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# Development and Testing of a Vocal Interactive Amazon Alexa Skill for Medication Adherence Support

TESI DI LAUREA MAGISTRALE IN
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# Abstract

The problem of medication adherence represents a major global challenge for the healthcare system. Studies show that, on average, one in two patients with a chronic disease does not take some or all of their prescribed medication correctly. If we add to this the fact that non-adherence increases with the number of drugs prescribed and that understanding the prescription remains a problem in many cases, the scenario becomes dramatic. The causes associated with non-adherence are varied; consequently, solutions to address this issue are evolving along with different approaches, such as the application of persuasive strategies aimed at changing behaviour in case of intentional and unintentional non-adherence.

The advent of technology also offers great potential in healthcare, and digitisation has made possible a rethinking of the role of the patient, who assumes a central profile in self-management. Technology has supported the development of solutions capable of connecting doctors and patients, guaranteeing remote monitoring. While the empowerment of patients means considerable progress, it also means sizeable active participation in the tasks they have to perform.

State of the art is full of solutions integrating technological potential, persuasion systems and remote monitoring: smart blisters, electronic pill bottles, as well as fully digital solutions such as smartphone applications for treatment planning and notification tools for intake or voice assistants for primary adherence support.

The research conducted in this thesis aims at realizing a framework able to fit into this context of use, i.e. allowing both the monitoring of adherence through voice technology with the supervision of an authoritative entity, guaranteeing the user the least possible burden to make the system transparent and functional. It was achieved by adding a new module to the IntakeCare platform, an apparatus for managing the treatment plan and remote adherence monitoring. A voice interface was created on Amazon's Alexa device to manage, help and guide the patient in planning and the observance of their treatment pathway. The module's design was based on research into strategies and persuasion models that could lead to behavioural change, specifically to correct incorrect adherence. Strategies were implemented to promote the primary task, enhance the dialogue and the credibility of the system.

The platform's architecture is based on the three-tier model; the database, the backend and the frontend, consisting of a voice interface for patients and a web application for doctors, were developed in parallel by several people in the IntakeCare team. Security, archiving, and data presentation logic were implemented. The module foresees that the doctor enters the medicines to be taken by the patients via the web application. It has a twofold reason: to limit misunderstandings about medication instruction and to relieve the subjects of the input task.

This thesis focused on the patient interface to develop an application named CareVoice for Amazon Alexa voice devices, which aims to solve the problem of non-adherence by offering support for the management of the treatment plan.

This technology, being directly linked to the web application used by the doctor, allows users to configure their prescribed treatments through simple steps that ensure they receive notification reminders when their medication is scheduled, with the possibility of confirming their intake. By processing this data, it is possible to report quantitative and detailed information on adherence both to the doctor, for supervision purposes, and to the patients, for richer insight into their progress.

The voice interface was tested on seven volunteers for a trial period of one week. All participants demonstrated the ability to complete the test by using the device correctly. Following the trial period, the system was evaluated from the perspective of usability using a semi-structured interview submitted to all participants, who expressed overall good opinions on the developed technology.

**Key-words:** adherence, digital health, voice interface.

# Abstract in italiano

Il problema dell'aderenza ai farmaci rappresenta una notevole sfida globale per il sistema sanitario. Gli studi evidenziano che in media un paziente ogni due affetti da malattia cronica non assume correttamente parte o l'interezza delle medicine prescritte. Se a questo aggiungiamo che la non aderenza aumenta all'aumentare del numero di farmaci prescritti e che la comprensione delle prescrizioni mediche rimane un problema in molti casi, lo scenario assume connotati drastici. Le cause associate alla non aderenza sono svariate e di conseguenza le soluzioni che mirano a risolvere questa problematica si stanno evolvendo seguendo diversi approcci come l'applicazione di strategie persuasive mirate al cambiamento del comportamento in caso di non aderenza intenzionale e non intenzionale. L'avvento della tecnologia anche in ambito sanitario offre una grande potenzialità e la digitalizzazione ha permesso di ripensare al ruolo del paziente, che assume un profilo centrale nell'autogestione. La tecnologia ha supportato lo sviluppo di soluzioni capaci di connettere medici e pazienti, garantendo il monitoraggio anche da remoto. Se da una parte l'emancipazione dei pazienti significa un notevole progresso, dall'altra significa anche forte partecipazione attiva nei compiti che devono svolgere.

Lo stato dell'arte è ricco di soluzioni che integrano potenzialità tecnologiche, sistemi di persuasione e monitoraggio da remoto: smart blister, electronic pill bottles, ma anche soluzioni completamente digitali come applicazioni per smartphone per la programmazione delle terapie e con strumenti di notifica per l'assunzione o assistenti vocali per il supporto nell'aderenza primaria.

La ricerca condotta in questa tesi mira alla realizzazione di un framework capace di inserirsi in questo contesto di utilizzo, che permetta cioè sia il monitoraggio dell'aderenza attraverso la tecnologia vocale, con la supervisione di un'entità autorevole, garantendo all'utente il minor numero di oneri possibili in modo da rendere il sistema trasparente e funzionale. L'obiettivo è stato raggiunto attraverso l'inserimento di un nuovo modulo alla piattaforma di IntakeCare, un sistema volto alla gestione del piano terapeutico e al controllo remoto dell'aderenza. È stata realizzata un'interfaccia vocale sul device Alexa di Amazon in grado di gestire, aiutare e guidare il paziente nella programmazione e nel rispettare il proprio percorso terapeutico. Il design del modulo si è avvalso di una ricerca sulle strategie e i modelli di persuasione che potessero portare al cambiamento di un comportamento, di correggere nello specifico quello della scorretta aderenza. Sono state implementate strategie di supporto al compito primario, al dialogo e alla credibilità del sistema.

L'architettura della piattaforma si basa sul modello three-tier; sono stati sviluppati parallelamente da più persone nel team di IntakeCare il database, il backend ed il frontend, composto da interfaccia vocale destinata ai pazienti e applicazione web pensata per i medici. Sono state implementate logiche di sicurezza, di archiviazione e di presentazione dei dati.

Il modulo prevede che sia il medico ad inserire tramite applicazione web le medicine che devono assumere i pazienti, al fine di limitare le incomprensioni e anche di alleggerire di questo compito i soggetti.

Questa tesi si è concentrata sull'interfaccia per il paziente, per sviluppare un'applicazione, dal nome CareVoice, per dispositivi vocali Amazon Alexa, che ha lo scopo di risolvere il problema della non aderenza offrendo un supporto per la gestione del piano terapeutico. Questa tecnologia, essendo direttamente collegata all'applicazione web usata dal medico, permette agli utenti di configurare i trattamenti prescritti attraverso semplici passaggi che garantiscono la ricezione di promemoria di notifica al momento in cui i farmaci sono programmati, con la possibilità di confermarne l'assunzione. Elaborando quindi questi dati, è possibile riportare informazioni quantitative e dettagliate relative all'aderenza sia al medico, con lo scopo di supervisione, che ai pazienti stessi, per una più ricca informazione sul loro percorso personale.

L'interfaccia vocale è stata testata su 7 volontari per un periodo di prova di 1 settimana. Tutti i partecipanti hanno dimostrato capacità nel portare a termine il test, utilizzando correttamente il dispositivo. A seguito del periodo di prova il sistema è stato valutato sotto il punto di vista dell'usabilità tramite un'intervista semi-strutturata sottoposta a tutti i partecipanti che hanno espresso nel complesso buone opinioni sulla tecnologia sviluppata.

**Parole chiave:** aderenza, sanità digitale, interfaccia vocale.

# Contents

# 1 Introduction

Changes in society and technological development have led to a rethinking of the organisation of the healthcare system. The role of the patient and that of the caregiver are no longer two separate entities. Population ageing leads to a twofold problem: increasing chronic illnesses and higher demand for healthcare support. More and more interconnected individuals make a solution possible, namely self-management and remote management. Patients become more autonomous and specialised; in short, they become their caregivers in some respects. Of course, this does not mutually exclude the role of the health care system, which, however, is relieved of a considerable burden on the one hand but has the possibility of outspread monitoring on the other.

The advent of eHealth has enabled more widespread care and lowered transport costs. The home and the workplace become spaces where clinical monitoring continues. Patients become emancipated and incorporate their care into everyday life. It enables high-level accessibility to all life activities without compromising them, even with chronic diseases. Electronics, information technology, applications and web-based solutions facilitate the care and greater awareness of the user. Chronic diseases are the foremost cause of human death. The most common are heart disease, respiratory disorders, cancer and diabetes. These are usually dependent on risk factors such as hypertension, overweight, high blood sugar and often depend, in turn, on habits, behaviour and lifestyle, with the increase in chronic disorders continuing to grow (O'Grady et al., 2009), thus constituting a considerable expense for nations and one of the sizeable challenges for health systems. Despite the prospects for longevity, only efforts to fight and change bad habits and a better organisation of their care can improve the quality of life of individuals. Although there is still little evidence to bring eHealth self-management tools into clinical practice, researchers are making efforts to prove the effectiveness of these technologies.

Chronic diseases, ageing, technological development represent the ideal storm, with self-monitoring as one of the solutions. In the following chapters, the problems and the solutions for monitoring health conditions will be examined. Firstly, the problem of treatment adherence will be explained. Secondly, how technology can fit into this context in terms of digital and persuasion-based solutions. Finally, an overview of digital solutions for autonomous and remote adherence monitoring will be presented.

## 1.1. The issue of non-adherence

Poor medication adherence has been identified by the World Health Organisation (WHO) as a significant public health problem contributing to increase morbidity and mortality as well as hospitalizations and consequently health care costs. Medication non-adherence is pervasive globally. Studies report that around 50% of patients in developed countries with long-term illnesses do not take their medication as prescribed (Sabate et al. 2003); this number is probably even higher in developing countries with fewer health resources. Accordingly, it is clear why this topic can be considered as one of the biggest challenges to our health.

The phenomenon of non-adherence has consequences not only for the health of the patient, which is adversely affected but also for the healthcare system as a whole, which has to guarantee to the patient the necessary assistance following any deterioration in health. The healthcare systems must manage these relapses with large financial and organizational resources that could potentially (at least partially) avoided. Estimates of the total costs of non-adherence range from $100 to $300 Billion each year and include both direct and indirect costs. To give a more practical numerical example, it is estimated that for every additional dollar spent to promote adherence in a prescribed medication, medical costs would be reduced by $7 for people with diabetes, $5.10 for people with high cholesterol, and $3.98 for people with high blood pressure (Bosworth et al., 2011).

To give an example, almost 1 in 4 cardiovascular patients suffering from hypertension, are partially or completely non-adherent in filling prescriptions after hospital discharge. Of those patients who are initially adherent, almost half tend to discontinue their antihypertensive medication within 6-12 months, and only 40%

are found to be continuing therapy when adherence is analysed 2 years after hospitalisation for the acute coronary syndrome (Baroletti et al., 2010).

Studies report that primary non-adherence leads to a significant increase in mortality at 1 year after hospitalization for myocardial infarction, while secondary non-adherence (not following the prescription correctly) leads to a significant increase in hospitalisations and consequent costs (Simon ST et al., 2021).

Figure 1 shows an example of adherence rates for the most common drugs for cardiovascular diseases, showing that real adherence is much lower than self-reported one.

| Medication | Self-Reported Adherence, % | Consistent Adherence, %* |
|---|---|---|
| Aspirin | 83 | 71 |
| Lipid-lowering agents | 63 | 46 |
| $\beta$-blockers | 61 | 44 |
| Aspirin+$\beta$-blocker | 54 | 36 |
| Aspirin+$\beta$-blocker+ lipid-lowering agent | 39 | 21 |

*More than 2 consecutive follow-up surveys over 6±12 months.

Figure 1: Adherence rates to common cardiovascular medications (Simon ST et al., 2021)

It needs to be also considered how the costs of care management are not only those borne by hospitals, but for example also the loss of work productivity that can affect the patient himself, or family members who take care for him. The combination of all these economic factors shows more adequately the enormous overall cost of non-adherence to medical treatment.

Although interest in the topic of patient adherence has increased considerably in recent years, supported by the large body of literature, there is still no uniformity in the terminology used. Vrijens et al. in 2012 in their review proposed a new taxonomy in which:

*"Medication adherence is defined as the process by which patients take their medications as prescribed"*.

The term adherence refers to three components: initiation, implementation, and discontinuation. Initiation occurs when the patient takes the first dose of the prescribed medication (start). Implementation or execution is the extent to which a patient's actual dosage corresponds to the prescribed dosage regimen (from start to the last dose). Discontinuation occurs when the patient at any time and for any reason stops taking the prescribed medication, marking the end of the therapy.

In addition, the term persistence refers to the length of time from the first intake to the last correct intake (Vrijens et al.,2012). Although its importance is well known and verified, the appropriate use of medications remains a challenge for both patients and providers. On the patient side, patients may not follow the medication and therefore fall within the definition of non-adherence at different stages of their treatment. Patients may decide not to start the treatment at all, or use the wrong doses of the prescribed treatment, or take it at the wrong time, or start the treatment in the correct way but stop it prematurely.

Primary non-adherence refers to the frequency with which patients fail to fill prescriptions (i.e., getting the drug at the pharmacy) when new medications are prescribed; secondary non-adherence refers to the medication not being taken as prescribed when prescriptions are already filled (Hugtenburg et al., 2013).

In Figure 2, a schematization of all the possible situations and steps in which a patient may decide to deviate from the prescription and thus be non-adherent to the medication are summarized.

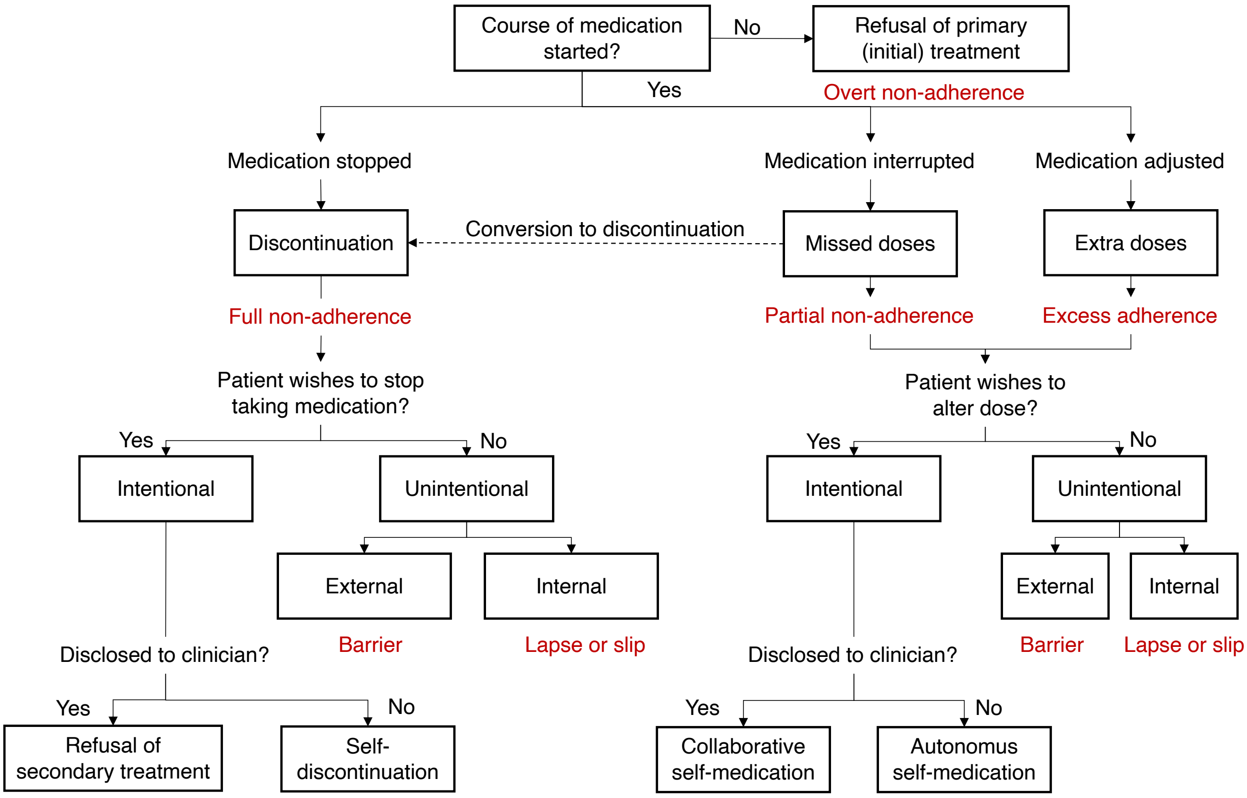



Figure 2: Representation of Adherence diagram. (Modified by Mitchell AJ et al., 2007)

### 1.1.1. Causes of non-adherence

As with any problem, the step before finding a solution is to identify the causes. The factors for non-adherence are various and highly dependent on the individual. The World Health Organisation (WHO) has grouped these factors into five main groups: patient factors, socio-economic factors, health system factors, prescribed therapy factors, and condition factors.

Patient-related factors are those that include the individual's personal beliefs about their treatment. Health illiteracy is a huge problem today. A person may or may not be aware of their illness and they may or may not agree on the need for intervention.

This problem is often worsened by fear of the potential side effects or toxicity associated with their medication. In addition, the psychological condition of the patient is also of high importance; an individual's cognitive ability and degree of forgetfulness are easily associated with non-adherence issues.

Socio-economic factors also inevitably have an impact, leading in some cases to an inability or difficulty for individuals to afford the medication. Individuals with a low socio-economic status (SES) were found to have a profound influence on health outcomes and poor medication adherence leading to subsequent adverse health events (Clark AM et al., 2009).

Another connected factor is related to the healthcare system. Effective communication between doctor and patient, which is necessary for patient understanding, may be hindered by the poor organisation between different hospital and outpatient care teams, between specialists from different health systems or even between providers and pharmacists. In addition, there are States where private health insurance is prevalent but requires costs that not everyone can afford, resulting in poor or no adherence to treatment.

Finally, the therapies prescribed and the conditions for which they are prescribed. Complicated dosage regimens lead to misunderstandings, strain, or forgetfulness on the part of the patient. As already mentioned, some drugs could have undesirable side effects and require extensive monitoring. These are all factors that could lead to reduced adherence to treatment.

Regardless of the various causes that lead a person to deviate from the prescribed therapy, non-adherence may be intentional or unintentional (Wroe AL et al.,2002). Intentional non-adherence refers to situations in which patients are aware of what medication they should take and when. However, they actively decide that they do not want to take their medication as prescribed by behaving as in one of the examples described above.

Unintentional non-adherence refers to unplanned behaviour and is less strongly associated with beliefs and level of cognition than intentional non-adherence. It is a passive process and is usually related to some form of forgetfulness or inattention that leads to the patient forgetting to take a dose, taking the wrong amount, repeating a dose, or taking the wrong medication. The change in routine may also result in unintentional non-adherence.

### 1.1.2. How to measure non-adherence

Once the meaning of adherence has been explained and its considerable importance in many respects clarified, one issue that arises is how to measure actual medication adherence. How does one know if the patient is taking the medication? Adequate quantification of medication adherence forms the basis of any effective adherence study. In addition, doctors need simple and straightforward ways to identify non-adherence and intervene to help patients follow treatment regimes.

It is possible to define two types of measures: subjective measures, which consist in patient' self-reports and evaluations by healthcare professionals, and objective measures, which consist of techniques to quantitatively measure adherence.

It is also possible to use technology to obtain indirect measures, such as pill counting, electronic monitoring, secondary database analysis, and biochemical measures. Subjective and objective measures have both advantages and disadvantages and should be used in combination. For example, among subjective measures, as the term indicates, we find a dependence of the results on the individual who might underestimate their non-adherence to avoid disapproval by their healthcare providers; among objective measures we certainly find higher costs and complexity of use of the systems.

Talking about subjective measurements, and so those involving clinician assessment and/or self-report, they could be structured interviews, online questionnaires, voice response systems, and so on. Among the advantages of these methods, there are lower costs, a high simplicity, and a great personalization in the analysis of a single patient; on the other side these methods can only weakly measure what is the adherence to the medication as they are subjective and therefore based on the hypothesis of the truthfulness of what is reported by the patient.

As already mentioned, these methods may use interviews made by clinicians with patients, where they are asked for example to estimate their progress on taking their medication by reporting an indicative number of missed doses, or the completion of self-reported questionnaires which are fully completed by the patient or their caregiver. The results of these questionnaires can be analysed and compared thanks to many scales that allow the results to be standardized.

In the review by Nguyen TM et al. published in 2014, 43 of these scales are considered and classified into five groups according to the information they are analysing: medication-taking behaviour, medication-taking behaviour and barriers to adherence, barriers to adherence only, beliefs associated with adherence and barriers and beliefs associated with adherence.

The various objective methods for measuring adherence include:

- Direct methods, i.e., the measurement of the medicine or its metabolite concentration in the body fluids, this measurement can be done at random times, following specific cadences, or only at the time of need. Obviously, this method on the one hand is the most accurate, it represents physical evidence and has simple and clear results (positive/negative); on the other hand, it is very expensive and difficult to implement, there can be a conflict in the results due to other medicines or food and it can be biased in case the subject knows when he/she will be tested;
- Measures that involve secondary databases and thus the analysis of sequences and patterns derived from data in systems such as e-prescriptions or pharmacy insurance claims. These data allow the quantification of adherence to various refill measures. Refill adherence is based on the concept that prescription refill patterns are a consequence of the patient's need for the medicine when it is finished and assume that the medicine is taken exactly as prescribed. From a mathematical point of view, two indexes are utilized: the medication possession ratio (MPR) and the proportion of days covered (PDC). These are the two most common formulas used to estimate medication adherence for chronic therapies. Both calculate the percentage of days for which the patient has available medication for their chronic conditions. In the MPR calculation, a patient who refills a medication 7 days before running out of it will have overlapping days supplied, which would wrongly elevate MPR. An adjustment is done in the PDC formula.

$$MPR = \left(\frac{Sum\ of\ days'supply\ for\ all\ fills\ in\ period}{Number\ of\ days\ in\ period}\right) \times 100\%$$

$$PDC = \left(\frac{Numbers\ of\ days\ in\ period\ "covered"}{Number\ of\ days\ in\ period}\right) \times 100\%$$

- Measures that involve electronic medication packaging (EMP) devices, devices incorporated in prescription medication. The Medication Events Monitoring System (MEMS) is the most used in medication adherence studies. the device has a built-in microprocessor which, whenever the medicine is removed from the container, can store the time and date of the event. These devices also allow audio-visual reminders to be programmed to remind the patient of the intake, allow real-time monitoring and even data storage. On the other hand, they assume that the patient who takes the medicine from the box, then actually takes it; however, these devices are subject to breakage or malfunctioning of the boxes, and have very high costs.

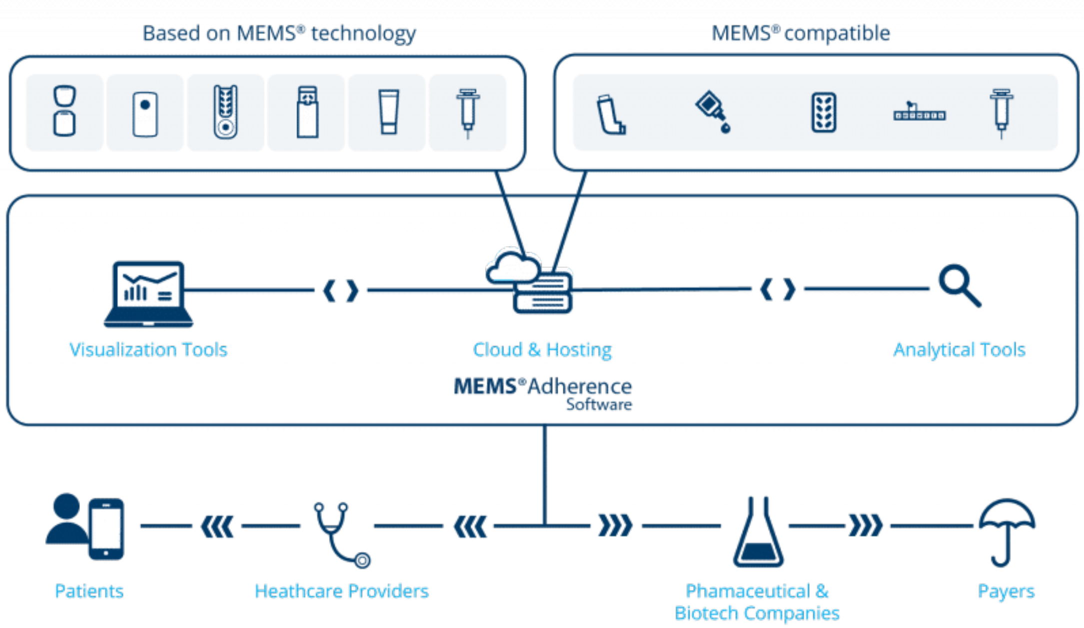



Figure 3: MEMS adherence systems (https://www.aardexgroup.com/)

Several ongoing studies are investigating the design of non-adherence prediction models using machine learning. This would benefit clinicians by allowing them to estimate in advance the risk of non-adherence in a specific patient and to act accordingly, and in a clinical trial context researchers may have the option of removing certain participants earlier in the study and thus save money and time.

Koesmahargyo et al. in 2020 published a study of over 4000 participants and used a decision tree-based machine learning algorithm to achieve high accuracy. The characteristics used for prediction were both static, such as the patient's primary diagnosis, trial complexity, demographics, and dynamic, using parameters such as frequency of adherence, delayed intake, and reminders received by the clinician from an earlier phase of the study. High levels of accuracy were seen in the results, which even improved when using real-time measurement data that can dynamically predict future adherence.

### 1.1.3. Solution to intentional and unintentional non-adherence

It is clear that an issue of such great importance has stimulated the development of many different strategies to improve adherence. These solutions involve the use of more or less innovative technologies and consequently greater or lesser ease of use. It must be highlighted that the appropriate solution must be personalized because, as previously seen, the causes of nonadherence can be various.

Among the different solutions currently available, a categorization could be made between the passive ones (i.e., that do not require any real interaction from the user after a reminder), and the active ones, which conversely require a certain degree of active involvement and participation from the patient. Passive solutions include, for example:

- Providing a personal diary to the patient at the start of therapy containing the dose regimen, effects of therapy and severity;
- Periodical monitoring supported by phone calls with a healthcare professional who has adequate knowledge about the patient's therapy;
- Interactive interventions with automatic voice response (AVR) systems or telephone voice messages delivered to the patient to remind them to take the

appropriate medication at the prescribed time encouraging continued adherence.

- Use of blister packs which are a type of medication packaging that allows the patient to access a certain dose of medication at a specific time labelled on the pack to make it less ambiguous as to the correct dose to take;
- Use of electronic pill bottles which are containers equipped with a microchip capable of recording the date and time the bottle is opened.

As already mentioned, these are solutions that might be useful in certain cases, e.g. when the reason behind low adherence is forgetfulness rather than complicated therapy, but do not in any way impact changing the patient's behaviour.

Active solutions, on the other hand, are technologies that need patient interaction and aim to empower the person by placing him at the centre of the treatment process, by creating some engagement. These include:

- Tools for collecting data and measuring adherence;
- Tools to remind therapy through alarms;
- Mobile applications for smartphones

Surely the solution with the most potential is the one that uses the smartphone and manages to encapsulate almost all the functionality covered by other technologies such as store information, monitor the analysis of stored data and provide notifications and alerts.

In the chapter dedicated to the state of the art, an overview will be given of some digital systems that assimilate all three of these categories. Mobile technologies and voice interfaces, which aim at collecting data and sending notifications related to adherence management, will be presented.

## 1.2. Digital health strategies to improve adherence

The question remains how digital health can contribute to improving adherence. First, treatment adherence must be considered as a behaviour, and non-adherence as the behaviour to be changed. Second, a focus on the strengths of the technology and how they can be used to modify behaviour has to be done. In this chapter, the peculiarities and effectiveness of mobile and IT-based devices are exposed, as well as models that theorise strategies leading to behaviour change.

A systematic review investigates the effectiveness of interventions mediated by mobile or computer-based technologies (Whitehead L et al., 2016). These technologies fall within the branch of eHealth called mHealth, a range of wireless, smartphone and tablet-based healthcare systems. These technologies take the form of software, apps and smart voice assistants. The survey investigates the use of mHealth systems for self-management outcomes of long-term conditions.

Especially for chronic diseases, they represent adaptable solutions that allow monitoring patients at any time and at a low cost. The market for these technologies is expanding very quickly: almost 84% of the world's population owns a smartphone, and this figure is growing continuously (https://www.bankmycell.com/blog/how-many-phones-are-in-the-world).

App stores can provide more than five million apps, and the downloads by 2020 were over 200 billion (https://financesonline.com/app-usage-statistics/). These statistics incorporate a very salient one, the time of use. It goes from around 110 hours per month in the 18-24 age group to 50 hours for the over 65s. During the pandemic, these data strongly grew. Estimates say that consumption has accelerated even faster. The need not only for educational applications but also for telemedicine has left numerous possibilities open.

Research findings can be confusing as it is burdensome to isolate usage of the apps alone from clinical intervention. Monitoring is most effective when conducted via apps. However, symptoms management may be affected by external support. It is also difficult to estimate the active drive of users to use apps, which is a fundamental requirement for the approach to technology. Evaluating applications is also not effortless because of the many ethical barriers and testing times required before the publication. From the users' point of view, the obstacles depend on their digitisation and availability of connection. Nevertheless, evidence points to statistically proven improvements in the use of applications in symptom management. The mHealth technologies can enhance the efficacy of chronic disease symptom self-management. However, cost-effectiveness analyses and actual implementation and delivery in the healthcare system will need more in-depth evaluations.

As evidence of the improved efficacy of eHealth and mHealth technologies, a study reports on an application to support nurses when administrating medication (Wentzel et al., 2014). The study also discusses the evaluation of the application: the results show positive comments and effective use of the platform. What often happens is that despite the desire of healthcare organisations to innovate, there is a lack of a rigorous method for implementing such systems. The gap between theory and practice of self-management systems development is compounding (Alpay L et al., 2019). In addition, such systems can be perceived as a distraction or as an impediment in the care of patients.

It is necessary to describe these technologies systematically and supplement them with persuasive strategies. Standardisation is an essential step, especially in the design phase. Without a standard, it would not be possible to identify the peculiarities and requirements of the problem we address. It is the case with CONSORT-EHEALTH, which stands for Consolidated Standards of Reporting Trials of Electronic and Mobile Health Applications and Online Tele Health (Eysenbach et al., 2011). It is a statement for reporting randomised controlled trials, which contains a checklist for standardising and analysing web-based and mobile health interventions.

Consideration must be given to the risk that the development of eHealth and mHealth will not affect inequalities in access to health and technology. A solution that can decrease these barriers should be designed. Poor economic conditions, low levels of digital literacy and health literacy lead to the exclusion of some people. Therefore, the effectiveness of interventions depends not only on the system used but also on how well it can bring about change through appropriate communication. Technology allows us to intervene in a targeted way and thus tailor the solution of a problem to the patient treated.

The core of technological change is linked to the accessibility and shareability of information. Information can therefore move faster and be ubiquitous. It is precisely the principle on which self-management is based. Self-management of patients is successful if it meets medical prerogatives. In other words, a patient is successful in self-management when he complies with the indications and prescriptions of his caregiver. Therefore the patient is positively autonomous if, for example, he manages to lose weight, stop smoking, remember to take his medication or have a proper diet, but we could give numerous other instances. The problem of adherence to a medical indication or prescription is a common issue in healthcare. Non-adherence, in particular, jeopardises the effectiveness of many interventions and doctors and nurses do not always have the time and willingness to follow patients in adhering to them.

### 1.2.1. Behaviour change support systems

Technology thus becomes a tool to support behaviour change. Technology is never neutral, never gets tired and is therefore always active: this allows for the layering of a persuasion strategy. Hence, it is mandatory to define how to convey this persuasion properly.

As defined by Oinas-Kukkonen:

*"A behaviour change support system (BCSS) is a socio-technical information system with psychological and behavioural outcomes designed to form, alter or reinforce attitudes, behaviours or an act of complying without using coercion or deception."*
(Oinas-Kukkonen at, 2013)

BCSSs can lead to changes in behaviour, attitude or task fulfilment, and there are three possible outcomes (Win, Khin Than et al., 2009):

- Reinforcement: the subject has a behaviour that needs to be stimulated, channelled or enhanced to make it more robust to change.
- Change or Forming: the subject must change, discard or recreate a behaviour from scratch.

- Shaping or Altering: a behaviour has to be blunted, modified or routed in the right direction. In this case, the intensity levels at which behaviour is reproduced are changed (e.g. decrease the number of cigarettes in a day).

It should be diversified the changing according to the target on which it is going to be leveraged:

- Fulfilment of a task: the subject does not need to have an inner drive to fulfil a duty; in this case, the system has the task of ensuring that the user performs that task (such as getting a patient to take his medication correctly). The subject's motivation is not changed. However, this system can affect higher spheres of human behaviour within enough time.
- Behaviour: the subject undergoes a more complex change that modifies behaviour. There are different types of behaviour and, not all of them are modifiable in the same way. e.g. short-term changes in behaviour are more straightforward to achieve than long-term changes.
- Attitude: the subject's change is visceral; in this case, the changing puts pressure on the motivational sphere and is more comprehensive. An attitude is more robust than behaviour to change.

Behaviour change promoted by BCSSs is based on influencing the subject. Generally, these systems are transformative, and change occurs because of persuasion, deception, coercion or nudging techniques. However, it must be excluded deception and coercion for obvious ethical reasons. The primary approach to achieving behaviour change is the one that uses the core element of persuasion, as expressed in the persuasive system design model.

It has been demonstrated that technologies that are designed in such a way that they support "behaviour change techniques" (BCTs) and "persuasive system design" (PSD) can have a positive effect on changing the behaviour, attitude, and motivation of their target audience (Asbjørnsen et al, 2019).

### 1.2.2. Behaviour change techniques

The study of the human psyche allows understanding cognitive models and how they are stimulated by the different communicative strategies mediated by technology (Torning et al., 2009). It is possible to recognise:

- Human-computer interaction: a subject communicates with a virtual interface.
- Computer-mediated communication: two subjects communicate via computer (email, messaging).
- Information systems: organisation and display of data using software and databases.
- Affective computing: how human emotions are processed, or how to arouse feelings through a virtual interface.

Obviously, in a system, these models can coexist and mix. An example is that of voice interfaces which combine some of the models listed above.

Before looking at how BCT and PSD systems unfold in real-life applications, it is necessary to understand their structure. Concerning behaviour change techniques, for example, a taxonomy of 93 distinct elements has been proposed (Michie et al., 2015). Structured lists of this kind are necessary to clarify and categorise studies and RCTs so that meta-analyses or systematic reviews can be developed. The Michie et al taxonomy groups the 93 BCTs into 16 macro-areas:

- Goals and planning: e.g. goal setting (both in terms of outcomes and behaviours), planning a specific action or sense of commitment.
- Feedback and monitoring: e.g. self-monitoring of one's outcome or behaviour, feedback statistics or surveillance of one's body values.
- Social support: e.g. practical support of a wingman or buddy (as in alcoholics anonymous), but also emotional support.
- Shaping knowledge: e.g. educate or instruct how to achieve a result or adopt a behaviour.
- Natural consequences: e.g. inform about social, fiscal or mental/emotional repercussions.

- Comparison of behaviour: e.g. can be demonstrative or social comparison.
- Associations: e.g. the use of totems, prompts or cues to suggest a definite behaviour, the removal or increased difficulty of obtaining a reward, but also overexposure to a context or behaviour to normalise it.
- Repetition and substitution: e.g. reinforce a practice already possessed by the subject or obtain an opposite habit substituting one behaviour with another.
- Comparison of outcomes: e.g. weighing up pros and cons, getting information from credible sources.
- Reward and threat: e.g. through incentives, rewards or material, social or autogenous punishments.
- Regulation: e.g. managing emotions, resources and medication in a more regularised way or giving exaggerated instructions to regulate or stop a behaviour (e.g. asking to smoke a lot more to stop smoking).
- Antecedents: e.g. restructuring or modifying situations that lead to a behaviour that you want to avoid (such as moving a box of biscuits to an inconvenient place) or that you want to stimulate (such as giving out free condoms to encourage protected sex).
- Identity: e.g. framing people, giving people a role (an unhealthy behaviour will be reduced to prevent setting a bad example), stimulating cognitive dissonance in contexts where a missing behaviour is widespread.
- Scheduled consequences: e.g. modification, removal, reduction of punishments and rewards.
- Self-belief: e.g. convincing people that they can change based on past successes or individual abilities.
- Covert learning: e.g. imagining punishments for desired behaviour or rewards for behaviour.

