indirect and intangabile costs.

DEVELOPMENT AND JUSTIFICATION

Throughout the last decades of medication adherence research, the mode of medication adherence measurement has evolved.

If a technology aims to monitor or measure adherence as part of the adherence management process it aims to facilitate, a broad range of options opens in terms of the measurement methods it can adopt, and which elements it targets, among those included in the causal (logic) model at the 'scientific core' of this process. To measure medication adherence, numerous methods have been developed: observing patients' medication intake directly, counting the remaining medication after a period of treatment, as well as various methods using self-report, electronic monitoring, electronic healthcare databases or laboratory tests. Moreover, measurement can target not only adherence behaviours but also adherence determinants, other self-management behaviours common in chronic care interventions (as described by Train4Health, a recent competency framework for the management of chronic conditions), and outcome measures such as health and quality of life. Users of the ENABLE repository may be interested to search for technologies that implement one type of measurement method, depending on the specificities of the setting in which they work (resources, acceptability, local expertise), or of the medication (e.g., mode of administration, pre-packaging). They may also be interested not only in measuring adherence behaviours, but also in technologies that integrate other elements of the causal model of self-management specific to the health condition they need to manage. Therefore, we have selected a range of measurement models (some of them with corresponding codes in SNOMED-CT, some based on methodological work in relevant domains), and followed the BCIO ontology and the Train4Health selection of self-management behaviours to offer the possibility to describe technologies from a measurement perspective.

Upper level	Sub-level 1	Sub-level 2	Sub-level 3	Definition
Printed material				Mode of delivery that involves use of printed material
	Brochure			Printed material mode of delivery that involves use of a printed publication within a brochure
	Printed media			Printed material mode of delivery that uses formats of printed media to communicate and share information
		Poster		Printed media mode of delivery that involves display of a poster in a public location.
		Newspaper/leaflet		Printed media mode of delivery that involves use of a printed publication in a newspaper or leaflet.
Human interaction				Mode of delivery that involves a person as intervention source who interacts with an intervention recipient
	Face to face consultations			Human interactional mode of delivery that involves an intervention source and recipient being together in the same location and communicating directly.
	Networks/patient groups			are groups that meet in person to discuss their 'issues' or experiences related to their health condition and or medication
Electronic				Mode of delivery that involves electronic technology in the presentation of information or the mode of motivation to an intervention recipient
	Smart phone/tablet			Electronic mode of delivery that involves communication processes
		Call		Electronic mode of delivery that involves a communication process in which a signal is sent by a caller to a recipient to alert them of the communication intent, giving the recipient the opportunity to engage with the communication.
			interactive messaging or chat	Call mode of delivery that involves textual information in the communication through interactive messaging or chat
			sms -short text message	Call mode of delivery that involves textual information in the communication.
			audio	Call mode of delivery that involves only audio information in the communication
			video	Call mode of delivery that involves video and audio information in the communication
		email		Electronic mode of delivery that involves communication by email.
		application		Electronic mode of delivery that involves the intervention recipient interacting with a mobile application

			interactivity	Application mode of delivery that is interactive
			diary	Application mode of delivery that uses a diary to delivery a medication adherence intervention
			reminder system	Application mode of delivery that uses a reminder system to delivery a medication adherence intervention
			gaming	Application mode of delivery that uses gaming features to delivery a medication adherence intervention
	Wearable electronic device			Electronic mode of delivery that includes medication related devices to support users to adhere to their treatment
		smart box		smart package that records the opening and closing of the box in which the medication is stored for use
		smart inhaler		smart package that records the use of the inhaler device in which medication is stored for use
		smart tube		smart package that includes a method to record the use of the tube in which medication in ointment or liquid form is stored for use
		smart buttom		smart package that includes a device attached to private pillbox where medication is stored for use and includes a button on which the person can press to record a dose intake
	digital media			Electronic mode of delivery that includes the use of electronic devices commonly used for mass-media communication
		Internet		Electronic mode of delivery that involves presentation of information through the internet
			patient portals	Internet mode of delivery that allows patients to interact and communicate with other patients having the same health condition, treatment, and so on. these patient portals are not controlled on the quality of information shared and are available on the Internet at all hours.
			website	Electronic mode of delivery that involves the intervention recipient interacting with a website.
		social media		Electronic mode of delivery defined as online communication channels disseminate information to a huge audience world wide
		broadcast media		Electronic mode of delivery that involves presentation of information through different mediums of media through a radio, television or billboard receiver.
			Radio	Electronic mode of delivery that involves presentation of audio information that is broadcast and received by a radio receive

TV	Electronic mode of delivery that involves presentation of information that is broadcast and displayed by television
Billboard	Electronic mode of delivery that involves presentation of information by an electronic screen positioned in a public location.

DEVELOPMENT AND JUSTIFICATION

Effective behaviour change interventions depend on a thorough evaluation and thoughtful selection of the mode of delivery of that specific intervention. The mode of delivery is defined as the 'physical or informational medium through which a given behaviour change intervention is provided'. To date, no ontology or other classification systems exist, to our knowledge, that categorize the mode of delivery of a medication adherence interventions. The Human Behaviour Change project, a collaborative research project aiming to create a 'Knowledge System' for using existing behaviour change interventions, is in process of creating ontologies to generate new insights about behaviour change. Within this project, scientists develop the Behaviour Change Intervention Ontology (BCIO), which is 'a set of definitions for entities and relationships used to describe behaviour change interventions, their contexts, effects and evaluations'. The modes of delivery attributes for the present repository were inspired from BCIO.

Upper Level	Sub-level 1	Sub-level 2	Sub-level 3
individual-level behaviour determinant			
	Capability		
		psychological capability	
			knowledge
			psychological skills
			memory, attention, decision
			behavioral regulation
		physical capability/skills	
	Opportunity		
		social opportunity/influences	
		physical opportunity/ environmental context and resources	
	Motivation		
		reflective motivation	
			role & identity

beliefs about capabilities

optimism

beliefs about consequences

intentions

goals

automatic motivation

reinforcement

emotion

Definition
modifiable causal influences on medication adherence that reside within an individual person
behaviour determinant referring to what an individual can do themselves to take medication as agreed
behaviour determinant referring to the mental capabilities that help individuals themselves take medication as agreed
psychological capability referring to what an individual knows about taking medication as agreed for their condition
psychological capability referring to what an individual is good at doing to take medication as agreed
psychological capability referring to the individual's abilities to retain information, to focus on specific things, and to choose between different things that help individuals take medication as agreed
psychological capability referring to what an individual can do themselves to keep track of taking medication and change their habitual ways of doing this
behaviour determinant referring to the physical capabilities that help the individual take medication as agreed
behaviour determinant referring to the conditions in the individual's external environment that can facilitate medication adherence
behaviour determinant referring to the conditions in the social environment
behaviour determinant referring to the conditions in the physical environment
behaviour determinant referring to what extent the individual feels driven/willing/energised to take medication as agreed
behaviour determinant referring to the extent of feeling motivated to take medication as agreed by thinking about it
reflective motivation referring to how the individual perceives what they need to do and how they are in their social personal and/or professional environment

reflective motivation referring to how the individual thinks about whether they can take their medication as agreed in various situations

reflective motivation referring to the confidence that the individual will succeed in their efforts to take medication and manage their condition

reflective motivation referring to what the individual thinks about the effects of taking medication on their health and/or other life goals

reflective motivation referring to whether the individual has taken a conscious decision to take medication as agreed

reflective motivation referring to how the individual represents in their mind the fact of taking medication as agreed, or other life goals related to their treatment

behaviour determinant referring to the extent of feeling motivated to take medication as agreed by emotions and impulses occurring automatically

automatic motivation referring to how taking medication as agreed is associated repeatedly to external stimuli that make it more likely to happen

automatic motivation referring to how taking medication as agreed is associated to individual's reactions to cope with personally significant stimuli

DEVELOPMENT AND JUSTIFICATION

Numerous factors influencing medication adherence have been identified in the research literature. The term commonly employed in research is 'determinants of behaviour', and an important distinction is made between modifiable and non-modifiable determinants, depending on whether these are amenable to change by an intervention within the specific context. Modifiable determinants are also named 'mechanisms of action' when they are part of a behaviour change intervention scenario as a process through which change is affected on a behaviour. Among the determinants studied and targeted by adherence support interventions/technologies, most are patient-related, although several may be related to the therapy/medication, condition, socio-economic context, or the healthcare system. Patient-related adherence determinants include for example the individual's beliefs about the medication, their health condition, their habits and ways of coping with changes in routine.

A substantial body of research has been conducted using a diverse range of concepts, theories and frameworks from health psychology and behavioural medicine. This research resulted in a vast number of constructs, not all relevant for adherence. Therefore, a selection was necessary for the purposes of the ENABLE repository. Recently, these have been systematized via literature review and expert consensus in the Capability, Opportunity, Motivation and Behaviour (COM-B) model, Behaviour Change Wheel and the Theoretical Domains framework, a group of related tools aimed to facilitate the description and development of interventions and the synthesis of scientific evidence on behaviour change. These tools have been increasingly used in health research, including in supporting medication adherence. Three main categories of individual determinants are proposed in the COM-B model, each with two subcategories: Capability (psychological and physical), Opportunity (social and physical), and Motivation (reflective and automatic). For each subcategory, up to six theoretical domains of behaviour determinants have been identified by grouping similar constructs from different sources, resulting in a total of 14 distinct domains. The terminology of behaviour determinants is currently evolving. Recently, 12 new categories have been added to the 14 TDF domains resulting in 26 mechanisms of action mapped onto the current classification of behaviour change techniques for evidence synthesis purposes. The Mechanisms of Action (MoA) Ontology is currently under development. Some determinant categories are named and structured differently in the MoA ontology version 1 as compared with COM-B and TDF structures, and the terminology is likely to continue to evolve in the following years. Therefore, we have adopted the COM-B/TDF classification, as it has been in use for research for the last years. Some simplifications have been applied from the structure proposed by Cane et al. (2012) to avoid duplication (i.e., the categories of role and identity and optimism were considered only in the reflective motivation category, although they can pertain also to automatic motivation); we kept the distinction between psychological skills and physical skills, as these are likely to be targeted separately in adherence technologies.

