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Mobile Therapeutic Attention for Patients with Treatment Resistant Schizophrenia

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with Treatment Resistant Schizophrenia

Deliverable 6.5 – M37

Lessons learned, guidelines and requirements for future deployment of m-RESIST

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Glossary/Abbreviations

RCT	Randomized Controlled Trial
ICT	Information and Communication Technologies
TRS	Treatment-Resistant Schizophrenia
EHR	Electronic Health Record
EMR	Electronic Medical Record
IT	Information Technology
CORE	Connected and Open Research Ethics
IRB	Institutional Review Board

1. Introduction

1.1 Purpose of this document

This deliverable reports on Task 6.5: Next steps for evolving the m-RESIST idea. The identification and documentation of lessons learned is a process that provides the best opportunity for improvement.

The main aim of this document is to gather all relevant information for better planning of later project stages and future projects, improving implementation of new projects, and preventing or minimizing risks for future projects. This document may be used as part of new project planning for similar projects in order to determine what problems occurred and how those problems were handled and may be avoided in the future. Additionally, this document details what went well with the project and why, so that other project managers may capitalize on these actions.

It also includes a description of existing legal and regulatory issues conditioning the future mainstream deployment of m-RESIST.

1.2 Document structure

In order to achieve this purpose, the structure of this document is as follows:

- Section 2 provides the set of lessons learned and identifies the areas that need more time and effort to improve.
- Section 3 describes the main requirements, focused in existing legal and regulatory issues, and provides recommendations conditioning the future mainstream deployment of m- RESIST.
- Section 4 gives the future steps needed to keep on progress with m-RESIST project, focusing mainly in the possibility of performing a Randomized Control Trial (RCT) and developing a Big m-RESIST Data Model to improve the basis of m-RESIST predictive model.
- Section 5 includes a last chapter with conclusions and suggestions for improving the future deployment of the m-RESIST solution.

2. Lessons learned and areas for improvement

This section synthesizes lessons learned during the development of the project, in order to identify issues that occurred, causes and strategies to avoid those problems in later project stages or future projects (a summary of key learning is at Annex 1). It is important to note that both, successes and improvements or shortcomings, have been included.

The key issues described below are:

- Assessment of goals and objectives,
- Identification of activities or areas needing additional effort,
- Identification of effective activities or strategies, and
- Assessment of the roles of partners in the project and the interactions among them

2.1 Goals and objectives

This project aimed to develop an innovative **disease management system, m-RESIST, a mobile ICT system addressed to empower patients with treatment-resistant schizophrenia (TRS), which will involve them to actively participate in the therapeutic process and will enable them to self-manage their condition. m-RESIST will become a step forward in improving and optimizing the clinical decision process.**

The **specific aims** for developing the m-RESIST programme were:

a. **Design** and develop the **m-RESIST system**.

b. **Design** the **m-RESIST programme** (services, care pathways or health routes).

c. **Test** the m-RESIST system and programme on **healthy volunteers and TRS patients**.

d. **Promote** an **active role of patients and** caregivers in the design of the m-RESIST programme and its apps: involvement in the process of users' needs identification.

e. **Promote** an **active role of patients and caregivers in the development and improvement** processes of the m-RESIST programme and its apps.

f. **Create a predictive model** based on a wide range of relevant data gathered by the system in order to identify risks and gaps in the treatments which will enable the prescription of personalised treatment and tools for patients, for managing co-morbidities and healthcare.

Once the project has finished, we considered that the specific aims of this project have been appropriate in order to achieve the main goal. An ICT solution based on mobile and platform components has been created and tested by TRS patients.

Regarding the specific objectives, two of them have been partially achieved. On one hand, it was not possible to *enrol enough caregivers* in the three sites to test the final product and collect their feedback for improvement. But in the case of TRS patients, we did not identify reluctance about new technologies; in fact the difficulties with devices seem to be more related to age than to the mental health condition.

On the other hand, the *basis for the predictive model* has been created but we did not get enough accurate sensor data to get significant results of the correlation between data and clinical outcomes. Mainly because of quick advances in technology, far more than clinical research, the wearables preselected at the beginning of the project were not available in the market when WP4 *Pre-trial with healthy users and system adjustment* started. This factor will be more developed in the next subsection 2.2.