### 1.2.3. Persuasive system design

Technology is often seen as a mere means of conveying information. However, evidence shows that when technology is integrated with means of persuasion it can be more effective (Kelders et al., 2012). The design of persuasion systems requires considerable effort. The models of Fogg and Nass, firstly, and Oinas-Kukkonen, secondly, allow to have a very comprehensive theoretical model.

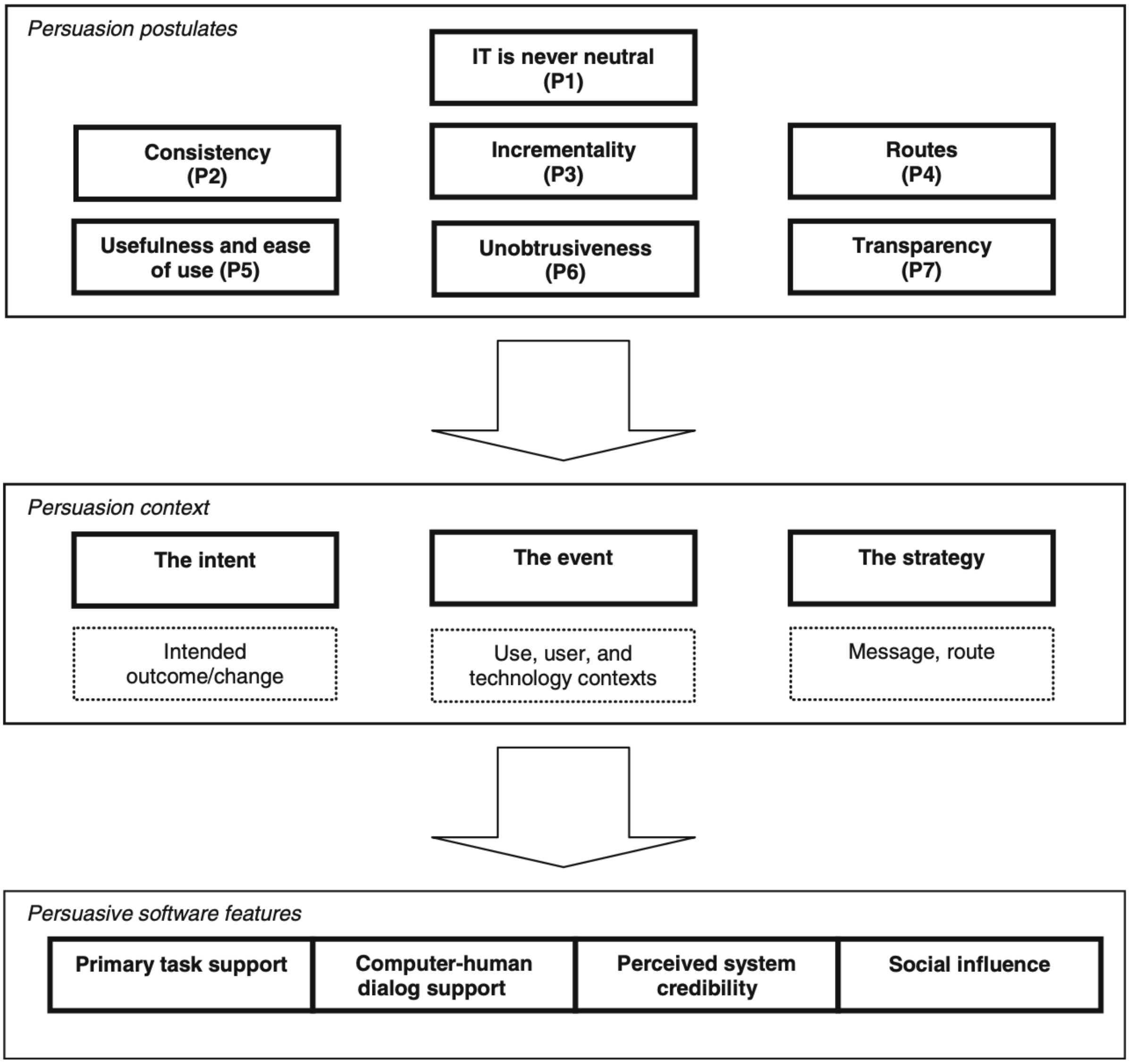



Figure 4: Representation of PSD Model (Oinas-Kukkonen at, 2013)

In this model, the starting point for building a persuasive system is to accept the following postulates:

- IT is never neutral: technology influences its recipient and does so with a purpose. Moreover, it is always active, and the persuasion process is not punctual but builds over time.
- Consistency: people are swayed when the purpose of persuasion appeals to a sense of commitment. In this way, the subject tends to allow himself to be persuaded so that his reality is more organised and consistent.
- Incrementality: the process of persuasion must be increasingly gradual.
- Routes: Persuasion can be both direct and indirect.
- Usefulness and ease of use: the user must perceive the technology as functional and straightforward; it must be efficient, responsive, safe and attractive.
- Unobtrusiveness: the technology must not be unwanted or intrusive but rather must be almost unnoticeable.
- Transparency: the purpose of persuasion must always be clear.

After defining the postulates, an investigation on the context of use is needed. A good design must consider the boundary conditions and shape the final product accordingly. We can distinguish three situations:

- The Intent: firstly, it must be considered the objective of the change. It can be a short-term behaviour, a long-term behaviour or an attitude. Achieving a momentary change is much easier than changing an attitude. The intent defines the context, and within this, it is possible to distinguish the change type (i.e. what it is wanted to change) and the persuader (i.e. who promotes the system of persuasion), which can be endogenous, exogenous or autogenous.
- The event: involves the three sub-areas of use, user and technology. Talking about use context, refers to the characteristics of the domain in which the persuasion system is involved. The user context is related to the features that have to do with the recipient of the persuasion system, such as imposed and self-imposed goals, lifestyle, motivation, inclination to face some challenges. The technology context, on the other hand, has to do with the type of persuasion technology used; for example, this may be mobile, computer-

based, a web application, and have different interface implementations such as computer-mediated or human-computer.

- The strategy: is composed of two elements, or rather the message and the route. The message differs in form and content; the form may be vocal, messaging, a pop-up, a dialogue, while the content may vary from information to mere data. The route may be direct or indirect and thus appeal to impulses, emotions and reasoning.

The next and final step in the design of a persuasion system is the definition of the system's features, which are divided into four dimensions:

- Primary task support refers to the primary tasks and persuasion strategies. It consists of Reduction (fragmentation of complex behaviours into simple tasks), Tunneling (guiding the user), Tailoring, Personalisation, Self-monitoring, Simulation, Rehearsal.
- Computer-human dialogue support refers to feedback and communication strategies. Embodies Praise, Rewards, Reminders, Suggestion, Similarity (communication imitates the user's language), Liking (attractiveness), Social Role.
- Perceived system credibility refers to the credibility that the system inspires. It is composed of Trustworthiness, Expertise (providing information knowledge-based), Surface credibility, Real-world feel (highlighting people behind the system), Authority, Third-party endorsements, Verifiability.
- Social influence: refers to influence strategies between people who adhere to the same system. It comprises social learning, social comparison, Normative influence (the target behaviour is normal), Social facilitation (an action is easier to perform if others also perform it), Cooperation, Competition, Recognition (public recognition of an individual or a group of people who adopt a target behaviour).

These solutions are the core of persuasion. However, there are no suggestions in the model for software requirements, how it should be deployed or how and which of these solutions should be included.

A rigorous cause-effect analysis using the partial least squares structural equation modelling method traces the primary system's persuasion factors that lead to the actual use of that system (Lehto et al., 2012). In this study, hypotheses are formulated and summarized in this diagram:

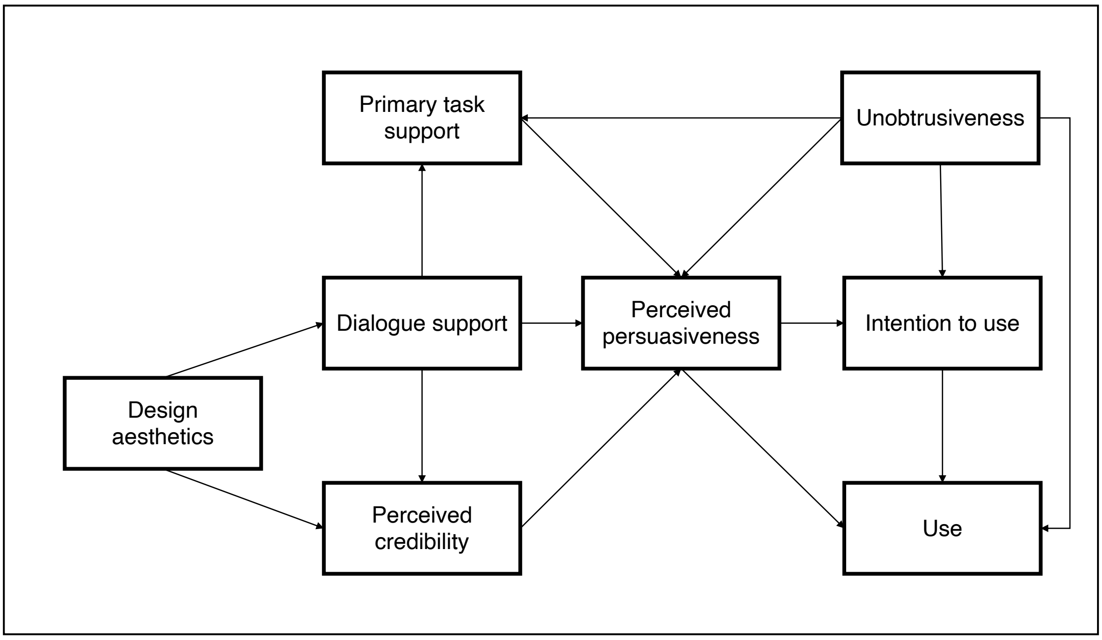



Figure 5: Hypotheses of factors influencing Perceived persuasiveness and Use (Lehto et al., 2012)

Primary task support is essential to enable users to perform their principal duties; therefore, it affects Perceived persuasiveness. Argumentation, feedback and interaction with the system are the main aspects of Dialogue support. Users are either trusted in the system or persuaded and helped to perform their job. Therefore, Dialogue support affects Primary task, Perceived persuasiveness and Perceived credibility. Credibility itself, in turn, influences the persuasiveness of a system, as a credible system is also more trustworthy. Aesthetics and design are visualization elements. They cannot be neglected because their form influences the system's credibility, while the message is a vehicle for information; thus, communication is the basis for dialogue. Unobtrusiveness encompasses the domains of privacy, usability, physical impediment, functionality, human interaction, routine, self-concept, and sustainability. It is a fundamental element for the daily performance achievement and thus the Primary task. An unobtrusive system is consequently more used. It has a positive relationship with Perceived persuasiveness, Intention to use and Actual usage. At this point, Perceived persuasiveness impacts Intention to use, which predicts Actual usage.

Based on the available data, a further study of the variance of the different factors was performed, leading to a rethinking of the model in which "Intention to use" was deleted because considered redundant. However, there are no considerations about Social support, which should be included. Figure 6 shows the final diagram:

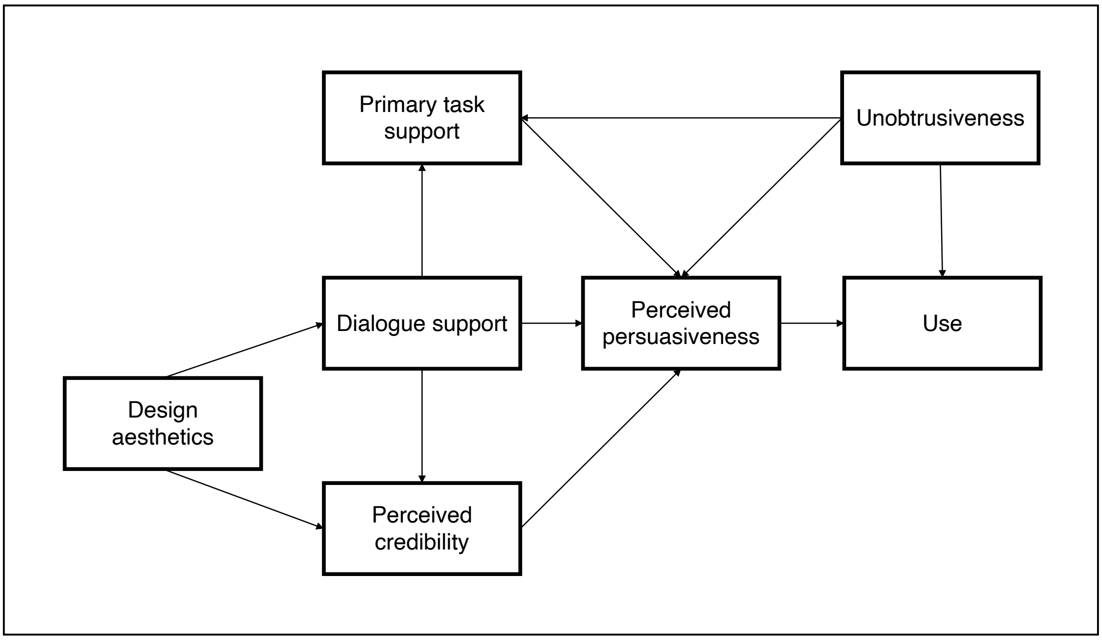



Figure 6: Resulting factors influencing Perceived persuasiveness and Use (Lehto et al., 2012)

As the theoretical models for persuasive systems are relatively recent, there is still little evidence to support their effectiveness. Behaviour change is quicker and easier to achieve than attitude or motivation change. However, there are considerations related to the timing of studies. The analysis and monitoring of the subjects of a study take a long time. Duration is extensive if the objective of the investigation is the measurement of the change of an attitude. Studies are often conducted on a population rather than individual subjects (Torning et al., 2009). Thus, it is a consequence that customisation solutions are more nuanced than their theoretical significance. Where such studies are possible, one should interface with ethical requirements and safety measures regardless. The design of these systems, therefore, remains a challenge.

There are studies proposing solutions and guidelines for incorporating persuasive systems in the context of healthcare self-management, as demonstrated in a publication of the Inholland University of Applied Sciences (Alpay et al, 2019). In this research, the models of PSD, CeHRes roadmap (i.e. an iterative phased action plan) and Fogg's (based on motivation, skills and triggers) are integrated.

There is also evidence of actual implementations, such as a persuasive and informative system for nurses (Wentzel et al., 2014). In this PSD, Reduction and Tunnelling strategies are exploited to enable simplified information search.

Some analytical studies and systematic reviews highlight the main persuasive strategies (Torning et al., 2009, Asbjørnsen et al., 2019, Kelders et al., 2012). For the primary task, Tailoring, Tunnelling, Reduction, Self-monitoring, Personalisation are among the most frequently used (in combination with Goal-setting). Rewards and Feedback, including Reminders, Praise are at the basis of dialogue support. Associations are the most used to stimulate adherence, Shaping knowledge for awareness-raising. Social support is also often mentioned, although it is tough to implement. It is also interesting to note that these strategies are often interlinked, e.g. Self-monitoring, Goal-setting and Feedback are the most common. Studies underline that Reminders are very effective in dealing with non-adherence. Given the nature of the results, it is evident that research in this field is still immature.

# 1.3. State of the art

## 1.3.1. Mobile health applications

Most of the apps in the app stores fall into categories of gaming, business and education. Only a minor percentage (around 3.6% in the Apple store) expresses the number of healthcare apps. (https://www.statista.com)

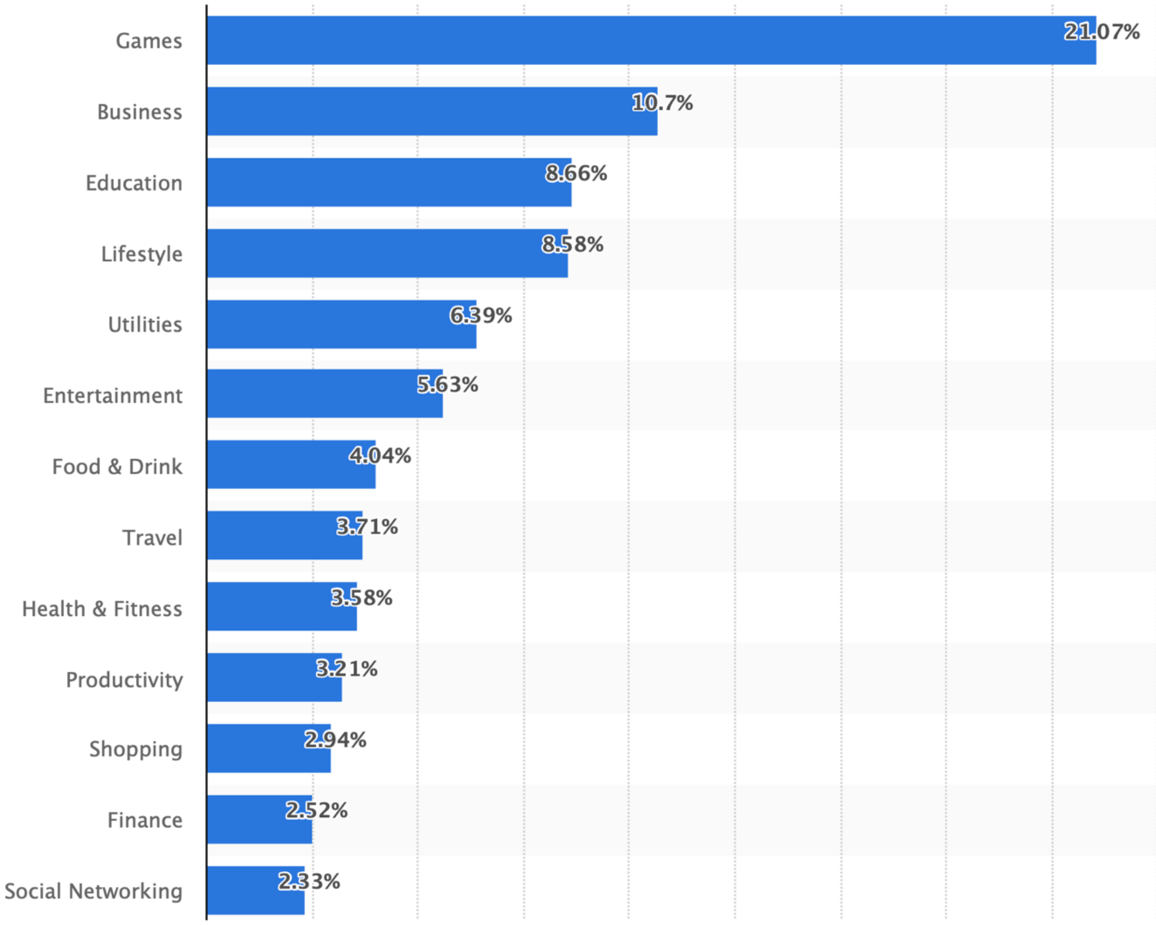



Figure 7: Most popular Apple App Store categories in December 2021, by share of available apps (https://www.statista.com)

However, it is interesting to note that the types of applications that are most used, in terms of hours of use, are mainly in the areas of social, communication and gaming:

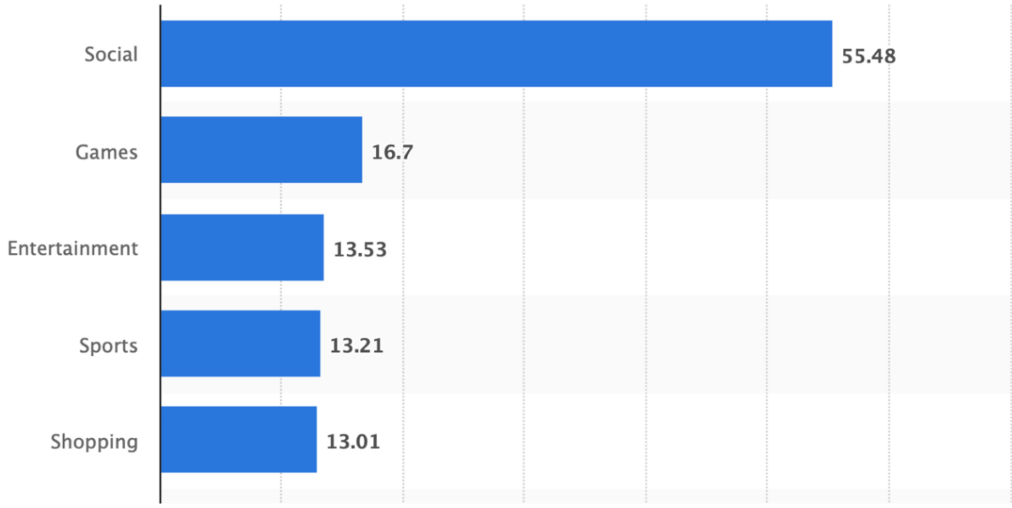



Figure 8: Average daily time spent by users worldwide on mobile apps from October 2020 to March 2021, by category (https://www.statista.com)

It is possible to observe data concerning the permeability (i.e. the level of potential consumers that an application can reach) of the various categories of applications (the available data only involve the Google Play app store):

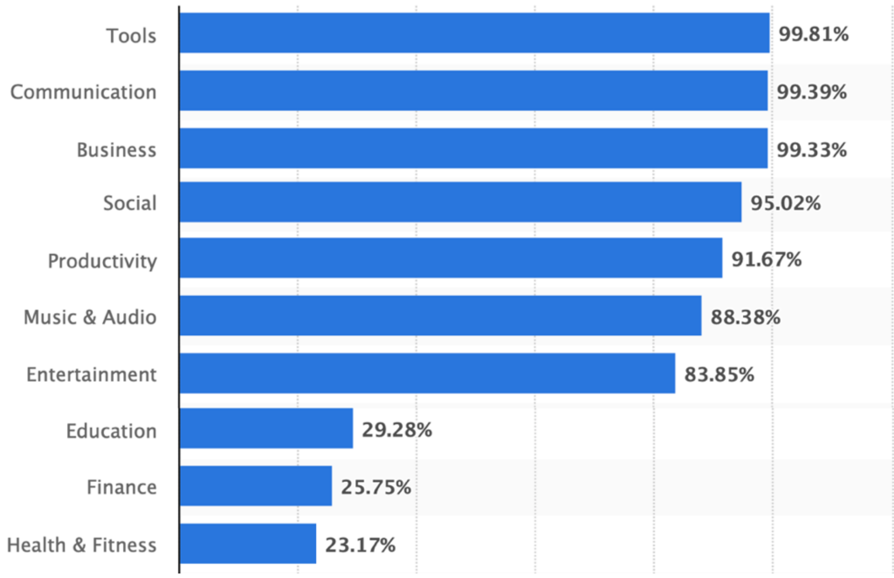



Figure 9: Market reach of the most popular Android app categories worldwide as of September 2019 (https://www.statista.com)

Healthcare apps are not all medical devices. It turns out that apps certified as medical devices by bodies such as the FDA or with CE mark account for only 0.5%

of the apps available on the market. We can therefore make a distinction between healthcare apps and medical apps. These, in turn, are divided according to the task they perform and the target audience. There are fitness apps, nutritional apps, apps specialising in gynaecology, cardiology, gastroenterology, dermatology, etc. However, it is not enough to deal with these sciences to make them conventional medical apps.

In our research, we mainly focus on apps supporting medication adherence. We principally analysed the most downloaded apps from the Italian app store (apple and google play).

There are nine applications that we have analysed:

- Promemoria Farmaci (MediSafe Inc.)
- Promemoria per Farmaci (Sergio Licea)
- Promemoria pillola (Benjamin Brewis)
- My pill reminder (Roman Baev)
- Mediteo: promemoria per farmaci
- Dosecast: promemoria pillola (Montuno Software)
- Medfox: Pill Reminder & Tracker
- Mr. Pillster: il ti ricorda pillole
- MyTherapy: promemoria per medicine

Each app was analysed in terms o fits main functions, features and persuasion strategies, according to the model below.

| *Primary Task Support* | *Dialogue Support* | *Credibility Support* | *Social Support* |
|---|---|---|---|
| Reduction | Praise | Trustworthiness | Social learning |
| Tunnelling | Rewards | Expertise | Social comparison |
| Tailoring | Reminders | Surface credibility | Normative influence |
| Personalization | Suggestion | Real-world feel | Social facilitation |
| Self-monitoring | Similarity | Authority | Cooperation |
| Simulation | Liking | Third-party endorsements | Competition |
| Rehearsal | Social role | Verifiability | Recognition |

Figure 10: Summary table of PSD (Win, Khin Than et al., 2009)

Some of the main aspects of these applications have been classified using the Oinas-Kukkonen persuasive design model. The functionalities of the foremost persuasion strategies have been mapped. In particular, it can be asserted that:

- The customization of the drugs in every aspect (image, time, dosage, frequency, mode of intake) is part of the Personalization strategy in the Primary Task Support;
- Adherence reports, calendars, graphs and tables on doses taken or missed are part of the Self-monitoring strategy in the Primary Task Support;
- Graphics and aesthetics of the interface (and its customization) contribute to Liking within Dialogue Support;
- Alarms and notifications for medication intake are part of the Reminders strategy, also within the Dialogue Support;
- The functionality of interacting with doctors is part of the Social role in the Dialogue Support;
- Expertise strategy within the Credibility Support is when one can have: information on medicines, contraindications, how to take them, pharmacies where to purchase them;
- The possibility to verify the manufacturer is part of Verifiability within Credibility Support;

- Good reviews, ranking in the app store and the developer (e.g. a large company) contribute to Trustworthiness and Surface credibility strategies in the Credibility Support;
- Strategies of alerts, notifications and cooperation with family members or caregivers are part of Cooperation within Social Support.

In Figure 11, the presence or not of each characteristic in the analysed apps has been summarized.

| | | Primary task support | | Dialogue support | | | Credibility support | | | Social support |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Personalization | Self-monitoring | Liking | Reminders | Social role | Expertise | Verifiability | Trustworthiness + surface credibility | Cooperation |
| Promemoria Farmaci MediSafe | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| Promemoria per Farmaci Sergio Licea | | ✓ | ✓ | ✗ | ✓ | ✗ | ✓ | ✓ | ✓ | ✗ |
| Promemoria pillola Brewis Benjamin | | ✓ | ✓ | ✓ | ✓ | ✗ | ✗ | ✓ | ✓ | ✓ |
| My pill reminder Roman Baev | | ✓ | ✓ | ✗ | ✓ | ✗ | ✗ | ✗ | ✓ | ✗ |
| Mediteo: promemoria per farmaci | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| Dosecast: promemoria pillola | | ✓ | ✓ | ✗ | ✓ | ✗ | ✓ | ✓ | ✗ | ✗ |
| Medfox: Pill Reminder & Tracker | | ✓ | ✓ | ✓ | ✓ | ✗ | ✓ | ✗ | ✗ | ✗ |
| Mr.Pillster: il ti ricorda pillole | | ✓ | ✓ | ✓ | ✓ | ✗ | ✗ | ✓ | ✓ | ✓ |
| MyTherapy: promemoria per medicine | | ✓ | ✓ | ✓ | ✓ | ✓ | ✗ | ✓ | ✓ | ✓ |

Figure 11: Mobile Application subdivided according to the PSDs they implement

Only the simplest and clearest applications have been included in the "Liking" field. It is clear that design and practicality are key elements. A user should not be disoriented, and it is often crucial to balance this against the number of functionalities provided. Some applications also offer the possibility to change tones and colours, among them, "Promemoria pillola", is one of the most configurable.

All applications allow for the customisation of therapy settings. It is the most important aspect to take into account if one wants to offer a generic service that can be extended to all types of prescriptions. Some applications, such as "Promemoria Farmaci", "Promemoria per Farmaci", "Dosecast", and "Mediteo" also allow the user to configure the icon for the pill/drug they wish to insert. Another feature present in all applications is the ability to provide reminders based on medication intake. However, only in some cases, such as the Medisafe app, it is possible to configure secondary alerts in case of missed intake. This functionality also includes alarms on refills. Below is an example of screens related to medication entry and reminder notification.

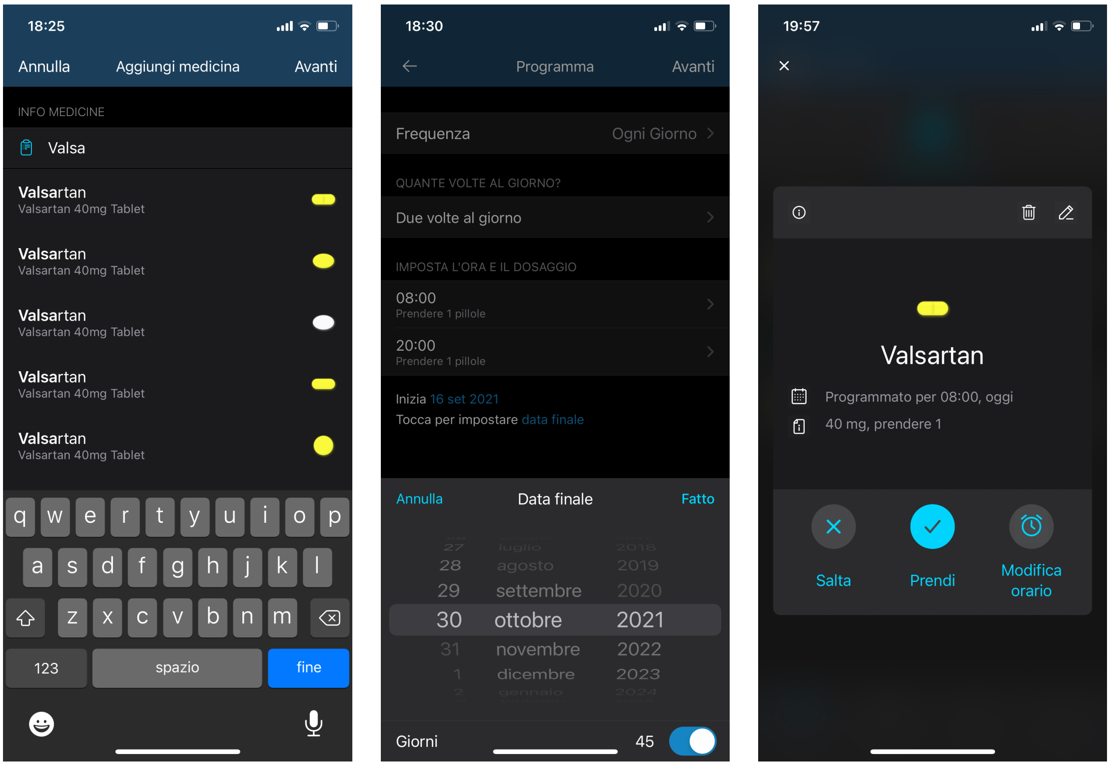



Figure 12: Medication search page, Medication scheduling page, Notification for taking the medication. Screens are taken from the Promemoria Farmaci (MediSafe Inc.)

"Dosecast" and "Pill Reminder", on the other hand, ensure association with various devices such as the Apple Watch or Fitbit so that notifications also arrive on other platforms. For features such as "Trustworthiness", "Surface credibility", and "Verifiability", ratings, comments, approval and certification of the apps were analysed. “Self-monitoring" is also one of the most common features, albeit to varying degrees: applications such as "Medisafe" and "Mediteo" provide informative reports. One of the most integrative aspects is certainly "Expertise". The degree of information can range from information on pharmacies in the vicinity, as offered by "Medfox", or drug insights, as for "Medisafe". Another important aspect is the inclusion of third parties (doctors, caregivers, nurses or family members), which allow better monitoring of "Social Role" and degree of assistance "Cooperation".

More detailed information for each of these applications can be found in the final appendix.

### 1.3.2. Vocal assistant in healthcare

Nowadays daily-used instrumentations are becoming more and more automated and many implementations have been developed in order to manage entire systems through voice commands. As a result, vocal-controlled devices have been widely studied over the past years. They are easy-to-use and they just need an internet connection in order to be constantly listening for the ‘wake-up word’ needed to be activated. This sound is transmitted via the internet to the cloud servers, where the entire processing takes place in order to give to the user the correct answer.

ISA (Interactive Smart Agents) devices, commonly known as smart speakers, have been on the market since November 2014 when Amazon launched Amazon Echo. After that, perceiving its great potential, other big companies like Google, Apple, and Microsoft responded with their own devices.

The voice assistant market is thriving: devices sold by 2020 are above 4 billion and as it is possible to see in the chart below, sales are estimated to double by 2024.

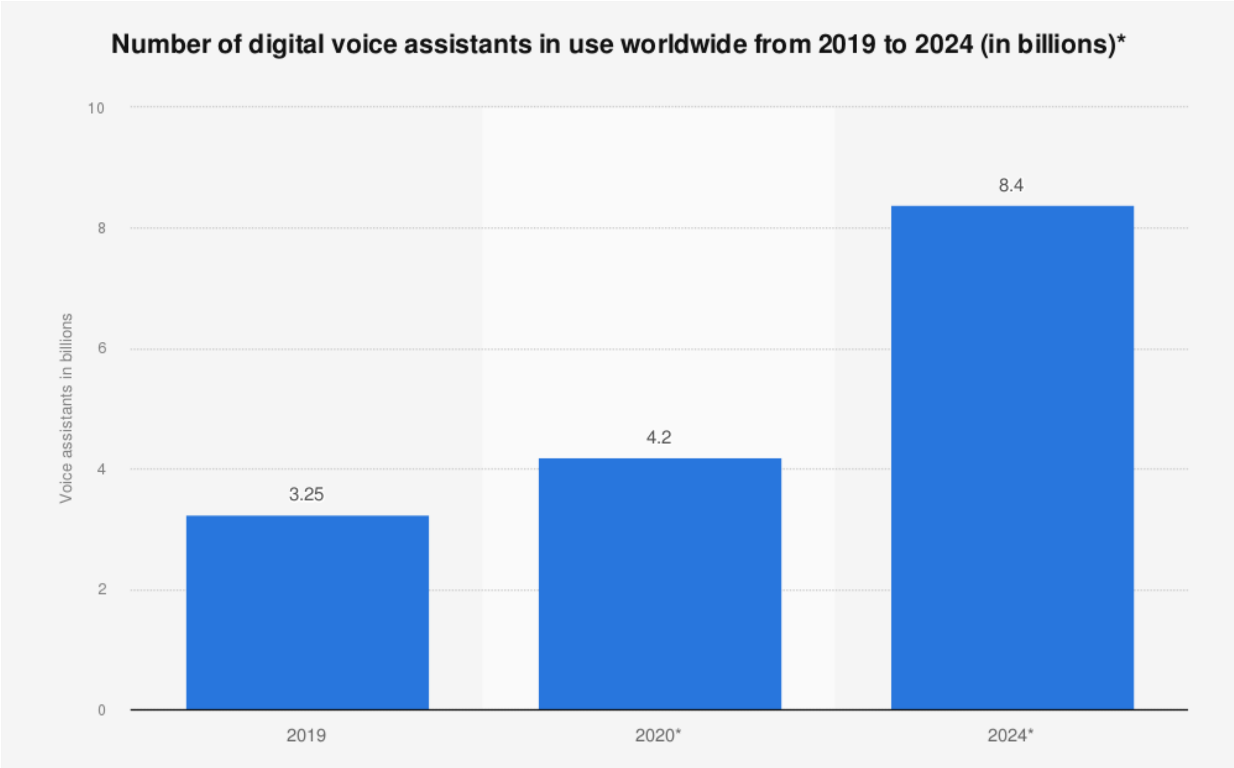



Figure 13: Number of digital voice assistants (Voicebot.ai, & Business Wire, 2020)

It is evident that ISA devices have endless possibilities of application in many fields. One of these is for sure the healthcare world where devices like these could potentially bring huge and consistent benefits, both in a domestic and in a hospital context, allowing different development strategies and functionalities. However, it must be remembered that the use of voice assistants in healthcare is certainly an innovation. Although several solutions are at a more or less advanced stage of development, it is not easy to find studies in the literature that have already been completed. Following research, it can also be seen that there are a very limited number of vocal assistants on the market that support people's well-being, and above all this is almost entirely an American market.