Upper Level	Sub-Level 1	Sub-Level 2	Definition
Acting on Capability			Group of behaviour change techniques aiming to influence what an individual can do themselves to take medication as agreed with the healthcare provider
	Feedback and monitoring		The technology includes options to record medication intake and its effects, and feed this information back to the user
		Biofeedback	The technology includes an option/activity to record physiological/biochemical effects of taking medication as agreed with the healthcare provider.
		Feedback or self-monitoring on behaviour	The technology includes an option/activity to monitor and feedback on adherence behaviours (by the medication users themselves or other people who can relay the information to them)
		Feedback or self-monitoring on outcomes	The technology includes an option/activity to monitor and feedback on a positive outcome of adherence behaviours (by the medication users themselves or other people who can relay the information to them)
	Repetition & substitution		The technology includes options/activities to perform certain actions repeatedly and systematically in order to enforce medication adherence behaviours and replace other behaviours not beneficial for medication adherence
		habit formation	The technology includes ways to prompt rehearsal and repetition of medication intake in the same context repeatedly at the planned time for intake, so that the context elicits adherence
		behavioral practice/ rehearsal	The technology includes ways to prompt practice or rehearsal of medication intake in a context or at a time when it may not be necessary, in order to increase adherence habit and skill
		graded tasks	The technology includes options to set easy-to-perform tasks related to medication intake, making them increasingly difficult until adherence becomes achievable in all situations
	Shaping knowledge		The technology includes options for the user to learn about how to take medication as agreed with the healthcare provider, what they can do themselves to stick to the schedule in difficult situations, and test different ways of doing this

Acting on Opportunity			Group of behaviour change techniques aiming to influence the conditions in the individual's external environment that can facilitate medication adherence
	Demonstration of behaviour		The technology includes an observable sample of how to take medication as agreed, directly in person or indirectly (video, pictures, drawings)
	Prompts & cues		The technology includes ways to prompt medication intake at the agreed time
	Restructuring the physical environment & adding objects		The technology includes advice on how to change the environment to make it easier to take medication as agreed with the healthcare provider.
	Identity		The technology includes ways of strengthening a positive identity that includes taking medication as agreed with the healthcare provider.
Acting on Motivation			Group of behaviour change techniques aiming to influence to what extent the individual feels driven/willing/energised to take medication as agreed with the healthcare provider.
	Goals and planning		The technology includes options to encourage setting goals related to adherence and planning to achieve them
		Action planning	The technology includes an option/activity for the user to plan concretely how they will take the medication.
		Discrepancy between current behaviour and goals	The technology includes an option/activity to compare the user's adherence-related goals with their current adherence behaviour
		Goal setting & reviewing (behaviour)	The technology includes an option/activity to set or agree on a goal in terms of an adherence behaviour, and review this goal in light of achievement
		Goal setting & reviewing (outcome)	The technology includes an option/activity to set or agree on a goal in terms of an outcome of adherence, and review this goal in light of achievement
		Problem solving	The technology includes an option/activity to identify barriers & facilitators of their own adherence and propose solutions to overcome / increase them
	pros & cons		The technology includes ways to identify and compare reasons for wanting or not wanting to take medication as agreed with the healthcare provider.

	Regulation		The technology includes advice and/or options/activities aiming to keep motivation for medication adherence within a range favourable for performing adherence-related behaviours.
		conserving mental resources	The technology includes advice on how to make taking medication less demanding for the person
		reducing negative emotions	The technology includes ways of reducing negative emotions in relation to taking medication
	Self-belief		The technology includes ways of increasing the person's confidence they can take medication as agreed with the healthcare provider.
	Imaginary reward		The technology includes advice on how to imagine correct performance of medication intake
Acting across domains			Group of behaviour change techniques aiming to influence determinants from more than one determinant group (capability, opportunity, motivation)
	Social support (emotional and practical)		The technology includes options to advise, arrange or provide social support (practical, emotional, other), or praise/reward taking medication as agreed with the healthcare provider.
	Social reward		The technology includes verbal/non-verbal rewards when the patient shows effort and/or progress in taking medication as agreed with the healthcare provider.
	Information about consequences		The technology includes information about consequences (health-related, emotional, social, environmental) of medication adherence (or non-adherence), and emphasise their relevance for the person

DEVELOPMENT AND JUSTIFICATION

To trigger/support change in a health behaviour like medication adherence, interventions (whether mediated by technologies or not) act by generating change in determinants of the target behaviour. They do so in the same way that medications act on improving health outcomes by triggering changes in pathophysiological mechanisms of the health condition they aim to treat. The 'active ingredients' for behavioural health interventions have been labelled behaviour change techniques (BCT). For example, a reminder set within a medication adherence app on the user's smartphone to prompt medication intake at the agreed time is an application of a BCT in the category 'Prompts & cues', that acts on the 'Opportunity' group of determinants as it modifies the conditions in the user's environment that can facilitate medication adherence.

Evidence on effects of these BCTs on different behaviours has been accumulating and has been recently systematized based on the BCT taxonomy, a consensus classification of 93 BCTs that organizes theoretical constructs in this field (ref). The BCT taxonomy is currently part of the Human Behaviour Change Project and interoperable with the models and ontologies used in the other descriptor groups. It has been used extensively in the last decade in intervention description, development, validation and implementation, as well as in evidence synthesis and training of healthcare professionals. However, not all techniques included in this taxonomy are relevant for medication adherence support. The ENABLE repository would need to include only BCTs relevant for adherence support technologies and be compatible with other tools used for behaviour change training and practice in healthcare systems.

Two applications of the BCT taxonomy to healthcare professional training on behaviour change simplify the structure and provide solutions for the ENABLE repository. The first, Cards for Change, is a simplified version of the taxonomy for development of training content for HCP behaviour change that has been used already in several countries as part of the Change Exchange Initiative (ref). It builds on a tool developed for coding training sessions in healthcare professional continuous education (ref) and includes the most used techniques in healthcare settings with examples of possible training activities. The second is the Train4health competency framework, a consensus-based framework for professionals who support self-management of chronic conditions in Europe developed by the Train4Health project, funded via the Erasmus+ programme (ref). The framework identified a set of 12 foundational competencies and 14 behaviour change competencies, including knowledge and abilities to identify relevant behaviours, intervention models, BCTs and apply these collaboratively to develop and implement self-management programmes. A panel of experts selected the most relevant BCTs for the 5 priority behaviours, including medication adherence support, physical activity, diet, smoking cessation and symptom monitoring and management.

We have therefore selected 24 categories of BCTs consistent with the selections operated by the Train4Health consortium and the Cards for Change team, to align the terminology with healthcare professionals training programmes that are currently using or will be developed in the future using these tools. Some BCT categories were merged due to common co-occurrence (e.g., feedback and monitoring; shaping knowledge techniques), and some BCTs are present in C4C but not in T4H since the former is more comprehensive than the latter. The initial ENABLE descriptor list includes only user-level BCTs (i.e., BCTs that can be included in technologies that provide support to medication users); if considered relevant, future versions can include HCP-level interventions (e.g., training programmes) or organisation/system-level BCTs. To align this set of descriptors with the ones referring to adherence determinants, we have grouped the 24 categories into 4 dimensions (i.e., acting on Capability, Opportunity, Motivation, cross domains), using the theoretical mapping described by Cane et al. and previously applied in evidence synthesis in health behaviour change. Mapping work is ongoing and likely to be updated with further iterations of these ontologies. We have therefore chosen the terms most used currently and expect back-compatibility in future versions.

It is important to note that a new classification by WHO is currently under development for health interventions which includes terminology for behavioural interventions: International Classification of Health Interventions (ICHI). Currently, ICHI is designed to be interoperable with the COM-B model via a series of extension codes. However, for describing categories of health interventions, the ICHI classification uses over 20 terms, different from the behaviour change literature, that cover measurement (Assessment, Testing), several broader categories on individual-level intervention

from the behaviour change literature, that cover measurement (Assessment, Testing), several broader categories on individual-level intervention (Training, Education, Advising, Counselling, Emotional support, Provision of products to support, Provision of peer support), as well as health system and societal level interventions (Providing opportunities for participation, Advocacy, Building partnerships, Public facilities, Environment modification, Capacity building, Awareness raising, Public health surveillance, Health alerts, Enactment and enforcement of legislation, Economic and non-economic incentives, Policy change, Other). Ensuring interoperability between ICHI and the BCIO ontologies is under discussion.

Upper level	Sub-level 1	Sub-level 2
health care professional		
	medical doctor	
		generalist medical practitioner
		specialist medical practitioner
	nursing professional	
	midwifery professional	
	pharmacist	
		community pharmacist
		hospital/clinical pharmacist
	dentist	
	associated health professional	
		community healthcare worker

health care assistant

psychosocial care professional

psychologist

Personal care worker

Personal provider

family member

parent or guardian

spouse or partner

other

carer

friend

peer

Definition
An intervention provider that applies scientific knowledge in medicine, nursing, midwifery, pharmacy, dentistry and/or health promotion to support patients in
A health professional that studies, diagnoses, treats and prevents illness, disease, injury and other physical and mental impairments.
A medical doctor that does not limit their practice to certain disease categories or methods of treatment, and may assume responsibility for the provision of continuing and comprehensive medical care to individuals, families and communities
A medical doctor that specializes in certain disease categories, types of patients or methods of treatment and may conduct medical education and research in their chosen areas of specialization.
A health professional that provides treatment, support and care services for people who are in need of nursing care due to theeffects of ageing, injury, illness or other physical or mental impairment, or potential risks to health.
A health professional that plans, manages, provides and evaluates midwifery care services before, during and after pregnancy and childbirth.
A health professional that stores, preserves, compounds and dispenses medicinal products and counsel on the proper use and adverse effects of drugs and medicines following prescriptions issued by medical doctors and other health professionals.
A pharmacist that practices in primary care/ community settings.
A pharmacist that practices in secondary care / hospital settings.
A health professional that diagnoses treats and prevents diseases, injuries and abnormalities of the teeth, mouth, jaws and associated tissues.
A health professional that performs technical and practical tasks to support diagnosis and treatment of illness, disease, injuries and impairments, and supports the implementation of health care usually established by medical, nursing and other health professionals
Associated health professional that provides health education, referral and follow-up, case management, basic preventive health care and home visiting services to specific communities.

Associated health professional that provides basic care services for the prevention and treatment of diseases and disorders, according to care plans and procedures established by medical, nursing or other health professionals.