2.2 Identification of activities needing additional effort

During the development of the project, the areas that were identified as needing a higher degree of attention and effort are the following:

- **Engagement of end-users:** this process needs time and effort in mHealth projects, mainly influenced by factors related with ICT such as **levels of familiarity with technology** and **training**. In m-RESIST project the first factor has had a major impact on the engagement with m-RESIST solution, particularly in caregivers. The research team had difficulties to promote an active role for them, and we consider that demographic and environmental characteristics of the target group should have been assessed in early stages of the project.
- **Training** is a factor with a high impact in mHealth projects. In order to ensure maximum usability of the specific devices used in the study, the participation of end-users in the creation of user guide material would be helpful. There is a need to invest more thought in the training material and training process for potential users, in order to create clear expectations from the system. There is also a need for interactive guidance procedures for clinicians in order to start creating new pathways of clinical routine, involving technological solutions. This process requires education for the users in order to engage them in changing the familiar pathways of providing and receiving care.
- **Decisions about technology:** in the m-RESIST project, we experienced a couple of disappointments owing to the **discontinuation** (e.g. Microsoft Band, Motorola 360) or **limitations** (e.g. Apple Watch, FitBit) of wearable hardware. The use of off-the-shelf hardware (e.g. Android Wear smartwatches) was not matched with a willingness to rely on commercial software and services (e.g. the activity tracking and recognition features of services like Google Fit or Apple HealthKit). This meant that we had to implement our own versions of existing technology instead of focusing on truly novel and domain-specific (i.e. geared towards mental health care) features. This could be avoided by considering multiple alternatives earlier in the project.

  Moreover, the **decision between providing smartphones or using participants' phones** has a high impact in the recruitment. In our project, patients were provided with a study smartphone in order to reduce potential bias in data collection. But in case of caregivers, they had to use their own phone. Theoretically this fact should have increased the likelihood that they understood faster how to use the solution. Instead of this, problems with compatibilities between m-RESIST app and caregivers' operating systems were found, so few caregivers could test the m-RESIST app. Collecting data of participants' smartphone devices ahead of time might be necessary to avoid this risk.
- **Involvement of the IT systems:** the status of the specific healthcare technological system used in each pilot site (Gertner, Semmelweis and Sant Pau) has been a barrier in m-RESIST solution integration with existing Electronic Health System in each site. The implementation of a new

mHealth solution in different clinical environments requires a **predefined planning to detail resources and time efforts**. Healthcare system is not still well-prepared for mHealth resources that need tools to enable communication between professionals, share decision making process and define a tailored patient-centred plan. For this reason it is important to involve the IT systems in the development of mHealth solutions since de beginning, in order to ensure an appropriate integration of tools, and to **identify blockages and constraints** in the healthcare system to achieve a continuous flow in functioning.

- **Transition from idea to a product-as-a-service business model:** inpatient and outpatient units are not well enough prepared to assume technological innovations in a quick and easy way. These types of initiatives should be addressed from the beginning to make them applicable in real assistance.

2.3 Identification of effective strategies

We consider that the most effective strategies to achieve the objectives of the project have been the following:

- **In-depth study of environment:** the implementation of a program/product should always take into account the cultural context, the health system and the legislation of each country involved.
- **Collection of qualitative data to get users' feedback:** the point of view of people involved in the project is essential since the beginning, and qualitative assessment is the best way to collect information about users' needs and opinions. In fact, a program should not be started without having previously worked on this part, as analysis of user opinions makes it possible to give a clear focus to the program.
- **Engagement strategies:** in order to generate motivation for engagement, *goals setting* and *personalized feedback* was included. For example, enabling and offering charts on the mobile app as functionality to patients has increased the transparency of the m-RESIST platform and helped patients feel in control of the data stored by the platform on their behalf. Moreover, providing personalization services and recommendations is usually achieved by analysing historical patient information, which is not available due to the enforcement of privacy rules which differ across institutions and countries. During the project we were able to create incremental history from the usage of m-RESIST, so the longer a patient was within our ecosystem, the better the personalization was.
- **Internal testing:** time for internal testing before and during the field-trials is necessary to identify and resolve bugs, a process where clinicians and technologists cooperate closely.
- **Ensure follow-up of technological bugs:** improvement of m-RESIST platform has been possible due to a continuous recording and monitoring of technological issues by means of a close communication between clinical researchers and technologists.
- **Translation of clinical procedures and intervention into technological forms:** the process of "translating" the clinical way of thinking into a "technical" format of "if, else" rules and exact specifications requires establishing a common "language" in order to provide efficient