Available solutions include both systems designed specifically for their purpose (hardware and software), and extensions (software only) that rely on existing technologies such as Amazon Echo or Google Home. In fact, these companies allow third parties to implement their software on their commercial hardware. This aspect produces important opportunities for all the researchers that want to develop their application and do not have enough competencies to create a voice platform. The powerful combination of deep learning and natural language understanding allows the implementation of human-machine verbal communication into the clinical field to optimize organizational performance and workflow.

Below are some of the most relevant solutions found. It should also be noted that the limited amount of information on the interaction models and functionalities of these technologies that can be accessed allows only a very limited analysis. Literature analysis revealed three main areas of applications for virtual assistants: Lifestyle, Social aspects, and Disease assistance.

Lifestyle is a very challenging and competitive field: smart watches, artificial intelligence and apps are created to support people's healthy living. One example is virtual coaching systems, including any kind of coaching that is delivered through an online platform. As free time for physical activity is limited due to people's busy lifestyles, a virtual coach that helps the individual to organise their days, their physical activity and their meals in a healthy way can be crucial for fitness and nutrition. These devices can also be integrated with other sensors to monitor the user's physical activity, not only giving suggestions, but also tracking results and progresses. Furthermore, acting as a human, a virtual coach can hold conversations, providing information and answering specific questions.

In this area, two specific devices on the market and found in the grey literature are:

SofiHub (https://www.sofihub.com/) : a personal reminder device aimed specifically at the elderly and people with disabilities. The system, called Home, includes a hub with several motion sensors positioned in different areas of the home, with the aim of observing the person's movement. During initial setup, through the online portal, assistants can add new / delete / edit reminders and do live text to voice messaging. The Home system can also help family members and care providers by giving useful insights into important behavioural patterns. Care providers can also access information through messages on a personal online portal so they can see when family members have not taken their medication or participated in important activities. Routines are monitored non-invasively through motion sensors that detect movement, or lack of movement throughout the home. If an anomaly is triggered due to a fall or a 'changed/absent routine', an alarm is sent to the assigned users, ensuring that help is never too far away.

Figure 14: SofiHub vocal assistant (https://www.sofihub.com/)

ElliQ® (https://elliq.com/): it aims to be a friendly, intelligent and inquisitive presence in the everyday life of its user. ElliQ is primarily targeted at older people and seeks to provide a source of companionship, entertainment and fun, while encouraging to achieve health and wellness goals. ElliQ interacts in a natural way through voice command, on-screen activities and proactive prompts and offers a wide range of functions to help leading a healthy lifestyle throughout the day - from daily conversation and inspiration, to reminders for medication, exercise, music and news, and so on.

The second main application is related to the social aspects. The population more prone to social isolation can develop depression and degenerative diseases. The elderly population, mainly, may experience this phenomenon for different reasons, such as problems with their motor system, embarrassment about their physical appearance, hearing problems, etc. This problem can be partially overcome through the use of voice assistants.

Studies have been conducted on groups of elderly people and have shown that devices such as Amazon Echo can be used either by the individual client who considers it as a virtual friend or by some users to stimulate social interaction, for example by playing songs or telling stories. This is supported by the results of a study (Tsiourti et al. 2016) involving 20 potential users of a device aimed at keeping the elderly 'company' for 12 weeks. At the end of this period, a qualitative and quantitative analysis was carried out, resulting in the 'virtual companion' to be appropriate and useful, and overall the results provided promising evidence on how such solutions potentially offer in assisting with daily living in independent living environments.

Regarding social isolation, other important factors could be related to communication, such as the ability to manage one's phone contacts and thus be able to call directly through these virtual assistants. Alexa represents a unique device in this kind of approach, as the Drop function allows to connect to other Alexa contacts.

Finally, the last area is the assistance in diseases. There are several areas where these solutions can fit into a health context. They range from management functionalities to assistive functionalities. As this is the specific area of interest for this project, the available solutions will be analysed in more detail.

The first example is an application programmed to be used with Amazon Echo and Google Home and it is called CardioCube. This application aims to standardize, automate and simplify the check-in, registration, and medical history, taking process through a direct link to the electronic health record (EHR). This functionality allows healthcare professionals to perform time-consuming paperwork during patient registration. This app was analyzed in a study involving medical staff and patients. On the medical side, it was rated highly due to its ability to automatically generate a summarised medical report that is immediately available in the web-based EHR. It also received positive feedback from the patient side and was considered "easy-to-use" (Jadczyk et al., 2019).

Vocal assistants and technologies using artificial intelligence can play a fundamental role in primary prevention and in the monitoring and treatment of people with chronic diseases. They can be useful in helping patients to maintain their independence. A substantial example is represented by Robin (Carroll et al., 2017), focused on helping people affected by dementia at first stages. Robin's purpose is to improve independence with a decision-support assistant during the routine, representing a sort of "electronic memory". The application is used to suggest necessity of intervention, such as reminding to take drugs or call the doctor, to program routines step by step, e.g. how to prepare the dinner, and to propose healthy activities. It is evident that this technology is essential for those patients that are not able to perform natural activities without any help and it could improve their lifestyle. Another example using Amazon's voice assistant aims to assist patients suffering from diabetes (Maharjan et al., 2019). The solution helps Native American diabetes patients to manage their daily diet and learn about food and nutrition. In particular, the main functions include suggesting a meal based on the user's context, local restaurant and restaurant menu recommendation, recipe recommendation, daily/weekly recall of diet history, saving food and recipe to the user's favourites list and more. A preliminary qualitative analysis shows very good accuracy and a high conversational succession rate.

Other solutions aiming more specifically at increasing medication adherence include:

Pillo (https://pillohealth.com/devices) voice assistant guides users through the loading process via on-screen voice and visual instructions. When it's time for a dose of medication, Pillow wakes up and proactively alerts users, improving engagement in health regimes by encouraging, guiding and connecting. Inside the device, 28 doses of appropriately scheduled medication can be kept. It is also possible to connect the device to an app to view the medication schedule on the go and keep track of health data. Through this app it is also possible to add a caregiver profile that can keep track of progress.


Figure 15: Pillo vocal assistant and smart dispenser (https://pillohealth.com/devices)

RxPense® (https://medipense.com/rxpense/) is a personal medication dispensing and remote monitoring solution targeted especially at the elderly, disabled veterans or chronically ill patients in residences, long-term care facilities or at home, in order to get the correct medication taken on time and inform caregivers or healthcare providers if a dose is missed. By implementing it with external sensors, it can also capture, monitor and store vital signs along with the patient's electronic medical record. Medications are organized as shown in the figure and securely locked in the device and can only be dispensed when the patient is authenticated at the right time.


Figure 16: RxPense technology (https://medipense.com/rxpense/)

An example of an App developed on Amazon Echo is MedBuddy. This app alerts users to take their medicines at a consistent time every day. The skill tracks whether participants reported taking or missing their medicine, giving the possibility to monitor the history. This app was tested in a study with 25 participants (Corbett et al, 2021) monitored for 60 days to see if they reported having taken or not their medication, or if they did not respond to the reminder. Of 23 participants who actually finished the study, only 1 reported missing a dose. Structured interviews administered after 60 days showed that around 80% of participants rated their overall experience with the Echo device as good or very good, and more than 50% confirmed the same opinion also for the developed App. Accordingly, most participants (15/23) said they would continue to use MedBuddy as a medication reminder if given the chance and would recommend it to others. Features of MedBuddy that participants appreciated were an external reminder separate from their phone, the ability to hear the reminder from a separate room, multiple reminders and verbal responses to reminders.

## 1.4. Aim of the work

A different concept for monitoring and improving adherence (the "Intake Care" concept), shown in Error! Reference source not found., by offering a modular approach with multiple solutions, has been recently proposed by the research group of Professor Caiani, and is currently under development.

It involves:

- The availability of a dashboard, by which the physician sets the therapy;
- The corresponding reminders are automatically set on different mobile technologies available to the patient;
- Different customizable solutions, based on patients' characteristics, are available to monitor pill intake:
    a. Through the phone's camera: the user photographs the blister pack. An artificial intelligence recognises the missing tablets from the blister photo. It then calculates how many pills have been taken and sends the data to the database.
    b. Through a smartwatch: the user takes medicine. A specially developed algorithm identifies gestures related to the behaviour of taking medications. The confirmation of the intake is sent to the database.
    c. Through Alexa's virtual interface: the user confirms the intake of the medicine by voice. The natural language processing system recognises the request and automatically reports the intake to the database.
- Proper and customized processing techniques automatically interpret such data;
- A reporting activity for the patient, the physician, and family members is present;
- A personalized engagement strategy to maintain adherence is embedded.

To put this concept in place, several Information Technology (IT) tools need to be developed, together with different data communication paths using multiple resources.

The aim of this thesis will be to contribute to this concept by expanding the ways reminders can be notified by developing a voice interface software ("skill") for the communication, management, notification and reporting of medication intake using Alexa. In addition, starting from the IntakeCare implementation in (Rossi, at 2020), the system's architecture was reorganized in order to cope with the requirements and limitations of the Amazon's voice system.

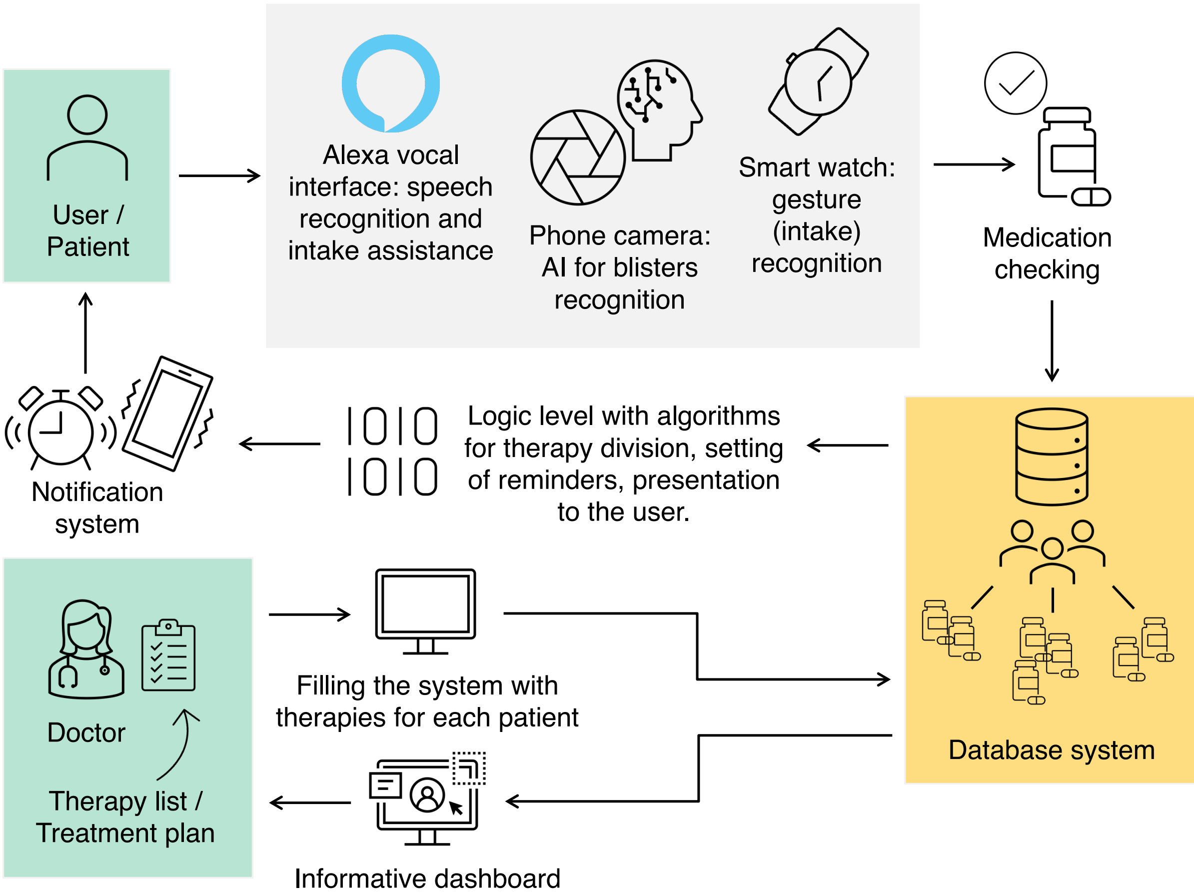



Figure 17: IntakeCare modular system

# 2 Material and Methods

The design of this system allows a physician to insert therapies for patients and check their adherence through a web application; on the other side, a patient will be able to keep under control his prescribed treatment plan thanks to the vocal interaction with Alexa. The two sub-systems can dialogue thanks to an underlying logic layer.

In this section, the requirements of the structure of this system is analyzed and consequently a solution for each component is proposed. The best architecture for this purpose is the three-tier web application one; it is described how each element is inserted inside this architecture, the relationship between all of them and then an insight on the Alexa segment is explained.

## 2.1. Three-tier architecture development

The modularity of the project identifies one of the most significant features: being able to keep separated each fragment is crucial for their singular development, and this can also guarantee the prevention of substantial failures consequent to any changes. That is made possible by the exploitation of the three-tier architecture. A three-tier web application consists of a presentation layer, a business logic layer and a data layer. It is defined as a client-server architecture, or rather, a system that allows making requests to specific services. As previously mentioned, one of the foremost advantages is the modularity that it offers: this grants different individuals to work separately through each section. Improved reliability, security and scalability are the other benefits: each module is independent from the others and can communicate with different and expandable modules. For example, it is possible to connect another database to the backend or to add new modules for future implementations, such as a smartphone application.

As visible in Figure 18, the architecture has been realized using different tools or platforms, which will be explained individually in the following paragraph.

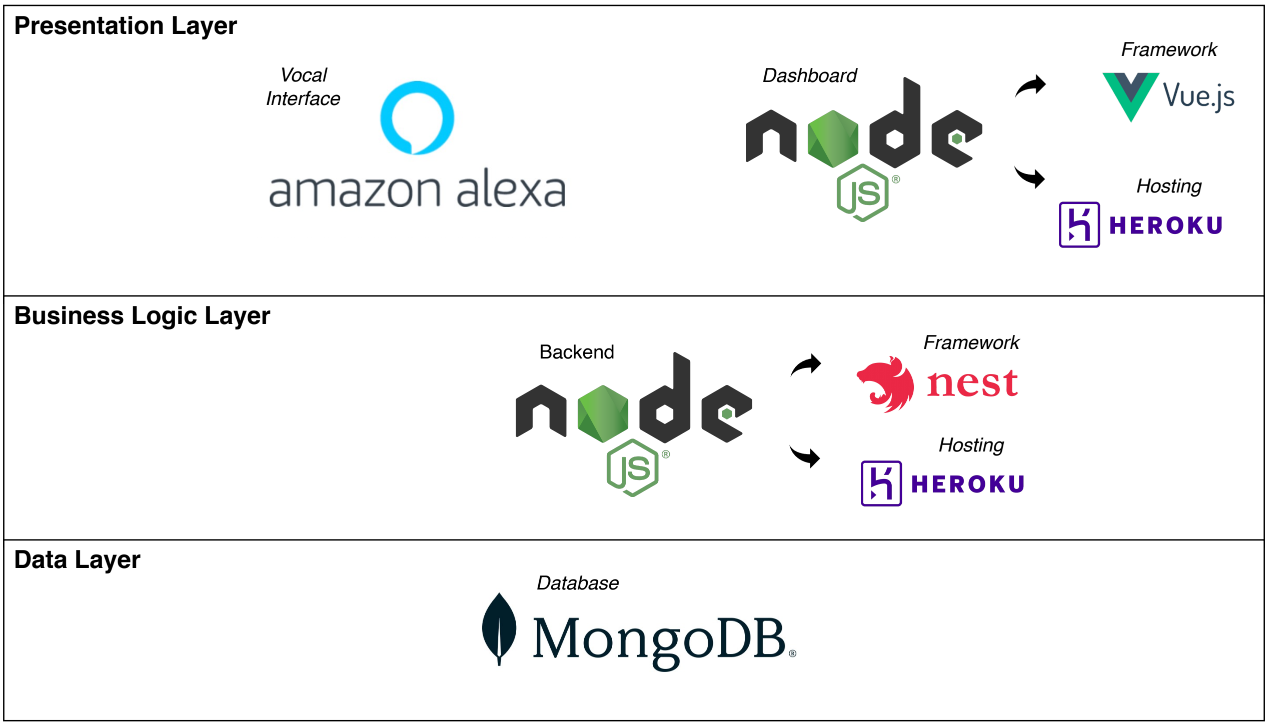



Figure 18: Representation of the Three-tier architecture with the frameworks exploited for each level

Each layer fulfils a specific function, but it is the integration of each of them that allows performing different higher-level tasks.

Figure 19 represents the use case of the platform. It summarises the usages of all the possible stakeholders interacting with the software: Administrators, Doctors, Patient and the System.

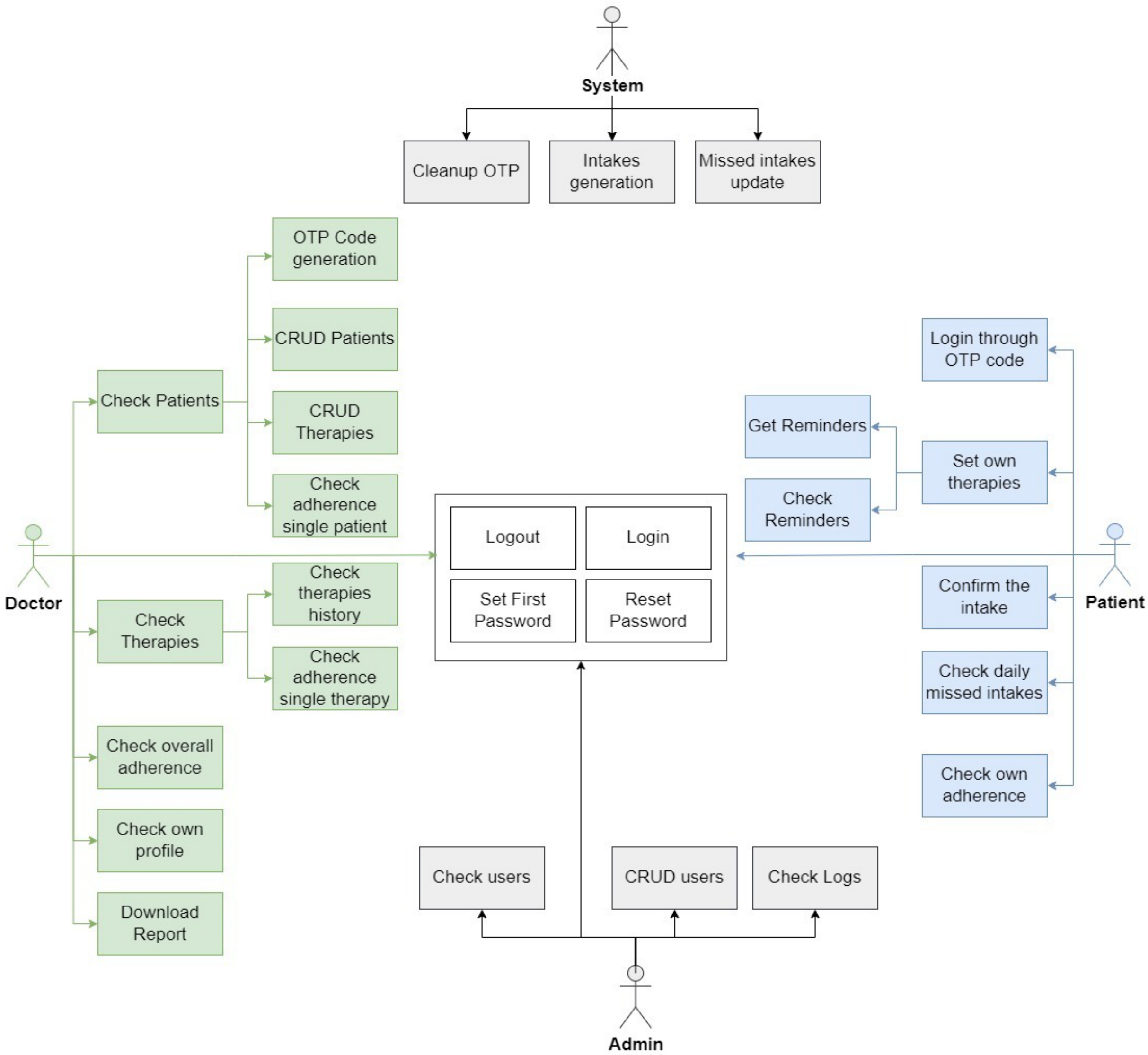



Figure 19: Use cases of the platform based on the different users. CRUD: Create, Read, Update, Delete. OTP: one-time password

In the following lines, an overview about the requirements and the corresponding functions of each architecture's layer will be explained.

### 2.1.1. Data Layer

The data are the bridge between doctors and patients: it is indispensable to have a platform to store, update and retrieve data. This platform is a database, and to this aim MongoDB (https://www.mongodb.com/cloud) was adopted in this project. MongoDB is a NoSQL database, a non-relational database. Differently from Database Management Systems (DBMS), which store information in relational tables, NoSQL databases store JSON files, and for this reason they are also called document databases. Although many users know DBMS because of their availability on the market for a longer time, NoSQL databases present many advantages. Capturing the differences and specificities of the two types of database allows one to understand the choice in using MongoDB. In particular, because of their characteristics, NoSQL databases are the most widely used in the medical field.

The compliance rules for DBMS are four properties of relational databases, and it is possible to summarise them in:

- Atomicity, namely every transaction must be bounded either when successful or not;
- Consistency, transactions are valid and not rolled back only when data complies with the database rules which are defined a priori;
- Isolation, which guarantees that the database can handle concurrent transactions, managing them as they are separated;
- Durability, data are saved permanently either when the transaction is successful or not.

NoSQL databases are newer and, for this reason, there are fewer frameworks able to interact with them. However, their structure allows remarkable flexibility since there's no need for strict rules for data validation. Less stringent consistency requirements mean improved performance when changing the data structure. A relevant difference between the two types of databases is their scalability. DBMSs can scale horizontally, which means that they need to increase the number of servers to guarantee higher performances. NoSQL databases scale vertically, which means that the database can scale when increasing the power of a single server. Vertical scaling is possible because of the unnecessary requirement of a data structure, with a significant advantage in terms of resources. One NoSQL database can scale horizontally by building a distributed architecture with disjoined servers: the result is the doubling of its performance.

Querying DBMSs is straightforward: therefore, this type of database is used when conducting data analysis. However, the documents collected by NoSQL databases are expandible without too many restrictions, thus allowing managing many and heterogeneous data with simplicity. One example is the medical record, a significant collection of different information and documents. Clearly, distinct patients can have very heterogeneous health records, from personal details to prescribed therapies or medical interventions. It is unlikely to use a DBMS for this purpose: because of the dissimilarities of its element, it should be created a sizeable database with unavoidable blank spaces. NoSQL databases optimize space and performances in these situations. Furthermore, DBMSs suffer SQL injections that are designed queries with malicious code, able to access data without permission. Similarly, NoSQL injections take advantage of weaknesses in the user queries.

| Features | DBMS | NoSQL |
|---|---|---|
| Popularity | Older, many user interfaces to access them | Newer, fewer tools to access data |
| Structure | Fixed, stringent | Flexible, few rules |
| Scalability | Horizontal (issues if the data is huge and heterogenous) | Mainly vertical and horizontal |
| Querying | Straightforward and quick | Less simple |
| SQL injection defence | Weak | Not suffering (but new cracking strategies in development) |

Table 1: DBMS vs NoSQL

Overall, MongoDB represents a new technology, a great system able to manage automatically different servers, and with high fault tolerance. Additionally, it collects data as close as possible to the user's location. MongoDB stores the records as Documents and accumulates them into Collections. In Figure 20, the Collections inside the database are listed. Each Collection defines a Schema, or rather a structure that all the Documents internal to the collection share. Anyhow, this doesn't affect the possibility to create heterogeneous Documents.

The implemented Collections are:

- Credentials: each Document stores the Username and the Hashed Password of one user. Bcrypt algorithm is used to obtain the hash value of the password. The Bcrypt is a function used in cryptography that is singularly robust to rainbow table and brute force attacks. The algorithm hashes strings merging them with a random one called Salt, whose purpose is to increase the complication in cracking the password.
- Pairings: each Document stores the OTP security code for a short temporal window. The one-time password (OTP) is a disposable authentication method. An authority generates and distributes the OTPs to the clients, which they can use just one time. If the value of the OTP correctly matches the one stored in the database, the OTP is valid. The authority enables the release of an Authentication Token, which is mandatory to access particular APIs. The client can use the Authentication Token only if the OTP is valid, which means exploiting the API of the program that (s)he wants to use. As the OTP is disposable, the authority deletes it after use.
- Users: each Document stores personal information (such as Name, Surname, Email, Telephone Number) and connects them with the associated Credentials. It collects the User Type (Admin, Doctor or Patient) and the Pairing ID (see above).
- Admins: each Document connects directly to the User Document. It empowers the user to do CRUD (*Create, Read, Update, Delete* ) operations on other Users.
- Doctors: each Document connects directly to the User Document. It allows the user to do CRUD operations on Therapies and Patients.
- Patients: each Document connects directly to the User Document and the associated Doctor.

- Therapies: each Document connects directly to the Doctor who prescribed the therapy and the referred Patient. It stores the Drug Name, the Delivery methods, the Duration (Start Date and End Date), the Posology and its relation with, Meals (After, During or Before the Meal). In addition, it stores the State of Validity of the posology (if in use or dismissed), the State of Editing (if New, Updated or Saved), the Validation method (i.e, the way to check the appropriateness of each Intake), and the Adherence score. Four Delivery methods can be distinguished, according to their Type: Daily, Weekly, Interval or Once. For Daily, the therapy repeats every day; In Weekly, it repeats just on specific days of the week. With Interval, the treatment repeats on interspersed days; with Once, it occurs just one time. The Delivery field contains many Options, each of them has three sub-fields: Cadence, Time and Maximum Delay. Cadence defines the occurrence rule: Cadence is 1 when the Scheduling Type is Daily or Once, >1 when it is Interval, and it is an array of days of the week when the Scheduling Type is Weekly. The Time field represents the hour at which the alarm of the Intake should occur. The Maximum Delay defines the interval beyond which the Intake is considered too late to be counted as valid.
- Intakes: each Document connects directly to the referring Therapy Document. It stores the Programmed Date (the scheduled moment of the Intake), the Maximum Delay, and the Status (Programmed, Taken or Missed).
- Logs: each Document connects directly to the User Document. It stores the Datetime and the Source for every specific Intent the user invokes interacting with Alexa (see Alexa Intents later).

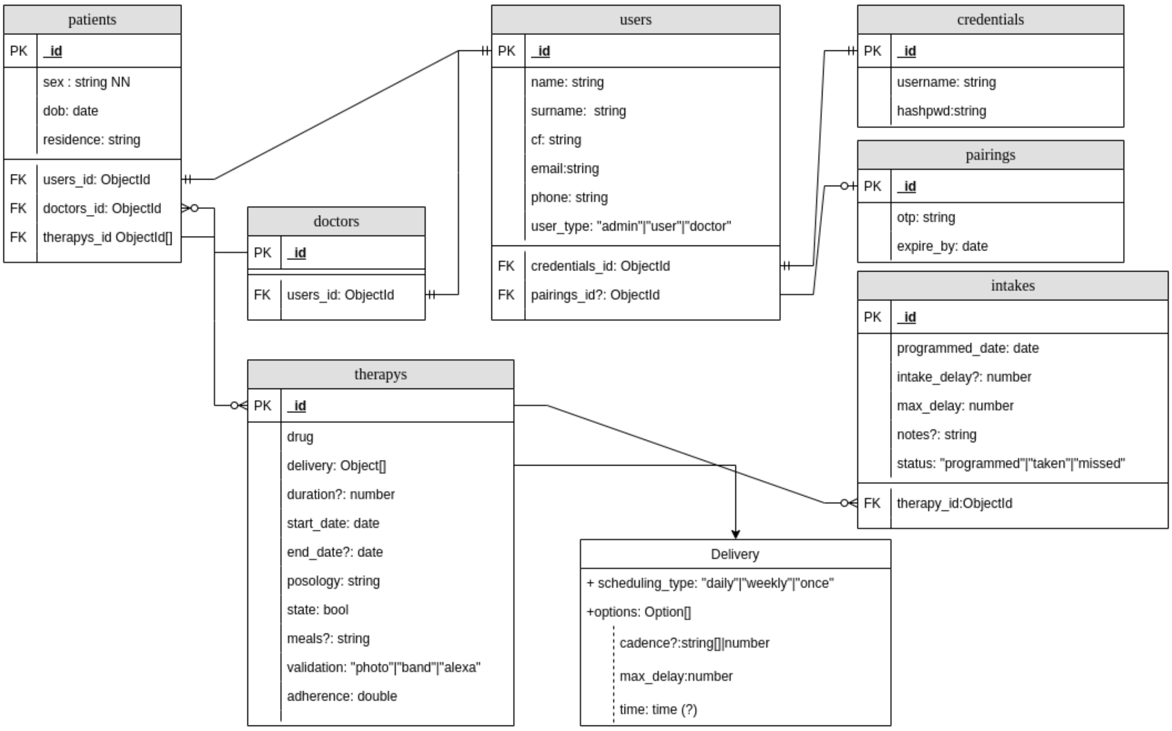



Figure 20: ER diagram

### 2.1.2. Business Logic Layer

The backend, or Business Logic layer, is the core of the functionalities of an application and represents the data access layer where all the services and the operations occur. A backend is programmed in different languages through several possible frameworks, and a platform should host it.

The framework that has been chosen for this work is Nest.js (Cancelliere, at 2022), which uses Node.js, a TypeScript runtime environment, which adds optional static typing to JavaScript. JavaScript is a high-level programming language and represents a core component of many Browsers; Node.js allows the exploitation of JavaScript to create server-side applications. To host the backend, Heroku has been used. Heroku is a PaaS (Platform as a Service): it principally is an on-demand available resource that allows storing and computing data, and for this reason, it is a cloud service.

The programming of the logic layer is comprehensive of several functions: CRUD operation for users and therapies, generation of intakes from a treatment, calculation of the adherence according to the taken or missed medications, etc.. The backend mirrors the tangible functionalities that each user can experience.

### 2.1.3. Presentation Layer

The top-most level of the three-tier architecture is the Presentation layer. Two separated interfaces have been designed: a dashboard, intended for the doctors' use, and an Alexa application, also called skill, intended for the patients. The dashboard was developed in a parallel study belonging to the same project by F.Cancelliere (Cancelliere, at 2022); the development of the Alexa skill was the focus of this thesis.

#### Dashboard

To develop the dashboard, Vue.js has been used, which is a simple, user-friendly and well-documented framework. In particular, it has a library for outlining the user interfaces, which is Naive UI. Many similar applications, minding the widespread standards, have been studied and analyzed in order to get inspiration for graphics and layouts. The dashboard progresses from an previously developed framework (Rossi, at 2020) that have been reshaped, keeping the foremost functionalities, but with a broader and in-depth analysis of each requirement. The main features are the forms for creating patients' profiles, inserting treatment plans, checking statistics of patients and displaying principal information about adherence and patients' therapeutic history. In the figures below, it's possible to see the most important pages of the dashboard.