An intervention provider that applies scientific knowledge in psychology, sociology and other social sciences to support individuals and families in a community in their well-being and life goals

A social professional that studies the mental processes and behaviourof human beings as individuals or in groups, and applies this knowledge to promote personal, social, educational or occupational adjustment and development

An intervention provider that delivers care, supervision and assistance for children, patients and elderly, convalescent or disabled persons in institutional and residential settings.

an intervention provider that is related to the person to whom the intervention is targeted through aspects of their personal lives.

A personal provider who is related to another person as they are descended from a common progenitor, related by marriage or other legal tie, or by a feeling of closeness.

A family member that is a mother, father or legal carer of the person to whom the intervention is targeted

A family member that is an individual who is married or in a committed relationship with the person to whom the intervention is targeted

A family member that is a child, sibling or in the extended family (e.g. uncle, aunt, nephew) with the person to whom the intervention is targeted

A personal provider who is an individual who cares, unpaid, for a friend or family member who is the person to whom the intervention is targeted

A personal provider who is an individual who is known, liked and trusted by the person to whom the intervention is targeted, typically exclusive of sexual or family relations

A personal provider who is described as similar to the person to whom the intervention is targeted on the basis of similarities in age, social status, gender, experience, health status

DEVELOPMENT AND JUSTIFICATION

The provider or source of intervention is a role played by a person, population or organization that provides/delivers a given intervention. This includes their occupational role, education, sociodemographic, knowledge, skills and any relatedness between them and the target population. In terms of medication adherence, the provider is often HCP. The quality of the HCP-patient relationships, especially communication skills, collaborative decision making, trust in the HCP and HCPs' cultural competences, are in correlation with patients' adherence. Several different professions of intervention providers were recognized as the most influential OR relevant in relation to medication adherence of patients using the Intervention Source Ontology Coding Guidelines and Gender, Sex, and Sexual Orientation (GSSO) ontology.

Upper level	Sub-level 1	Sub-level 2	Sub-level 3	Definition
Physical setting				Intervention setting that consists in a physical environment where the medication adherence technology is used.
	Residential facility			A physical setting that has at least one housing unit as part in which a person to whom the intervention is targeted lives.
		Household residence		Residential facility where a person to whom the intervention is targeted lives alone or with one or more persons.
			Residential care or assisted living	Household residence where many vulnerable persons live.
			Student residence	Household residence where many students live.
	Healthcare facility			A physical setting that is administered by a health care organisation for the purpose of providing health care to a patient population.
		Hospital facility		healthcare facility that is run by a hospital organisation and is the bearer of a hospital function.
		Doctor-led primary care facility		A healthcare facility led by doctors
		Care home facility		A healthcare facility that is run by a care home organization and is the bearer of a care home function
		Hospice facility		A healthcare facility that bears a function to provide healthcare to the sick or terminally ill
		Pharmacy facility		A healthcare facility whose function is to store, prepare, dispense and monitor the usage of pharmaceutical drugs among patients in a given area or encountered in a given healthcare provider organization
		Psychiatric facility		A healthcare facility designed and staffed to house and treat individuals that need assistance with mental health
		Community healthcare facility		A healthcare faclity providing healthcare services to people in a certain area.
		Dentist facility		A healthcare facility where dental healthcare is provided
	Educational facility			A physical setting in which formal education is provided to a student population

	Community facility		A physical setting used by a group of people living in the same area or having a particular characteristic in common
		Social centre or Community Hall facility	A community facility used for socialising by those living in a given area.
Virtual setting			Intervention setting that consists in a virtual environment where the medication adherence technology is used.
	Telemedicine		Virtual setting through which healthcare services are delivered by medical doctors
	Telepharmacy		Virtual setting through which healthcare services are delivered by pharmacists

DEVELOPMENT AND JUSTIFICATION

Implementation and behavioral science emphasize the importance of understanding and describing the environment in which a certain intervention is delivered as it can significantly influence its outcomes. In addition, not every intervention is applicable or transferable to every setting. Similar to the mode of delivery, we can distinguish between physical and virtual settings. Healthcare services may be provided in different healthcare facilities using different technologies and adherence intervention models. Thus, the efficacy of direct in-person models of adherence intervention may be different than indirect interventions such as electronic strategies. Some interventions may be applicable in both types of settings, or require a combination of physical and virtual settings in order to be performed. The classification was made using the Intervention Setting Ontology, which is a component of the Behaviour Change Interventions Ontology (BCIO).

Upper Level	Sub-Level 1	Sub-Level 2
D3.1.1 General quality indicators		
	ISO certification	
	Evidence from scientific evaluation	
		Research base on development
		Research base on effectiveness
		Ethical and legal aspects
	Development standards	
		Development process
		User-centered design process
		Conflict of Interest
		Updating of information sources
	Technological standards	
		Performance
		Data protection

		System integration testing
		Inter-device portability
D3.1.2 Research-related quality indicators		
	Theory base	
	Measurement validity	
		content validity
	Intervention validity	
		coherence of the intervention model
	Measurement reliability	
		Internal consistency
		Inter-rater reliability
		Test-retest reliability
D3.1.3 Policy-related quality indicators		
	Cost and economic evaluation	
		Cost-effectiveness

			Cost-utility
			Cost-consequence
			Cost-benefit
			Cost-minimisation
			Budget impact
			Country(ies) where evaluation performed
		Current use of the technology	
			Regulatory status
D3.1.4 Use-related quality indicators			
		Usability	
			Simplicity
			Cleanliness
			Intuitiveness
			Reliability

Satisfaction	
	Satisfaction test
Customisation	
	Customisation of language
Aesthetics	
Readability	

Sub-Level 3	Sub-Level 4
Quality of evidence on development	
Quality of evidence on effectiveness	
Usability tests	
Reliability of interactive components	
Design scalability of the technology	

Data encryption

Antivirus with supported maintenance

Data storage place

Data storage capacity

Protection against theft or physical attacks

face validity

language validation

target population validation

vs no intervention

vs other interventions

Authorisation status

Country(ies) where approved

Approval body(ies)

Indication(s) approved

Reimbursement status

Country(ies) where

Indication(s) reimbursed

Definition
Quality indicators that that evaluate MATech characteristics relevant for all stages of the technology development, adoption and use.
General QI referring to whether the MATech has obtained one or more ISO certification labels relevant for its content and purpose.
General QI referring to whether the MATech has been evaluated through the systematic, rigorous, and meticulous application of scientific methods, and the evidence obtained.
Evidence from scientific evaluation is available to support the design of the MATech.
Attribute of the research base on development referring to the "grade (or strength) of recommendation", decided based on levels of evidence (sometimes called hierarchy of evidence) assigned to studies based on the methodological quality of their design, validity, and applicability to patient care.
Evidence from scientific evaluation is available to support the effectiveness of the MATech (excluding cost-effectiveness, outlined in section D2.1.3 and implementation outcomes, outlined in section D3.2).
Attribute of the research base on effectiveness referring to the "grade (or strength) of recommendation", decided based on levels of evidence (sometimes called hierarchy of evidence) assigned to studies based on the methodological quality of their design, validity, and applicability to patient care.
Attribute of the scientific evaluation of the MATech referring to whether the research has ethical approval, has considered and addressed any risks for the target population, complies with the current laws on research on humans and data privacy and safety, and has shared information about how it meets these requirements.
General QI referring to whether the MATech has been developed according to standards established in the development of health technologies.
All development activities undertaken with respect to MATech are clearly described, such as activities related to preparation, development and optimization of product components as well as the manufacturing, validation and distribution process.
The MATech was developed in an iterative design process in which designers involved the target users and their needs in each phase of the design process. The users's requirements, objectives, and feedback were taken into account during the development process.
Usability tests were performed and the results are available (e.g., described or available on a link) with a statement, how the findings influenced the MATech.
The provider's conflicts of interest are clearly described, if any, to ensure trust and transparency.
Information sources are periodically verified (proven to still be correct and accurate) and updated (new information added or design changed).
General QI referring to whether a MATech corresponds to criteria commonly used to assess the technical functioning of electronic components, if applicable.
The MATech works fast and accurately without bugs or errors.
The interactive components (e.g. alarm system) are secure and these characteristics are maintained even when the system grows.
The MATech shows efficiency even with a large volume of users / data.
Collected data are properly protected to prevent sensible data leakage.

Encrypting takes a part of the data and translates it into a new form so that only people with access to the key can read it, in order to protect the confidentiality of digital data.

The MATech has software installed for data protection against online theft and attacks, and regularly revised to fulfil the function of acting against malicious code or programs.

Data storage on MATech devices is not connected to network to further ensure data safety against network attacks.

How much storage space is provided by the MATech to contain data.

The MATech has measures in place for protection against burglary, theft, vandalism and terrorism.

The developed MATech conforms to the requirements in terms of technical, privacy and security requirements of health care systems.

The MATech can be connected with several other devices.

Quality indicators that evaluate if the research on the MATech has been performed according to standards established in measurement and intervention research.

The MATech is developed based on theory, evidence, and/or theoretical frameworks.

The MATech measurement components measure exactly what they propose to measure (the used measure represents the intended variable)

Type of validity referring to the extent to which a measure in the MATech “covers” the construct of interest

Type of content validity referring to the extent to which a measurement method in the MATech appears “on its face” to measure the construct of interest.

Type of content validity referring to whether the MATech and corresponding materials were validated for the available languages.

Type of content validity referring to the whether the MATech was tested and validated for the target population.

The MATech intervention components have the potential to influence the behaviour determinants they target.

The use of behaviour change techniques in the intervention components of the MATech is evidence based, i.e. there is scientific evidence that the chosen techniques are likely to be effective in influencing the chosen behaviour determinants.

The MATech measurement components reproduce a measurement result consistently in time and space.

Type of measurement reliability referring to the consistency across items or indicators of the same construct

Type of measurement reliability referring to consistency across different researchers

Type of measurement reliability referring to the consistency over time

Quality indicators related to Health Technology Assessment (HTA) procedures and concepts that inform decision-making regarding implementation and use of health technologies.

an economic analysis has been performed to inform value-for-money judgements about the MATech with information about costs, health-related outcomes and economic efficiency

CEE that examines the costs and health outcomes of one or more interventions, to estimate how much it costs to gain a unit of a health outcome, like a life year gained or a death prevented.

Cost-effectiveness analysis where the control group is represented by a population receiving no intervention (treatment as usual)

Cost-effectiveness analysis where the control group is represented by a population receiving other interventions.