communication routes. Clear definitions about the targets of intervention and the chain of actions needed to achieve goals were done. Thus, technologists could have an idea about the aim of each feature.

- **Continuous update of relevant literature***:* systematic and extensive review of legal, ethical and scientific progress aimed at developing a platform connected to reality, and in line with the latest findings and recent developments.

2.4 Assessment of roles and interactions among partners

Clear and open communication between all partners involved is a key factor for success. Establishing a good communication generates the effect that people get to know and trust each other, leading to a better understanding of each other's work and challenges that may come along with it. The m-RESIST consortium has followed the key principle in Living Lab management related to the need for good and clear flow of communication between all partners involved. Since the beginning the consortium considered relevant to organise and implement it well from the start of operations. Thus, potential problems (technological or clinical) could be detected and solved in time, and we ensured that major project milestones were being met.

The social interactions at consortium assemblies contributed a great deal of mutual understanding and willingness to collaborate. But for WP3 and WP5 in particular, the most helpful to progress were **scheduled weekly meetings** to manage collaboration (particularly software development). Organize frequent "stand-up" type conference calls[1] at fixed, recurring times, and across geographically distributed people, proved to be highly valuable. In addition to conference calls, the use of instant messaging (e.g. Slack), as opposed to email, proved valuable.

In case of WP3, intensive day or series of consecutive days were planned to work face-to-face or remote on the configuration of m-RESIST solution. This strategy "'pushed'' the solution into a version ready for field trials and usability testing. In case of blockages or constraints in the development, **short meetings of a small group of people** lead to better and faster outcomes, easing that clinicians and technologists can work side-by-side. A clear example was during the task of developing the content of clinical interventions that should be imported to the app. Full working days focused on a task, where partners contributed with their input about resources available, helped solidify and get ready a solution for initial field testing. During periods of rapid development, key individuals from the technology and clinical teams often had **daily check-ins**. Such brief, focused meetings also reduce the need for reorientation between diverse stakeholders, a procedure that is invariably required with less frequent meetings

[1] https://en.wikipedia.org/wiki/Stand-up_meeting

3. Future mainstream deployment of the m-RESIST solution

In the light of the experience acquired during the performance of the m-RESIST project, the following requirements and recommendations are key for successful developments in mHealth.

3.1 Requirements for a successful implementation of the m-RESIST solution in clinical practice

One important requirement is referred to **interoperability**. This functionality is critical to allow the integration of the m-RESIST system with other existing EHR/EMR systems of any health IT department that requests it. This integration must be based on the use of international standards to structure and to exchange patients' data and will allow a better processing and structured management of health data, considering the requirements of the project. This issue, interfaces with the different institutional information systems, was addressed in deliverable D3.2 m-RESIST Back-End Design.

Integration between eHealth platforms and IT health systems is a complex task. It was not within the scope of the current project to achieve a complete integration between m-RESIST and the EHR systems in each pilot site, but the goal of the development, in this area, was to create a system which was capable of being integrated. The next steps for the successful implementation of the system include acquiring approvals from the IT managers of each clinical site using the m-RESIST solution, and a pilot period to test the interoperability options, fixing bugs and developing improvements.