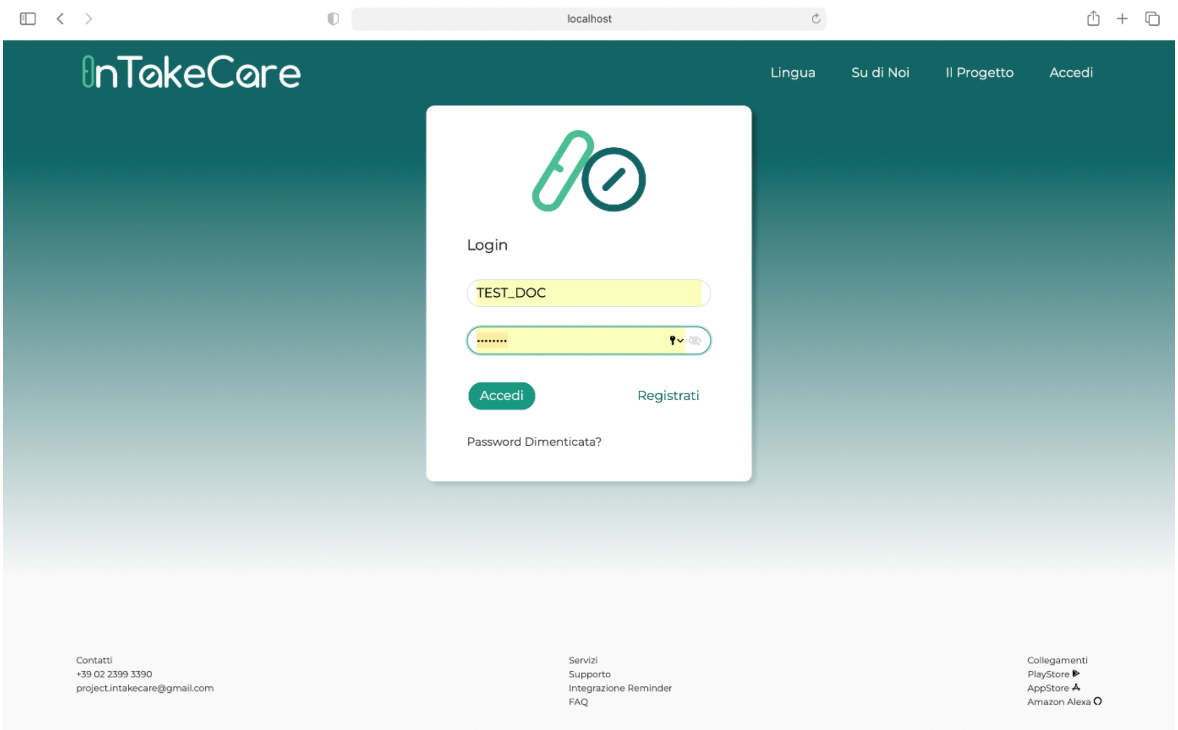



Figure 21: Login page

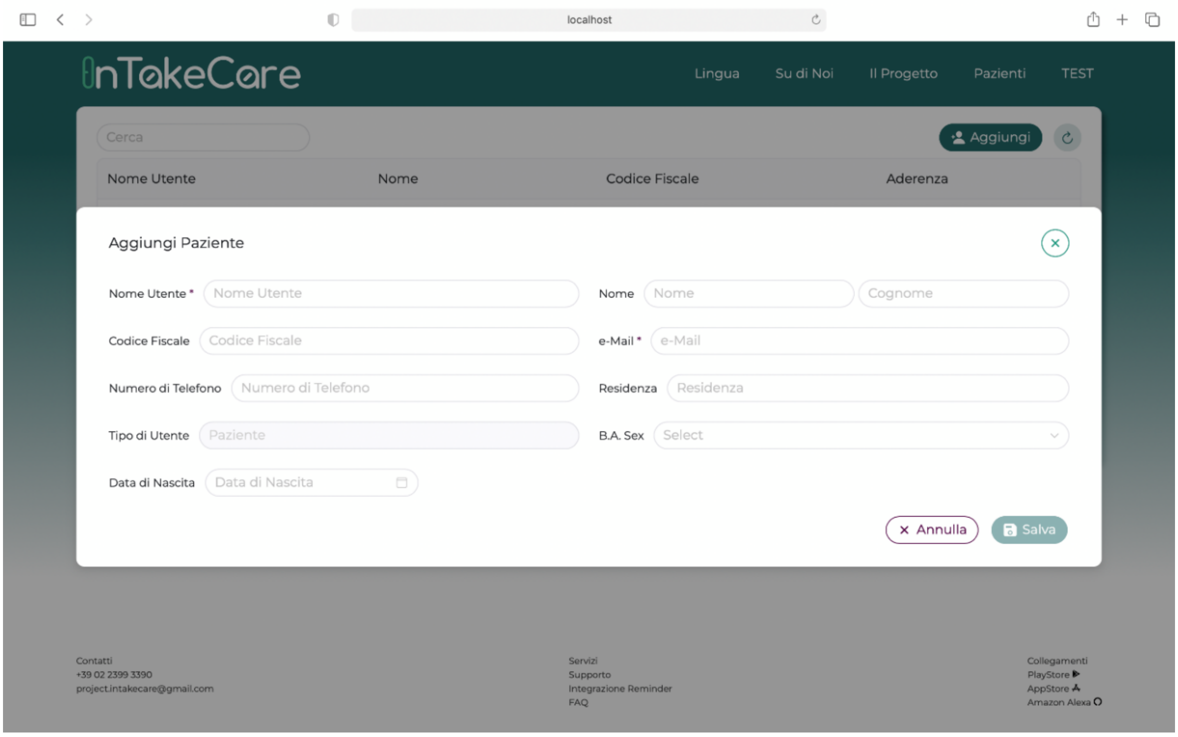



Figure 22: New patient form

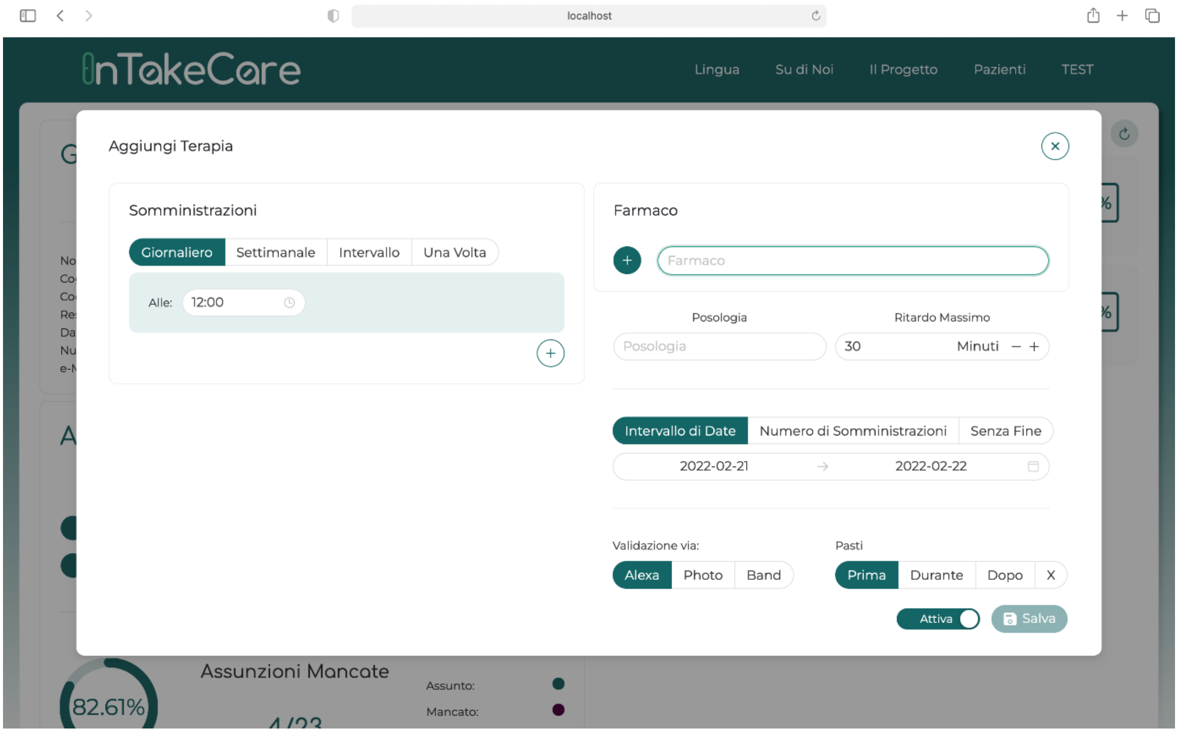



Figure 23: New therapy form

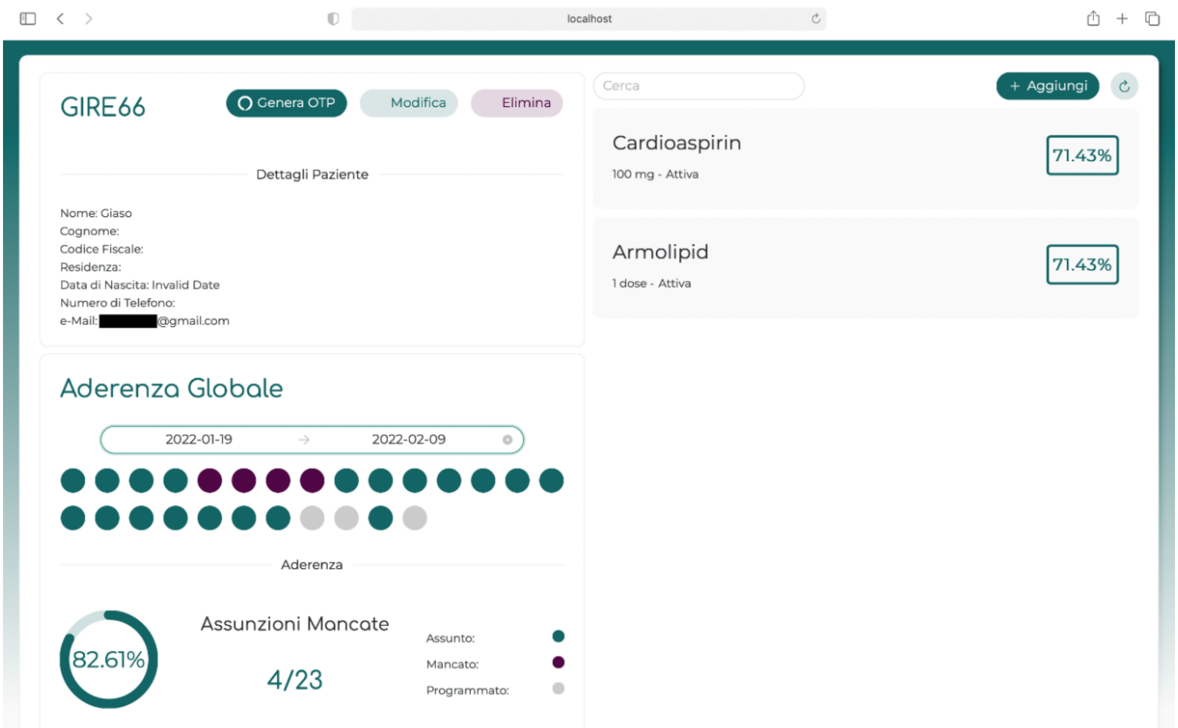



Figure 24: Patient overview

### Amazon developer console and Alexa skills

Alexa is a service in the cloud offered by Amazon, divided into two basic parts.

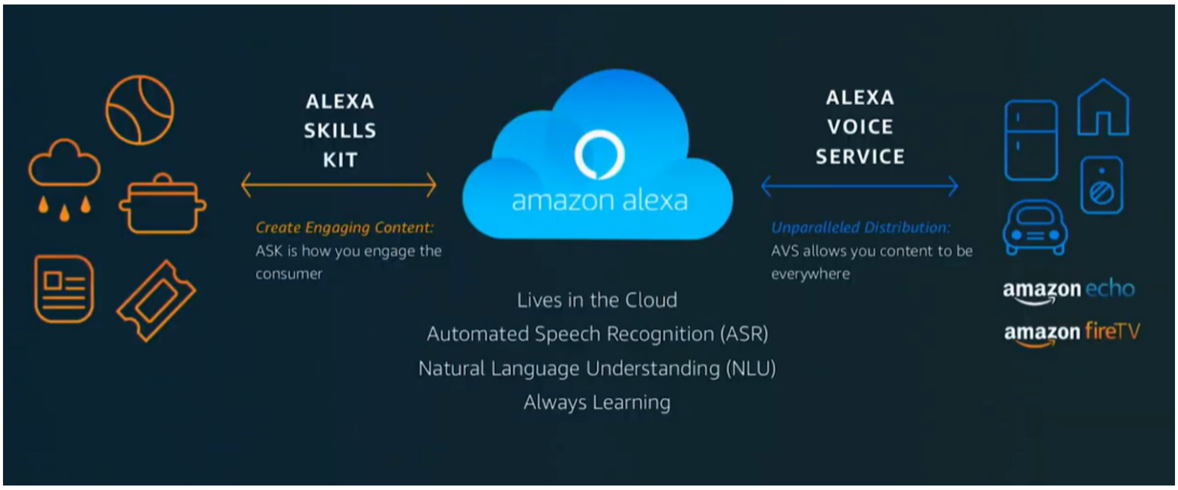



Figure 25: Amazon Alexa

The first part is the Alexa Voice Service, i.e., how devices of all kinds can be interfaced with the Alexa service. The figure below shows just a few of the existing examples. These include the Echo Dot or the Echo Show, which are devices produced directly by Amazon, but also third-party products such as domotic devices.

Specifically, the Echo Dot devices have a purely vocal interface, with slight differences in audio quality and design between the various generations. The Echo Show devices have a small touch screen and a video camera both for vocal and visual interaction. Again, the various models vary in size and audio and video quality.


Figure 26: Examples of Alexa-Enabled Devices

Once all these products are connected to Alexa, the desired functionality has to be set. This is done via skills. Skills "teach" Alexa new things.

Amazon Alexa skills are like apps for Alexa that allow the development of methods useful to share new content or services. It is possible to enable and disable the Skill using the Alexa app or the web browser, in the same way as the one used to install and uninstall apps on a smartphone or tablet. It is either possible to view all the available Skills and activate or deactivate them using the Alexa app. Alexa, with its interactive voice interface, offers users a simple, hands-free way to interact with the skill. The skills developed can also take advantage of the automated speech recognition and natural language understanding implemented in the Alexa device (https://developer.amazon.com/en-US/alexa/alexa-skills-kit).

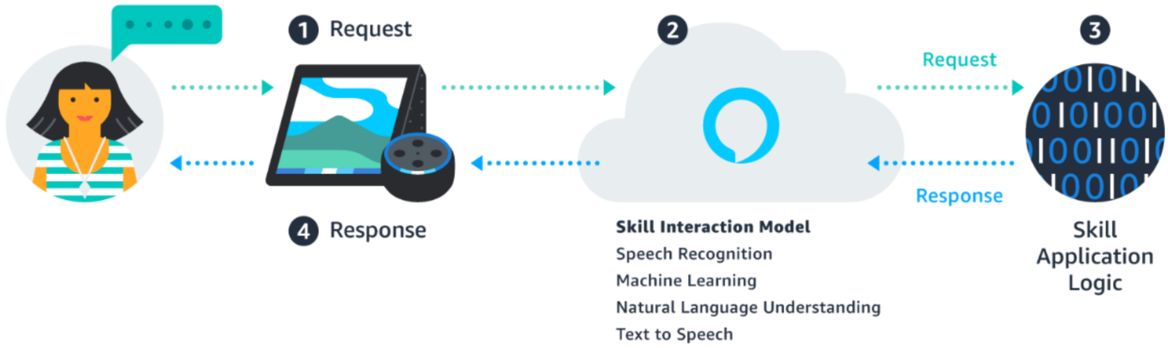



Figure 27: Alexa skill diagram

New skills can be developed and subsequently published by organizations or individuals to reach users on hundreds of millions of Alexa devices. Support for the development of an Alexa Skill is provided by the Alexa Skills Kit (ASK). This kit consists of tools, application program interfaces (APIs), Skill components, code samples, and documentation that enable a developer to add expertise to the more than 10,000 voice recognition capabilities already available in Alexa.

The general architecture of the Alexa system is shown in Figure 28. When a user speaks, the sound the user makes is processed by the device. The only thing the device can do is figure out if the user has said the starting word called "wake-word": Alexa. Once it senses the Alexa word, it sends everything else to the Alexa service. This service does two things: it converts sound into text (automatic speech recognition) and then interprets the meaning of the text. Machine Learning algorithms and Natural Language Processing techniques are used to do this.

The process starting with the voice request (input) and ending with Alexa's response (output), visible in the next figure, has a maximum duration of 8 seconds. This aspect is crucial for the Skill development phase and its implications will be analysed in the Discussion chapter.

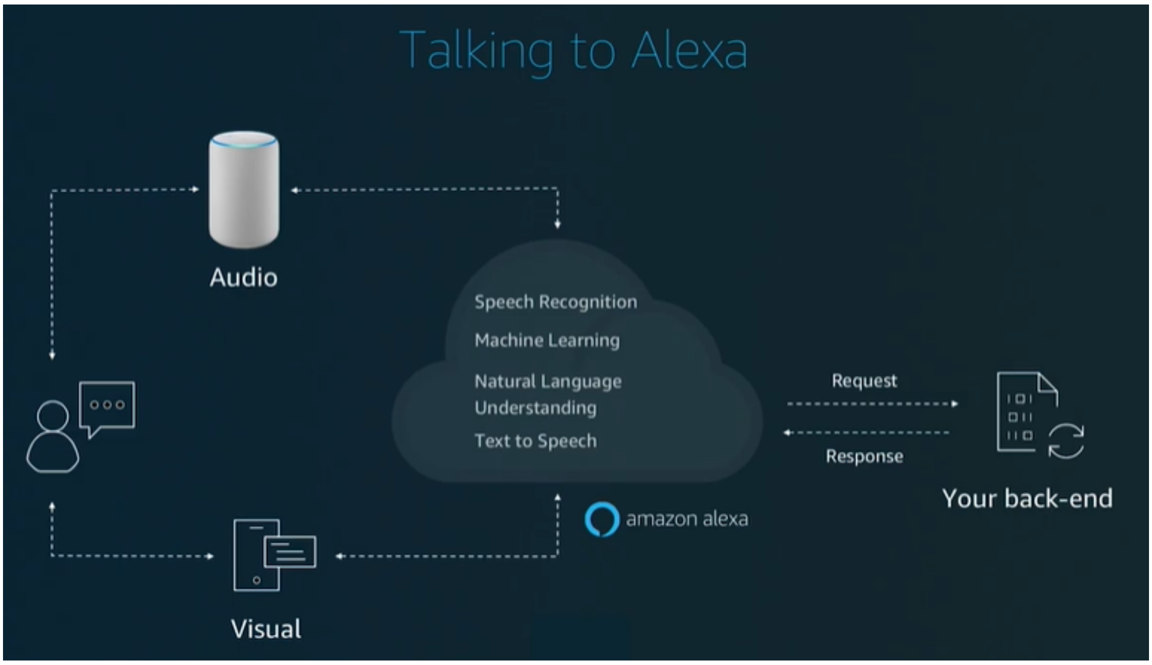



Figure 28: Architecture of Alexa skills

To develop a Skill, two different components must be designed. The Voice Interaction Model, i.e. how the voice communication between the user and Alexa takes place, and the implementation logic, i.e. the back-end where all the necessary functions and reasoning reside.

The various steps to be taken are shown in Figure 29 and described subsequently.


Figure 29: Alexa skill steps

*Design the skill:*

The first step in creating a Skill is to choose the voice interaction model. In this first design step, it is necessary to design voice interactions adapted to the way users express their intent naturally through speech (https://developer.amazon.com/en-US/docs/alexa/ask-overviews/voice-interaction-models.html). Each Alexa skill has a voice interaction model that defines the words and phrases, called *utterances*, that users can say to Alexa to make the skill do what they want.

Alexa supports two types of interaction models:

- Pre-built voice interaction model – a set of predefined utterances by Alexa;
- Custom voice interaction model – Developer defines the utterances that users can say to interact with the skill. The custom voice interaction model allows enormous flexibility and control. In fact, the developer designs the set of utterances (words and phrases) needed to activate each feature of the skill. In particular, at the time of designing the custom voice interaction, it is essential to define:
    - The invocation name that identifies the skill. The user will speak this name whenever they want to initiate a conversation with the skill;
    - The intents that will be managed in the skill. The intents represent the actions that the user can exploit, where each intent invokes functionalities of the skill;
    - The utterances that users must cite to invoke the intents. The interaction model of the skill is represented by the mapping of utterances. An utterance can trigger only one intent, but one specific intent can be invoked by several similar utterances. A wide choice of utterances defining the same purpose can increase the naturalness of the language and interaction between the user and Alexa. Utterances may contain optional or mandatory arguments, called slots, which collect variable values that your skill needs to satisfy the user's request.

*Build the skill:*

Once the developer has chosen the voice interaction model and the type of skill to be developed (https://developer.amazon.com/en-US/docs/alexa/build/build-your-skill-overview.html), it is possible to start the building phase.

To start building a skill using a customized speech interaction model, it is necessary to be aware of the required resources, here listed:

- Reinforcement: the subject has a behaviour that needs to be stimulated, channelled or enhanced.
- An accessible endpoint from the Internet to host the cloud-based service. When creating an Alexa skill, it is possible to decide whether to store the code and manage the backend resources on Amazon Web Services (AWS) Lambda or build and host the skill as an HTTPS web service (for this option, a cloud hosting provider and an SSL certificate are needed), or just take advantage of Alexa-hosted skill. The latter method stores the code and resources on AWS and allows to quickly starting programming using one of the skill templates available in the developer console. Using an Alexa-hosted skill also avoids the need for an AWS account as Alexa itself provides the AWS needed resources directly from the developer console. Alexa places the files and resources in an individual account, which is of course strictly separated from the accounts of other users. By choosing the Alexa-hosted skill option (https://developer.amazon.com/en-US/docs/alexa/hosted-skills/build-a-skill-end-to-end-using-an-alexa-hosted-skill.html), development takes place directly in an online code editor in the developer console.
- An appropriate development environment for the programming language that is intended to use to code the skill. If the Alexa-hosted skill option is chosen, the available languages are Node.js or Python.
- An accessible website to host any media used in the skill. If the Alexa-hosted skill option is chosen, Alexa assigns an Amazon S3 bucket to store the content.

*Test the skill:*

Once the Skill is programmed, a testing phase is necessary. The Alexa Skills Kit (ASK) includes tools that allow testing and debugging the skill. The skill test can be carried out using the Alexa simulator in the developer console (it does not support simulation of all functionalities), the Alexa app installed on the desktop or smartphone, or an Alexa-enabled device. If it is done on the Alexa app or an Alexa-enabled device, such as an Amazon Echo, a log in with the same email address used to sign up for the account on the Amazon developer portal is needed.

Another existing option before the release of the Alexa skill is to test the beta version of the skill with a limited set of users. This option also allows testing any changes to an already published skill while keeping the skill available to the public. Any user associated with an email address can be included as test users, with a maximum of 500 invitations per skill, and at any time it is possible to add and remove testers, or end the beta test period.

A prerequisite for the use of the skill beta is that the beta tester logs into the Alexa device with the same email address as the one entered by the developer in the invitation. During the beta test phase, the Beta Test section in the developer console provides a dashboard showing which testers have accepted the invitation. From here it is possible to add and remove testers, send reminders (one reminder per tester is allowed during the whole duration of the beta test) and request to testers, or decide to end the test phase (https://developer.amazon.com/en-US/docs/alexa/custom-skills/skills-beta-testing-for-alexa-skills.html).

Another useful test to run is the utterance test. When building the interaction model using the utterance profiler, it is possible to enter utterances and see how they resolve with intents and slots, thus verifying that the utterances invoke the right intent and do not risk triggering unwanted intents (https://developer.amazon.com/en-US/docs/alexa/custom-skills/test-utterances-and-improve-your-interaction-model.html).

*Certify and publish the skill*

After the design, construction, and testing phase, certification is necessary to carry out the publication in the Amazon Alexa Skills Store. The certification phase requires the fulfilment of policy, security, functionality, voice interface, and user experience requirements (https://developer.amazon.com/en-US/docs/alexa/certify/certify-your-skill.html).

*Monitor the skill*

After the skill is certified and published, it is possible to monitor its usage and perform analytics to help the developer understand how users interact with the skill. It is possible for example to monitor the number of unique customers, the percentage of users who invoked a particular interaction path of intent, and more.

## 2.2. CareVoice

The solution developed and proposed by this thesis project has been called CareVoice. CareVoiceis an Alexa Skill, designed to be available on any voice interface device provided by Amazon (e.g. Echo Dot, Echo Show, and others), as a smart solution that allows users to keep their pharmacological treatment plan under control.

In the following paragraphs, the implementation logic of the entire application is shown, divided into the first part of Voice Interaction Model and the second part of Programming Logic.

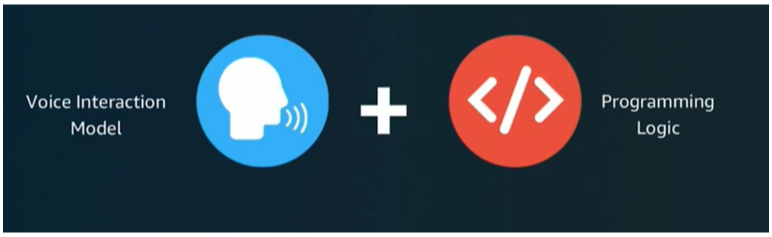



Figure 30: CareVoice components

Referring to figure 30, it is possible to identify the design phase with the voice interaction model and the build phase with the construction of the programming logic. The object of study of this thesis exploits the beta test functionality. The certification and monitoring of the skill, on the other hand, will be the subject of future developments because they follow its publication.

### 2.2.1. Interaction model

The following block diagrams summarise the possible voice paths programmed in the CareVoice skill. The user's voice interactions are marked in green in the figures, while Alexa's responses are in blue. The phrases users pronounce to trigger the various CareVoice intents (or functions) may be slightly different because the skill has been programmed including aliases corresponding to synonyms or variations, provided the meaning remains the same. Some voice paths are compulsory, such as the identification phase of the user through the OTP; others are triggered according to the user's will, such as processes linked to information on one's adherence status.

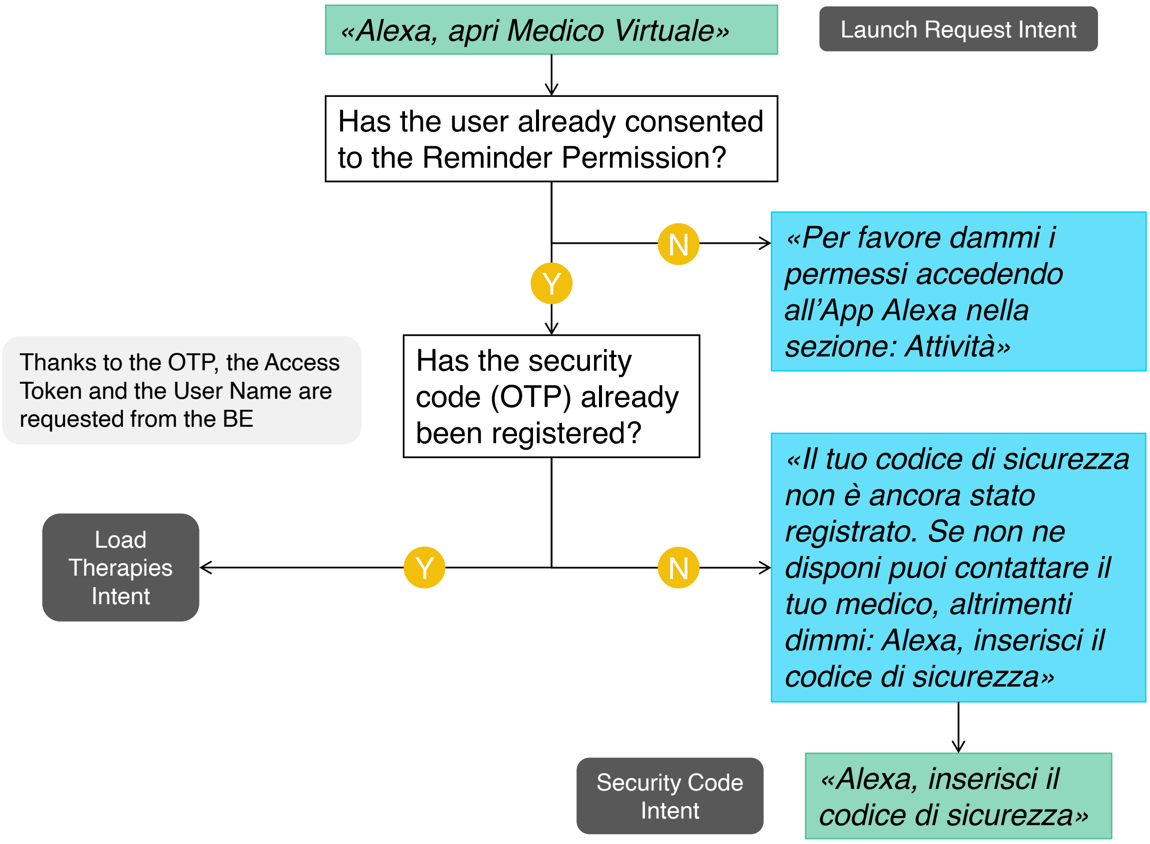



Figure 31: CareVoice Launch phase

The 'Virtual Doctor' must be invoked for opening the skill. During the first opening of CareVoice, the system will check if the user has already enabled the skill to send reminders. If not, Alexa will ask for such permissions. This procedure will be explained in the algorithm section below. Afterwards, it will be necessary to open the skill a second time.

If this step has not performed before, the system will ask to combine the Amazon user profile with that of a patient in the CareVoice doctor's logbook. This step requires the entry of an OTP that has been given to the patient in advance by the physician. If the user says "Alexa, enter the security code", the intent that handles the OTP will be triggered (Figure 32).

In this intent, Alexa will ask the user to pronounce the digits of the Security Code and if it is correct, Alexa will greet the user by saying its name, and suggesting the phrase to proceed to trigger the actual configuration of therapies (e.g. "Hello Maria! Tell me: Alexa configures my therapies, to proceed"). The combination with the OTP is essential for security reasons and to obtain the token from the database to access all user's data.

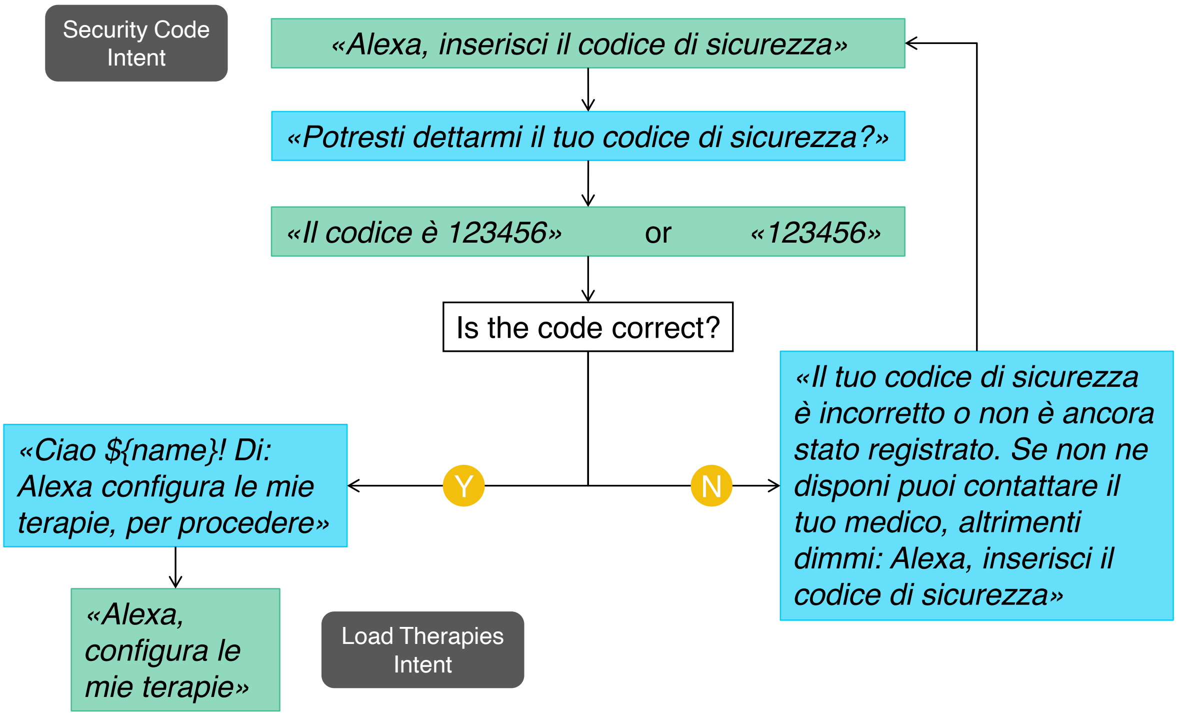



Figure 32: CareVoice Security pairing phase

If the Amazon user profile has been already associated to a patient in the CareVoice doctor's logbook, when CareVoice opens Alexa will immediately notify the user if therapies to configure are present. Alternatively, pronouncing the trigger phrase "Alexa, configure my therapies" the therapies are loaded from the database and will be available to the skill in its session. Figure 33 shows the voice interface diagram concerning the configuration of medications.

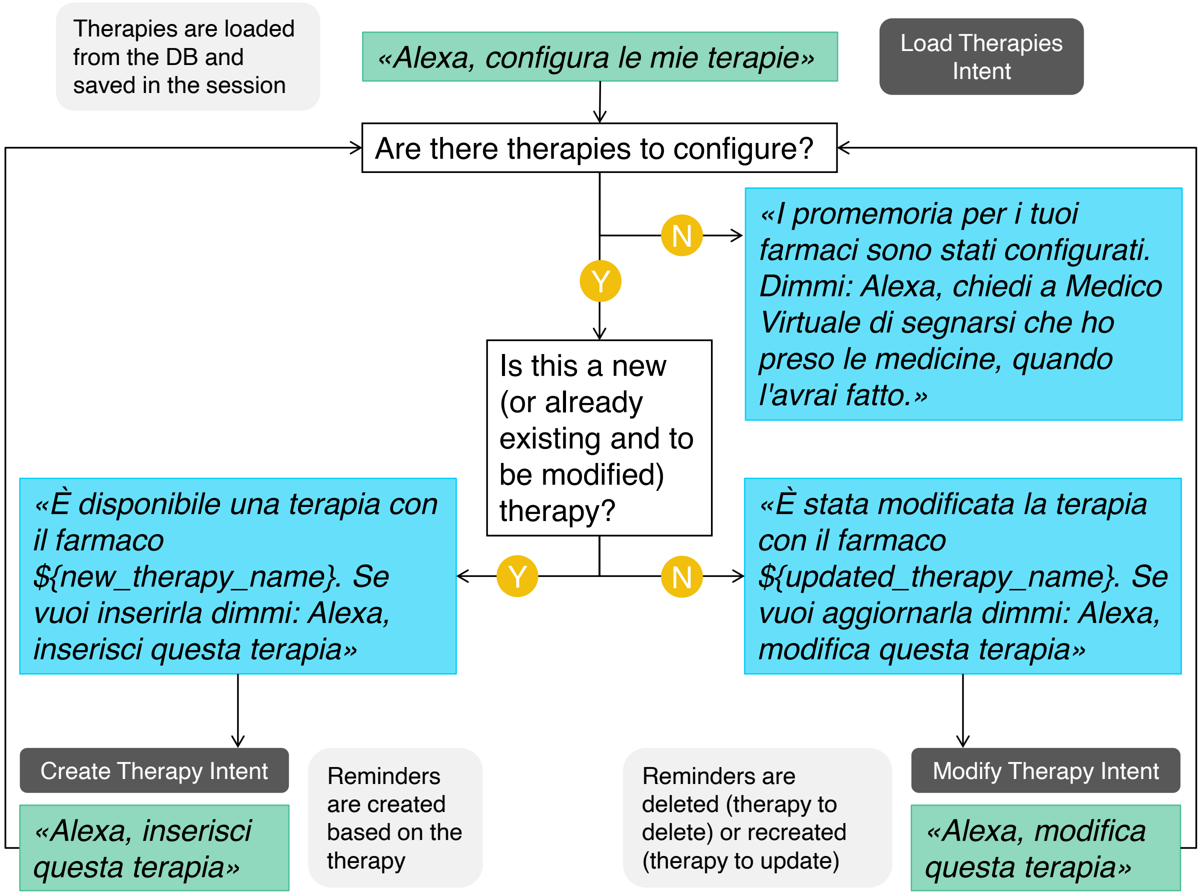



Figure 33: CareVoice Therapies configuration phase

The system checks if new therapies, or changes in existing therapies, have been inserted by the physician. In the former case, Alexa will inform about the new drug and ask for consent in order to allow the system to schedule reminders for that medication, as prescribed by the physician. In the latter case, the user will have to confirm the modification. The system will consequently edit the reminders if the therapy needs to be updated or remove them if the medication needs to be erased.

Once there are no more therapies to configure, Alexa will say: "The reminders for your medication have been configured. Say: Alexa, ask Virtual Doctor to mark that I have taken my medication when you have done so".

As previously anticipated, the algorithm automatically set all the reminders, so that the user only has to worry about confirming that the medication has been taken.

When a reminder is triggered, after taking the medication the user has to activate the confirmation phase with the uttering: "Alexa, ask the Virtual Doctor to note that I have taken my medication" (see figure 34). At that point, the system will create the list of intakes scheduled in the 60 minutes preceding this interaction. If the list is empty, Alexa will say: "There are no medications to take at this time. Try again later or check your reminders". If there are items in the list, Alexa will ask iteratively for each item if the drug has been taken, for example: "Have you taken 100mg of Cardioaspirin?". The user will have to answer either yes or no.

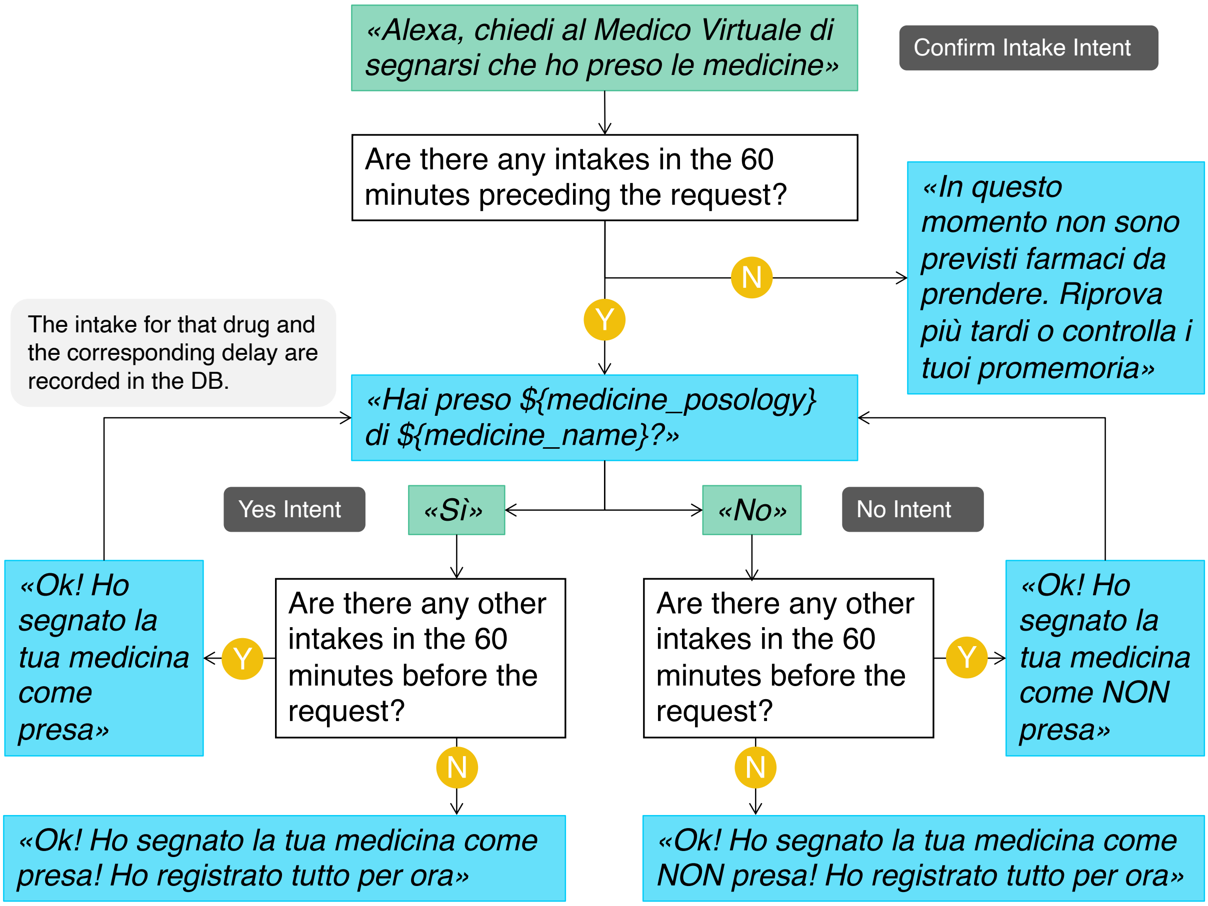



Figure 34: CareVoice Intakes confirmation phase

Once the list is complete, this message will be followed by: "I have recorded everything for now".

The user can also ask about its adherence. There are two intents that are triggered by different sentences.