CEE in which the incremental cost of a technology from a particular point of view is compared to the incremental health improvement expressed in the unit of quality adjusted life years (QALYs)

CEE in which a wide range of costs and consequences (effects) of the technology is assessed and reported separately. It includes all types of effects, including health, non-health, negative and positive effects, both to patients and other parties (e.g., caregivers).

CEE consisting of a systematic process to sum the potential rewards expected from the technology and then subtract the total costs associated with that technology; some analysts also build models to assign a monetary value on intangible items.

CEE consisting of applying basic rules to determine what mix of labor and capital produces output at the lowest cost, i.e., what the most cost-effective method of delivering goods and services would be while maintaining a desired level of quality.

CEE that estimates the financial consequences of adopting a new technology which is usually performed in addition to a cost-effectiveness analysis; it evaluates whether the high-value intervention is affordable.

Healthcare system or country where the economic evaluation has been performed

Specifies the regulatory status (authorization and reimbursement) of the technology. These information are country or system specific, thus the repository also needs to specify where these indicators apply.

The stage in which the MATech is in the process of obtaining necessary authorisations and being considered for reimbursement by authorities in order to be adopted in routine practice in a health system or country.

HTA CUR indicator specifying whether the technology is approved for clinical use by an appropriate local regulator via marketing authorisation and/or CE marking.

Healthcare system or country where the technology has received authorization.

Name of the body which has issued the technology approval for clinical use in the respective country (eg., NICE)

Diagnoses, clinical conditions or social conditions for which the MATech has been approved for clinical use

HTA CUR indicator specifying whether the technology cost is fully or partially covered for the patient by a reimbursement authority (eg., NHS, insurance company)

Healthcare system or country where the technology is reimbursed.

Diagnoses, clinical conditions or social conditions for which the technology is reimbursed

Quality indicators that evaluate if the MATech meets users expectations and provides a pleasurable experience of interaction with the technology.

The MATech is easy to use, and easy to learn or understand, as assessed in objective ways (as opposed to user-friendliness, which is subjective).

The interface is not overly complex, but instead is straightforward, providing quick access to common features or commands.

The interface is well-organized, making it easy to locate different tools and options.

The interface makes sense to the average user, requires minimal explanation for use, and provides clear explanations for how to use it.

The MATech is reliable and does not malfunction or crash.

The level of satisfaction of the end user with the MATech has been explored and found appropriate.

The manner in which the level of satisfaction from the patient with the MATech was assessed, e.g. online or telephone survey about satisfaction made by research staff.

The MATech or some parts of it can be customized to the needs of the individual user.

The MATech gives the option to customize language to adapt to different users.

The MATech has been evaluated as aesthetic (size, layout, graphic, font size etc. support the use of MATech) in a research project or external review.

The text included in the MATech is written in a style easy to understand, i.e. readers are able to recognize (decode) the words as well as comprehend the meaning of the text.

DEVELOPMENT AND JUSTIFICATION

Quality indicators are standardized, evidence-based, and measurable items for monitoring and evaluating the quality of healthcare performance. With their statement about the structure, process, or outcomes of care, review criteria and standards can be developed to help operationalize quality indicators.

No classification or list of criteria could be identified in the literature that provides a formal description of quality indicators specific to medication adherence technologies. However, several related sets of criteria refer to ehealth applications in general -such as the Mobile Application Rating Scale (MARS)- or guide reporting of research on ehealth applications -such as the Consort-EHEALTH guideline. These checklists and guidelines include relevant concepts of technology quality but are neither comprehensive nor specific to medication adherence technologies. MATech represent an important type of health technology and therefore should adopt HTA procedures and concepts to inform decision-making regarding their implementation and use. Two HTA domains were considered relevant for MATech: (i) Cost and economic evaluation (ECO) informs value-for-money appraisal with information about costs, health-related outcomes and economic efficiency; (ii) Current use of technology (CUR), specifies the authorization and reimbursement status of the technology. The indicators in both domains are often country or system specific, thus the repository also needs to specify where these indicators apply. Other HTA domains include assessment elements that are either captured in other attribute groups or not applicable to MATech.

Therefore, we decided to develop a checklist for assessing the quality of ehealth applications, building on the work of an ongoing project involving a systematic review of existing items and criteria in the literature. We synthesized the quality indicators identified in this work into a comprehensive list and adapted the items to be appropriate for medication adherence technologies for the ENABLE repository. This new list of items was discussed, adjusted, concretized, and refined in several rounds with SC members, and additional constructs were generated until consensus was reached.

As MATech follow different stages of development and implementation and need to meet quality standards specific or common to all stages, from research to adoption by decision-makers to routine use in specific settings, we decided to group quality indicators according to their relevance to these stages. We considered some indicators relevant to all stages, while others would be likely to be more research-related, policy-related, or use-related.

Upper Level	Sub-Level 1	Definition
implementation outcome		characteristic of the techology regarding its implementability in clinical practice, as supported by evidence
	Acceptability	Implementation outcome referring to whether stakeholders reported satisfaction with various features of the technology and the experience of using it to support medication adherence
	Feasibility	Implementation outcome referring to whether stakeholders perceived the technology as practical and fit for use in supporting medication adherence
	Sustainability	Implementation outcome referring to whether stakeholders perceived the technology as appropriate for routine sustained use in supporting medication adherence
implementation strategy		characteristic of the technology that facilitate implementation and maitenance of the technology in a setting
	training	Implementation strategy referring to activities to teach stakeholders about the technology and how to use it and integrate in the medication adherence support processes
	educational materials	Implementation strategy referring to materials stakeholders may consult to learn about the technology and how to use it and integrate in the medication adherence support processes
	funding	Implementation strategy referring to financial strategies and/or additional costs to facilitate adoption of the technology into medication adherence support practice
	expertise sharing	Implementation strategy referring to information from previous implementations on what helped adopt the technology into medication adherence support practice
	technical assistance	Implementation strategy referring to systems to support implementation of the technology into medication support practice
	consultation	Implementation strategy referring to accessing direct support from experts for the implementation of the technology into medication support practice

accreditation & legal approvals	Implementation strategy referring to credentials and/or licensing to acquire or prove to be able to use the technology in a setting in the conditions necessary for optimal safety and effectiveness
collaborations	Implementation strategy referring to involving multiple institutions in delivering the medication adherence support solution that uses the technology
access to additional resources	Implementation strategy referring to access to data, space, laboratory facilities

DEVELOPMENT AND JUSTIFICATION

Medication adherence support technologies (as medications themselves) work only if they are adopted by individual users or by a group of healthcare providers and users in a healthcare setting, if their use is maintained for the duration in which they are designed to be used to bring about the expected benefits, and if they are used as intended for this duration. Evidence in implementation sciences is accumulating in recent years on how to facilitate the adoption and use of technologies (or interventions) in real-world settings. This question needs to be addressed separately, as most interventions are developed in contexts not representative for real-world situations and many additional challenges occur, particularly when scaling-up such interventions within care delivery. To move from research/development settings into clinical care, researchers need to consider implementation challenges already from the technology development stage.

The field of implementation sciences is relatively new, and only recently efforts have been made to structure terminology and propose concepts to be used in a standardized way. To ascertain whether the implementation of an intervention has been successful, specific consideration needs to be given to implementation outcomes, i.e., "the effects of deliberate and purposive actions to implement new treatments, practices, and services", which are intermediary to the service and client outcomes envisaged by an intervention. Among the 8 outcomes proposed in the taxonomy of Proctor et al (2011) following literature review and expert panel discussions, some refer primarily to the process of implementation and use (e.g. adoption, penetration, fidelity) and to the application of the technology is a specific setting (appropriateness, implementation cost), others can be construed as mostly referring to the technology itself across settings and were selected for the ENABLE repository. The Expert Recommendations for Implementing Change (ERIC) project has compiled a list of 73 implementation strategies, i.e., "methods or techniques used to enhance the adoption, implementation, and sustainability of a clinical program or practice". This taxonomy, the result of a Delphi expert consensus process with input from numerous stakeholders, achieves a similar goal of aligning language and provides a comprehensive range of options from which implementers may choose strategies to boost the scaling-up of their innovation in a clinical setting. As for implementation outcomes, many of these strategies refer to the process of implementation itself and are highly dependent on the setting; thus, an implementation team may decide to start with assessing local needs, to conduct iterative tests of change, to create new clinical teams, to develop and implement tools for quality monitoring, etc. in response to barriers or facilitators identified during project planning, However, some implementation strategies are also dependent on the technology itself and can be addressed at least partly in the development and implementation of the technology across settings; we have therefore examined the ERIC compilation and selected strategies that could be technology-specific and addressed across settings. The conceptual structuring of this field is in constant evolution; however, these two classifications have already gained notoriety and are likely to be used by stakeholders to generate and use evidence on medication adherence technologies.

Following this preliminary work on the ENABLE repository, three implementation outcomes were selected and adapted from the taxonomy of implementation outcomes to target early-, mid-, and late-implementation phases. They refer to whether stakeholders are satisfied with the technology and using it (acceptability), whether they perceive it as practical and fit for use (feasibility) and appropriate for routine use on the long term (sustainability).

Eight implementation strategies were selected and adapted from the ERIC compilation of implementation strategies, following the interventienet.nl format. Thus, the ENABLE repository will aim to collect information on whether there is any information available, any benefit/need, and any support already provided for the following topics: training stakeholders and users for working with the technology, accessing education materials about the technology, any financial strategies or additional costs applicable, any expertise to share from previous implementations, any consultation to access for support in implementation/use, any accreditation or legal approvals necessary, and whether the involvement of multiple institutions is needed for implementing the technology into clinical care.

ENABLE Repository Delphi survey - study information letter

What is this study about?

Adherence to medication has been found to be suboptimal in numerous chronic conditions and to have a negative impact on chronic disease management, patient's general health status, quality of life and working abilities as well as health care costs and waste. Numerous technologies exist to support medication adherence, yet few are implemented into practice. An online interactive repository of available technologies may facilitate their selection and adoption by different stakeholders. Developing such repository is among the main tasks of the ENABLE COST Action (CA19132), within the remit of Working Group 2. To meet this challenge the ENABLE Action includes a large interdisciplinary network of experts in medication adherence from 39 European countries and has initiated several activities towards these goals. A definition of medication adherence technologies and a framework of attributes were developed. The framework was structured into three domains (product and provider information, medication adherence descriptors and evaluation and implementation) branching in attribute groups, which branch further into sublevels with related labels and definitions.