The implementation of mHealth in healthcare routes is continuously evolving regarding **legal and regulatory issues**. Regular updates are needed. In the case of the m-RESIST project, it is a part of the largely evolving field of research utilizing the potential of mobile, digital and passive sensing technologies in healthcare. Clinical potential of mobile and communication technologies opens a variety of new opportunities, while presenting new challenges regarding unintended consequences of revealing personal passively-collected digital data. These challenges were addressed at the initial stage of the project's development. The three clinical sites involved in the pilots collected information on the legislation and regulations regarding the conduct of clinical trials, specifically with vulnerable populations such as patients with mental health disorders, as well as the use of ICT in healthcare. A comparison was done on the legislation and regulations in each country, resulted in an ethical roadmap (Ref.1) that was developed for all aspects of the project, including the development of the digital platform (e.g. data security) and the conduct of the pilots.

Regarding the future deployment of the solution after the pilot stage, it must be taken into account that the literature on **ethical and legal aspects of clinical trials involving mobile technology** is rapidly evolving, due to the accumulated and updated experience of researchers in the field. Potential solutions to address ethical and legal challenges of technology-enhanced research have been recently proposed and described.

For example, Torous and Nebeker (Ref.2) propose an accessible and dynamic resource to bridge a growing gap between researchers, who capture personal health data via mobile, imaging, pervasive sensing, social media, and geolocation tracking tools, and the Institutional Review Boards (IRBs) charged with reviewing these research proposals. The proposed tool is called *Connected and Open Research*

Ethics (CORE), and it is addressed to researchers and IRBs. The CORE is a free, web-based resource that aims to convene stakeholders in the digital mHealth ecosystem to collectively shape dynamic and responsive ethical and responsible research practices. Using a participatory approach to inform the CORE design and function, the CORE team invited input from individuals representing interdisciplinary, cross-disciplinary, and cross-sector perspectives with a vested interest in advancing dynamic and responsive ethical standards. Focus groups and key informant interviews were convened with IRB representatives and researcher stakeholders to inform the initial CORE platform functionality and design.

The CORE platform, released in 2016, hosts a growing global network of over 200 individuals representing 10 countries and a majority of the United States with expertise in privacy, technology, bioethics, research ethics, regulations, sciences, engineering, and even a few participants. The key features include a Forum where Network members can share informational resources and post or answer questions, and a Resource Library where researchers can upload language used in their IRB-approved protocol application and informed consent documents. The goal is to help other researchers who are beginning to use new digital tools in research and who want to see examples of successful IRB protocol and consent language, and receive feedback from experts when writing their own IRB applications. Likewise, IRBs that are beginning to review m-Health and digital medicine research studies can post questions on the CORE Forum, as well as contribute to or search the Resource Library, to see what others have found to be acceptable. This saves time and, ideally, increases the consistency for how IRBs evaluate and mitigate potential risk to research participants.

Another recently published article presents a *legal framework developed to support designers in development and assessment of digital health services* (Ref 3.). The presented framework was created based on concepts and regulations identified through interviews with authority representatives, and a process of stakeholder review and iterative revision of the developed framework confirmed that it was in accordance with current regulation, legislation, and practice. In table 1 the *decision algorithm* for researchers is showed:

Is the Product a Medical Device? A medical device is a product with a medical purpose, such as: to prove, prevent, monitor, treat or mitigate a disease, and to prove, monitor, treat, mitigate, or compensate an injury or disabilities. A product is a medical device if it has a medical purpose such as to: • Prove, prevent, monitor, treat, or mitigate a disease. • Prove, monitor, treat, mitigate, or compensate an injury or disability. • Examine, change, or replace anatomy or a physiological process. • Control fertilization.
Is the Product an eHealth Service? An eHealth service has a purpose to: • Mediate health service or information and interaction between health care and an individual. • Mediate information exchange between patients and health care professionals, hospitals, and other professionals within health care and networks for health information and telemedicine. • Use ICT to improve the preventive work, diagnoses, health care, monitoring, or

administration.
Is the Service Recommended/Supplied by the Health Care? Usually referred to health professionals' medical professional liability in the care and treatment of a patient and the medical responsibility in a comprehensive organizational plan.
Is There Any Risk of Care Damage? Care damage is a damage that could have been avoided if adequate measures were taken by health care. If medical device or eHealth service, the risk of care damage is determined by the level of care, the vulnerability of the target group, and how the usage is being monitored or followed up by the health care.
Is Personal Data/Personal Information Handled? Personal data is defined as all information that can directly or indirectly be assigned to a physical person who is alive. Handling of personal data is defined by the following: every action or series of actions taken regarding personal data (automatically or not). For example, collection, registration, usage, storage, organization, processing, and distribution.
Does the Service Lack User Agreement? Consent is defined as any freely given specific and unambiguous expression by which the registered person, after receiving information, accepts handling of personal data relating to him or her.