The first one is to check on scheduled medications that the user could have forgotten to take during that day until the moment of the request. In case of not taken medications, Alexa will list them with a sentence like: "Hi! Today you forgot to take two medications. Specifically, you didn't take: 100mg of Cardioaspirin at 19:00 and 1 pill of Lisitens at 12:30!". As can be seen, the posology field can vary to indicate dosage in pills or grams. Alternatively, a supportive message will be given: "Congratulations! Today you have taken all the medicines you have scheduled so far!" (see Figure 35).

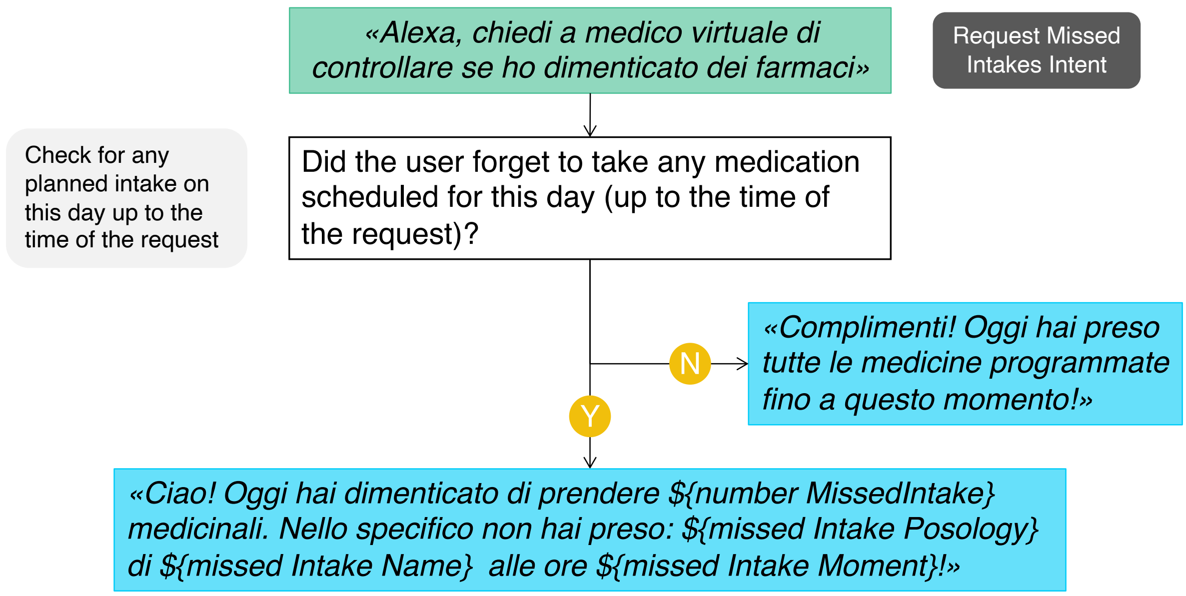



Figure 35: CareVoice Missed intakes request

The second intent is the request for the adherence. Alexa will reply: "Great!" if adherence is greater than 80%; a neutral sentence if it is less than 80% but greater than 30%, and an invitation to pay more attention when adherence is less than 30% (see Figure 36). How the adherence value is calculated will be discussed in the algorithm paragraph below.

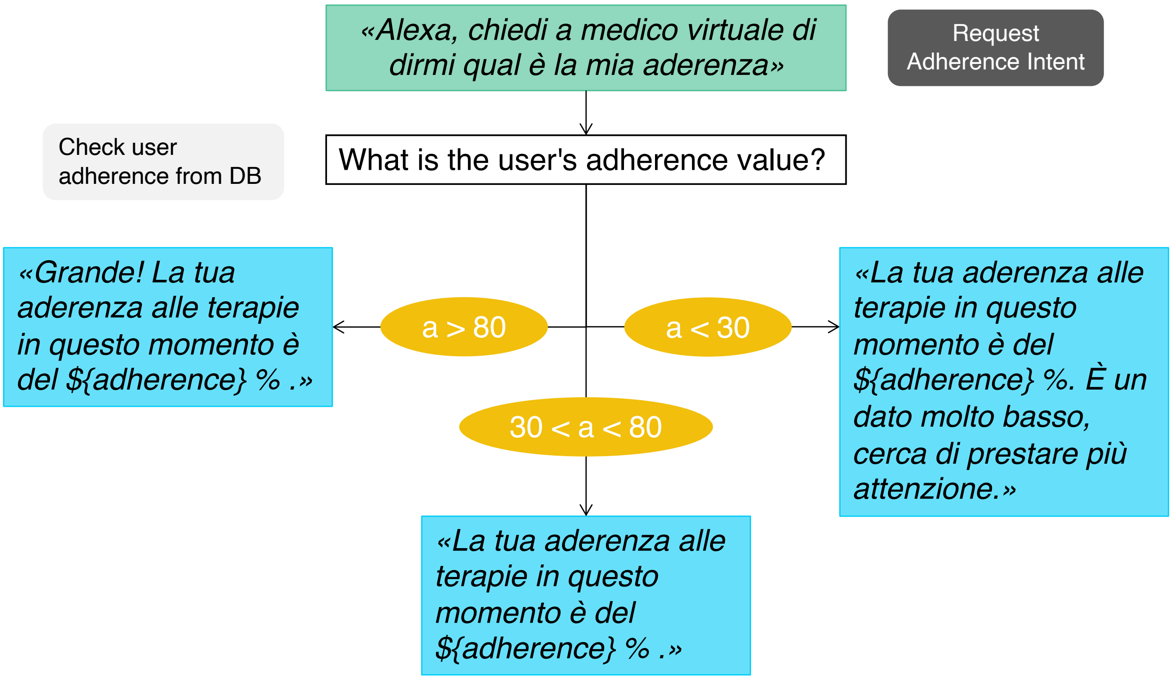



Figure 36: CareVoice: Adherence score request

## 2.2.2. Logic model

In the *Code* section of the Alexa developer console, it is possible to write or import the code of the Skill. The programming language can be defined when the Skill is created. In this case, the Alexa-hosted environment with Node.js is used. The code can be distributed over several files into which the libraries of the desired functionality are imported. This section presents the libraries and APIs needed to design CareVoice Skill and consequently, the algorithm developed for the various phases.

### Libraries and APIs

*AWS-SDK:*

The SDK (Software Development Kit) is a set of documentation, APIs, tools and libraries that allow the development of applications within AWS (Amazon Web Services). AWS is the cloud computing platform provided by the Amazon group that offers storage services, artificial intelligence, security, computing tools and more. One of the most important for this project is the Amazon S3 (Simple Storage

Service) resource, which acts as a repository of data and objects of all kinds for Internet applications. In particular, the S3 bucket makes it possible to store various files (even large ones) permanently. By using interceptors (i.e. codes dedicated to reading and writing files) to address the attributes contained in the session on the S3 bucket, it is therefore possible to save them persistently. For CareVoice, interceptors have been used to populate the S3 memory with the data contained in the session. This is done to guarantee the saving of some data between the various accesses of the user on Alexa.

*AXIOS:*

Axios (https://axios-http.com) is a Javascript library that allows to connect with the backend API and manage requests made via the HTTP protocol. The advantage of Axios is that it is promise-based, allowing the implementation of asynchronous code. The asynchronous code will allow a page to load several elements at the same time instead of sequentially, which will significantly reduce loading times. This library is of particular importance as it has been used to make possible any link between the Alexa Skill and the database on the Mongo.

*MOMENT.JS:*

Moment.js (https://momentjs.com) is a stand-alone open-source JavaScript framework used as an alternative to native JS date objects which are often cumbersome to use. It is useful for date formatting, parsing, validation but also for managing time zones and supports dates in international languages.

*ALEXA REMINDERS API:*

To manage reminders in the Skill, the Alexa Reminders API was used. To query this API, the ReminderManagementServiceClient must be used, allowing the creation, editing, deleting or accessing one or more selected reminders.

```
class ReminderManagementServiceClient extends BaseServiceClient {
  deleteReminder(alertToken: string): Promise<void>;
  getReminder(alertToken: string): Promise<services.reminderManagement.GetReminderResponse>;
  updateReminder(alertToken: string, reminderRequest: services.reminderManagement.ReminderRequest):
Promise<services.reminderManagement.ReminderResponse>;
  getReminders(): Promise<services.reminderManagement.GetRemindersResponse>;
  createReminder(reminderRequest: services.reminderManagement.ReminderRequest): Promise<services.reminderManagement.ReminderResponse>;
}
```

Figure 37: Function of ReminderManagementServiceClient

It is therefore possible to make a reminder creation request via this service. The necessary parameters to insert in the body of the request made to the Alexa Reminder Management API are:

- *requestTime*: the time instant when the request is made (valid ISO format);
- *timeZoneId*: the id of the time zone in which the reminder configuration is to be performed;
- *startDateTime*: start date of the reminder schedule. Defined both with date and time. Default is 'now';
- *endDateTime*: end date of the reminder schedule. Defined both with date and time. Default is 'no end time';
- *recurrenceRules*: the recurrence pattern for a repeating alert. The explications of the rules defining the cadence vary according to the type of frequency the reminder has. The Alexa reminder system supports the following *FREQ RRULE* patterns: *FREQ=DAILY*, *FREQ=WEEKLY*, *FREQ=MONTHLY*, and *FREQ=YEARLY*. The *BYDAY* parameter is used to define the desired days of the week in the case of weekly frequency; the *BYMONTHDAY* parameter is used to define the desired days of the month in the case of monthly frequency. The *INTERVAL* parameter is used to set the frequency. The minimum interval between two recurrence values is one hour for the en-US localization and four hours for all other supported localizations. The maximum interval for daily, weekly and monthly patterns is 31 days. Each of these frequencies also supports programming times defined in the parameters *BYHOUR*, *BYMINUTE*, *BYSECOND*;
- *locale*: the language of the message that will be activated when the reminder starts;
- *text*: a string that includes the text of the message that Alexa will say at the scheduled time;

- *pushNotification*: Contains information about the push notification. If ENABLED, the Alexa app receives a push notification when the reminder goes off.

```
{
   "requestTime" : "2019-09-22T19:04:00.672",
   "trigger": {
        "type" : "SCHEDULED_ABSOLUTE",
        "timeZoneId" : "America/Los_Angeles",
        "recurrence" : {
          "startDateTime": "2019-05-10T6:00:00.000",
          "endDateTime" : "2019-08-10T10:00:00.000",
          "recurrenceRules" : [
            "FREQ=DAILY;BYDAY=SU;BYHOUR=17;BYMINUTE=15;BYSECOND=0;INTERVAL=1;",
            "FREQ=MONTHLY;BYMONTHDAY=5;BYHOUR=10;INTERVAL=1;"
          ]
        }
   },
   "alertInfo": {
        "spokenInfo": {
            "content": [{
                "locale": "en-US",
                "text": "walk the dog",
                "ssml": "<speak> walk the dog</speak>"
            }]
        }
    },
    "pushNotification" : {
         "status" : "ENABLED"
    }
}
```

Figure 38: Example body of a Create Reminder Request

## Algorithm

In this section, the functionalities designed and described in the voice interaction model chapter are reviewed. More specifically, the implementation logics that allow to proceed from input data to voice response are addressed.

*Configuration:*

The Figures below (39 and 41) show the entire process of the previously described configuration. It could be divided into two phases, firstly a check of needed permissions required both by the Alexa system and the access to the database is done and then all the therapies and reminders are managed.

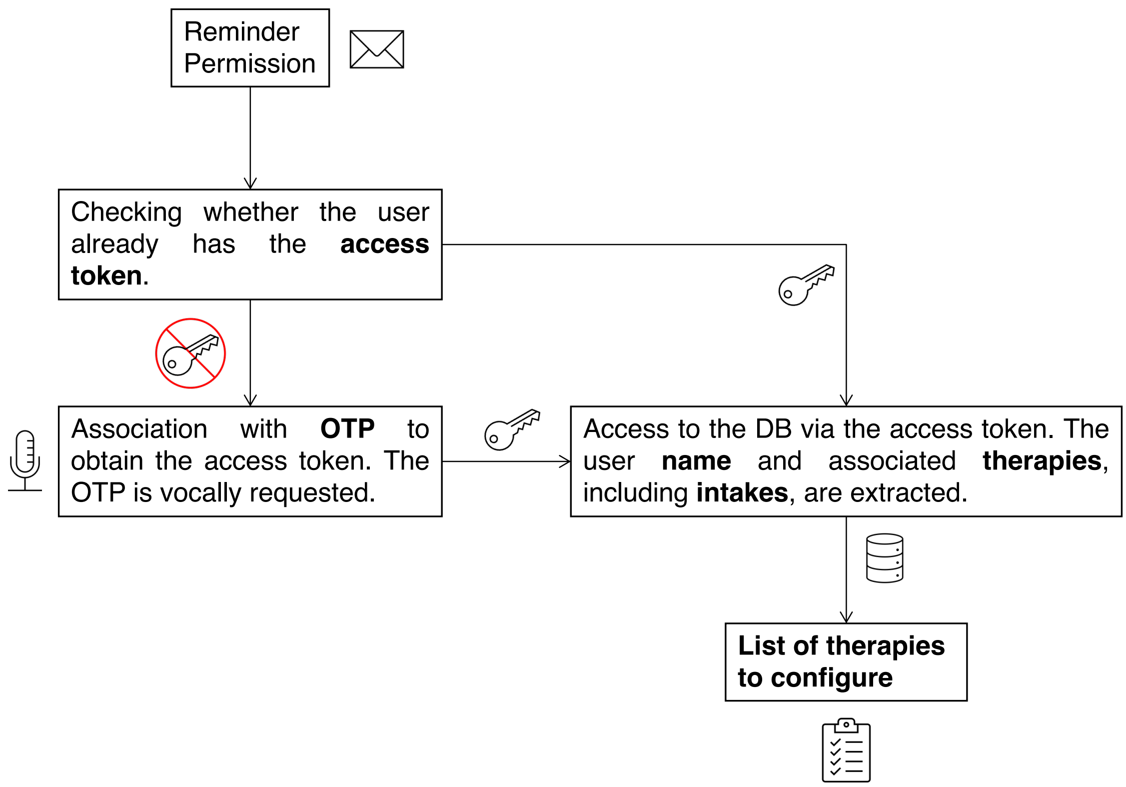



Figure 39: Configuration process (access)

The system, as the first step, checks the permissions that the user must give to Alexa to allow to create, update and delete reminders linked to that Skill. If these permissions are not granted, such as in the case of the first time the user logs on to the skill, a card (shown in the Figure 40) is generated on the Alexa App to notify the user. Through that notification, the user can update such authorizations.


Figure 40: Alexa App - "Authorisation required. Reminders: Allow this Skill to create and edit reminders. This Skill can only see reminders created using it."

Next, a check is made on the access token, an opaque string identifying a user used in token-based authentication to allow an application to access an API. This access token makes it possible to communicate with the Database and thus to operate the entire skill. The access token and the username are obtained the first time the Skill is accessed by the user entering an OTP (one-time-password) generated by the back-end when a new patient is registered. The OTP code is a disposable password, valid only for a single access session or transaction, which guarantees high-security standards and solves the problems associated with the use of traditional passwords.

Once all the permissions and authorizations have been granted, it is possible to move on to the actual phase of configuring the Skill's functions.

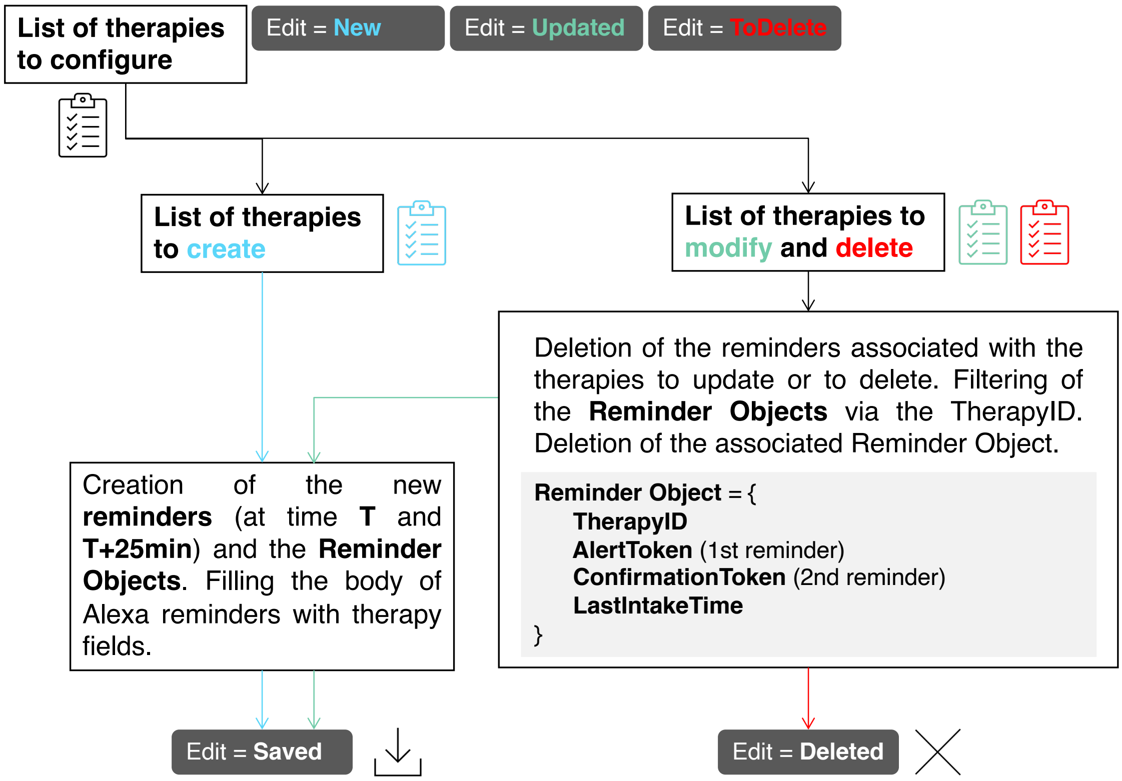



Figure 41: Configuration process (therapies)

A request is made to the database to obtain all the therapies referred to a specific user, programmed in a time interval defined by the developer. In order to set this time interval, it is necessary to pay attention to the time zone in which the user is located. To facilitate later access, objects containing therapies are saved in the session.

In the next step, the saved therapies are extracted and analyzed individually. In particular, the two fields that define the following configuration mode are the field *edit* and the field *status*. The *edit* field can be *new, updated, saved, todelete* and *deleted;* the *status* field can be *true* or *false*. In Table 2 all the possible combinations are explained.

| | | State | |
|---|---|---|---|
| | | True | False |
| Edit | New | The therapy has never been entered into the system via a configuration. When opening CareVoice, the user will be asked to confirm the creation of the therapy. | The doctor created a new therapy which (s)he dismissed before the user set it up on Alexa. |
| | Updated | The therapy has already been entered into the system through a configuration. When opening CareVoice, the user will be asked for confirmation to change the therapy. | The doctor updated a therapy which (s)he dismissed before the user changed it on Alexa. |
| | Saved | Once the new or modified therapy has been configured, the edit field is updated to notify the successful configuration. | The doctor suspended a treatment but did not cancel it. |
| | ToDelete | - | The doctor has decided to permanently delete a therapy. This status is transient but necessary: it ensures the deletion of reminders on Alexa. When opening CareVoice, the user will be asked for confirmation to change the therapy. |
| | Deleted | - | Once the reminders related to the therapy 'to delete' have been removed, the edit field is updated to notify the deletion. |

Table 2: Combination of the field State and Edit

Based on the combination of these two fields, the user is asked to trigger the appropriate intent via the respective voice command. As every user interaction is done vocally, strategies have to be found to minimize the risk of misunderstandings due to ambiguous terms. Thus, in order to avoid possible mistakes made when pronouncing the names of medicines, the system has been set up so that it is Alexa that pronounces them and only asks the user for confirmation. The confirmation phrase will be "*Alexa, configura questa terapia*" (Alexa configures this therapy) is case of a new therapy to be set, or "*Alexa, modifica questa terapia*" (Alexa modifies this therapy) in case of a therapy that have to be deleted or updated.

In order to create the reminder for a specific therapy, it is necessary to extract from the therapy object all the necessary parameters. The first parameter extracted is the scheduling type that allows to understand if it is a reminder that must be set once (once), daily (daily), at intervals of days (interval) or weekly (weekly); then the start date and the end date of the therapy (in the case of type is once only the start date is available); then, the parameters that contain the time (hours and minutes) at which the reminder must be set, and finally parameters that are used to create the text message that is spoken by Alexa at the time of the reminder: among these are the name of the drug, the dosage and relation of the intake to meals.

Creating reminders for a therapy involves setting two alarms with a flexible time interval for each programmed intake. After the first alarm set for the exact time of the intake as decided by the physician, if the participant tells Alexa that they have taken their medicine, no subsequent alarm will be triggered. Otherwise, a second alarm is scheduled 25 minutes later. The number of repetitions per single reminder (i.e. two) was chosen as a compromise between sufficient insistence and risk of annoyance to the user. Each of these reminders is associated with an identification code called a token.

Since it is necessary to keep the data in session to use it transversally between the different intents, for each set therapy a reminderObject containing the following fields is created:

ReminderObject = {

*therapy_id*: unique therapy identifier

*alertToken*: unique identifier referred to the first alarm

*confirmationToken*: unique identifier referred to the second alarm

*last_intake_time*: date and time of last scheduled intake

}

When a therapy has to be modified or deleted, the Modify Intent is triggered. The two id tokens (alertToken and confirmationToken) are extracted from the reminderObject associated with the therapy through the therapy id. Using these tokens, the reminder can be deleted from the Alexa device. Subsequently, the reminderObject in the session, which is now superfluous, is also deleted. In the specific case of an update, the reminder will be recreated (following the same procedure described above) with the modified characteristics as intended. A new reminderObject is also saved in this case.

At the end of the creation phase of a new therapy or modification of a pre-existing therapy, the database is notified to change the *edit* field referred to that therapy to be *saved*. In case of a permanently deleted therapy, the *edit* field is changed to *deleted*.

*Confirm of the intake:*

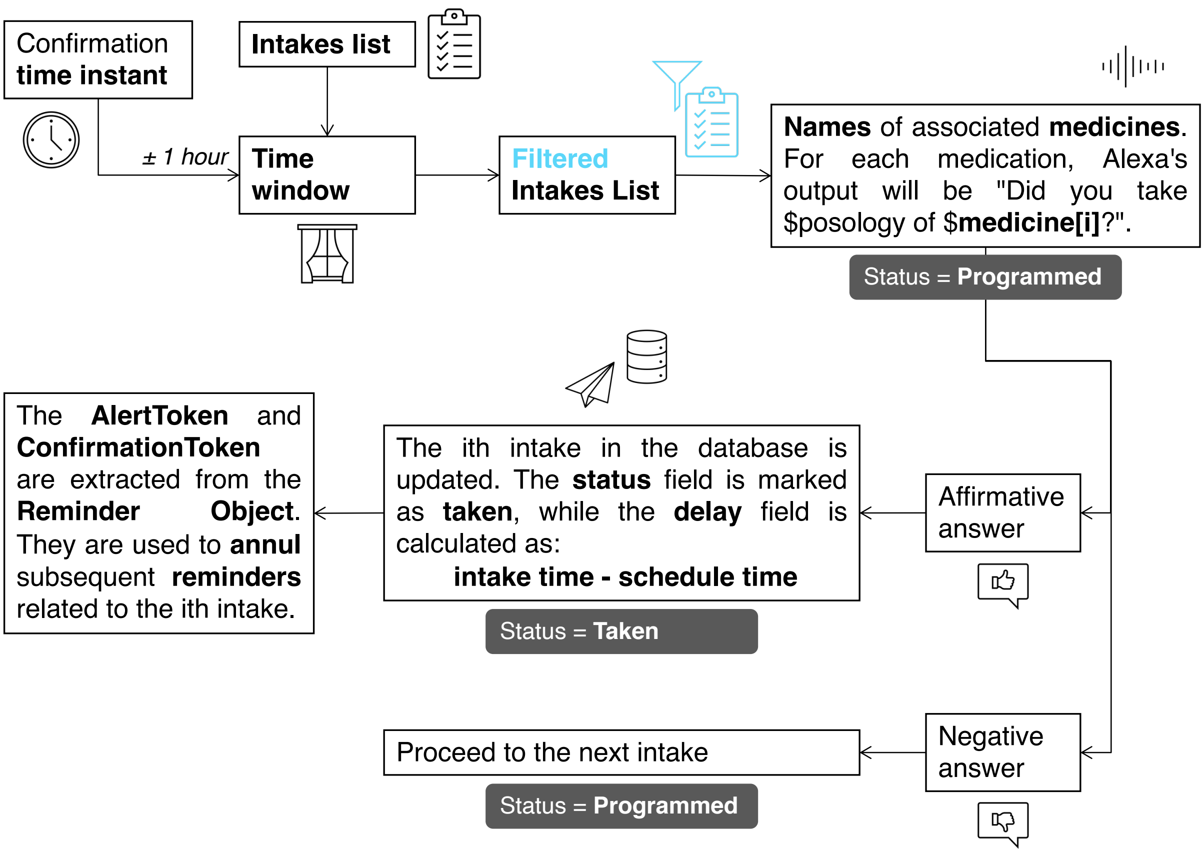



Figure 42: Confirmation of the intake process

When the user confirms to Alexa that the intakehas been done, the time instant is saved. Through this instant, the scheduled intakes in the adjacent time window (flexible and editable) are selected. For each intake in this interval, the name of the relevant medicine is extracted and reported in Alexa's voice output. The name of the medicine is in fact the most natural way to interface with the user. At this point the user can confirm or not that the announced intake is related to that specific medicine.

A negative response triggers the No Intent which simply runs the cycle to the next intake in the adjacent interval, a positive response triggers the Yes Intent.

In the last case, the Database is notified that the specific intake has been taken by modifying the field *state* to taken and by assigning to the field *delay* the time difference between the time of intake and the time at which the intake is scheduled (this delay may be negative if the intake occurs earlier than the reminder).

Through the reminderObject, alertToken and confirmationToken are extracted to allow the cancellation of the subsequent reminders referring to that intake, superfluous if the intake had already been recorded.

The Yes and the No Intent are pre-set Alexa intents that can be used only once within an entire skill due to the fact, as previously explained, that the utterances used to call an intent must be unique, as well as the corresponding code.

*Request of adherence info:*

It is possible to get insights into the adherence in two ways. The former is to ask how many doses have been missed on the current day: the system asks the database for all the intakes of that day and those with the status still on programmed are selected. For each of them, Alexa will alert the user of their missed doses; alternatively, it will indicate that all therapies have been followed correctly.

The latter allows to have a more global view of the user's adherence to the whole treatment plan. Adherence is calculated as the ratio of all the intakes taken to those planned up to the time of the request and is expressed as a percentage. An adherence of more than 80% is considered optimal (Haynes RB at 1980). The range below this percentage was broken down into very poor adherence if below 30%, and average adherence for the percentages between 30 and 80%.

*Logs:*

In order to study the interaction of the user with the individual functions of the skill, logs are sent to the database to mark the use of or access to specific function.

```
LogObject = {

        _id: unique log identifier
        from: string which identifies where the log comes from
        user_id: unique user identifier
        date: time of the log
}
```

### 2.2.3. Persuasive strategies

The CareVoice skill has been designed with some persuasion strategies in mind. Firstly, the postulates defined in the Oinas-Kukkonen theory were respected:

- The non-neutrality of the technology is ensured by the motivation behind the design (i.e. patients should comply with the prescribed treatment plan);
- The consistency of the patients' actions is achieved by creating a sense of commitment to their duties;
- Incrementality is obtained through practicality and persistent use of the technology;
- Routes are mainly direct and achieved through Alexa's suggestions;
- The application is also useful and easy to use, which makes it safe and efficient;
- The system is unobtrusive because it is a voice interface that does not complicate the user's daily activities in any way;

- Transparency of intent is enshrined in the agreement between doctor and patient, and the purpose is benevolent as it aims at maximum patient adherence.

Secondly, usability frameworks were defined:

- The intention is to maximise adherence to prescribed therapies;
- The event has to do with the use, the user and the technology. The context of use is the home environment, which is closely related to the technology context. Alexa needs a continuous power supply and a constant internet connection. Therefore, the typical user is identified as someone who spends their days mainly at home or in a fixed location (ideally, Alexa could also be taken to the workplace). The user must possess sufficient technical skills to understand how to interact with the technology and thus have adequate digital literacy. However, it is worth noting that the device works perfectly well even in the absence of an the smart phone apposite application, except when configured for Reminder Permission. The Alexa application is in fact not a prerequisite, except when it comes to downloading skills and approving certain permissions. This is a task that even a technician or supervisor can carry out, counteracting the difficulties that a user with poor smartphone handling skills might encounter. A vocal interface is easier to manage than a mobile application, and it allows the expansion of the users' pool to those who are not very practical with mobile phones. Ideally, the installation will be guided by technicians. It would make interfacing with the Alexa application unnecessary. The latter, however, represents a cardinal potential: through the Alexa application, it is still possible to use the voice interface and thus confirm the intake of medication. The app also allows receiving reminder notifications. It can be seen as an opportunity to broaden both the pool of users and the context of use. It means that the technology is versatile. It can be used by capable users as well as people more unfamiliar with technological solutions, both at home and in outdoor situations;
- The strategy, which consists of message and Route, is mainly based on the dialogue and, therefore, on direct interaction.

The main features of the developed system are summarised in Table 3, divided into the four dimensions of the PSD: Primary Task Support, Computer-human Dialogue Support, Perceived System Credibility and Social Influence.

| Persuasive design dimension | Persuasive strategy principles | CareVoice Features |
|---|---|---|
| Primary Task Support | Reduction | CareVoice helps the user to mark all therapies in their treatment plan. It does this through a fast and secure configuration, which updates the user step by step. The system supports the user who no longer has to remember every therapy. |
| | Tunneling | CareVoice guides the user through all the steps to set up and take the medication. It does this through a guided and personalised process. |
| | Personalization | CareVoice guide allows any therapy to be entered, depending on the user's needs. Reminders are organised in four ways: daily, weekly, interval, PRN. The message is also comprehensive: the therapy, dosage and time of intake concerning meals are well defined. |
| | Self-monitoring | Through the functions of feedback on missed medication during the day and insight into adherence, CareVoice allows users to monitor their performance at all times. |
| Dialogue Support | Praise | When users request adherence data from the Virtual Doctor, they will get a praise response if they have good adherence results and have taken all the daily medications. |
| | Reminders | Reminders are the crucial aspect of CareVoice. Through these notifications, users are always encouraged to take their medication. There are also two reminders, so the second alarm will still sound |

| | | |
|---|---|---|
| | | if users have not confirmed their intake. It is also a relevant aspect: the system does not get tired of sending notifications, while users will try to signal their intakes to deactivate them. |
| | Liking | Alexa is a design device and can be purchased in different shapes and colours. However, it is complex to appreciate a voice interface for how visually attractive it is. |
| | Social Role | The specialist doctor who prescribes the treatment is a cornerstone of this project. A direct channel is established between patient and doctor when CareVoice is used. The patient will communicate needs and requests regarding their treatment plan to the doctor. The doctor will give advice and modify the patient's medication settings. |
| System Credibility Support | Surface Credibility | A first glance at CareVoice can guarantee the security of use and thus perceived credibility. The Alexa skill has, indeed, passed an initial ethical check, but the project's progress, which is still moderately immature, does not allow more comprehensive conclusions on credibility. |
| | Real-world Feel | Although in CareVoice the user-device interaction is through a Virtual Doctor (and therefore a digital and fictitious entity), it is worth considering that every instruction driven on Alexa is at the behest of a doctor. The Virtual Doctor is just a voice interface that communicates remotely with the patient. |

Table 3: Persuasive features in CareVoice

It can be observed that many strategies related to Credibility Support and Social Support are not present. This is due to evident reasons connected to the implementation and realisation of the Skill, still in the design and testing phase.

## 2.3. Usability Testing Protocol

A test phase was carried out with the aim of studying the invasiveness and usability in daily life of the developed application. The test's purpose was to keep track of the accesses (logs) to the various functions (intents) of Skill CareVoice. It allows identifying the path the testers follow during the test, which functions are used most and how often they are used. Also, the actual users' weekly adherence was measured, checking how many and which intakes have been taken and which ones have been missed, besides the measure of increase in adherence using the developed solution was not one of the primary goals in this phase.

The enrolled participants were patients who take at least one medication in their daily life and who have a good knowledge of their treatment plan. To simplify the organizational aspect of the protocol, each therapy was inserted in the dashboard by the patient himself, with the same posology ordered by the treating physician, under the supervision of a technical operator.

The patients/testers then had the task of continuing with their treatment plan with the support of Alexa for a week, during which they were alerted to take their medication and had the various features of the skill at their disposal. Among these functionalities, of particular importance for the test, is the feedback to the system on the actual medication intake. The testers were provided also with the CareVoice user manual, in which the functionalities are explained and the most important statements summarised.

At the end of the test, the Skill is programmed to stop sending notifications or collect any further data as there will be no more therapies scheduled.

An individual meeting was then arranged with each participant to administer a semi-structured interview and a usability questionnaire, to obtain a qualitative assessment of the Skill and the used protocol.

The test protocol was approved by the Etichcal committee of Politecnico di Milano, which reviewed the procedure. Each volunteer receives a set of forms, which are listed here:

- Declaration of consent to the processing of personal data. It comprehends the project description, the methods of acquisition, the use and the storage of data and those responsible for it;
- Information form, explaining the purpose of the study, the benefits it brings and the purpose of data processing;
- Informed consent form, in which the tester declares to have read and accepted the previous forms;
- Profiling form, in which the (pseudonymised) subject describes its pre-existing health conditions;
- Treatment plan form. The user enters for each therapy the drug name, the time of intake, the dosage and any notes (this is used to enter the parameters in the dashboard);
- Pre-test questionnaires, in particular, the Morisky Medication Adherence Scale and the IT-eHEALS;
- Post-test questionnaires, in particular, the System Usability Scale (IT-SUS) and a semi-structured interview to assess the usability specifications of the Skill;
- Instruction manual to use the CareVoice Skill.

### 2.3.1. Protocol

Each volunteer, who has previously filled in and signed the test forms, was given an Alexa Echo Dot device. As all Amazon Alexa devices equally support the CareVoice Skill, in case a device was owned by the volunteer, that device was used.

Alexa devices need to be connected to power and a Wi-Fi network for proper operation. From the Amazon Alexa Console, the tester's email was entered in the Beta Test field of the Distribution section. The Skill, not being public, is usable only by those into the Beta Test. The volunteer must accept the invitation to use the Skill in their email before using it. The associated email must be the one with which the tester has an account on Alexa (if they did not have one, this was created at the time of installation). The Alexa device was associated with the Alexa application (as per protocol for any Alexa user).

Figure 43: Amazon Alexa Echo Dot used for tests

The tester's data were entered in the dashboard through a fake doctor's account (to create the Patient object), and the volunteer was asked to enter each therapy's data into the dashboard. Caution was advised to ensure correspondence between the reminders and the medication's intakes scheduling times. The entire configuration phase was carried out with the support of an operator.

The dashboard also generates the OTP with which the user can securely associate with his Patient object, and thus receive all associated data on Alexa from the database. The security code remains active for 24 hours. The first time CareVoice was started, a Card was sent to the Activity section of the Alexa application, asking to grant permissions to the reminders. Afterwards, the tester was asked by Alexa to identify himself through the security code. When this was done, the user was able to configure the therapies in a guided way. Each therapy created corresponded to reminders that were activated at set times.

### 2.3.2. Pre-test questionnaire

In this phase, participants were presented with two questionnaires: the Morisky 8-item Medication Adherence Scale and the IT-eheals (IT- eHealth Literacy Scale).

The IT-eheals (Bravo, at. 2018) aims at obtaining a more quantitative idea of the subject's characteristics, and represents the adapted and validated Italian version of the eheals. The eheals is a short self-report test with an 8-item questionnaire aiming at measuring the digital health literacy (DHL) of the user. (Norman CD, at. 2006). It helps determine how people deal with electronic health information, specifically to identify potential difficulties in accessing, evaluating, and using online health information. The 8 items are rated on a 5-point subjective Likert scale ranging from "completely disagree" to "completely agree". Figure 44 shows the Italian version of the eHEALS.