What to expect from study participation?

The proposed definition and framework will be evaluated in a real-time online Delphi study by stakeholders from 39 countries with research, practice, policy, patient representation and technology development backgrounds. It is expected that you and other invited stakeholders evaluate the proposed the relevance, clarity and completeness of the definition and repository attributes. All participants have multiple opportunities to reconsider their evaluations based on aggregated feedback updated in real-time.

Participants are invited to rate the degree of relevance and clarity of the proposed definition of medication adherence technologies, and of each attribute group, by placing a dot on a 2D-grid; the position of the dot on the vertical axis indicates clarity (low to high = bottom to top), and its position on the horizontal axis indicates relevance (low to high = left to right). Participants are encouraged to provide their comments and suggestions (anonymously) on the comments section and engage with other participants' comments.

We will stop the survey when a predefined number of participants will respond, and when stability of responses will be reached. We will summarize the results descriptively and compare evaluations across stakeholder groups and countries. We will quantify agreement among stakeholders on proposed attribute groups using the IPRAS analysis technique from RAND/UCLA Appropriateness Method.

COST is supported by the European Commission Framework Programme of the European Union

How to participate?

Firstly, by this email we extended our invitation to you and are asking for authorization to use your email within the scope of this study. If after considering this information you agree to participate, please access directly the link provided in the email sent from the eDelphi.org. You will be formally asked about your consent to participate when you will access the survey after a brief introduction, and the questions will appear only once you will consent to this study.

How are data collected and stored?

For this study it is necessary to collect some personal data. This includes your name and email address, as well as your age, gender, field of work/expertise, country, education level and the role of your participation with years of experience in it (researcher/academic; healthcare practitioner; policy/decision maker; patient representation; eHealth/IT specialist). Your name and email address are not linked to other data you provide by answering the survey. The personal data will not be visible to other respondents. The personal data used for conducting this study will be stored until the end of the COST Action ENABLE (October 2024) and then erased.

Ethical and data protection approvals

This study obtained ethics approval from Malaga Regional Research Ethics Committee in April 2021. In addition, the Delphi protocol was determined as compliant regarding data protection and security by Data Protection Officer from University of Basel.

For more information about your rights on data processing, and further questions about the project please contact the ENABLE-R Delphi at wg2enablecost@gmail.com.

On behalf of the ENABLE WG2 Steering Committee,

Alex Dima and Urska Nabergoj Makovec

COST is supported by the European Union Framework Programme of the European Union

Summary of the Delphi survey

Welcome

Instructions for the Delphi survey (2 pages)

Agreement with the GDPR statement

Demographic information (gender, age, country, education, professional field)

Through which perspective are you answering today?

	Research/education professional	Healthcare practitioner	Policy/decision makers	Patient perspective	eHealth/ IT specialist
Less than 5 years experience					
10 to <15 years experience					
15 to <20 years experience					
20 to <30 years experience					
More than 30 years experience					

What is a "medication adherence technology"?

For the purpose of this repository, we propose the following definition: **"Medication Adherence Technologies (MATech) are devices, procedures or systems developed based on evidence to support patients to take their medications as agreed with the healthcare providers (i.e. to initiate, implement, and persist with the medication regimen)."**

1) Please rate your level of agreement with the proposed MATech definition (X axis).
2) Please rate the CLARITY of the MATech definition (Y axis).

Detailed explanation of the definition and repository scope:

- **devices, procedures or systems** emphasize the inclusion of all technologies, irrespective of their mode of delivery (whether based on electronic or printed supports, delivered through human interaction, or a combination of these) with the aim to construct a comprehensive repository in which users can identify diverse technologies to fit their potentially diverse needs.
- **developed based on evidence** encompass the requirement of evidence/research that supports at least a potential contribution to either measurement or intervention on medication adherence (e.g., validation study on measurement of medication adherence, or pilot study with medication adherence among outcomes). Thus, technologies that are not (yet) supported by evidence (e.g., are in earlier stages of development and testing), or clinical practice protocols without an evidence base on at least one aspect (safety, efficacy, effectiveness, cost-effectiveness, appropriateness, social and ethical values or quality), will not be (yet) included in the repository until such evidence is produced and reported.
- **support patients to take their medications as agreed with the healthcare providers (i.e., to initiate, implement, and persist with the medication regimen)** encompass the contribution of the technology to medication adherence management – either directly in patients' self-management, or by supporting professionals to offer such services to patients through all phases of medication adherence. Thus, technologies that focus on other medication management goals, but do not target adherence specifically would be out of scope for this repository.

The MATech definition and scope of the repository is based on the WHO definition of health technologies, the WHO publication "Adherence to long-term therapies: evidence for action", the ABC taxonomy and the European Commission definition of best practice.

D1.1 Product and provider information

The product and provider domain entails basic information about the product and provider organization as well as the description of the repository entry and source of information.

1) Please rate the RELEVANCE of this attribute group (X axis).
2) Please rate the CLARITY of this attribute group (Y axis).

Further explanation:
Domain 1 consists of one attribute group and includes the attributes for the description of basic product and manufacturer/developer information, as follows:

1. **Product** is a device, procedure or system, that could be used to manage adherence to medication described by its name, brand, type, release date, ...
2. **Provider organization** is the organization that produces and/or makes the product available for users described by its name, type, domain activity, contact details...
3. **Repository entry** is a description of a health technology by a repository author account (ID, date of entry, update, verification).
4. **Author of the product description** is a person or group of persons who enters information about at least one MATech in the ENABLE-R database (ID, name, date, contact details).

The definitions of domain 1 are based on the ITEMAS ontology. For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

Table of contents for Domain 2 – medication adherence descriptors

D2.1 Target use scenario

Target use scenario is the type of common adherence management activities that the technology is intended to be used for (i.e., for self-management of adherence or support service use).

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation:

Target use scenario entails:

1. **Adherence self-management** is the scenario in which the technology is used for adherence self-management activities and can be further defined by:
    - Person in the healthcare environment (*patient or caregiver*)
    - Patient age group (*adult, adolescent, child, infant*)
    - Patient functional status (*mental functions, sensory functions, movement-related functions*)
    - Patient literacy (health literacy, including medication literacy)
    - Patient polypharmacy
    - Patient multimorbidity

2. **Adherence support use** is the scenario in which the technology is used for activities supporting taking medication in a health/social care provision setting and can be further specified by the following user types:
    - Professional health and social care provider
    - Health (system) manager

The definitions of target use scenarios are based on several taxonomies -SNOMED-CT, and WHO International Classification of Functioning, Disability and Health (ICF), and Digital Health Interventions (DHI)- and research literature sources. For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

D2.2 Target health conditions

Target health conditions are the type of diseases or health problems the technology is intended for.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation:

Target health conditions entail:

1. Blood
2. Cancer and neoplasms
3. Cardiovascular
4. Congenital disorder
5. Ear
6. Eye
7. Infection

8. Inflammatory and immune system
9. Injuries and accidents
10. Mental health
11. Metabolic and endocrine
12. Musculoskeletal
13. Neurological
14. Oral and gastrointestinal
15. Renal and urogenital
16. Reproductive health and childbirth
17. Respiratory
18. Skin
19. Stroke
20. Generic health relevance

The definitions of target health conditions are based on The International Classification of Disease (ICD-11) and The Health Research Classification System (HRCS) from the UK clinical research association. For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

D2.3. Medication regimen

Medication regimen attributes are the prescribed schematic form/therapeutic plan of medication therapy that the technology is intended for.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation:

Medication regimen attributes entail:

1. **Type of intention** as the purpose for which the medication is prescribed (*e.g., preventive or therapeutic*).
2. **Duration of treatment** presents the intended interval of treatment and relates to the clinical course and disease conditions (*e.g., short or long-term*).
3. **Route of administration** is the route in which medications/doses are administered to unfold pharmacological effects (*e.g., oral, inhaled, injections/subcutaneous, infusion/parenteral, patches, topical*).
4. **Number of monitored medications** defines how many distinct medications are monitored by the technology, if applicable (*e.g., single medication, multiple medication*).
5. **Prescribed dosing frequency** defines the dose-taking patterns recommended for medicines administration, in which doses should be taken at defined time intervals over a defined time period (*e.g., once-daily, multiple daily dosing at fixed intervals, once per week dosing, multiple dosing per week in fixed intervals, dose adjustment recommendations*).

The definitions of medication regimen attributes are based on several taxonomies: SNOMED-CT; National Cancer Institute Thesaurus (NCIT) and Medical Subject Headings (MeSH). For a more detailed view of the respective sub-levels with lables and definitions please check the interactive graph or the Excel file under supporting information.

D2.4.1. Phase of medication adherence

A medication adherence phase is a time interval between the prescription start and end dates that is behaviourally (i.e., linked with specific determinants and outcomes) and metrically (i.e., requires specific estimation methods) distinct.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation

Medication adherence phases include

1. **Initiation** is the phase of adherence that covers the start of a prescribed treatment, i.e., the period from when the prescription is issues to the first dose taken (i.e., the initiation event)
2. **Implementation** is the phase of adherence from the initiation until the last dose taken during which one can estimate the extent to which the patient's dose taking and timing are linked to the prescribed dosing regimen.
3. **Discontinuation (Persistence)** is the phase of adherence that refers to the end of treatment execution and covers the period until last dose is taken, e.g. end of therapy or termination by patient. Persistence is the period between initiation and discontinuation.

The definitions of adherence management are based on the ABC Taxonomy. For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

D2.4.2.A Monitoring/measurement type of management

Medication adherence monitoring, or measurement, is type of adherence management that refers to estimating (repeatedly) medication adherence behaviours, determinants, and/or outcomes.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation

Medication adherence monitoring/measurement entails:

1. **Measurement method** is a way in which information is gathered and summarized by the technology about the patient's medication adherence. It is further specified into the following:
   - **Direct observation method** is a measurement method consisting in observing medication intake directly.
   - **Pill count method** is a measurement method consisting in calculating left over pills in containers/blisters at a specific time point.
   - **Self-report method** is a measurement method using data reported by patients or caregivers about themselves (*e.g., diary, questionnaire, interview/consultation*).
   - **Electronic monitoring method** is a measurement method using data from devices that record medication taking events electronically (*e.g., smart packages, smart pill, digital event record system*).
   - **Electronic healthcare database method** is a measurement method using routinely collected data as part of a longitudinal healthcare process (*e.g., electronic medical records, claims/dispensing, record linkage system*).
   - **Laboratory method** is a measurement method based on clinical assessment through invasive procedure (*e.g., measuring drug concentration, biomarker or treatment response in samples from body fluids*).