Table 1. A Legal Framework to Support Development and Assessment of Digital Health Services.

As can be seen from the above examples, the field of technology-enhanced research requires brain-storming, an ongoing process resulting in formulation of guidelines for designers and developers through the legal and ethical challenges in development work in the digital health domain.

3.2 Recommendations for implementing m-RESIST in clinical practice

Implementation of any telemedicine or eHealth service in clinical practice requires a multi-disciplinary approach, which considers both clinical and technological issues. Different attempts have already been made to define key success factors aiming to move from telemedicine pilots to scale, like the list of 18 Critical Success Factors identified in the Momentum Project[2]. This list identifies deployment strategies, management of organizational change, legal, regulatory and security perspective, and ICT. The activities performed during the m-RESIST project have helped the consortium to identify key aspects for the implementation of telemedicine services such as m-RESIST, as clinical tools that can be used not only in mental health, but also in other medical fields.

[2] https://www.ehtel.eu/references-files/ehtelconnect-support-documentation/MomentumLeaflet2015BlueprintInANutshell.PDF

The following recommendations for m-RESIST implementation follow the structure of success factors identified in the Momentum Project:

- **Deployment strategy:** the m-RESIST system has been deployed in three centres in different countries (Spain, Hungary, and Israel) with different clinical practices, cultural readiness and vision of mHealth. In all the countries, health professionals involved in m-RESIST have played an essential role in the execution of the pilots, dealing both with their own clinical teams and the patients enrolled. Scaling of such solutions can be leveraged by creating awareness in management bodies of health centres about the benefits of the project, including economic assessment, clinical outcomes and main challenges.

- **Organizational Change:** m-RESIST has identified current health intervention in the three countries, and has proposed novel therapeutic processes and clinical interventions (healthy lifestyle, treatment adherence symptom management) to address treatment-resistant schizophrenia patients. Explaining the benefits of m-RESIST to both the Management Board and Clinical Board of the centres involved is essential to reach an agreement about the scaling of m-RESIST in Psychiatric Services in Spain, Israel and Hungary. Adapting the clinical interventions defined to each centre's reality is necessary to scale up the m-RESIST solution.

- **Legal, regulatory and security:** the next big step in data protection in Europe is the entry into force of the new EU General Data Protection Regulation[3]. The Ethical Roadmap defined in WP2 (Ref. 1), has to be updated to the new legislation, in order to fulfil all the requirements set by the new regulation. One of the key changes is that each centre will have to appoint Data Protection Officers, to deal with all the data processing activities and processes.

- **ICT perspective:** m-RESIST has developed novel therapeutic processes supported by ICT tools. The integration of these tools with existing Health Information Systems is essential to scale up m-RESIST solution. Interoperability requirements were gathered during WP2 activities, incorporated in the design documents (Ref.4). However, given the difficulty to involve IT Departments in each centre, and their generally low receptiveness when integrating their systems with external sources and 3rd party applications, it has not been possible to fully integrate m-RESIST solution in the three centres involved. However, positive outcomes have been produced, like the development of a database with the main outcomes in TRS condition assessment, which has been integrated in IR-HSCSP database for future research in mental health. More effort should be invested in incorporating IT Department's representatives in future activities related to scaling up of m-RESIST.

[3] https://www.eugdpr.org/

4. Next steps for evolving m-RESIST project

We consider that one of the next steps in this project should be to perform a **cost-effectiveness clinical randomised trial**, which includes the most relevant variables accounting for complexity in TRS according to m-RESIST predictive model results, and to provide a communication tool in healthcare technological system where professionals can communicate, share decision-making and set tailored patient-centred interventions. m-RESIST is an innovative developmental project in which a difficult clinical challenge was met using modern m-health approached. Nobody has previously carried out such a project. The aims of the project were to develop a clinical model and preliminary test acceptability, usability and satisfaction of using the m-RESIST solution in TRS patients, caregivers and clinicians. These limited aims were a good decision here but larger follow-ups on outcomes are needed in future.