**IT-eHEALS**

| | 1 - Decisamente in disaccordo | 2 | 3 | 4 | 5 - Decisamente d'accordo |
|---|---|---|---|---|---|
| So come trovare su Internet informazioni utili sulla salute | ☐ | ☐ | ☐ | ☐ | ☐ |
| So come usare Internet per rispondere alle domande riguardo alla mia salute | ☐ | ☐ | ☐ | ☐ | ☐ |
| So quali informazioni sulla salute sono disponibili in Internet | ☐ | ☐ | ☐ | ☐ | ☐ |
| So dove trovare su Internet informazioni utili sulla salute | ☐ | ☐ | ☐ | ☐ | ☐ |
| So come usare le informazioni sulla salute che trovo su Internet in modo che mi possano essere d'aiuto | ☐ | ☐ | ☐ | ☐ | ☐ |
| Ho le capacità che mi servono per valutare le informazioni sulla salute che trovo su Internet | ☐ | ☐ | ☐ | ☐ | ☐ |
| Posso distinguere la bassa o alta qualità delle informazioni sulla salute che trovo su Internet | ☐ | ☐ | ☐ | ☐ | ☐ |
| Mi sento sicuro nell'usare informazioni che trovo su Internet per prendere decisioni riguardo alla mia salute | ☐ | ☐ | ☐ | ☐ | ☐ |

Figure 44: IT-eheals

The ideal score of the IT-eheals is reported in the radar plot in Figure 45.

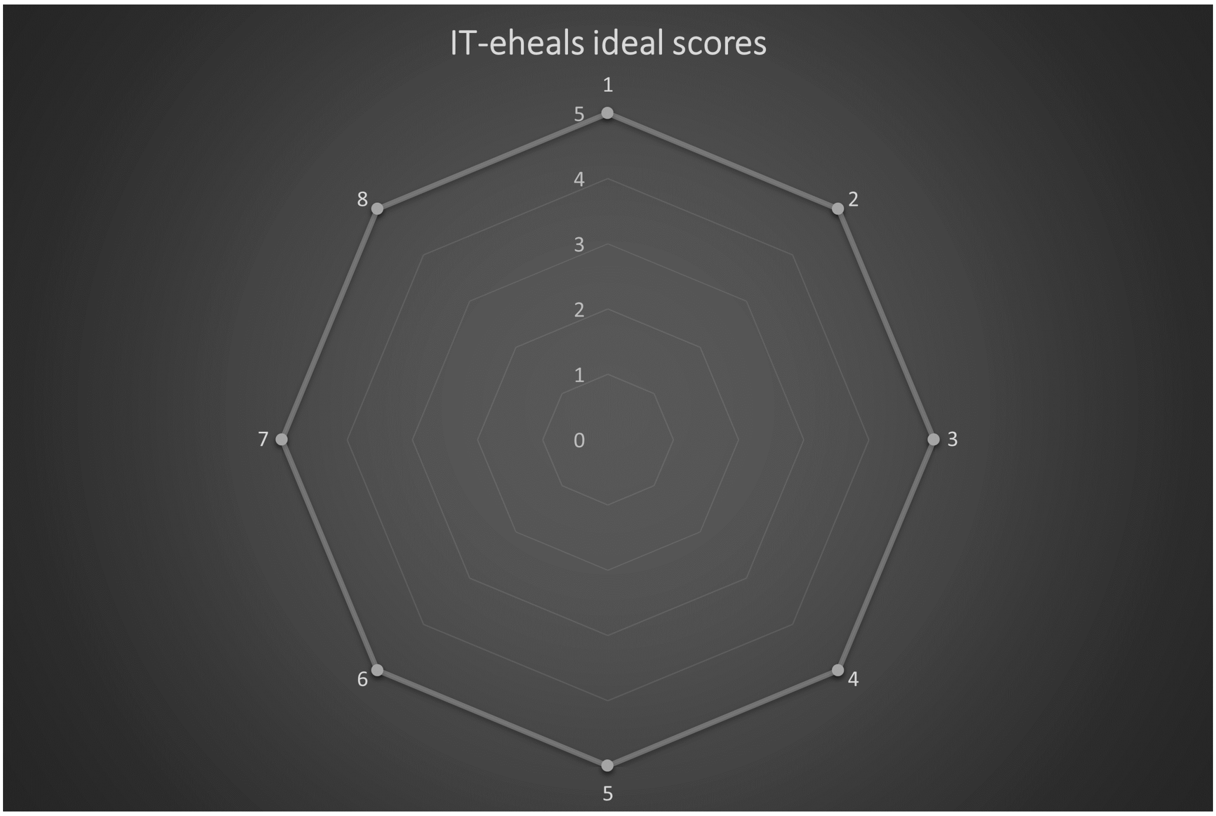



Figure 45: Radar Plot IT-eheals ideal scores

The Morisky 8-item Medication Adherence Scale (MMAS-8), instead, allows obtaining useful data in order to make a more objective evaluation of the propensity to adherence of the subject.

The MMAS-8 has been demonstrated as a valid measure to detect patients' risk of non-adherence (Morisky, at. 1986). The first 7 items have dichotomous responses (0 = Yes; 1 = No) and the last one includes a 5-point Likert scale response.

In the current study, in order to make the questionnaire more understandable to the subjects, the validated Italian version (Fabbrini, at. 2013) was used after a very slightly readjustment to make it disease-independent and generalized, being originally formulated for Parkinson's patients.

Figure 46 shows the Italian version of the MMAS-8.

**Morisky Medication Adherence Scale 8**

| | Sì | No |
|---|---|---|
| 1. Qualche volta si dimentica di prendere le pillole? | ☐ | ☐ |
| 2. Nelle ultime due settimane, ci sono stati dei giorni in cui non ha preso le medicine? | ☐ | ☐ |
| 3. Ha mai ridotto o smesso di prendere le medicine senza dirlo al suo medico perché si sentiva male quando le prendeva? | ☐ | ☐ |
| 4. Quando viaggia o esce di casa, si dimentica di portare con sé i farmaci? | ☐ | ☐ |
| 5. Ieri ha preso tutte le sue medicine? | ☐ | ☐ |
| 6. Quando sente che i suoi sintomi sono sotto controllo, a volte smette di prendere le sue medicine? | ☐ | ☐ |
| 7. L'assunzione quotidiana dei farmaci è un vero e proprio disagio per alcune persone. Si sente mai infastidito o sente di avere delle difficoltà nell'attenersi al piano di trattamento? | ☐ | ☐ |
| 8. Quanto spesso le capita di avere difficoltà a ricordarsi di prendere tutti i suoi farmaci? | ☐ Mai<br>☐ Raramente<br>☐ Qualche volta<br>☐ Spesso<br>☐ Sempre | |

Figure 46: MMAS-8 Italian version

In order to obtain an overall Morisky score (Okello et al., 2016), the sum of all answers must be calculated by considering each "no" answer as a value of 1 and each "yes" answer as a value of 0, except for item 5 where the evaluation is opposite.

For item 8, the score varies from 0 ("Always") to 1 ("Never") with intervals of 0.25 for intermediate answers.

The total MMAS-8 scores can thus vary from 0 to 8 and identify the three levels of adherence: high adherence (score = 8), medium adherence (score 6 to < 8), and low adherence (score<6).

### 2.3.3. Post-test semi-structured interview and questionnaire

At the end of the test week, a second meeting with the subject was organized. During this meeting, a semi-structured interview was carried out and at the end the subject was given a questionnaire.

The semi-structured interview included 18 specially designed questions, whose answers were reported by the interviewer himself. Mixed types of answers were allowed: from "Not at all" to "Very much", "Yes" or "No", and some open-ended. They can be divided into four groups.

- Skill configuration phase:

1. Al primo accesso ti è stato chiesto di impostare il codice univoco sul dispositivo Amazon Alexa. Quanto è stato complesso?

| Per niente | Poco | Abbastabza | Molto | Moltissimo |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

2. Al primo accesso ti è stato chiesto di configurare vocalmente le terapie. Quanto è stato complesso?

| Per niente | Poco | Abbastabza | Molto | Moltissimo |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

- Use of the CareVoice Skill:

3. Ti è capitato di non ricevere i promemoria per una data terapia?

4. Hai trovato delle difficoltà nel comunicare con il Medico Virtuale?

5. Hai trovato utile la funzione del doppio promemoria?

6. Ritieni che il tempo a disposizione per prendere il medicinale sia adeguato?

7. Ti è capitato di utilizzare altre funzioni del Medico Virtuale oltre al rispondere alle notifiche (i.e. controllare aderenza)?

8.a. Se SÌ, quali e perché?

8.b. Se NO, perché?

9. Quali sono gli aspetti del Medico Virtuale che hai trovato più utili o interessanti?

10. Quali sono gli aspetti del Medico Virtuale che hai trovato meno utili o di disturbo?

11. Quanto è stato intrusivo l'utilizzo del Medico Virtuale nelle tue normali attività giornaliere?

12. Complessivamente, su una scala da completamente insoddisfatto a completamente soddisfatto, quanto sei soddisfatto della settimana di utilizzo del Medico Virtuale?

| Completamente insoddisfatto | Leggermente insoddisfatto | Indifferente | Abbastanza soddisfatto | Completamente soddisfatto |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

- Use of the Alexa device in general:

13. Prima di questo test utilizzavi già un dispositivo Amazon Alexa?

14. In generale, saresti interessato/a ad utilizzare nella tua vita quotidiana Alexa per monitorare la tua aderenza?

14.a. Se NO, perché? Preferisci utilizzare altri strumenti? (ad esempio smartphone, calendario fisico)

15. In generale, saresti interessato/a ad utilizzare nella tua vita quotidiana Alexa per altro oltre il monitoraggio dell'aderenza?

15.b Se NO, perché?

- Perception of adherence:

16. Su una scala da molto bassa a molto alta, come pensi fosse la tua aderenza prima dell'esperimento?

| Molto bassa | Bassa | Buona | Alta | Molto alta |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

17. Pensi che la tua aderenza sia rimasta uguale, migliorata o peggiorata durante l'esperimento?

☐ Migliorata

☐ Rimasta uguale

☐ Peggiorata

☐ Altro ____________________________________________

18. Hai dei consigli o suggerimenti da darci su come migliorare la Skill?

At the end of the semi-structured interview, the IT-SUS usability questionnaire, representing the adapted Italian translation (Borsci et al., 2009) of an international standard questionnaire called system usability scale (SUS) (Bangor et al., 2008), was subministered to the user. This questionnaire was created in 1986 with the aim of measuring the perceived usability of electronic systems in the office by the user, but is now used more generally utilized for any technological application. It aims to measure how easy or difficult it is to use a specific technology taking into account its layout, design, implemented functions, etc.

It consists of 10 questions that can be answered with a five-point Likert scale from "Strongly Disagree" to "Strongly Agree". The structure of the questionnaire was designed to minimise the subject's propensity for automated responses. It provides for redundant questions but with positive and negative answers in an alternating manner. This strategy allows for more reliable results. The questionnaire is shown in Figure 47.

### System Usability Scale (IT-SUS)

18. Rispondi alle seguenti domande su una scala da 1 (molto in disaccordo) a 5 (molto d'accordo).

| | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| Penso che mi piacerebbe utilizzare questo sistema frequentemente. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Ho trovato il sistema complesso senza che ce ne fosse bisogno. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Ho trovato il sistema molto semplice da usare. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Penso che avrei bisogno del supporto di una persona già in grado di utilizzare il sistema. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Ho trovato le varie funzionalità del sistema ben integrate | ☐ | ☐ | ☐ | ☐ | ☐ |
| Ho trovato incoerenze tra le varie funzionalità del sistema. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Penso che la maggior parte delle persone potrebbero imparare ad usare il sistema facilmente. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Ho trovato il sistema molto macchinoso da utilizzare. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Ho avuto molta confidenza con il sistema durante l'uso. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Ho avuto bisogno di imparare molti processi prima di riuscire ad utilizzare al meglio il sistema. | ☐ | ☐ | ☐ | ☐ | ☐ |

Figure 47: IT-SUS questionnaire

In the radar plot in Figure 48 the ideal score of the IT-SUS questionnaire is reported.

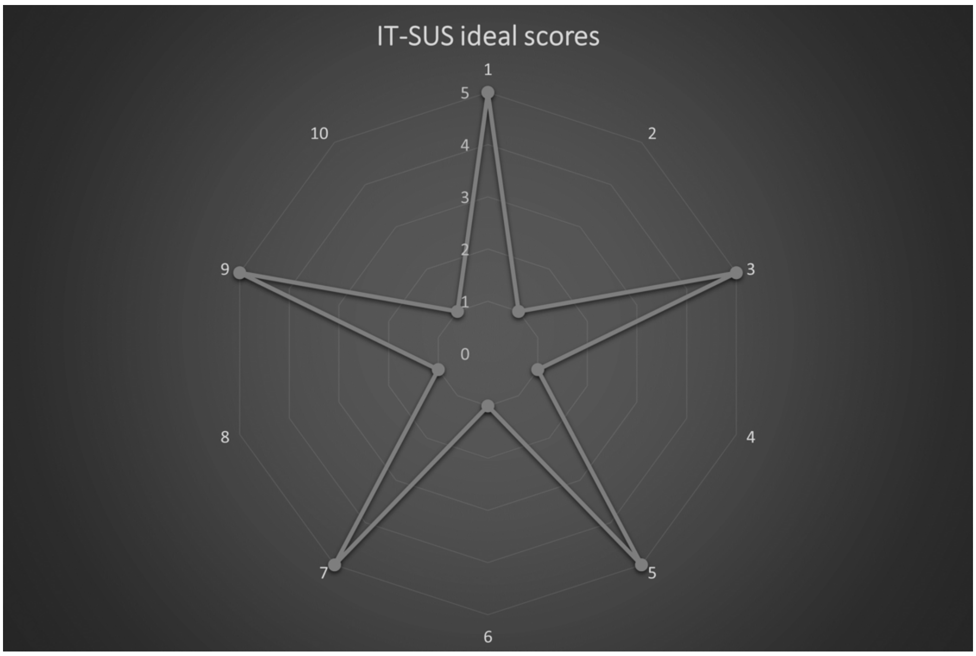



Figure 48: IT-SUS ideal scores

In order to calculate the overall SUS score, it is necessary to go through different operations (Brooke et al., 1995) for the group of questions with positive content (questions 1,3,5,7,9) and for the group with negative content (questions 2,4,6,8,10).

For the first group of answers, which has an ideal value of 5, a value equal to the score itself minus 1 was calculated for each answer. For the group of answers with negative content, which has an ideal value of 1, a value equal to 5 minus the score of the answer was calculated.

At the end of this operation, all the obtained values were added together and then multiplied by 2.5.

The used formulas are shown below:

$$Adjusted\ Single\ Score\ (group\ 1) = \ Single\ Score - 1$$

$$Adjusted\ Single\ Score\ (group\ 2) = \ 5 - Single\ Score$$

$$SUS\ Score\ = \left(\sum Adjusted\ Single\ Score\ (group\ 1) + \sum Adjusted\ Single\ Score\ (group\ 2)\right) * 2{,}5$$

The obtained overall SUS score is on a scale from 0 to 100 (with 100 being the optimal value). In the literature, an overall SUS score higher than 68 indicates respondents' appreciation of the device in terms of usability (J. Sauro et al., 2011).

# 3 Results

This section will highlight the main results of the testing protocol. 7 volunteering patients (with at least one drug to take every day) were involved as testers. All testers were assigned the device for 7-8 days (14 days only in some cases), which was configured to meet the stated ethical requirements. The testers were also asked to fill in the pre and post-test questionnaires. In the first paragraph, the test group is described. Then the results of adherence (measured directly with the CareVoice skill on Alexa) and those of the semi-structured interview questionnaires will be reported.

## 3.1. Test group

The population of subjects studied was classified to assess the prevalence of definite characteristics in the group, including gender, age, pre-existing medical conditions, therapies the testers were required to take (how many, which, when, how) and whether the volunteers were already able to use an Alexa device.

The test group consisted of 7 subjects: in Table 4 the specific information about gender, age, pre-existing chronic condition (if declared) and ownership or previous use of an Alexa device are reported. As it is possible to note, 4 subjects (57%) were males and 3 (43%) females. Only one subject was aged between 30 and 40, three between 40 and 50, none in the 50-60 bracket, two subjects between 60 and 70 and only one >70.

Five subjects (71%) were already familiar or owned an Alexa device.

In Table 5, the number of assumed medications/day, their frequency and posology are reported, based on the therapeutic plans inserted by the volunteers. Number of drugs went from 1 to 3, where most of the subjects were taking 1 or 2 medications everyday, with the most complex treatment plan in Subject G (3 drugs and 4 different intakes).

| User profiling | | | | |
|---|---|---|---|---|
| **User** | **Sex** | **Age** | **Pre-existing health conditions** | **Used to Alexa** |
| **A** | M | 47 | Hypertension | No |
| **B** | M | 66 | N/A | No |
| **C** | M | 43 | N/A | Yes |
| **D** | M | 75 | Hypertension | Yes |
| **E** | F | 61 | N/A | Yes |
| **F** | F | 31 | N/A | Yes |
| **G** | F | 46 | Hypertension | Yes |

Table 4: Test group summary: user profiling

| | Medication | | |
|---|---|---|---|
| **User** | **Number** | **Frequency** | **Posology** |
| **A** | 2 | Everyday 1 time - Everyday 1 time | 40mg - 20mg |
| **B** | 2 | Everyday 1 time - Everyday 1 time | 100mg - 1pill |
| **C** | 1 | Everyday 1 time | 1pill |
| **D** | 2 | Everyday 1 time - Everyday 1 time | 5mg - 5mg |
| **E** | 1 | Everyday 1 time | 1pill |
| **F** | 1 | Everyday except Sunday 1 time | 50mg |
| **G** | 3 | Everyday 1 time - Everyday 1 time - Everyday 2 times | 1/2pill - 1pill - 1pill |

Table 5: Test group summary: treatment plan

## 3.2. Pre-test questionnaires results

The results of the IT-eheals questionnaire are reported in Figure 50 as radar plots for each participant.

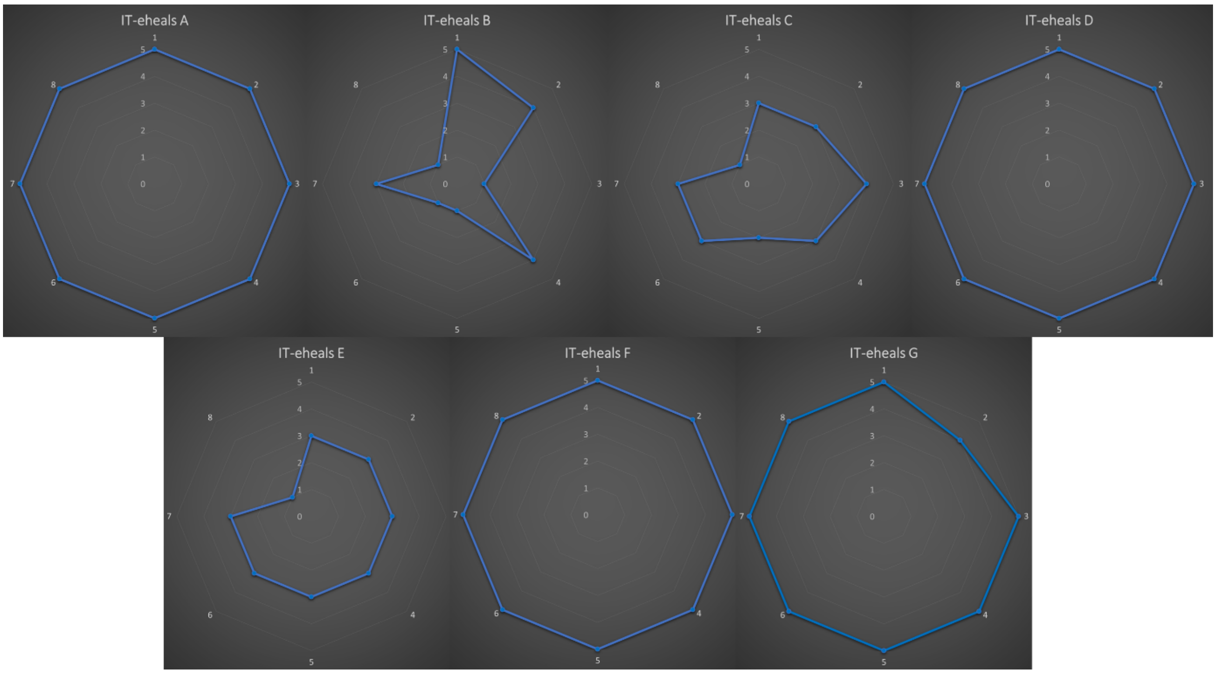



Figure 49: Radar Plot IT-eheals results

As can be seen, in four subjects the results showed results corresponding to a very good digital health literacy, while for the other three the level was moderate. Calculating the overall score of the IT-eheals as the sum of all answers ranging from 1 to 5 gives a range from a minimum of 8 to an optimal maximum of 40.

In Table 6, the overall score of the IT-eheals for each subject is reported, together with the results of the MMAS-8 self-questionnaire used to to assess the perceived adherence before the start of the test.

| User | IT-eheals score (min: 8; max: 40) | MMAS-8 Score (min:0; max:8) | Perceived Adherence |
|---|---|---|---|
| **A** | 40 | 3.5 | LOW |
| **B** | 20 | 8 | HIGH |
| **C** | 21 | 4.5 | LOW |
| **D** | 40 | 4.5 | LOW |
| **E** | 22 | 3.5 | LOW |
| **F** | 40 | 4.5 | LOW |
| **G** | 39 | 6 | MEDIUM |

Table 6: MMAS-8 and IT-eheals total scores

As can be noted, the majority of participants reported low adherence propensity, one reported medium adherence, while high adherence was associated with only one subject.

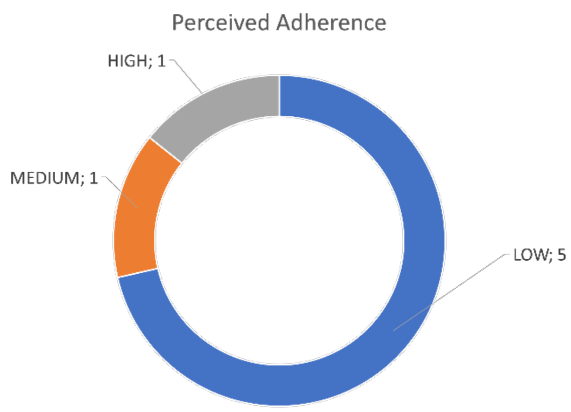



Figure 50: Perceived Adherence from MMAS-8 results

## 3.3. Post-test questionnaires results

*Ad-Hoc Semi structured Interview Results*

Below are charts containing the distributions of the answers (with notes if any) given to the ad-hoc questions the subjects were asked. As previously described, the questions can be divided into four macro groups according to their theme: Setup Configuration, Skill Usage, Alexa Device and Adherence.

With regard to the setup configuration , it can be seen in the Table 7 that almost all the subjects (with the exception of one) found the phase of accessing the skill by means of a security code and configuring the reminders not at all complex.

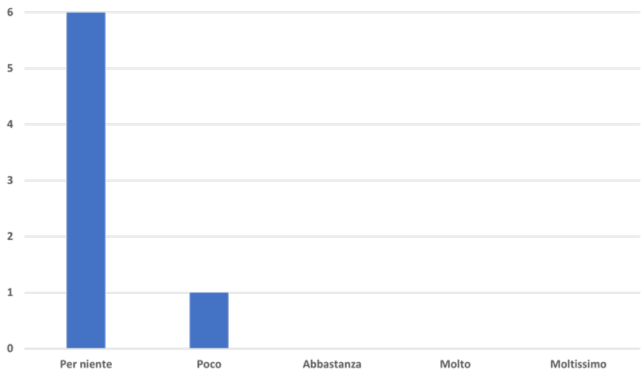
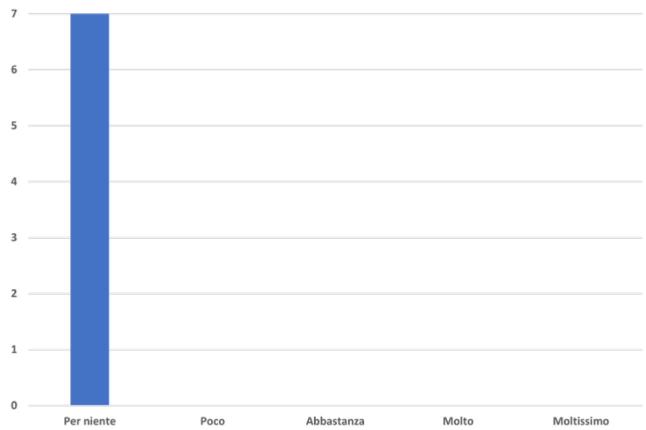
| Question | Chart | Notes |
|---|---|---|
| *1: "Al primo accesso ti è stato chiesto di impostare il codice univoco sul dispositivo Amazon Alexa. Quanto è stato complesso?"* |   | |
| *2: "Al primo accesso ti è stato chiesto di configurare vocalmente le terapie. Quanto è stato complesso?"* |   | |

Table 7: Ad-hoc results: Setup Configuration

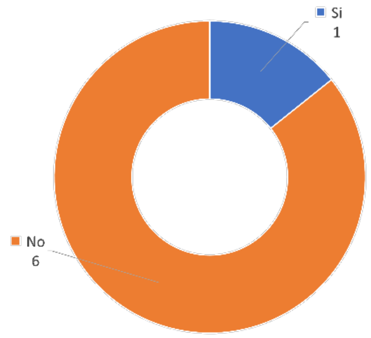
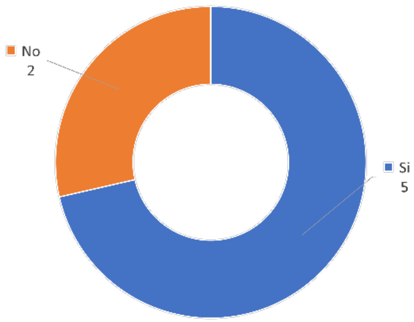
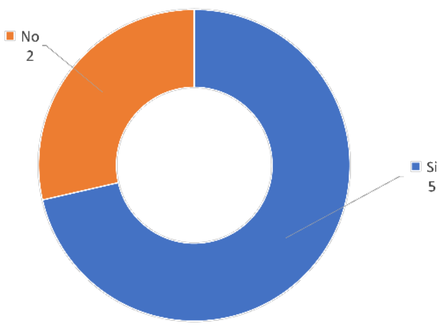
Questions from 3 to 12 referred to the use of the CareVoice Skill.

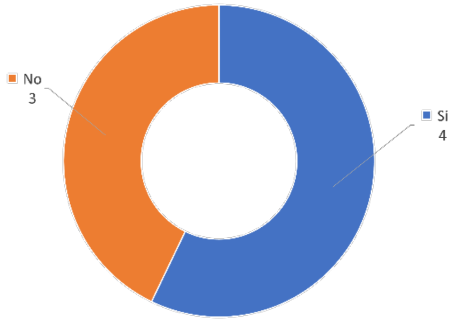
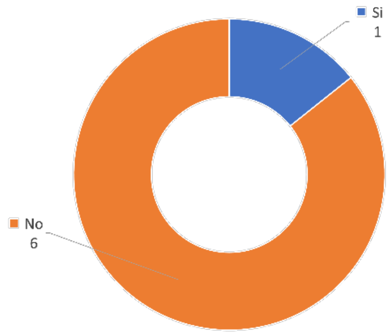
Only one patient did not receive notifications fo specific intakes, while 5 out of 7 found some difficulties in the communication with the CareVoice skill, in most cases due to complexity of the utterances to be used.

The repetition of the notification 25 minutes after the first one was an appreciated feature in 5 out if 7 patients, but in 3 out 7 the interval of time (that ranges from 60 minutes before to 60 minutes after the programmed time of the intakes) to take the medication was judged not enough.

Generally, functions other than replying to the notification to confirm adherence were not tested. The proposed system was considered not intrusive in personal life from 4/7, but for the other 3 there were some intrusive aspects to be considered. Also, 2 subjects underlined the inutility of functionalities they did not use, 1 subject considered unnecessary to repeat the dosage every notification, while 1 subject considered the notifications too repetitive.

Positive aspects were the automated reminder setting, the possibility to communicate by voice, and the ability to use the skill also from the Alexa App. The last question of this part, analyses the overall evaluation through response that could be "Completamente insoddisfatto", "Leggermente insoddisfatto", "Indifferente", "Abbastanza soddisfatto" or "Completamente soddisfatto". This question reports full satisfaction for 3 subjects, enough satisfaction for other 3 and the lowest score is indifference reported by 1 subject.

| Question | Chart | Notes |
| --- | --- | --- |
| *3: "Ti è capitato di non ricevere i promemoria per una data terapia?"* |  | |
| *4: "Hai trovato delle difficoltà nel comunicare con il Medico Virtuale?"* |  | -utterance for confirmation of intake too long;<br>-problem with communication for 2 days; utterances complex, manual needed; mobile app does not work;<br>-utterance too complex |
| *5: "Hai trovato utile la funzione del doppio promemoria?"* |  | |

| | | |
|---|---|---|
| *6: "Ritieni che il tempo a disposizione per prendere il medicinale sia adeguato?"* |   | Those who answered 'no' felt that time was not enough |
| *7:" Ti è capitato di utilizzare altre funzioni del Medico Virtuale oltre al rispondere alle notifiche (i.e. controllare aderenza)?"* |   | The person who answered yes asked for the Medicines missed due to absence of notification and out of curiosity. Those who answered no justify with low interest in the short period of use. |
| *9:" Quali sono gli aspetti del Medico Virtuale che hai trovato più utili o interessanti?"* | - Reminder;<br>- Opportunity to communicate by voice<br>- Ability to use the skill also from the Alexa App | |
| *10: "Quali sono gli aspetti del Medico Virtuale che hai trovato meno utili o di disturbo?"* | - 3 subjects answered none<br>- 2 subjects answered functionalities they have not used<br>- 1 subject considers it unnecessary to repeat the dosage every notification<br>- 1 subject considers the notifications too repetitive | |

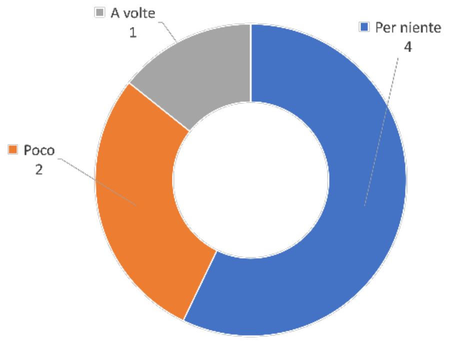
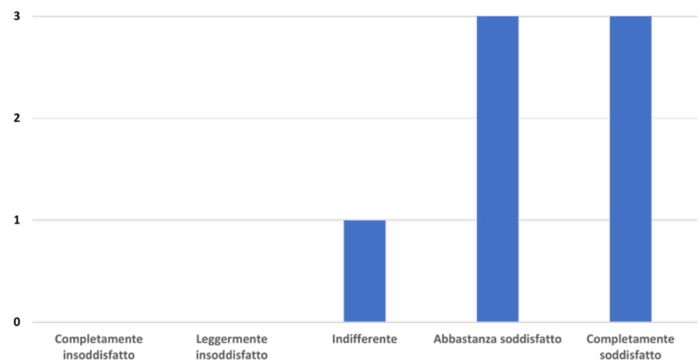
<table>
<tr>
<td>11:" Quanto è stato intrusivo l'utilizzo del Medico Virtuale nelle tue normali attività giornaliere?"</td>
<td>
</td>
<td>The person who answered "A volte" (sometimes) found the reminder set at an early time in the weekend disturbing</td>
</tr>
<tr>
<td>12:" Complessivamente, su una scala da completamente insoddisfatto a completamente soddisfatto, quanto sei soddisfatto della settimana di utilizzo del Medico Virtuale?"</td>
<td colspan="2">
</td>
</tr>
</table>

Table 8 : Ad-hoc results: Skill Usage

As regards the use of the Alexa device in general, from Table 9 can be seen that both users that were already using the device and those that did not use it before will be interested in using it to monitor adherence, and also for other purposes.

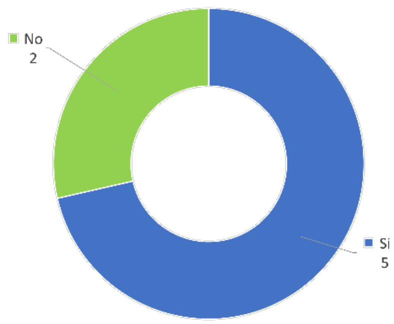
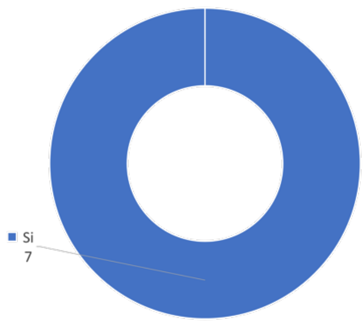
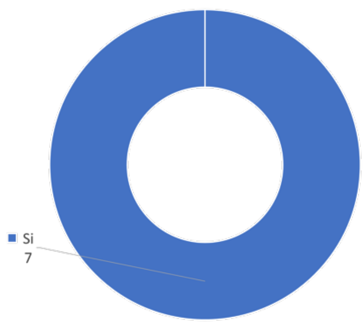
| Question | Pie Chart | Notes |
|---|---|---|
| *13:" Prima di questo test utilizzavi già un dispositivo Amazon Alexa?"* |   | |
| *14:" In generale, saresti interessato/a ad utilizzare nella tua vita quotidiana Alexa per monitorare la tua aderenza?"* |   | |
| *15: "In generale, saresti interessato/a ad utilizzare nella tua vita quotidiana Alexa per altro oltre il monitoraggio dell'aderenza?"* |   | |

Table 9: Ad-hoc results: Alexa Device

In terms of perception of adherence, before the start of the trial it varied widely between subjects, ranging from Low to Very High. In spite of this variety, surprisingly 4/7 subjects reported that their adherence improved during the testing phase, while in the other 3/7 it remained the same.

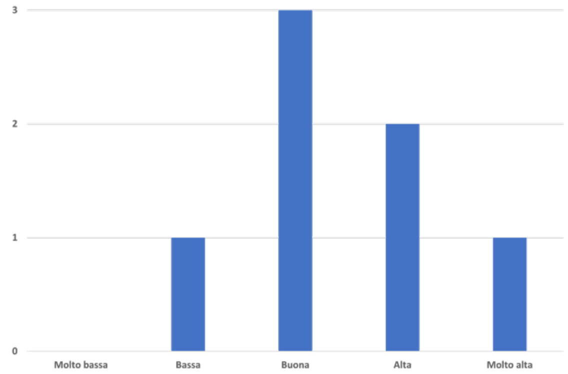
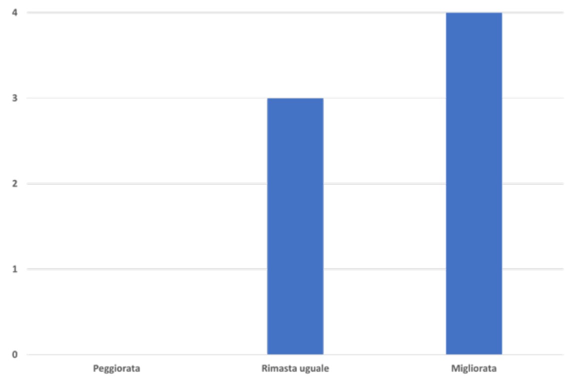
| **Question** | **Chart** | **Notes** |
|---|---|---|
| *16:" Su una scala da molto bassa a molto alta, come pensi fosse la tua aderenza prima dell'esperimento?"* |  | |
| *17:" Pensi che la tua aderenza sia rimasta uguale, migliorata o peggiorata durante l'esperimento?"* |  | |

Table 10: Ad-hoc results: Adherence

*SUS Questionnaire Results*

To evaluate the usability perceived by the participants in the study, the results of the SUS questionnaire were analyzed both as an overview and in detail by studying each response.

In figure 51 the radar graphs for each subject are reported. This type of graph allows to have an immediate vision of the results obtained for the single subjects and for the single answers. Subjects who reported being Alexa users since before the test are shown in blue, those who did not use it previously are shown in green. This distinction was made because pre-existing familiarity with the device could mean better-perceived usability. In the background of each radar plot, the ideal result for each response is shown in grey.