2. **Measurement target** is a component of the adherence causal (logic) model measured by the technology. It is further defined by:
   - **Determinant measure** is measurement targeting causal influences on the behaviour that can be modifiable (amenable to intervention with a medication adherence technology).

- **Behaviour measure** is measurement targeting a self-management behaviour (*e.g., adherence, diet, physical activity, tobacco use, symptom monitoring and management*).
- **Outcome measure** is the measurement targeting the effects of the behaviour or change of behaviour on the patient's status (*e.g., health outcome, quality of life*).

The definition of adherence monitoring/measurement is based on the ABC Taxonomy. The definitions of measurement methods and targets are based on several taxonomies -SNOMED-CT, the Train4Health (T4H) behaviour change competency framework and the behaviour change intervention ontology (BCIO)-, as well as scientific literature and the methodological expertise of the repository Steering Committee. For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

D2.4.2.B Support/intervention type of management

Medication adherence support and/or intervention is a type of adherence management that refers to generating change in medication adherence determinants and thus behaviours and outcomes.

1. **Please rate the RELEVANCE of this attribute (X axis).**
2. **Please rate the CLARITY of this attribute (Y axis).**

Attribute groups further describing medication adherence support/intervention type of management are presented for your review in the next pages.

The definitions of adherence management types are based on the ABC Taxonomy.

D2.4.2.B.1 Intervention modes of delivery

Intervention modes of delivery are the ways used to deliver a medication adherence intervention.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation

Intervention modes of delivery entails:

1. **Printed material** is the mode of delivery involving use of printed material (e.*g., brochure or printed media such as poster, newspaper/leaflet*)
2. **Human interaction** is the mode of delivery involving a person as intervention source who interacts with an intervention recipient (*e.g., face to face consultations or network/patient groups*)
3. **Electronic mode** is the mode involving electronic technology in the presentation of information or the mode of motivation to an intervention recipient (*e.g., smartphone/tablet, wearable electronic device like smart box, smart inhaler, smart tube, smart button or digital media like internet, social media, broadcast media, billboard*).

The definitions of intervention modes of delivery are based on the Behaviour Change Intervention Ontology (BCIO), specifically a taxonomy of mode of delivery of behaviour change interventions (BCI). For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

D2.4.2.B.2 Target behaviour determinants

Target behaviour determinants are causal influences on medication adherence that can be modifiable (amenable to intervention with a medication adherence technology).

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation

Target behaviour determinants entails:

1. **Capability** is a group of determinants referring to what an individual can do themselves to take medication as agreed with the healthcare provider (*e.g., psychological/cognitive capability or physical capability/skills*)
2. **Opportunity** is a group of determinants referring to the conditions in the individual's external environment that can facilitate medication adherence (*e.g., social opportunity/influences or physical opportunity/environmental context and resources*)
3. **Motivation** is a group of determinants referring to what extent the individual feels driven/willing/energized to take medication as agreed with the healthcare provider (*e.g., reflective motivation or automatic motivation*)

The definitions of target behaviour determinants are based on the Capability, Opportunity, Motivation and Behaviour (COM-B) model, the Theoretical Domains Framework (TDF) and the Behaviour Change Intervention Ontology (BCIO), specifically The Mechanisms of Action (MoA) Ontology currently in development. For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

D2.4.2.B.3 Behaviour change techniques

Behaviour change techniques (BCTs) are options/activities included in the technology that aim to influence determinants (barriers and facilitators) of medication adherence behaviours.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation

BCTs entails:

1. **BCTs acting on capability:**
    - **feedback and monitoring** means the technology includes options to record medication intake and its effects and feed this info back to the user (*e.g., biofeedback, feedback or self-monitoring on behaviour, feedback or self-monitoring on outcomes*).
    - **repetition and substitution** means the technology includes options/activities to perform certain actions repeatedly and systematically in order to enforce medication adherence behaviours and replace other behaviours not beneficial for medication adherence (*e.g., habit formation, behavioural practice, graded tasks*).
    - **shaping knowledge** means the technology includes options for the user to learn about how to take medication as agreed with the healthcare provider, what they can do themselves to stick to the schedule in difficult situations, and test different ways of doing this.

2. **BCTs acting on opportunity:**
   - **demonstration of behaviour** means the technology includes an observable sample of how to take medication as agreed with the healthcare provider, directly in person or indirectly (video, pictures, drawings).
   - **prompts & cues** means the technology includes ways to prompt medication intake at the agreed time. restructuring the physical environment & adding objects means the technology includes advice on how to change the environment to make it easier to take medication as agreed with the healthcare provider.
   - **identity** means the technology includes ways of strengthening a positive identity that includes taking medications agreed with the healthcare provider.

3. **BCTs acting on motivation:**
   - **goals and planning** means the technology includes options to encourage setting goals related to adherence and planning to achieve them (*e.g., action planning, discrepancy between behaviour and goals, goals setting and reviewing, problem solving).*
   - **pros & cons** means the technology includes ways to identify and compare reasons for wanting or not wanting to take medication as agreed with the healthcare provider.
   - **regulation** means the technology includes advice and/or options/activities aiming to keep motivation for medication adherence within a range favourable for performing adherence-related behaviours (*e.g., conserving mental resources, reducing negative emotions*).
   - **self-belief means** the technology includes ways of increasing the person's confidence they can take medication as agreed with the healthcare provider.
   - **imaginary reward** means the technology includes advice on how to imagine correct performance of medication intake.

4. **BCTs acting across all three determinant groups:**
   - **social support** means the technology includes options to advise, arrange or provide social support (practical, emotional, other), or praise/reward taking medication as agreed with the healthcare provider. social reward means the technology includes verbal/non-verbal rewards when the patient shows effort and/or progress in taking medication as agreed with the healthcare provider.
   - **information about consequences** means the technology includes information about consequences (health-related, emotional, social, environmental) of medication adherence (or non-adherence) and emphasize their relevance for the person.

The definitions of behaviour change techniques are based on the Capability, Opportunity, Motivation and Behaviour (COM-B) model, the Theoretical Domains Framework (TDF), the Behaviour Change Techniques (BCT) taxonomy v1, and the Behaviour Change Intervention Ontology (BCIO). For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

D2.4.2.B.4 Intervention provider

Intervention provider is a role played by a person who uses the technology to assist the patient in their self-management of medication adherence.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation

Intervention provider entails:

1. **Health care professional** is an intervention provider that applies scientific knowledge in medicine, nursing, midwifery, pharmacy, dentistry and/or health promotion to support patients in managing their health (*e.g., medical doctor, nursing professional, pharmacist, dentist, associated health professional*).
2. **Psychosocial care professional** is an intervention provider that applies scientific knowledge in psychology, sociology and other social sciences to support individual and families in a community in their well-being and life goals (*e.g., psychologist*).
3. **Personal care worker** is an intervention provider that delivers care, supervision and assistance for children, patients and elderly, convalescent or disabled persons in institutional and residential settings.
4. **Personal provider** is an intervention provider that is related to the person to whom the intervention is targeted through aspects of their personal lives (*e.g., family member, carer, friend, peer*).

The definitions of the intervention provider attributes are based on several taxonomies: BCIO, in particular the Intervention Source Ontology, and Gender, Sex and Sexual Orientation Ontology (GSSO). For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

D2.4.2.B.5 Intervention setting

Intervention setting is the social and physical environment in which the technology is or can be used to manage medication adherence.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation

Intervention setting entails:

Physical setting is an intervention setting that consists in a physical environment where the medication adherence technology is used (*e.g., residential facility, healthcare facility, educational facility, community facility*).

Virtual setting is an intervention setting that consists in a virtual environment where the medication adherence technology is used (*e.g., telemedicine, telepharmacy*).

An intervention can be applied or applicable to one type of settings, or to both.

The definitions of the intervention setting attributes group are based on the BCIO, in particular the Intervention Setting Ontology. For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

Table of contents for Domain 3 – evaluation and implementation

D3.1.1.A ISO certification

ISO certification is a general quality indicator referring to whether the MATech has obtained one or more ISO certification labels relevant for its content and purpose.

1. **Please rate the RELEVANCE of this attribute (X axis).**
2. **Please rate the CLARITY of this attribute (Y axis).**

The definitions of quality indicators are based on a checklist of e-health quality criteria (under development), Mobile Application Rating Scale (MARS), and the Consort-EHEALTH guideline.

D3.1.1.B Evidence from scientific evaluation

Evidence from scientific evaluation is a group of general quality indicators referring to whether the evaluation of MATech has been performed through the systematic, rigorous, and meticulous application of scientific methods, and the evidence obtained.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation

The evidence from scientific evaluation entails:

1. **Research on development** means evidence from scientific evaluation is available to support the design of the MATech. This also encompasses the classification of quality of the presented evidence.
2. **Research on effectiveness** means evidence from scientific evaluation is available to support the effectiveness of the MATech (excluding cost-effectiveness, outlined in section D2.1.3 and implementation outcomes, outlined in section D3.2). This also encompasses the classification of quality of the presented evidence.
3. **Ethical and legal aspects** means the MATech research has ethical approval, has considered and addressed any risks for the target population, complies with the current laws on research on humans and data privacy and safety, and has shared information about how it meets these requirements.

The definitions of quality indicators are based on a checklist of e-health quality criteria (under development), the Mobile Application Rating Scale (MARS), and the Consort-EHEALTH guidelines. For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

D3.1.1.C Development standards

Development standards are a group of general quality indicators referring to whether the MATech has been developed according to standards established in the development of health technologies.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation

The development standards entail:

1. **Development process** means all development activities undertaken with respect to MATech are clearly described, such as activities related to preparation, development and optimization of product components as well as the manufacturing, validation and distribution process of the MATech.
2. **User-centred design process** means the MATech was developed in an iterative design process in which designers involved the target users and their needs in each phase of the design process. The users' requirements, objectives, and feedback were taken into account during the development process.
3. **Conflict of interest** means the provider's conflict of interests are clearly described to assure trust and transparency.
4. **Updates of information sources** means information sources are periodically verified (proven to still be correct and accurate) and updated (new information added or design changed).