The m-RESIST project cannot give full answers about how effective, cost-effective or generalizable the developed model is. In the future, we could benefit from even more proactive and earlier planning of future grant applications. The aim of this future project should be to evaluate an integrated care intervention for TRS, aimed at improving patient outcomes whilst saving European healthcare organisations a considerable amount of resources. We have planned to set up a multicentre randomized study aimed to compare **the effectiveness between** m-RESIST and standard program **in adults with TRS and their caregivers**. This study would be performed again in European and non-European regions with different healthcare systems (Spain, Hungary and Israel), where an active engagement of end-users (patients and caregiver) to identify expectations and demands will be promoted in the early stages of the project. This new project would bring evidence-based practice for improving the intervention in TRS by evaluating available research evidence showing whether and why a treatment works, clinical evidence to rapidly identify each patient's risks and benefits of potential interventions, and patients' preferences and values, compatible with the organizational context. Other future step will be the **improvement of the m-RESIST platform**. Pilot testing and outcomes of user experience has been useful to identify the areas that need more technological and clinical development.

Regarding technological area, alternative wearable to gather sensor data will be considered in order to promote participants' engagement and ensure data accuracy. Improvements in activity reports delivered to patients by the app will also be needed, in order to promote and reinforce specific behaviours. The inclusion of gaming tools will be evaluated. The integration of a communication tool for participants (e.g. forum) will also be examined, since it was one of the best valued tools during focus groups with users. On the other hand, the clinical intervention package has not been completely developed in this project. Content for recommendations and clinical modules for social communication and recovery should be made and included.

The **development of a Big m-RESIST Data Model** would be another future step for m-RESIST project. As was stated in the m-RESIST proposal (Nº 643552), the m-RESIST solution was not envisioned as a system only addressed to collect patient data, but also to let a modeller tool work and create a predictive model for the patient. The keys to observe and understand what are happening, and to predict what will happen in the future are: have a good organization of the data, an extensive repertoire of modelling tools, and an extensive experience in the analysis of predictive models' results.

The Big Data approach would give fast and straight access to unprecedented amounts of data related to TRS condition, creating an opportunity for deeper insight, earlier intervention and patient engagement.

A Healthcare Data Model would redirect 80% of time spent organizing data towards analysing the data. In addition, it would extend the data source field including analytics on unstructured clinical notes, discharge summaries, genomics etc. By linking Big Data mining tools with a high level predictive model, m-RESIST would open a new technical approach to health treatments. Predictive models could exploit patterns of behaviour found in multiple variables of the patient in order to identify risks and gaps in the treatments, and guide decision making.

Similar than in ethical and legal issues, an updated of Big Data requirements will be necessary. In 2016, the European Commission published a study on big data in public health, telemedicine and healthcare[4], where ten policy recommendations in this field were outlined:

Recommendation 1 on Awareness Raising Develop and implement a communication strategy to increase the awareness of the added value of Big Data in Health and encourage a positive public mind set	**Recommendation 2 on Education and Training** Strengthen human capital with respect to the increasing need for a workforce that can utilize the potential of Big Data in Health
Recommendation 3 on Data Sources Expand existing and explore new sources of Big Data in Health and secure their quality and safety	**Recommendation 4 on Open Data and Data Sharing** Promote open use and sharing of Big Data in Health without compromising patients' rights to privacy and confidentiality
Recommendation 5 on Applications and Purposes Increase target-oriented application of Big Data analysis in health based on the needs and interests of stakeholders including patients	**Recommendation 6 on Data Analysis** Identify the potentials of Big Data analysis, improve analytical methods and facilitate the use of new and innovative analytical methods
Recommendation 7 on Governance of Data Access and Use Implement governance mechanisms to ensure secure and fair access and use of Big Data for research in health	**Recommendation 8 on Standards** Develop standards for Big Data in Health to enhance and simplify its application and improve interoperability
Recommendation 9 on Funding and Financial Resources Ensure purposeful investment steered by the European Commission to warrant cost-effectiveness and sustainability	**Recommendation 10 on Legal Aspects and Privacy Regulations:** Clarify and align existing legal and privacy regulation of Big Data in Health.