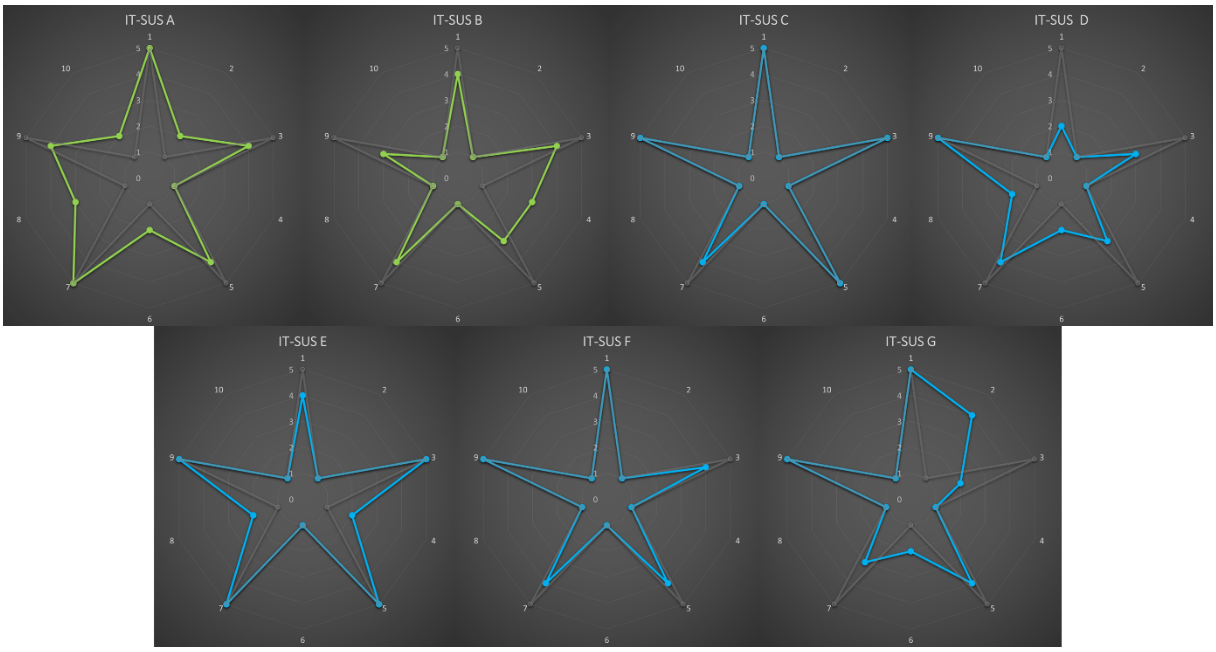
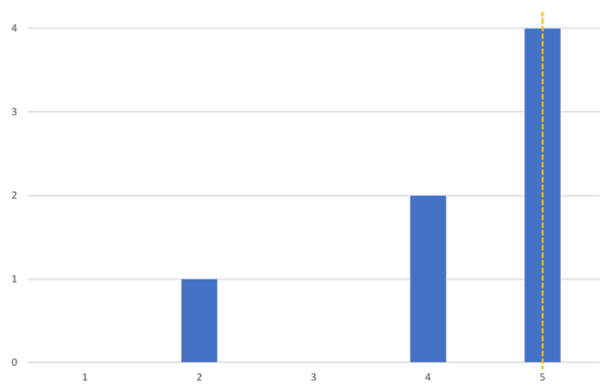
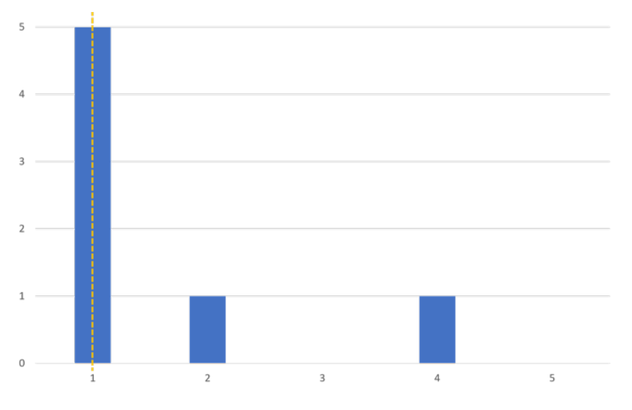
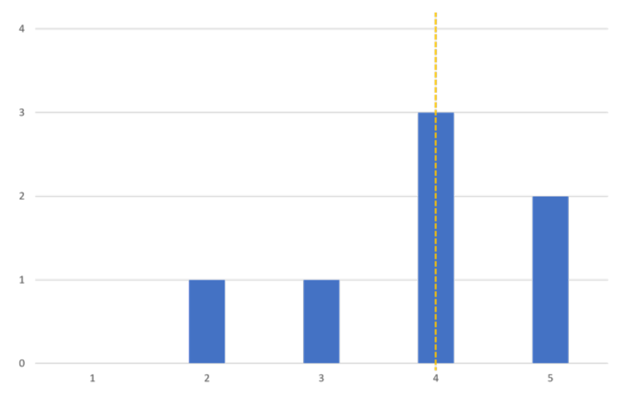
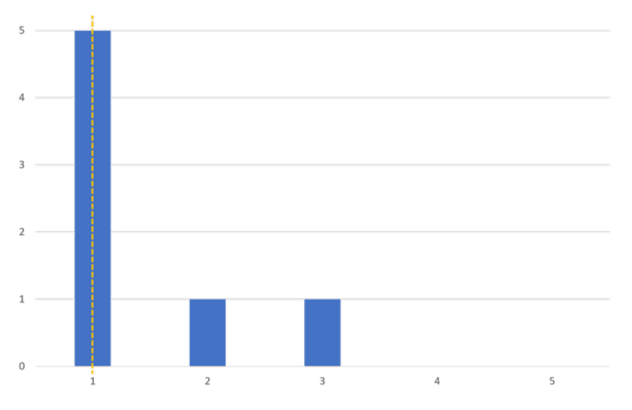
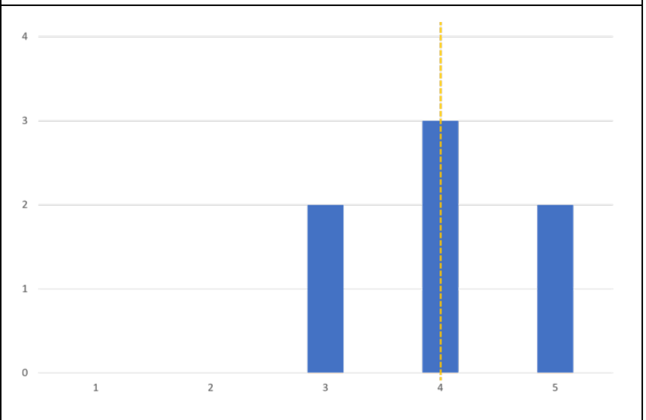
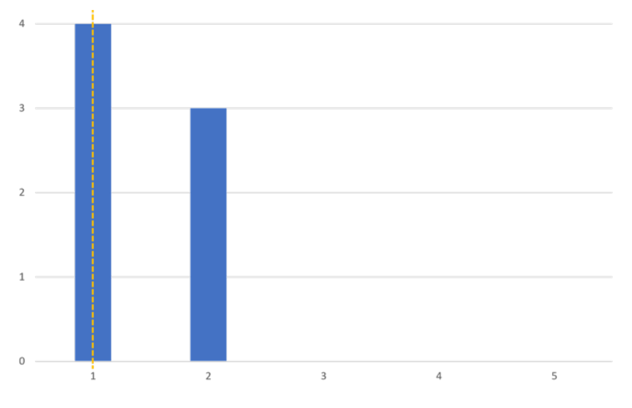
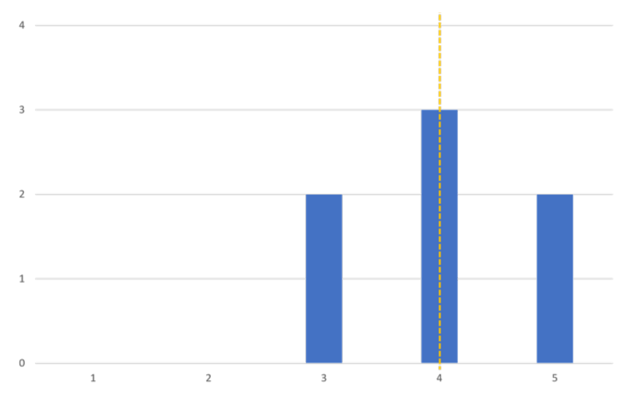
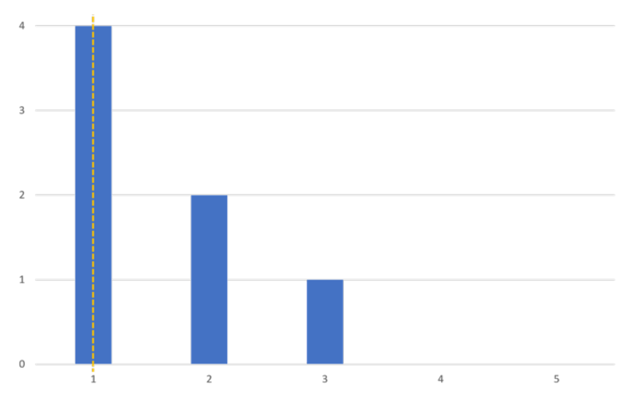
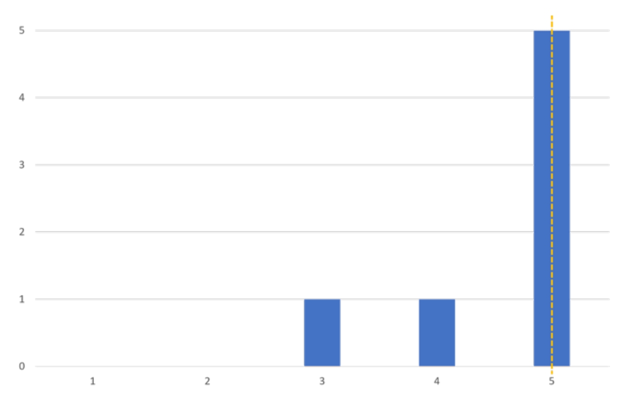



Figure 51: Radar Plot SUS results

To investigate which questions had the most critical feedback, a bar chart was drawn showing the distributions of the answers for each question. On the x-axis the scores from 1 to 5 are reported and on the y-axis the population for each score. The median value was calculated for each answer and shown for each graph reported as yellow lines.

| Item | Bar chart |
|---|---|
| *1: "Penso che mi piacerebbe utilizzare questo sistema frequentemente."* |   |

| | |
|---|---|
| *2: "Ho trovato il Sistema complesso senza che ce ne fosse bisogno"* |  |
| *3: "Ho trovato il sistema molto semplice da usare"* |  |
| *4: "Penso che avrei bisogno del supporto di una persona già in grado di utilizzare il sistema"* |  |
| *5: "Ho trovato le varie funzionalità del sistema ben integrate"* |  |

| | |
|---|---|
| *6: "Ho trovato incoerenze tra le varie funzionalità del sistema."* |  |
| *7: "Penso che la maggior parte delle persone potrebbero imparare ad usare il sistema facilmente."* |  |
| *8: "Ho trovato il sistema molto macchinoso da utilizzare."* |  |
| *9: "Ho avuto molta confidenza con il sistema durante l'uso."* |  |

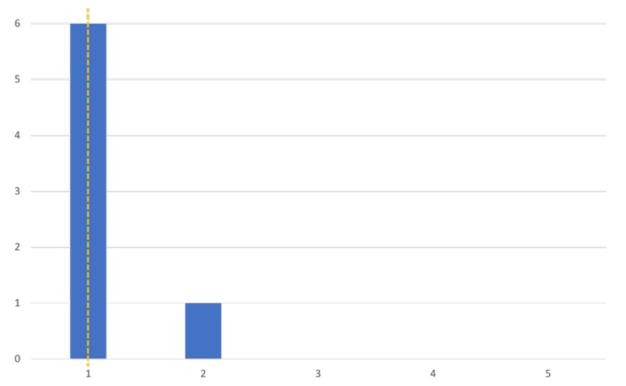
| | |
|---|---|
| *10: "Ho avuto bisogno di imparare molti processi prima di riuscire ad utilizzare al meglio il sistema."* |  |

Table 11: Bar Chart SUS response

In answers 1,2,4,6,8,9 and 10 it can be seen that the median (marked in the bar chart with a yellow dotted line) coincides with the ideal value of this answer.

For the remaining answers 3,5,7, however, a very good result can be seen, as the median deviates in all three cases by only one point from the optimum value. In particular, these three responses concern issues such as ease of use, immediacy in learning the technology and the presence of well-integrated features.

In Table 12, the SUS score for each subject is reported:

| User A | User B | User C | User D | User E | User F | User G |
|---|---|---|---|---|---|---|
| 80 | 77,5 | 97,5 | 75 | 92,5 | 92,5 | 75 |

Table 12: Total score SUS results

As a score above 68 is considered good, and the lowest reported score is instead 75, it can be highlighted that for all subjects the results in terms of usability were very good, up to a maximum of 97.5 for subject C and median ($25^{th}$ percentile, $75^{th}$ percentile) equal to 80 (76.25; 92.5)with interquartile range equal to 16,25.

## 3.4. Logs and adherence results

Table 13 shows the main data collected examining the interactions of the subject with Alexa, in accordance to the data inserted in the database. They have been divided by testers and identify the intake collected through the CareVoice skill functions. In yellow the two testers whose data acquisition occurred in correspondence with the resolution of some code bugs are highlighted. With reference to the Algorithm section of the Materials and Methods chapter, the various columns show the sum of all LogObjects with identical "from" field for each subject. For each feature then, the times a tester used that specific feature were summed up to calculate the final value. In any case, all interaction models and their features (i.e. the "from" field) are shown in the "Interaction Model" section in the "Materials and Methods" chapter.

The "Security Code" column represents access to the functionality that allows the Alexa profile to be associated with the system profile via OTP.

The "Load Therapies" column indicates the feature for configuring therapies.

The "Confirm Intake" column identifies the interaction the user has with Alexa to confirm the intake of the medicine(s).

The "Yes" column represents the times when the user answers yes to the question following the trigger of the "Confirm Intake" function. Here we have to make a specification: the "Confirm Intake" function cycles through all therapies programmed for the same time. A person who has taken all the relevant medication will answer affirmatively to the confirmation for each medication. The sum of the "Yes" logs will then equal the number of times "Confirm Intake" is used multiplied by the number of drugs scheduled at the time "Confirm Intake" was triggered. This is true only if the user has taken all of the scheduled medications at the same time and then confirmed the intake to CareVoice, and the response time between the skill's question and the yes answer about the intake has not elapsed. In all other cases , this rule no longer applies and the number of calls to the "Confirm Intake" function may increase.

The "Request Missed Intakes" column, on the other hand, indicates the number of times the user explicitly asked CareVoice whether or not they had missed any intakes.

Similarly, the "Request adherence" log indicates how many times the user requested information about their adherence.

| | | Logs | | | | | |
|---|---|---|---|---|---|---|---|
| **User** | **# Therapies** | **Security Code** | **Load Therapies** | **Confirm Intake** | **Yes** | **Request Missed Intakes** | **Request Adherence** |
| **A** | 2 | 1 | 8 | 15 | 12 | 0 | 0 |
| **B** | 2 | 1 | 6 | 27 | 20 | 0 | 1 |
| **C** | 1 | 1 | 1 | 12 | 6 | 0 | 0 |
| **D** | 2 | 1 | 1 | 10 | 12 | 1 | 0 |
| **E** | 1 | 1 | 1 | 8 | 7 | 0 | 0 |
| **F** | 1 | 1 | 1 | 7 | 3 | 0 | 0 |
| **G** | 1 | 1 | 3 | 31 | 29 | 7 | 2 |

Table 13: Tester data collected through the database

Here are some considerations on the logs under analysis:

- Security Code Log: a value of 1 indicates that access to the user's association function via the OTP code occurred only once. This value is correct in all subjects, showing that pairing occured as expected only when the skill was first opened in Alexa.
- Load Therapy Log: its value depends on how many times therapies have been set up, reset or where the user accesses this function having already

configured all therapies and therefore not continuing with any interaction. In the basic test, this value was expected to be 1, as the therapies have been set up by each tester at the beginning, and were not supposed to be changed again. However, some values >1 are present: for the first testers A and B marked in red, this was due to the initial resolution of some code errors that requested to reinsert the therapies. For tester G, however, this was due to the fact that the user accessed the function but had nothing to configure.

- Confirm Intake Log: this value indicates how many times the user interacts with Alexa to confirm the intake of the medication. This value can vary widely and does not represent the adherence to intake, as a user may confirm after too long and have to invoke this function again (Alexa remains active only for a limited number of seconds, after which it exits the command which has to be called a second time), or a subject with several medications (programmed for the same moment) could take only one drug and confirm it, and only later he could take and confirm the intake of the second tablet. For subjects A and B some problems with confirmation were also initially present, so their values are less significant then others.
- Yes Log: the number of each confirmed drug intake is reported in this field. The Yes Log represents how many intakes are taken and therefore it should be an indicator of a subject's adherence; its value must be identical to the intakes taken (in the table below). If the adhesion is 100% then the number of Yes will be equal to the number of Total Intakes calculated as:

$$Total\ Intakes = \left(\sum Intakes\ for\ therapy\ in\ a\ day * number\ of\ day\ in\ which\ the\ therapy\ is\ scheduled\right)$$

for each therapy prescribed.

For each drug confirmed as taken, the intake “status” field is updated in the database.

In Table 14, the main data collected examining the interactions of the subject with Alexa, in accordance to the data visualized through the dashboard are presented. The total intake therefore equals the number of individual tablets the patient has to take: it is calculated as described above, i.e. as the sum of all the planned intakes for each therapy in the treatment plan, where all the intakes for a therapy on one day are multiplied by all the days on which the therapy is planned. At this point the intakes recorded as taken by CareVoice will constitute the "Taken" elements and vice versa those not recorded will constitute the "Missed" column.

| | | Intakes | | | | |
|---|---|---|---|---|---|---|
| **User** | **# Therapies** | **Total** | **Taken** | **Missed** | **Test days** | **Adherence** |
| **A** | 2 | 30 | 12 | 18 | 14 | 40% |
| **B** | 2 | 28 | 21 | 7 | 14 | 75% |
| **C** | 1 | 7 | 6 | 1 | 7 | 85.71% |
| **D** | 2 | 16 | 12 | 4 | 8 | 75% |
| **E** | 1 | 8 | 7 | 1 | 8 | 87.50% |
| **F** | 1 | 6 | 3 | 3 | 7 | 50% |
| **G** | 3 | 32 | 29 | 2 | 8 | 90.63 % |

Table 14: Tester data collected through the dashboard

The final adherence calculated and presented in the dashboard takes into account all the intakes compared to the total ones.

It is possible to note that the duration of the tests is different only for the first two testers, as it has been deliberately extended to solve technical problems. It is important to underline that the first acquisitions have been fundamental to test the code and consequently for the resolution of the errors.

# 4 Conclusion and discussion

The objective of this work was to create and update components in the structure of the IntakeCare platform, a digital health solution aimed at managing the treatment plan and remote monitoring of adherence. In detail, a new method has been integrated to support the management of reminders and related confirmation of intakes. The new personalized solution involves the use of an application ('Skill') via a voice interface, managed via the Alexa device, through which the subject can communicate, notify and report medication intake. One of the most fundamental aspects is the connectivity between the elements of this platform, in particular between doctors and their patients. The developed framework includes several IT solutions, which are used to fulfill the main tasks relevant to communication and adherence monitoring. While the doctor can remotely enter the patients' medication and view their progress and compliance, the patients are supported by a system that notifies and records their intakes.

One of the fundamental aspects that makes the developed solution unique and innovative is the creation of a direct and automated link between the control platform used by the doctor to insert the patient’s drug posology and the Alexa device used by the patient. This step is of main importance as the misunderstanding of drug labels and prescriptions provided by doctors is one of the major problems contributing to adverse drug events. As shown in a cross-sectional study carried out (Patel MJ at 2013) on a total of 181 patients with different levels of formal education, the majority failed to understand the different medical terminologies referring to therapies and their scheduling, with subjects with low formal education and older more prone to misunderstanding.

The main key points developed in this project were:

- Direct entry by the doctor of prescriptions on a web platform;
- Storage of all prescribed treatment instructions in a database;
- Voice playback through Alexa in compliance with the instructions entered by the doctor;
- Appropriate voice-mediated notification;

- Tracking of intakes via the voice interface;
- The saving of intakes in the database;
- Monitoring and representation of adherence;
- Feedback to the patient and results displayed on the doctor's control dashboard;
- Persuasive approaches were implemented in the workflow:. incrementality in confidence through continuous use of the interface, non-neutrality of the technology, primary support to counteract non-adherence, transparency and unobtrusiveness of the system not to be perceived as invasive during daily life, dialogue support for comprehensible interaction, and techniques to support credibility for a more authoritative perception.

Compared to many existing state-of-the-art solutions, where the user is in charge of self-administration, the IntakeCare's platform has a significant advantage: scheduling and confirming intake are activities reserved to the doctor and the patient, respectively. In this way, users will not be overloaded with additional tasks that could also require specific digital skills to be performed, in managing their treatment pathway. The platform guarantees the seriousness in the scheduling of the treatment plan, as it is in the doctor's responsibility, and its immediate adaptability based on modifications introduced by the control dashboard. Moreover, control is promoted, thanks to the patients' feedback on the intakes of the planned medications.

## 4.1. Technological aspects

As already mentioned, an implementation peculiarity of the Alexa software is the maximum time interval available to the system to process the request and complete the response. This interval, which goes from the moment in which the vocal request is made, to the moment in which Alexa has to give a vocal output, has a maximum duration of 8 seconds. If the computational time of the implementation processes necessary to fulfil the given request exceeds 8 seconds, Alexa will go into standby and will not be able to complete the objective. This value is fixed, and although it helps to make Alexa an effective and responsive tool, on the other hand, it limits the processing possibilities.

In the specific case of this project, when setting up the reminders, a call is made to the Reminders API which implies a variable processing time between 0.5 and 2 seconds. Since two reminders have been set for each intake schedule, this has the consequence of duplicating the time required.

For example, in the case of a medicine that has to be taken three times a day, considering two reminders per event, a time that is six times the API call time will be required (on average 6x1sec). It is clear, once again, that the more complicated the prescription, the closer we get to the time limit, with the risk that the whole operation will fall down and, therefore, the configuration will fail.

In an initial implementation phase, the idea was to have all therapy reminders configured in a single step. Given the time limitation described above, a change in approach was necessary. It was therefore decided to configure one therapy at a time (one medicine at a time) in order to reset the 8 seconds available for each new therapy.

This solution has two limitations: first, in the initial configuration phase of the therapy, for each drug it is necessary to confirm the input to obtain a dynamic interaction that respects the time limit. This ould result in a very long configuration process in case the user has many drugs to confirm.

In addition, even though it would be a very uncommon case, it is not feasible to confirm therapies with more than four intakes per day, as this would exceed the maximum of 8 seconds imposed by Alexa, as specified above. For these rare cases, in future implementations it could be possible to split the configuration of the same therapy into several phases to circumvent the time limit, for example by dividing it into morning, afternoon and evening configurations. Future updates from Amazon could allow a better management of this requirement in the communication with Alexa, so to make the process even more natural and efficient, leading to further optimization of the configuration time. Although it could be perceived as a cumbersome step, in reality this structure guarantees a final supervision to the users of the therapeutic plan with which the Alexa reminders will be set and therefore protects them from malicious entries and has to be accomplished only one time, in the first configuration, or in correspondence to a change in therapy agreed with the physician.

Another aspect related to Alexa is that utterances have a rigid and binding structure. Although they can be cumbersome and difficult to remember (as expressed by some testers), the phrases to interact with the device must have a fixed structure. For example, it is the case of the intake confirmation: "Alexa, ask the virtual doctor to mark that I took my medicine", which has as elements the invocation (Alexa), the target skill (ask the virtual doctor) and the function that one wants to use (to mark that I took my medicine). Only the latter can be modified and syntactically lightened. Following the results obtained, alternative synonym phrases were added to those implemented at the outset and are given in the Appendix B. These are also subject to the strict structure above described; however, it would be interesting to study how different phrases could influence the sense of complication perceived by the testers.

The Alexa skill can only be tested by entering the email of the participants in the appropriate section and approved by them by accessing the message in their inbox. This step will be overcome when the skill will be published on Alexa skill store because each patient will be able to download it automatically. However, the approval path to publish the skill requires an unspecified amount of time for verification before publication is granted, which needs to be taken into consideration.

An important detail is that as the structure of the platform assigns the decision-making role to the physician, so patients cannot change their therapies (schedules, frequencies, etc.). Besides it would be possible to integrate the platform with the possibility for the patient to send a request to change the therapy, this would be managed more easily through an application than through a voice interface.

## 4.2. Comment on results (usability aspects)

Some considerations could be made relevant to the usability results, the enrolled test group and the relevant satisfaction with the experiment.

First, it needs to be underlined that for most of the enrolled subjects the posology consisted in daily medications, and with a reduced number of drugs to be assumed every day. This represents a dimension of not complex therapies, which may change in different clinical situations or age groups. However, CareVoice can potentially handle all types of the complexity in the treatment plans thanks to the way in which the drugs are inserted in the control dashboard.

The variability in the small sample size of studied patients was very high, both in terms of age, ehealth literacy and level of perceived adherence, and also the fact of already having and using Alexa or not represents a possible bias.

The study was necessarily focused on the patient's usability of the proposed solution, in a time frame of 7 days that was considered enough to capture possible barriers for utilization without extending too much the duration of the test. Although most users appreciated almost all aspects of the developed Alexa skill, the results show that some aspects still need to be improved. Among these, the time limit for taking medication (set at 1 hour before and after the reminder for this test) was considered too short. In a real scenario with the physician involved, this value can be easily set by the doctor together with the patient, depending on how important it is to take a medicine with certain time precision.

The second point of less satisfaction was that of the communication interaction with Alexa (question 4): in many cases, the utterance "Alexa, chiedi a Medico Virtuale di segnare che ho preso le medicine" was considered too long to be pronounced, and double reminders about individual drugs were also considered unnecessary by some (it should be remembered that if the drug is taken before the second reminder, it lapses). Others expressed concern about the integrated functions of the skill, such as the request of the adherence score.

Another factor that could impact the perceived usability is that during the configuration phase the skill asks the user to confirm the insertion of one medicine at a time (and consequently set the relevant notifications automatically). This step could appear long if the number of insertion cycles increases. However, a specific analysis on this aspect was not carried on due to the small size of the test group and to the low number of therapies they had to insert.

Overall, the results showed a high level of satisfaction with the technology, both in terms of its persuasive elements and its non-intrusiveness in daily life. Some testers rated it as “a useful assistant that I missed when the period of the test was over”.

As previously observed, the SUS score showed a very good level of usability associated to the developed solution.

The results obtained can be considered as an additional value to what was reported in Beaney's study (Beaney et al., 2020): subjects used only the basic functionality of Alexa to create the reminders. At the end of the study, they reported positive feedback on how the digital reminders supported them in remembering their medication. In their conclusions, it was pointed out that “The basic functionality exists, so if a medication 'skill' (app) could be developed to solve these problems, it would make the device even more useful". CareVoice, the skill developed in this thesis, can be considered as exactly the specialised extension they mentioned. In fact, the skill allows subjects no longer to set the reminders themselves, but rather to perform a single skill configuration step in which all the data and information entered by the doctor are retrieved. As suggested by Beaney's study, the functionalities of notification and confirmation of the intakes remain.

As originally stated, demonstrating the improvement in adherence using the solution was not the primary aim of the conducted pilot study; in fact, to prove that, a randomized clinical trial in a larger patient’s population for a longer time period should be performed, with the same group of patients exposed to the digital solution or not for at least one months. However, interestingly, in 4/7 patients the perceived adherence during the study was improved, and in none of the participants was decreased. This result show high promises for what is the final goal of the implemented solution.

In order to evaluate how the level of adherence could be estimated by the usage of the Alexa skill, the logObjects relevant to its use were analyzed. to understand which elements could be relevant for this analysis. The Confirm Intake Log, due to its great variability relevant to its usage, does not show to guarantee reliable data, as already pointed out earlier. Conversely, the Yes Log seems to represent the best indicator of adherence, as it counts the number of doses that have been confirmed as taken to the CareVoice skill. Accordingly, adherence can be computed as the ratio between the number of Yes Log and the total intakes scheduled in a certain time interval, which can be selected by the doctor in the dashboard.

A final remark must be made also about the the Request Missed Intakes and the Request Adherence Logs: besides the fact that their value was close to zero, this should not be interpreted in the sense that the possibility for the patient to ask for missing doses or visualize the computed adherence was considered useless. In fact, the testers were mainly involved in a usability test and for a very short time, so that they were not stimulated in tracking their adherence, nor was any specific technique adopted to push them to do so.

The limitations regarding the usability test are mainly two: the first one is that no physician was involved together with his/her patients. The testers were all volunteers, and the process of drug entry took place in the way approved by the ethics committee of Politecnico di Milano. It included supervision by the researchers on the testers during the entry of their therapies using the physician's dashboard. This modality does not reflect the final idea envisioned for the use of this platform, but it was adopted for its simplicity (involving physicians and patients would have required additional Ehtical Committees approvals from the involved institutions, besides that this activity is currently planned), and because the attention was focused in this case on just the patient'usability of the interaction with Alexa, that did not require the physician's involvement.

The second limitation is about the small number of participating subjects up to now, due to the limited availability of Alexa devices to be used (two), to the difficulty in recruiting volunteers, and the time needed to complete the test in each subject.

## 4.3. Future developments

Being a very new and innovative system, it is clear that there are many possible future developments. First and foremost is the improvement of the doctor's control dashboard graphical interface to be used as both a mobile and tablet application. With the reactive tools of JavaScript, this functionality has already been implemented and very preliminary tested for usability in a parallel thesis (Cancelliere, at 2022). The idea of a specific mobile application that can be used by everyone and which, depending on permissions and roles, will allow the user to perform tasks and functions will need also to be further explored.

Additional functionalities could be added to the system (i.e., computation of weekly, monthly, as well as separate adherence for each drug). Thinking in a larger upscaling perspective, the system will need to be linked to the hospital EHR system. Reminders about the need to re-fill the medications could also be integrated, as well as checking on expiration date (if inserted by the patient).

As regards communication with the patient, more complex interactions including voice emotion features, as well as pre-recorded messages, could be added in order to increase engagement and avoid repetitiveness of the same sentences, also in view of achieving a personalization of the solution to the preferences and characteristics of the patient.

As the adopted system architecture allows for a modular development where many functions can be added, communication with other devices exploiting Alexa capability to extensively interact with third-party devices and objects could be added. In this perspective, a mirror model could be conceived in which an Alexa device could be used by the doctor to set the input of medicines in a vocal form, then returning confirmation to the doctor and connecting to the patient's device to configure the intake reminders.

In conclusion, a main contribution to the concept of the IntakeCare platform was given in this work by expanding the ways reminders for medication adherence can be notified to the patient by developing a novel voice interface software ("skill") for the communication, management, notification and reporting of medication intake using Alexa. Also, initial usability testing in the field provided the first reassuring and promising feedbacks from the enrolled patients about the way the interaction with Alexa and the developed skill have been conceived. Specific areas to further explore were highlighted, as well as current limitations and barriers to be tackled.