The definitions of quality indicators are based on a checklist of e-health quality criteria (under development), Mobile Application Rating Scale (MARS), Consort-EHEALTH guideline. For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

D3.1.1.D Technological standards

Technological standards are a group of general quality indicators referring to whether a MATech corresponds to criteria commonly used to assess the technical functioning of electronic/digital components, if applicable.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation

The technological standards entail:

1. **Performance** - the MATech works fast and accurately without bugs or errors (*e.g., reliability of the interactive components, design scalability*).
2. **Data protection** - collected data is properly protected to prevent sensible data leakage (*e.g., data encryptions, antivirus supported maintenance, data storage place and capacity and protection against theft or physical attacks*).
3. **System integration** - evidence of MATech meeting the technical, privacy and security requirements of health care systems.
4. **Inter-devices portability** - the MATech can be connected with several devices.

The definitions of quality indicators are based on a checklist of e-health quality criteria (under development), Mobile Application Rating Scale (MARS), Consort-EHEALTH guideline. For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

D3.1.2 Research-related quality indicators

Quality indicators that evaluate if the research on the MATech has been performed according to standards established in measurement and intervention research.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation

The research-related quality indicators entail:

1. **Theory base** means the MATech is developed based on theory, evidence, theoretical framework.
2. **Validity of measurement** means the MATech is valid for certain conditions, populations, etc. (content validity)
3. **Validity of intervention** means the use of BCTs in the MATech is evidence based, i.e., there is scientific evidence that the chosen BCTs are likely to be effective in influencing the chosen behaviour determinants.
4. **Reliability of measurement** means the MATech shows a high test-retest reliability, internal consistency, and inter-rater reliability.

The definitions of quality indicators are based on a checklist of e-health quality criteria (under development), Mobile Application Rating Scale (MARS), Consort-EHEALTH guideline. For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

D3.1.3 Policy-related quality indicators

Quality indicators related to Health Technology Assessment (HTA) procedures and concepts that inform decision-making regarding implementation and use of health technologies.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation

The policy-related quality indicators entail:

1. **Economic and cost evaluation (ECO**) means an economic analysis has been performed to inform value-for-money judgements about the MATech with information about costs, health-related outcomes and economic efficiency. It entails several types of analysis (e.g., cost-effectiveness, cost-utility, cost-benefit, budget impact), which can be country or system specific, thus the repository also needs to specify where these indicators apply.
2. **Current use of technology (CUR)** specifies the regulatory status (authorization and reimbursement) of the technology. These information are country or system specific, thus the repository also needs to specify where these indicators apply.

The definitions of policy-related quality indicators are based on Health Technology Assessment (HTA) Core Model, version 3.0 and O'Rourke et al. (2020). "The new definition of health technology assessment". For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

D3.1.4 Use-related quality indicators

Quality indicators that evaluate if the MATech use meets users' expectations and provides a pleasurable experience of interaction with the technology.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation

The use-related quality indicators entail:

1. **Usability** means MATech qualities such as simplicity, organization, intuitiveness and reliability. High usability is indicated when MATech is simple, well organized, intuitive and reliable.
2. **Satisfaction** means satisfaction with MATech assesments were performed to control the level of satisfaction of the end user.
3. **Customization** means the MATech or some parts of it can be customized to the needs of the individual user.
4. **Aesthetics** is the perception of the product, which can be described as aesthetic (size, layout, graphic, font size etc.) as this was evaluated in a research project or external review.
5. **Readability** means the ease of understanding or comprehension achieved by the style of writing. The reader must be able to recognize (decode) the words in the medical device patient labelling as well as comprehend the meaning of the text.

The definitions of quality indicators are based on a checklist of e-health quality criteria (under development), the Mobile Application Rating Scale (MARS), and the Consort-EHEALTH guideline. For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

D3.2.1 Implementation outcomes

Implementation outcomes are characteristics of the technology regarding its implementability in clinical practice, as supported by evidence.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation

Implementation outcomes entail:

Acceptability means whether stakeholders reported satisfaction with various features of the technology and the experience of using it to support medication adherence

Feasibility means whether stakeholders perceived the technology as practical and fit for use in supporting medication adherence

Sustainability means whether stakeholders perceived the technology as appropriate for routine sustained use in supporting medication adherence

Definitions of implementation outcomes and strategies are based on Proctor et al. (2011) "Outcomes for Implementation Research: Conceptual Distinctions, Measurement Challenges, and Research Agenda", the Consolidated framework for advancing implementation science (CFIR), the Expert Recommendations for Implementing Change (ERIC) and the Interventienet.nl website. For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

D3.2.2 Implementation strategies

Implementation strategies are characteristics of the technology that facilitate implementation and maintenance of the technology in a setting.

1. **Please rate the RELEVANCE of this attribute group (X axis).**
2. **Please rate the CLARITY of this attribute group (Y axis).**

Further explanation

Implementation strategies entail:

1. **Training** are activities to teach stakeholders about the technology and how to use it and integrate in the medication adherence support processes.
2. **Educational materials** are materials stakeholders may consult to learn about the technology and how to use it and integrate in the medication adherence support processes.
3. **Funding** are financial strategies and/or additional costs to facilitate adoption of the technology into medication adherence support practice.
4. **Expertise sharing** are information from previous implementations on what helped adopt the technology into medication adherence support practice.
5. **Technical assistance** are systems to support implementation of the technology into medication support practice
6. **Consultation** means accessing direct support from experts for the implementation of the technology into medication support practice.
7. **Accreditation & legal approvals** are credentials and/or licensing to acquire or prove to be able to use the technology in a setting in the conditions necessary for optimal safety and effectiveness.
8. **Collaborations** means involving multiple institutions in delivering the medication adherence support solution that uses the technology.
9. **Access to additional resources** means access to data, space, laboratory facilities.

Definitions of implementation outcomes and strategies are based on Proctor et al. (2011) "Outcomes for Implementation Research: Conceptual Distinctions, Measurement Challenges, and Research Agenda", the Consolidated framework for advancing implementation science (CFIR), the Expert Recommendations for Implementing Change (ERIC) and the Interventienet.nl website. For a more detailed view of the respective sub-levels with labels and definitions please check the interactive graph or the Excel file under supporting information.

Thank you and see you soon!

Dear panellist,

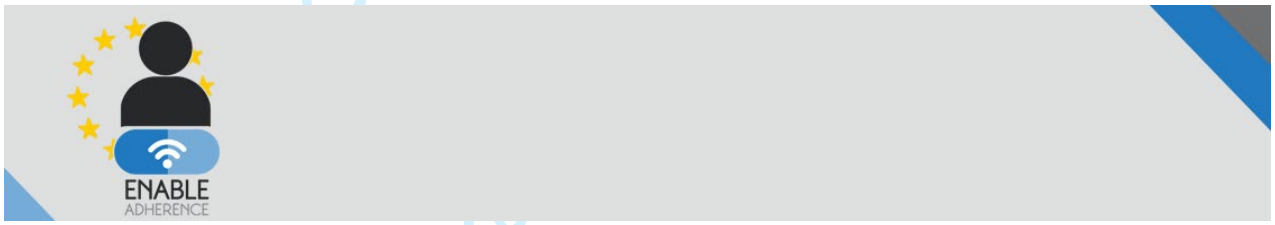
you have made it to the end of the survey. We appreciate your effort and valuable contribution to development of the ENABLE repository of medication adherence technologies.

Please remember to visit the survey several times during the study period to reconsider your answers based on the aggregated feedback and discussions with the other anonymous panellists. Reminders will be sent every 2 weeks to remind you to log in and participate again.

Please don't hesitate to contact us on wg2costenable@gmail.com in case of any questions.

Best wishes,

The ENABLE WG2 Steering Committee



General data protection statement (GDPR)

By continuing the survey, you declare that you have read, understood and agreed with the following statements:

1. *This Delphi survey is performed by the COST Action ENABLE (CA19132) Working group 2 with principal investigators Alexandra Lelia Dima and Urska Nabergoj Makovec.*
2. *The aim of the study is to explore the level of agreement on the proposed structure for a repository of medication adherence technologies*
3. *Participation in the survey is voluntary and the study is designed to ensure participants' anonymity as one of the key features of the Delphi approach.*
4. *The collected personal data will be used exclusively for conducting the study and analysing and reporting results in an aggregated form.*
5. *In order to illustrate some study findings, we might quote statements provided by individual respondents in open text fields; however, the Delphi platform ensures that no personal data can linked to such statements.*
6. *A data protection assessment was carried out by the Data Protection Officer at the University of Basel. According to this instance the Delphi study protocol was determined as compliant with data protection and security standards.*
7. *The personal data used for conducting this study will be stored until the end of the COST Action ENABLE (October 2024). You can address your rights regarding access to, correction of or limitation of use of your personal data through the email wg2enablecost@gmail.com anytime during that time period.*

COST is supported by the European Commission Framework Programme of the European Union

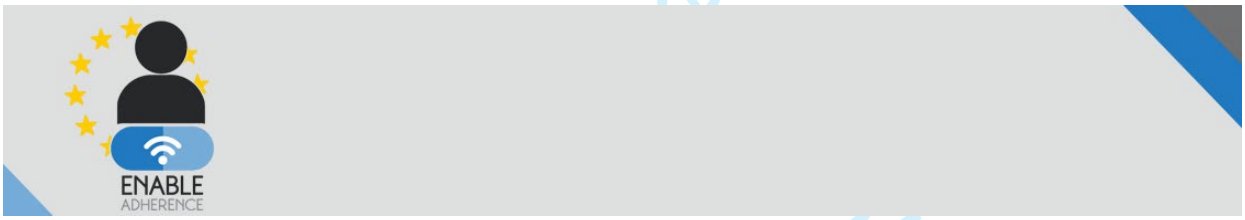
Welcome to the ENABLE-R real time Delphi survey!

ENABLE is a European Cooperation In Science and Technology (COST) project ("CA19132 - European Network to Advance Best practices & technoLogy on medication adherencE") that aims to raise awareness of medication adherence technologies and best practices, and to foster and extend multidisciplinary knowledge on medication adherence at patient, treatment and system levels. COST is supported by the EU Framework Programme Horizon 2020. ENABLE currently has members from 39 European countries.