Table 2. Fields of policy recommendations

As this discussion, regarding the potential benefits and challenges of further Big Data development in Health, is still on-going and expecting to flow for the next years, a continuous task of revision related to this framework will have to be done.

[4] https://ec.europa.eu/health/sites/health/files/ehealth/docs/bigdata_report_en.pdf

5. Conclusions

The m-RESIST project has been a 3-years period of serious scientific, clinical and technological working, with the main objective of delivering an mHealth solution for people with treatment-resistant schizophrenia and their caregivers, that was acceptable, usable and satisfactory for them.

As a final conclusion of the project we would like to summarize the main challenges, success factors and top recommendations that could help to better planning future m-RESIST steps, and to improve implementation of new projects, and preventing or minimizing risks for future projects.

5.1 Primary challenges

The primary challenges that m-RESIST project has had to deal with are the involvement of end-users, the translation of clinical procedures into technological rules, and the tight schedule to develop a new digital solution in this target population.

First challenge, regarding the end-users, was the process of recruitment and their compliance. TRS patients characterise for their persistent symptoms, suspiciousness, isolation, low motivation and reluctance to changes in their clinical treatment and/or in daily routines. Patients with better engagement and fidelity with their clinical team were more likely to consent. Other factor was the absence of caregivers in some cases, which was included as exclusion criteria. Any issue rose regarding their compliance with protocol, but strategies to motivate and retain patients were needed in case of m-RESIST usage. For example, by reporting and reinforcing regularly their activity, and by being available face-to-face or online to solve technological issues with the devices. The sense of “not being alone” has been one of the main factors in patients’ retention.

The second challenge of the project has been to integrate knowledge from different areas (technological and clinical). The complexity to translate complex clinical interventions into specific system functionalities, workflows and ICT tools has been one of the main sources of delays and difficulties to achieve system readiness. Regarding user-system interactions, some specifications were not detailed enough, which required further discussions. Also, some difficulties were found in the definition of the clinical significance of sensors data acquired and their relation with treatment flows developed into the clinical intervention modules, which added more complexity to the definition of data management. Throughout the project, different approaches have been made to tackle this complexity, such as dedicated face-to-face meetings, virtual meetings, hackatons, testing sessions and similar activities. At the end of the project, there has been a good exchange of knowledge between technological and clinical partners.

Finally, the third challenge has been the time frame. The project duration has allowed developing and testing the m-RESIST concept. However, in order to further analyse data which correlates clinical outcomes and data gathered by the m-RESIST system, more data and time is needed. Once the validity of m-RESIST tools has been tested in a selected group of patients, a larger test needs to be implemented, with more patients and over a longer period of time.

5.2 Success factors

Different success factors can be identified. The main success factor to develop a project of these characteristics has been the consortium attitude towards communication within the project. The proactive role of the different project members, both from the technological and clinical side, and the regular participation of all partners in all the project's meetings (scheduled and unscheduled), have enhanced fluid communication to efficiently solve the different and complex issues that have arisen throughout the project.

Another remarkable factor has been the planning of strategies to assure and promote participants' engagement, to monitor achievements and milestones, and to assess the risks and plan alternatives. Patient's receptiveness has been one of the major concerns to achieve the project's results. Through different methods (focus groups, workshops, pilots), clinicians involved have approached patients by explaining the benefits of the project, making them "part of the team", and emphasizing their role as "testers" and the importance of their feedback. In some cases, patients felt responsible for the "good results" of the project, in which cases clinicians explained to them that "any result is a good result", as the main objective of m-RESIST has been to develop and test an innovative disease management solution based on a mobile ICT system and a therapeutic intervention program, by promoting an active role of patients, caregivers and professionals.