ENABLE-R will be **an online repository of medication adherence technologies (ENABLE-R)**, which will describe a wide range of technologies relevant for different potential users: patients, healthcare professionals, managers of healthcare organisations, policy makers, researchers. The aim is to develop a user-firendly repository, where users will be able to search technologies with specific attributes, that would fit their context and needs.

This Delphi survey aims to explore the level of agreement with the proposed scope and structure of the repository. A steering committee has been working since October 2020 to define medication adherence technologies and propose a repository structure that considers many aspects of such technologies and their use in different settings. To ensure that the scope and structure is in line with stakeholders' needs and expectations, we created this Delphi survey to consult with stakeholders across Europe on several key elements of the proposed scope and structure. The study obtained ethical approval and positive data protection assessment. Please consult the survey information letter or contact us at wg2costenable@gmail.com f you have any questions.

You were recognized as a stakeholder in the area of medication adherence and are invited to participate in this Delphi survey. Thank you for taking time to complete this survey. We value your contribution.



Instruction for the Delphi survey

The content and structure of the survey

The survey includes **23 questions** related to repository structure, each presented on a separate page. Before starting the survey, we request some **basic information** about you and your experience in medication adherence.

- We present the proposed **definition of the medication adherence technologies (MATech)** for your consideration.
- We invite you to take some time **to explore the full framework of attributes**. It consists of **three domains** (D1. Product & provider information; D2. Medication adherence descriptors; D3. Evaluation & implementation) with underlying attribute groups. Each attribute group branches further in sublevels with related labels and definitions and is labeled with domain number and consecutive number according to the level it represents (e.g. D2.1 or D2.1.1). The complete framework is presented in an interactive graph and in a Excel document detailing proposed structure, labels, definitions and justifications; you may open these documents in separate windows so that you can consult them throughout the survey. After familiarizing yourself with the framework, we ask you to **provide general comments about any missing attributes** relevant for a future MATech repository.
- We describe each domain on one page and present each attribute group and respective sublevels for your consideration on separate pages and ask you to rate **their overall relevance and clarity** and provide **comments or suggestions for improvement** of attribute labels or definitions, and any specific thoughts about any missing attributes in this particular group.

The real time Delphi approach

This survey uses **a real-time approach**, which means that, once you answer a question, you will immediately see other's responses and comments and aggregated feedback on your screen. The strength of the Delphi approach lies in participants having the opportunity to revisit their answers based on other's answers and comments. Hence, it is very important that you **visit the survey two or more times during the study period and reconsider your answers based on the aggregated results and discussions in the comments section**. You are also encouraged to engage in the discussion by explaining the reasons for your responses and making suggestions for improvement. These will also appear in real-time and allow (anonymous) exchanges among stakeholders.

We will regulary check the platform, send updates on the study progress and reminders to (re)visit the survey.

Completing the survey

It should take you **45 to 60 minutes** to complete the survey the first time, and approximately **30 to 60 minutes** for revisiting your answers at a later moment (depending on the level of engagement in discussions you prefer).

You can **navigate across pages** in the survey by clicking on the **blue arrow above the page number**. An index window opens and you can choose which questions you would like to answer. For the first

visit to the survey, we recommend following the order provided. You can **log in and out of the survey** and upon return continue answering where you stopped the last time.

Format of the questions

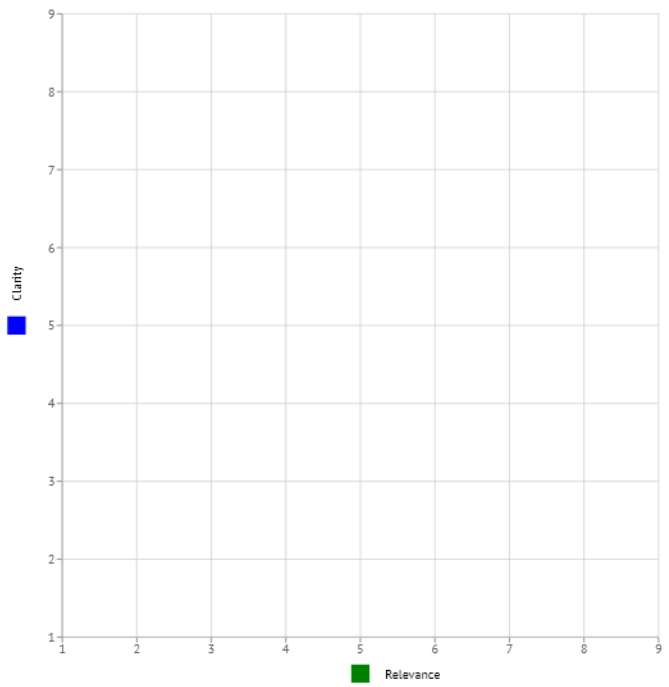
For each attribute, an **interactive 2D grid with two axes** (*see below*) will appear:

- the **horizontal (X) axis** represents **RELEVANCE** of the proposed attribute group for the repository structure on a scale from **1-9 (left-right)**, where 1 indicates extremely not relevant (*far left*) and 9 indicates extremely relevant (*far right*). By relevance, we mean **the extent to which these attributes are important in order to make informed choices regarding their adoption and use.**
- **the vertical (Y) axis** represents **CLARITY** of the attribute group labels and definitions on a scale from **1-9 (bottom-top)**, where 1 indicates extremely not clear (*bottom*) and 9 indicates extremely clear (*top*). By clarity, we mean **the extent to which the labels and definitions of these attributes are easy to understand and apply by repository users.**
- after deciding on your rating on both axes, you can mark your answer in the grid and **a blinking dot** will appear representing both your ratings. **One dot for two ratings: left-right RELEVANCE, bottom-up CLARITY.**
- the scale is continuous, which means you can click anywhere in the grid and thus rate using decimal values (e.g. 4.7)
- after providing your answer, you will be able **to see other participants' ratings represented as dots on the same grid**, and aggregated feedback on the right side of the 2D grid.
- You can change your ratings any time during the study period, by **moving the blinking dot on the grid**. Moreover, you are **encouraged to revisit your answers** on multiple occasions in light of other participants' answers.

Each attribute page also contains **a comments section**. Below the 2D grid you can find open text fields to provide comments or suggestions on the attribute and related sublevels. All comments are displayed anonymously. Please provide your comments in the relevant pre-defined category:

- revisions of attribute labels and definitions
- missing attributes in this group

There you can also see other participants' comments and suggestions and respond to them. Please remember to **save your comments** before leaving a page so that they can be recorded and displayed.



Distribution of answers

X-axis

Answer count	23.00
Lower quartile (Q1)	4.01
Median (Q2)	4.50
Upper quartile (Q3)	6.00

Y-axis

Answer count	23.00
Lower quartile (Q1)	4.33
Median (Q2)	5.01
Upper quartile (Q3)	6.40

Revisions of attribute labels and definitions | Missing attributes in this group

REVISIONS OF ATTRIBUTE LABELS AND DEFINITIONS

SAVE

COMMENTS Select the amount of shown comments 10 Newest first Oldest first

Servicio Andaluz de Salud
CONSEJERÍA DE SALUD

Dra. Dña. Gloria Luque Fernández, Secretaria del CEI Provincial de Málaga

CERTICA:

Que en la sesión de CEI de fecha: 29/04/2021 ha evaluado la propuesta de D/Dña.: Pilar Barnestein Fonseca, referido a la MS1 del Proyecto de Investigación: "COST Action "European Network to Advance Best practices & technoLogy on medication adherencE" (ENABLE) ".

Este Comité lo considera ética y metodológicamente correcto.

La composición del CEI en esta sesión es la siguiente:

Dra. Ana Alonso Torres (UGC Neurociencias)
Dra. Encarncación Blanco Reina (Farmacología Clínica)
Dra. Begoña Jiménez Rodríguez (UGC Oncología)
Dra. Marta Blasco Alonso (Obst. y Ginecología)
Dr. Rafael Carvia Ponsaille (Anatomía Patológica)
Dª. Ana Díaz Ruíz (Licenciada en Derecho)
Dr. José C. Fernández García (UGC Endocrinología y Nutrición)
Dr. Manuel Herrera Gutiérrez (UGC UCI)
Dra. Mª Victoria de la Torre Prados (UMA)
Dr. José Leiva Fernández (Médico Familia)
Dra. Mª Dolores López Carmona (Medicina Interna)
Dr. Jesús López del Peral (Esp.Protec.Datos)
Dña. Carmen López Gálvez del Postigo (Miembro Lego)
Dª. Inmaculada Doña Díaz (Alergología)
Dra. Gloria Luque Fernández (Investigación)
Dra. Cristobalina Mayorga Mayorga (Laboratorio)
Dra. Mª Angeles Rosado Souvirón (UGC Farmacia)
Dra. Leonor Ruíz Sicilia (UGC Salud Menta.)
Dra. Elena Sánchez Yáñez
Dr. Antonio López Téllez (Médico de Familia)

Lo que firmo en Málaga, a 29 de abril de 2021

CONSEJERÍA DE SALUD Servicio Andaluz de Salud C.E.I. PROVINCIAL DE MÁLAGA C.I.F.: Q-9150013-B

Fdo.: Dra. Gloria Luque Fernández
Secretaria del CEI

Universität Basel

Verwaltungsdirektion

Universität Basel, Verwaltungsdirektion, Postfach, 4001 Basel

Mrs Janette Ribaut
Bernoullistrasse 28
4056 Basel

Basel, 25. Mai 2021

Data Protection Assessment of your project "Developing a medication adherence technologies repository: an online real-time Delphi survey protocol"

Dear Ms. Ribaut

I would like to confirm, that we have reviewed your project with regard to data protection and data security. Based on the documents provided to us, we can confirm that data protection is complied with in your project. In particular, since you collect the survey responses exclusively anonymously and no conclusions can be drawn about individual persons.

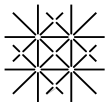
Yours sincerely,

Danielle Kaufmann
Data Protection Officer

Seite 1/2

Universität Basel
Verwaltungsdirektion
Petersgraben 35, Postfach 2148
4001 Basel, Switzerland

Danielle Kaufmann, lic. iur.
Datenschutzbeauftragte
T +41 61 207 30 22
M +41 79 381 20 72
Danielle.kaufmann@unibas.ch



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