5.3 Top recommendations

Based on our experience, we recommend: defining properly the requirements and expectations of the projects; determining in detail the role and responsibilities addressed to the partners of a consortium; selecting one partner responsible for clinical and technological partners to act as a bridge between these two knowledge areas, to establish proper channels of communication, to involve end-users from the beginning of the project, and to plan and promote dissemination process.

Regarding involvement of health professionals and patients, it is important to perform more research and to adapt the defined therapeutic interventions in m-RESIST (treatment adherence, symptom management and healthy lifestyle) to each centres' reality, in order to assimilate the work performed and to scale up the m-RESIST solution in the clinical practice. These steps require definition of practical information on "how to" further implement m-RESIST in a psychiatric service, following the recommendations described in this deliverable.

6. References

Ref. 1 D2.1Ethical Roadmap, dated from 8/04/2016

Ref. 2 Torous J, Nebeker C. Navigating Ethics in the Digital Age: Introducing Connected and Open Research Ethics (CORE), a Tool for Researchers and Institutional Review Boards. J Med Internet Res 2017;19(2):e38Garrel.

Ref. 3 Garell, C., Svedberg, P., & Nygren, J. M. (2016). A Legal Framework to Support Development and Assessment of Digital Health Services. JMIR Medical Informatics, 4(2), e17.

Ref. 4 D2.4 m-RESIST System Requirements, dated from 30/07/2015.

ANNEX 1. Key learning and recommendations for future projects

Project Area / Overall Impact on Project	Key Learning	Recommendations for Future Projects
Project Management	**Strengths:** Importance of effective and inclusive leadership **Areas to improve:** The roadmap in WP should be more specific in deciding partner roles	• More operative description of responsibilities and tasks of different partners • Conduct workshops with other groups working on telepsychiatry solutions to share knowledge and knowledge
Project Planning	**Strengths:** Plan to monitor achievements and milestones, and to assess risks and plan alternatives **Areas to improve:** Lack of preliminary analyse and subsequent implementation of certain resources in clinical centres	• Include in the planning of tasks the monitoring and regular collection of information related to this deliverable
Technological Requirements	**Strengths:** Study in-depth of environment during WP2- User requirements and Healthcare routes. **Areas to improve:** Acquiring approvals from IT managers of each field-trial site; getting to know interoperability options; access to ECR/EMR	• IT involvement since the beginning of the project • Evaluate in detail the technological knowledge of the caregivers and use of digital tools
People and Their Roles	**Strengths:** Paper and role of clinical and technological coordinators; work of clinical and technological partners in close partnership; regular meetings apart from general assemblies	• More operative description of responsibilities and tasks of different partners • Include in clinical teams people with knowledge in new technologies: intermediate figure that speeds up the

	Areas to improve: Identification and definition of the communication tools to be used	creation of the technological solution
Project Communication	**Strengths:** regular communication of project results in scientific community and mass-media **Areas to improve:** Promote a more active role in social media such as twitter, and increase number of published papers	• Engage partners in the dissemination process by using social-media and writing scientific papers • Monitor regularly the state of these tasks
Testing / Quality Assurance	**Strengths:** Users involvement since the beginning of the project Enable a fluid and dynamic channel of issues communication Involvement of clinicians in internal testing process **Areas to improve:** Detailed knowledge about profile of potential participants (personal characteristics, technological devices)	• Promote a proactive role in testing internally the solution • Define engagement strategies for other users than patients (e.g. caregivers)
Architecture/ Technical Solution	**Strengths:** m-RESIST app and platform adapted to users requirements Co-participation of users in design and improvement **Areas to improve:** Integration between components and selection of wearables	• Create the list of selected wearables in early stages of the project, and update regularly their availability • Create a dictionary of terms to improve the understanding of main clinical and technological ideas • Include a “hybrid” figure between technological patners and clinicians, such as a biotechnologist
Training	**Strengths:** Availability of brief and easy-reading	• Involve end-users in material creation; include video-tutorials adapted to patients’

	guides for users Technological knowledge of clinical partners **Areas to improve:** Type of material	characteristics
Deployment	**Strengths:** Ready for implementation **Areas to improve:** Connection with EHR/EMR	• IT involvement since the beginning of the project