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# 6 Appendix

## A. CareVoice manual

English version

| Process | Utterance | Function |
|---|---|---|
| Setting up of the treatment plan | "*Alexa*, apri *Medico Virtuale*" | This leads to the *CareVoice* function. The *CareVoice* will initially ask to grant permissions from the app, then the following reopening will ask to enter the security code. Once these parts have been completed, it will greet the user each time it is opened and advise them to configure their therapies. |
| | "*Alexa*, inserisci il codice di sicurezza" | *CareVoice* will ask to dictate the security code and wait for the answer. It is important to ensure that the code is accessible. If the code dictated is correct, he will greet the user and advise him to configure the therapies. |
| | "*Alexa*, configura le mie terapie" | *CareVoice* will ask to confirm whether to proceed with the insert of each individual therapy prescribed by the doctor or, alternatively, to modify it if the doctor has updated any existing ones (deleted therapies are considered as updated). |
| | "*Alexa*, inserisci questa terapia" | The user confirms to *CareVoice* to proceed with inserting or modifying the therapies |

| | | |
|---|---|---|
| | ---<br>“*Alexa*, modifica questa terapia” | that the treating doctor has prescribed or updated. The procedure is repeated for each therapy within the treatment plan. |
| Confirmation of intake | “*Alexa*, chiedi al *Medico Virtuale* di segnarsi che ho preso le mie medicine” | The user prompts *CareVoice* to mark a specific intake as taken. The time interval in which it is possible to confirm the intake is limited. If the intake is confirmed, subsequent reminders are silenced. |
| Request info on adherence | “Alexa, chiedi al Medico Virtuale di controllare se ho dimenticato dei farmaci” | *CareVoice* will check whether the user has missed any doses during the current day. If so, it will report which drugs have not been taken, otherwise it will confirm that everything is OK and that the therapy has been respected. |
| | “Alexa, chiedi a Medico Virtuale qual è la mia aderenza” | *CareVoice* will respond with the adherence index calculated as the ratio of confirmed hires to planned hires to date. |

Italian version

| Procedimento | Frase di attivazione | Funzione |
|---|---|---|
| Fase di configurazione del piano terapeutico | “*Alexa*, apri *Medico Virtuale*” | Si entra nella funzione *MedicoVirtuale*. Il *Medico Virtuale* chiederà inizialmente di conferire i permessi dall’app, in seguito alla successiva riapertura chiederà di inserire il codice di sicurezza. Una volta completate queste parti ad ogni apertura saluterà l’utente e gli consiglierà di configurare le terapie. |
| | “*Alexa*, inserisci il codice di sicurezza” | Il *Medico Virtuale* chiederà di dettargli il codice di sicurezza e aspetterà la risposta. È importante assicurarsi di avere il codice a |

| | | |
|---|---|---|
| | | portata di mano. Se il codice dettato è corretto saluterà l'utente e gli consiglierà di configurare le terapie. |
| | "*Alexa*, inserisci questa terapia"<br>---<br>"*Alexa*, modifica questa terapia" | Si conferma al *Medico Virtuale* di procedere con l'inserimento o con la modifica delle terapie che il medico curante ha prescritto o aggiornato (le terapie cancellate vengono considerate come aggiornate).<br>Il procedimento si ripete per ogni terapia all'interno del piano terapeutico. |
| Fase di conferma dell'assunzione dei farmaci | "*Alexa*, chiedi al *Medico Virtuale* di segnarsi che ho preso le mie medicine" | In questo modo si chiede al *Medico Virtuale* di annotare l'effettiva assunzione dei farmaci (teoricamente previsto dopo il promemoria generato da Alexa). Nel momento in cui viene confermata l'assunzione, i promemoria successivi riferiti a quella stessa assunzione, vengono silenziati in quanto ormai superflui. |
| Fase di controllo delle dosi mancate | "Alexa, chiedi al Medico Virtuale di controllare se ho dimenticato dei farmaci" | Il *MedicoVirtuale* controllerà che l'utente abbia assunto tutti i farmaci della giornata e che non abbia saltato delle dosi. In tal caso segnalerà quali farmaci non sono stati presi, altrimenti confermerà che tutto è a posto e che la terapia è stata rispettata. |
| Fase di richiesta aderenza | "Alexa, chiedi a Medico Virtuale qual è la mia aderenza" | Il *MedicoVirtuale* ti risponderà sull'indice della tua aderenza calcolata come il rapporto tra assunzioni confermate e assunzioni programmate fino a quel momento. |

# B. Utterance dictionary

| **Intent name** | | **Utterances** |
|---|---|---|
| Launch Request Intent | Main Utterance | *"Alexa, apri Medico virtuale."* |
| Security Code Intent | Main Utterance | *"Inserisci il mio codice di sicurezza."* |
| | Synonyms | *"Inserire il codice di sicurezza."* |
| | | *"Ti dico il codice di sicurezza."* |
| | | *"Il mio codice di sicurezza è {otp}."* |
| | | *"Il codice di sicurezza è {otp}."* |
| | | *"Che il mio codice di sicurezza è {otp}."* |
| | | *"Che il codice di sicurezza è {otp}."* |
| Load Therapies Intent | Main Utterance | *"Configura le mie terapie."* |
| | Synonyms | *"Configura le terapie."* |
| | | *"Guarda le mie terapie."* |
| | | *"Inserisci le mie terapie."* |
| | | *"Configurare le mie terapie."* |
| | | *"Inserire le mie terapie."* |
| | | *"Guardare le mie terapie."* |
| Create Therapy Intent | Main Utterance | *"Inserisci questa terapia."* |

| | | |
|---|---|---|
| | Synonyms | *"Inserisci {medicina}."* |
| Modify Therapy Intent | Main Utterance | *"Modifica questa terapia."* |
| | Synonyms | *"Edita questa terapia."* |
| Confirm Intake Intent | Main Utterance | *"…segnarsi che ho preso le mie medicine."* |
| | Synonyms | *"…ho preso le mie medicine."* |
| | | *"…ho preso le medicine."* |
| | | *"…annota le medicine."* |
| | | *"…segna le mie medicine."* |
| | | *"…segna le medicine."* |
| | | *"…segnarsi l'assunzione delle medicine."* |
| | | *"…annotarsi le mie medicine."* |
| | | *"…segnarsi le mie medicine."* |
| | | *"…annotarsi le medicine."* |
| | | *"…segnarsi le medicine."* |
| | | *"…annotarsi che ho preso le mie medicine."* |
| | | *"…annotare che ho preso le mie medicine."* |
| | | *"…annotarsi che ho preso la mia medicina."* |
| | | *"…annotare che ho preso la mia medicina."* |
| | | *"…confermare che ho preso la mia medicina."* |

| | | |
|---|---|---|
| | | *"…confermare che ho preso le mie medicine."* |
| | | *"…segnare che ho preso la mia medicina."* |
| | | *"…segnarsi che ho preso la mia medicina."* |
| | | *"…segnare che ho preso le mie medicine."* |
| | | *"…ho preso la mia medicina."* |
| | | *"…confermo di aver preso la mia medicina."* |
| Request Missed Intakes Intent | Main Utterance | *"…di controllare se ho dimenticato dei farmaci."* |
| | Synonyms | *"…ho dimenticato dei farmaci."* |
| | | *"…ho dimenticato di prendere qualche medicina oggi."* |
| | | *"…ho preso tutte le medicine di oggi."* |
| Request Adherence Intent | Main Utterance | *"…qual è la mia aderenza."* |
| | Synonyms | *"…mostrami la mia aderenza."* |
| | | *"…mostrarmi la mia aderenza."* |
| | | *"…dirmi la mia aderenza."* |
| | | *"…dirmi qual è la mia aderenza."* |

# C. Applications features

**Promemoria Farmaci (MediSafe Inc.)**

Main features:

- Clarity and simplicity;
- Report sharing (viewing and sharing with doctor);
- Integration with apps that measure blood glucose, blood pressure, weight, pulse and temperature;
- Family interaction (allows management of many people under one account);
- Reminders for medication supplies (in case of new prescriptions or empty blisters);
- Saves prescriptions for medication as needed (PRN or pro re nata, so allergies, constipation, pain and therefore to be taken without a schedule);
- Assistance for nurses thanks to the Medfriend extension;

Extension in the premium version:

- No limitations of Medfriend;
- 20 or more medical measurements supported;
- Configurable tones, colours and styles;
- No advertising banners;

| Page | Features |
| --- | --- |
| Home | Possibility of registration or access |
| | Possibility of adding or not a medicine |
| | The home page displays the list of medicines to be taken during the day |

| | |
|---|---|
| | By scrolling through the calendar, one can view past and future prescriptions |
| | Notifications will remind the user of prescriptions |
| Add medicine | Integration with medicine database (often classified by colour and shape of the dispensing method and commented with principal information, such as dosage) |
| | Possibility to change dosage, units and appearance |
| | Possibility to change the shape and colour of the medicine for easier visualisation and better association with reality |
| Scheduling | Frequency and dosage selection |
| | Possibility of adding and modifying several repetitions in a day concerning dosage |
| | Possibility to select start and end dates of prescription (with unlimited intake option) |
| Stock management | The app keeps track of the pills in stock (e.g. blister capacity) and send notifications before they run out to remind the user to go to the pharmacy or doctor to repeat the order if necessary. |
| | A confirmation message is displayed at the end of the operation |
| Consent | Pop-ups will appear to ask the user permission to receive reminders and for a guide to quick instruct in using the app |
| Medication menu | Displays a summary list of medications |
| | Insight of medicine by clicking on it |
| | Change or edit all the medication parameters |
| | One can also suspend or delete the selected medicine |

| | | |
|---|---|---|
| Settings | The user can add information such as managing the treating doctors, writing notes in a diary, marking their appointments and viewing a report (weekly, monthly, or yearly) of adherence and what has been taken or missed |
| | One can control alerts and alert tones, display phrases, manage users and measurements |
| | In the premium version, the offer is by paying 5€ |
| Profile management | One can manage and add profiles |
| | The Medfriend function allows associating the profile with one or more people who will be notified when the user does not take medications |

**Promemoria per Farmaci (Sergio Licea)**

Main features:

- Simplicity
- Allows the creation of many types of reminders
- Tracks the amount of medication remaining
- Reliably tracks whether or not the medication is taken
- PRN included
- Allows reminders for medical appointments
- Allows to view reports and email them to the doctor
- Supports multiple users

Extension in the premium version:

- No longer just two reminders but unlimited

| Page | Features |
| --- | --- |
| Home | Display of medications to be taken by the day and scrolling calendar |
| | Medication entry menu, reminders (i.e. prescriptions), calendar display, and other features |
| Add medicine | Function that allows to add drugs and save them in the profile |
| | Controllable parameters include dosage, quantities, and other optional data |
| | FDA database |
| | Possibility of controlling the dosage even up to eighths of a pill |
| | Possibility of selecting the desired photo to link to the drug image |
| | Stock and expiry management with alarms |
| | Options for editing and integration with other data |
| Scheduling | Adding PRN |
| | Displaying the calendar |
| | Management of reminders according to repetitions, dosages and periods |
| | Insertion of ringtones for early and late alarms |
| Consent | Requesting consent to notifications |
| Medication menu | Adherence reports |
| | Possibility to mark medication as taken or not taken |
| Settings | Manage ringtones, messages and backups |

| | |
|---|---|
| | In-app payment for the premium version |
| Profile management | Adding appointments with editable parameters |

**Promemoria pillola (Benjamin Brewis)**

Main features:

- No advertising
- User friendly and clear
- Simple design, customisable
- Allows to manage multiple users
- Allows to share the profile with an assistant
- Supports contraceptives
- Configures medication refill notifications and custom images
- Notifications on Apple Watch, Fitbit and has widgets on iOS14
- Allows inserting widgets in the phone menu

| Page | Features |
|---|---|
| Home | Brief introduction/guide |
| | Profile creation (access through face ID to increase security) |
| | Account customisation with photo and colour |
| | The main screen presents the day's reminders |
| | The "go-to today" button takes back to the current day |
| Add medicine | Quick drug entry with customisable times and doses |

| | |
|---|---|
| | Parameters: name (no reference database) and photo (customisable) |
| Scheduling | Can also be on specific days of the week or fixed intervals |
| | Contraceptive cycle adjustment is also available |
| | A calendar menu allows you to view past and future reminders |
| | By scrolling left and right, you can quickly determine whether or not to take the medication marked in the reminder |
| Stock management | Possibility of programming the order of a new medicine |
| Consent | The application requests the user's consent to send notifications |
| Settings | Possibility to change the users and the medicines they have taken |
| | In the premium version (1.99€ per month), it is possible to increase specific functions |
| Profile management | Family Sharing option |

**MyTherapy: promemoria per medicine**

Main features:

- Simplicity
- Sharing of pdf reports by email (viewing and sharing with doctor)
- Other people/family members can view a user's progress
- Reminders for medication supplies
- Medical appointment entry

| Page | Features |
|---|---|
| Home | Possibility to register or log in |
| | Option to enter voluntary information such as gender and year of birth |
| | Possibility to add a reminder or not |
| | The Today section displays the medications that are still to be taken during the day |
| Add medicine | Integration with medicine database |
| Scheduling | Possibility of adding and modifying several repetitions in the day concerning dosage |
| | Possibility to select prescription end dates |
| | Possibility to set reminders every 5 min until confirmed |
| Stock management | Possibility to enter quantities for inventory |
| Consent | By clicking 'Get started', one accepts the conditions and terms of use |
| Medication menu | The Progress section displays the medication 'taken', 'missed' or 'unmarked' |
| | One can extract a PDF of the progress and email it |
| Profile management | Appointment entry |
| | Enter doctor contacts |

**Mediteo: promemoria per farmaci**

Main features:

- Simplicity
- Clarity and simplicity and good design
- Completeness and richness of features
- Sharing of pdf reports via email (viewing and sharing with doctor)
- Interaction with family (possibility of adding users to view one's progress)
- Reminders for medication supplies
- Input of vital parameters with reports and statistics in CSV format

| Page | Features |
|---|---|
| Home | Possibility of registration (to connect to the electronic patient record) or without an account |
| | Short initial demo |
| | Visualisation of medicines of the current day in the Daily section |
| | By scrolling through the calendar, one can view past and future prescriptions |
| | Notifications will remind the user of prescriptions |
| Add medicine | Integration with medicine database by name or barcode scan |
| | Possibility of changing the appearance and colour of the medicine for easier visualisation and association with reality |
| | Possibility to insert notes or photos of the medicine |
| Scheduling | Frequency and dosage selection |
| | Configuration menu |

| | |
|---|---|
| | Selection of start and end of therapy |
| | Final synthesis pre-saving new drug |
| Stock management | Refill insertion |
| Consent | Country selection and confirmation Terms and conditions |
| Medication menu | List of medications entered in the Treatment section |
| | Report with weekly, daily and punctuality references |
| | By clicking on the calendar, one can select the day and see the medicines to be taken on that day |
| | One can enter parameters and get statistics and reports to share (CSV file and soon available in PDF format) in the My Diary section |
| Profile management | Enter contacts of doctors, pharmacies or generics |

For the following applications, we only report the main features. In particular, these applications generally have fewer features or differ little from the previous ones.

**My pill reminder (Roman Baev)**

Main features:

- Flexible
- Notifies hiring times
- View past hires in the calendar
- Organise hires and non-hires
- View upcoming hires with a widget

**Dosecast: promemoria pillola (Montuno Software)**

Main features:

- Reliable notifications
- Avoids overdoses by pre-determining how many doses are allowed for a maximum of 24 hours
- Doses and instructions are editable
- Allows postponing reminders
- Smart silencing (sleep tracking)
- Private and secure
- Allows synchronization with other devices (with Dosecast CloudSync)
- Multiple types of administrations are available
- Offers dose history and compliance reporting
- Tracks quantities and alerts for refills
- Supports multiple people
- Tracks doctors and pharmacies prescribing or dispensing medication
- Has a database for medications
- Allows customization of medication photos

**Mr.Pillster: il ti ricorda pillole**

Main features:

- Statistics with graphs on the app
- Possibility to manage multiple family members (designed for caregivers)

**Medfox: Pill Reminder & Tracker**

Main features:

- Map with nearby pharmacies

# D. Test modules

**DICHIARAZIONE DI CONSENSO AL TRATTAMENTO DEI DATI PERSONALI AI SENSI DELL'ART. 13 DEL REGOLAMENTO UE N. 679/2016 DEL 27 APRILE 2016**

**Titolo del progetto di ricerca**
Studio di usabilità di software per il monitoraggio dell'aderenza alla terapia farmacologica attraverso l'utilizzo di dispositivo a comando vocale Amazon Alexa.

**Breve descrizione del progetto di ricerca**
Il progetto di ricerca si propone di valutare l'usabilità di una soluzione digitale progettata per monitorare l'aderenza alla terapia di pazienti cronici attraverso l'utilizzo di dispositivi a comando vocale Amazon Alexa. Il partecipante allo studio sarà dotato di una "skill" appositamente sviluppata da installare sul dispositivo Amazon Alexa, che sarà a lui messo in dotazione per la durata dello studio in caso non ne abbia già uno personale (in questo caso, se necessario uno sperimentatore provvederà alla installazione del dispositivo presso il domicilio del paziente, ed alla relativa disinstallazione al termine dello studio, in sua presenza).
La Skill è collegata tramite codice univoco ad un database cloud privato ed anonimizzato, all'interno del quale il partecipante inserisce le terapie e le relative posologie (tempistiche, modalità e dosi) tramite un'interfaccia web. La Skill genererà dei promemoria per ricordare al paziente quale terapia assumere, quando ed in che modo, registrandone la risposta per monitorarne l'aderenza per 7 giorni consecutivi, che costituiscono la durata della sperimentazione. All'inizio dello studio sarà richiesta la compilazione di due brevi questionari in italiano, al fine di ottenere delle informazioni sulla aderenza farmacologica, e sulla eHealth literacy del partecipante. Al termine dei 7 giorni, verrà richiesto di partecipare ad una intervista semi-strutturata per ottenere una valutazione qualitativa della soluzione testata, e la compilazione di un questionario relativo alla usabilità della stessa.
Da tale studio si prevede la produzione di materiale scientifico per divulgazione a conferenze o pubblicazioni in riviste di settore, nonchè indicazioni utili sulla effettiva usabilità della soluzione proposta.

**Responsabile della ricerca:** Prof. Enrico Gianluca Caiani, Politecnico di Milano.

Si forniscono ai sensi dell'art. 13 del GDPR (General Data Protection Regulation), regolamento UE n. 679/2016 del 27 aprile 2016, le seguenti informazioni.

**Titolare del trattamento dati**
Politecnico di Milano - Direttore Generale su delega del Rettore pro-tempore – mail: dirgen@polimi.it.

**Responsabile interno del trattamento**
Prof. Enrico G. Caiani, Politecnico di Milano, enrico.caiani@polimi.it
I dati saranno trattati da ulteriori soggetti autorizzati e a tal fine istruiti nel rispetto della normativa vigente.

**Responsabile protezione dati e punti di contatto**
Dott. Vincenzo Del Core - privacy@polimi.it tel.: 0223999378

**Finalità del trattamento**
Il team dello sperimentatore principale, afferente al Politecnico di Milano, presso il quale viene effettuato lo studio, in conformità con le responsabilità previste con il Regolamento UE generale sulla protezione dei dati personali 679/2016 (di seguito "RGPD") e il Decreto Legislativo n. 196 del 30 giugno 2003, tratterà i Suoi dati personali, come specificato di seguito, esclusivamente nella misura in cui siano essenziali per la conduzione dello studio e il raggiungimento dei suoi obiettivi.

**Base giuridica e natura del conferimento dei dati**
La base giuridica di tale trattamento è da rinvenirsi, ai sensi dell'art. 6, 1° comma, lett. a) del Regolamento, nel Suo consenso, libero e facoltativo.
La partecipazione al progetto è facoltativa. Il conferimento dei dati richiesti tuttavia è indispensabile allo svolgimento dello studio: il rifiuto di conferirli non Le consentirà di parteciparvi.

**Modalità di trattamento e natura del conferimento dei dati**
Il trattamento dei dati avverrà attraverso strumenti informatici e telematici, con logiche di organizzazione ed elaborazione correlate esclusivamente alle finalità della ricerca e, comunque, in modo da garantire la sicurezza e la riservatezza degli stessi in conformità alla normativa vigente.
Le registrazioni dei dati potranno essere conservate, informatizzate e raccolte unicamente ai fini scientifici. In tal caso il Politecnico di Milano si impegna a:
- trattare i dati tramite i ricercatori specificatamente designati;
- curare le successive fasi di elaborazione e di memorizzazione dei dati raccolti in modo da non identificare direttamente gli interessati, procedendo all'anonimizzazione di tutte le informazioni;
- comunicare i dati e/o memorizzarli, in forma anonima, in un database accessibile a tutti i partecipanti al progetto di ricerca;
- diffondere i risultati soltanto in modo aggregato e/o anonimo.

**Comunicazione e diffusione**
I dati personali, se oggetto di comunicazione e/o diffusione (per esempio per mezzo di pubblicazioni scientifiche, congressi, seminari, lezioni ecc..), saranno in ogni caso previamente resi anonimi e trattati in forma aggregata in modo da escludere qualsiasi possibilità di identificazione del minore.
Si precisa che la comunicazione o diffusione dei dati sopra descritti avverranno, con il Suo consenso, solo previa valutazione della pertinenza e non eccedenza del trattamento rispetto alle finalità della raccolta.

**Periodo di conservazione dei dati**
I dati raccolti saranno utilizzati con strumenti informatici e telematici e saranno conservati esclusivamente per il tempo strettamente necessario per la trascrizione dei contenuti e per la loro anonimizzazione e, comunque, non oltre 5 anni.

**Diritti degli interessati**
In qualità di soggetto interessato può chiedere in qualsiasi momento al Titolare:
□ la conferma dell'esistenza o meno di dati personali che lo riguardano;
□ l'accesso ai suoi dati personali ed alle informazioni relative agli stessi; la rettifica dei dati inesatti o l'integrazione di quelli incompleti; la cancellazione dei dati personali che la riguardano (al verificarsi di una delle condizioni indicate nell'art. 17, paragrafo 1 del Regolamento e nel rispetto delle eccezioni previste nel paragrafo 3 dello stesso articolo); la limitazione del trattamento dei suoi dati personali (al ricorrere di una delle ipotesi indicate nell'art. 18, paragrafo 1 del Regolamento), la trasformazione in forma anonima o il blocco dei dati trattati in violazione di legge, compresi quelli di cui non è necessaria la conservazione in relazione agli scopi per i quali i dati sono stati raccolti o successivamente trattati.

In qualità di soggetto interessato ha inoltre diritto di opporsi in tutto o in parte:
□ per motivi legittimi al trattamento dei dati personali che lo riguardano, ancorché pertinenti allo scopo della raccolta;
□ al trattamento di dati personali che lo riguardano a fini di invio di promozione di iniziative formative ed eventi culturali del Politecnico di Milano.

Tali diritti sono esercitabili rivolgendosi a privacy@polimi.it.

Qualora ritenga che i suoi diritti siano stati violati dal titolare e/o da un terzo, ha il diritto di proporre reclamo all'Autorità per la protezione dei dati personali e/o ad altra autorità di controllo competente in forza del Regolamento.

**CONSENSO AL TRATTAMENTO DEI DATI PERSONALI**

Il/La sottoscritto/a …………………………………………………………………………………………………
nato/a a …………………… il ………………………… residente a ..………………………………………
via ………………………………………………………………………………………......……….. n. ……… ;
presa visione dell'informativa ai sensi dell'art. dell'art. 13 del GDPR (General Data Protection Regulation), regolamento UE n. 679/2016 del 27 aprile 2016

**AUTORIZZA**

il Politecnico di Milano al trattamento dei propri dati personali nell'ambito del progetto di ricerca "Studio di usabilità di software per il monitoraggio dell'aderenza alla terapia farmacologica attraverso l'utilizzo di dispositivo a comando vocale Amazon Alexa" per le finalità indicate nell'informativa di cui sopra.

☐ *acconsente* ☐ *non acconsente*
*al trattamento dei propri dati, anche di natura particolare, per finalità di ricerca statistica e scientifica con le modalità e per gli scopi descritti [adesione al progetto]*;

Luogo e data ……………………………………….

(firma leggibile) ……………………………………….

**MODULO INFORMATIVO**
**PER SOGGETTO ADULTO**

**Titolo dello studio:** Studio di usabilità di software per il monitoraggio dell'aderenza alla terapia farmacologica attraverso l'utilizzo di dispositivo a comando vocale Amazon Alexa.

**Sperimentatore Principale: Prof. Enrico G. Caiani, Politecnico di Milano, enrico.caiani@polimi.it**

Gentile Signora / Egregio Signore,
Le è stato chiesto di partecipare ad uno studio sperimentale e questo documento ha lo scopo di informarLa sulla natura dello studio, sul fine che esso si propone, su ciò che comporterà per Lei una tale partecipazione, sui suoi diritti e le sue responsabilità.
La prego di leggere attentamente queste informazioni scritte prima di prendere una decisione in merito ad una eventuale Sua partecipazione allo studio. Lei avrà a disposizione tutto il tempo necessario per decidere se partecipare o meno.
Potrà, inoltre, porre liberamente qualsiasi domanda di chiarimento e riproporre ogni quesito che non abbia ricevuto una risposta chiara ed esauriente.
Nel caso in cui, dopo aver letto e compreso tutte le informazioni ivi fornite, decidesse di voler partecipare allo studio, Le chiederò di voler firmare e personalmente datare il modulo di Consenso Informato allegato a questo documento.
**I Suoi dati personali saranno trattati come descritto nella sezione informativa sulla riservatezza dei dati personali, nel rispetto del Regolamento generale sulla protezione dei dati personali UE 2016/679 e del D. Lgs. 196/2003. Questa informativa e la relativa richiesta di autorizzazione al trattamento dei dati Le saranno sottoposte separatamente.**

**Che cosa si propone lo studio**
Lo studio ha come obiettivo quello di valutare l'usabilità di una soluzione digitale in fase di sviluppo, progettata per monitorare l'aderenza alla terapia di pazienti cronici attraverso l'utilizzo di dispositivi a comando vocale Amazon Alexa, attraverso l'uso di un apposito software (una "Skill" di Alexa) sviluppato appositamente dal nostro team di ricerca.
Per poter aderire allo studio, Lei deve disporre di una rete Wi-fi per il collegamento ad internet presso il suo indirizzo di residenza.
Inoltre, deve esserle stata diagnosticata almeno una patologia cronica e Lei deve essere sottoposto a trattamento farmacologico, raccomandato dal suo medico curante, che richieda l'assunzione di almeno un medicinale con cadenza giornaliera.

**Quali sono le caratteristiche di questo studio**
Si tratta di uno studio di usabilità che si svolge valutando l'efficacia della interazione vocale tra lei ed il dispositivo presso la sua casa, per un periodo di 7 giorni, e che le richiederà non più di pochi minuti al giorno, con lo scopo di ricordarle al momento giusto il farmaco da assumere per la sua terapia.

**Cosa comporta la sua partecipazione allo studio**
*(Indicare tempi, i trattamenti e modalità di svolgimento dello studio e del follow up. Se studio randomizzato esplicitare la modalità di assegnazione al trattamento, i trattamenti previsti nei diversi gruppi)*

Se hai i requisiti sopra indicati ed accetterà di partecipare alo studio, La informiamo che esso prevede inizialmente che Lei fornisca i dati richiesti nella "scheda raccolta dati" circa la sua età, altezza, peso, genere e condizioni preesistenti. Le sarà inoltre richiesto di compilare la "scheda terapie", indicando quali terapie farmacologiche sta seguendo e le relative posologie (tempistiche, dosi e modalità), come definito dal suo medico di fiducia. Inoltre, le sarà chiesto di compilare due brevi questionari al fine di comprendere la sua propensione alla aderenza alla terapia farmacologica che le è stata prescritta dal suo medico, e sulla sua abilità ad interagire con tecnologia digitale nel contesto della salute (eHealth literacy).

Dopodichè le sarà mostrato come inserire i dati relativi alla sua terapia tramite una interfaccia web. Un operatore sarà disponibile ad aiutarla in tale inserimento, dove occorrerà che lei verifichi e inserisca per ogni farmaco che sta assumendo la corretta posologia. Questi dati, infatti, andranno a generare automaticamente degli "allarmi", o notifiche tramite messaggi vocali sul dispositivo Alexa, che le ricorderanno nel corso della giornata il momento in cui è prevista l'assunzione del farmaco, e la relativa dose.
Le verrà anche spiegato, e avrà modo di provare, ad interagire in modo vocale con Alexa, così da sapere come avverrà l'interazione relativamente ai farmaci da assumere.

Al termine di questo passaggio, se Lei già dispone di un dispositivo Amazon Alexa, Le sarà inoltre consegnato (via email o in forma cartacea) il codice alfanumerico necessario per poter fare il download e la relativa impostazione della "Skill" sul suo dispositivo Amazon Alexa. In questo caso, occorre che lei attivi la Skill entro 24 ore. Dopodichè, per i successivi 7 giorni il dispositivo Amazon Alexa provvederà a ricordarle, agli orari impostati dalla sua terapia, quale medicinale assumere e con quale posologia.

Nel caso in cui Lei già non disponga del dispositivo Amazon Alexa, si metterà d'accordo con un membro del nostro team per un appuntamento al suo domicilio, così che possiamo fornirLe il dispositivo Alexa, procedere alla sua installazione, e attivare con lei la Skill relativa, per poter poi iniziare la sperimentazione di utilizzo per 7 giorni.

Ogni volta che Alexa le comunicherà il momento di assuzione di un dato farmaco, La invitiamo a controllare che tale messaggio corrisponda con quanto da Lei dichiarato nella "Scheda terapie" compilata inizialmente, e di cui riceverà copia cartacea.
Durante i 7 giorni di esperimento potrà, in qualsiasi momento, richiedere assistenza per qualsiasi dubbio o problematica relativa all'esperimento ai ricercatori attraverso i contatti che le saranno messi a disposizione.

Al termine dei 7 giorni le verrà chiesto di partecipare ad un'intervista di circa 30 minuti con i ricercatori per ottenere la Sua opinione relativamente alla soluzione digitale che avrà avuto modo di testare, ed alla compialazione di un breve questionario atto a misurare la sua impressione in relazione alla usabilità di tale soluzione. In tale occasione Le verrà anche richiesto di restituire il dispositivo che Le è stato fornito, nel caso non ne fosse dotato apriori di uno personale.

**Quali sono i benefici che potrà ricevere partecipando allo studio**
Partecipando allo studio potrà "toccare con mano" la possibilità di usare nuove tecnologie per aiutarla a gestire la sua aderenza alla terapia farmacologica, fornendoci così utili indicazioni per le ulteriori fasi di sviluppo di tale soluzione, contribuendo così allo sviluppo della conoscenza in questo campo.

**Quali sono i rischi derivanti dalla partecipazione allo studio**
Non sono stati identificati possibili eventi avversi, rischi o inconvenienti legati alla sua partecipazione a questo studio. Come sopra indicato, ogni volta che Alexa le comunicherà il momento di assuzione di un dato farmaco, La invitiamo a controllare che tale messaggio corrisponda con quanto da Lei dichiarato nella "Scheda terapie" compilata inizialmente, e di cui riceverà copia cartacea. In caso di problemi, può contattare un membro del nostro Team in ogni momento, a qualsiasi ora e giorno della settimana.

**Cosa succede se decide di non partecipare allo studio**
La partecipazione allo studio è del tutto volontaria: Lei è libero/a di non partecipare allo studio oppure, se decide di partecipare, avrà il diritto di ritirarsi dallo studio in qualsiasi momento e senza l'obbligo di fornire spiegazioni, dandone tuttavia comunicazione ai ricercatori, e restituendo il dispositivo Amazon Alexa nel caso lo abbia ricevuto.
In tal caso non saranno raccolti ulteriori dati che La riguardano e, nei limiti previsti dalla normativa, potrà chiedere la cancellazione di quelli già raccolti.

**Riservatezza dei dati personali**
In accordo agli artt. 13 e 14 del Regolamento generale sulla protezione dei dati personali UE 2016/679 e del D. Lgs. 196/2003 si riportano i requisiti prescritti dal Garante della Privacy circa le finalità del trattamento dei dati, il titolare del trattamento, la natura, le modalità del trattamento, diffusione e comunicazione dei dati.

**Finalità del trattamento**
Il team dello sperimentatore principale, afferente al Politecnico di Milano, presso il quale viene effettuato lo studio, in conformità con le responsabilità previste con il Regolamento UE generale sulla protezione dei dati personali 679/2016 (di seguito "RGPD") e il Decreto Legislativo n. 196 del 30 giugno 2003, tratterà i Suoi dati personali, come specificato di seguito, esclusivamente nella misura in cui siano essenziali per la conduzione dello studio e il raggiungimento dei suoi obiettivi.

**Titolari del trattamento**
Per le finalità di cui al paragrafo precedente sono autonomi Titolari del trattamento:

a) Politecnico di Milano:
Il Prof. Enrico G. Caiani, Sperimentatore Principale di questo studio, è la persona preposta dal Titolare al trattamento dei dati relativi allo studio.

Dati di contatto del Responsabile della protezione dei dati per il Politecnico di Milano:
Direzione Generale tel. 0223992243 email: pecateneo@cert.polimi.it

**Conferimento e Natura dei dati**
Il conferimento dei dati personali per lo studio è indispensabile al suo svolgimento ed il rifiuto di conferirli non Le consentirà di parteciparvi.
I Suoi dati personali includeranno: Nome, Cognome, Luogo e Data di nascita, Residenza, Domicilio, Telefono, E-mail, Genere, Altezza, Peso, Condizioni mediche preesistenti, terapie in corso e relative posologie (di seguito chiamati "dati personali", "scheda raccolta dati" e "scheda terapie").

**Modalità del trattamento, Diffusione e comunicazione dei dati**
I dati acquisiti, trattati mediante strumenti anche elettronici, saranno diffusi solo in forma rigorosamente anonima, ad esempio attraverso pubblicazioni scientifiche, statistiche e convegni scientifici.
Il personale autorizzato al trattamento afferente al Politecnico di Milano presso il quale viene effettuato lo studio avrà accesso ai Suoi dati personali.
Inoltre, per finalità ispettive e di controllo, l'accesso ai Suoi dati contenuti anche nella documentazione originale, è consentito al Comitato Etico, se richiesto dalla legge applicabile e con modalità tali da garantirne la riservatezza.

Il Politecnico di Milano presso il quale viene effettuato lo studio e il Promotore adotteranno tutte le misure di sicurezza adeguate e gli idonei accorgimenti tecnici ed organizzativi per effettuare un trattamento conforme alla vigente normativa e a tutela dei Suoi dati personali, della Sua dignità e riservatezza.
Per le finalità sopra indicate, i Suoi dati personali saranno raccolti dal personale autorizzato afferente al Politecnico di Milano presso il quale viene effettuato lo studio e trasferiti in forma pseudonimizzata, mediante mezzi elettronici o di altro tipo, al personale interno preposto alle analisi dei dati.

La pseudonimizzazione dei dati personali significa che i Suoi dati personali saranno trattati in modo che non possano più essere attribuiti a Lei senza l'utilizzo di informazioni aggiuntive a condizione che tali informazioni aggiuntive siano conservate separatamente e soggette a misure tecniche e organizzative di protezione. In altre parole, il Politecnico di Milano presso il quale viene effettuato lo studio La identificherà con un codice identificativo al momento del Suo coinvolgimento nello studio. Tale codice identificativo verrà utilizzato al posto del relativo nominativo in ciascuna comunicazione dei dati collegati allo studio. Lo Sperimentatore

Principale del Politecnico di Milano presso il quale viene effettuato lo studio sarà l'unico ed esclusivo soggetto a poter associare il codice identificativo ai Suoi dati personali. Inoltre, tale codice sarà conservato in documenti riservati e sarà accessibile solo quando indispensabile ai fini dello studio e per periodi di tempo limitati (per es.: durante le attività di monitoraggio e verifica).

**Conservazione dei dati**
Il Suoi dati saranno conservati per un periodo non superiore a quello necessario per le finalità dello studio per i quali sono stati raccolti (5 anni). Qualsiasi dato personale sarà eliminato dopo la scadenza del periodo di conservazione applicabile.

**Esercizio dei diritti**
Lei ha il diritto di accedere ai Suoi dati personali trattati per lo studio e richiedere la loro rettifica, limitazione, eliminazione o esportazione. Inoltre, potrà revocare il Suo consenso alla partecipazione allo studio e alla raccolta di ulteriori dati in qualsiasi momento.

Per queste richieste, contatti per iscritto/email lo Sperimentatore Principale dello studio presso il Politecnico di Milano Lei ha il diritto di ritirarsi dallo studio in qualsiasi momento e non saranno raccolte altre informazioni su di Lei. Lei può inoltre esercitare il diritto all'oblio (art. 17 del GDPR) e dunque richiedere la cancellazione dei dati personali raccolti e trattati.

**Per informazioni in merito al trattamento dei dati e per i diritti connessi, si prega di contattare il Responsabile della protezione dei dati del Centro di sperimentazione.**

**Ulteriori informazioni**
Non riceverà alcun compenso economico per la partecipazione allo studio.
Il protocollo dello studio che Le è stato proposto è stato approvato dal Comitato Etico del Politecnico di Milano.

Lei potrà segnalare qualsiasi fatto ritenga opportuno evidenziare, relativamente alla ricerca che La riguarda, al Comitato Etico di questa Università.

Per ulteriori informazioni e comunicazioni durante lo studio sarà a disposizione il seguente personale:

| | | |
|---|---|---|
| Prof. | Caiani | Enrico Gianluca |
| Telefono | 338.7163426 | |
| Email | Enrico.caiani@polimi.it | |

_______________________________ __/__/____ ________ _______________________

Nome per esteso dello sperimentatore Data Ora Firma

**MODULO DI CONSENSO INFORMATO**
**PER SOGGETTO ADULTO**

**Titolo dello studio:** Studio di usabilità di software per il monitoraggio dell'aderenza alla terapia farmacologica attraverso l'utilizzo di dispositivo a comando vocale Amazon Alexa.

**Sperimentatore Principale: Prof. Enrico G. Caiani, Politecnico di Milano, enrico.caiani@polimi.it**

Io sottoscritto/a ________________________________________________________________
nato/a a ______________________ il ___/___/_______ residente a ______________________________
via/piazza _________________________________________________________________ n. ___________
tel. ___________________________ email __________________________________________________
domicilio (se diverso dalla residenza) __________________________________________________

**DICHIARO**

1. di aver ricevuto dal Dottor ________________________________________ esaurienti spiegazioni in merito alla richiesta di partecipazione alla ricerca in oggetto, secondo quanto riportato nella scheda informativa, facente parte di questo consenso, della quale mi è stata consegnata una copia in data ____________ alle ore ______________ (*indicare data e ora della consegna*);
2. che mi sono stati chiaramente spiegati e di aver compreso la natura, le finalità, le procedure, i benefici attesi, i rischi e gli inconvenienti possibili;
3. di aver avuto l'opportunità di porre domande chiarificatrici e di aver avuto risposte soddisfacenti;
4. di aver avuto tutto il tempo necessario prima di decidere se partecipare o meno;
5. di non aver avuto alcuna coercizione indebita nella richiesta del Consenso;
6. che mi è stato chiaramente spiegato di poter decidere liberamente di non prendere parte allo studio o di uscirne in qualsiasi momento senza fornire giustificazione, e che tali decisioni non modificheranno in alcun modo i rapporti con i docenti e con il Politecnico di Milano (nel caso il soggetto sia uno studente);
7. sono consapevole che devo ricevere una copia del presente modulo di consenso

**e pertanto:**

□ **acconsento** □ **NON acconsento**
di partecipare allo studio.

□ **acconsento** □ **NON acconsento**
al trattamento dei dati necessari per la conduzione dello studio nei limiti e con le modalità indicate nell'informativa facente parte di questo consenso.

□ **acconsento** □ **NON acconsento**
di essere informato sui risultati della ricerca.

| | | | |
|---|---|---|---|
| ______________________________ | __/__/____ | ________ | ______________________ |
| Nome per esteso del soggetto | Data | Ora | Firma |
| ______________________________ | __/__/____ | ________ | ______________________ |
| Nome per esteso del rappresentante legale | Data | Ora | Firma |

Modulo informativo e di consenso informato per soggetto adulto
Versione n.1 del XX/11/2021
Codice Studio:XXX

| |
|---|
| Io sottoscritto Prof./Dr. ……………………… *(Cognome)* ………………..… *(Nome)* |
| Dichiaro che il soggetto ha firmato spontaneamente la sua partecipazione allo studio.<br>Dichiaro inoltre di:<br>● aver fornito al soggetto esaurienti spiegazioni in merito alle finalità dello studio, alle procedure, e rischi connessi;<br>● aver verificato che il soggetto abbia sufficientemente compreso le informazioni fornitegli<br>● aver lasciato al soggetto il tempo necessario e la possibilità di fare domande in merito allo studio<br>● non aver esercitato alcuna coercizione od influenza indebita nella richiesta del Consenso<br><br>______________________________ ___/___/______ _________ ____________________<br>Nome per esteso dello sperimentatore che ha fornito le informazioni e raccolto il consenso informato — Data — Ora — Firma |

| |
|---|
| **NOTA BENE**<br>una copia del presente modulo, firmato e datato, allegato al “Modulo informativo per soggetto adulto”, dovrà essere consegnata al Paziente stesso |

CODICE PER PSEUDONIMIZZAZIONE PAZIENTE: ........................................................

## INFORMAZIONI PERSONALI

| | |
|---|---|
| COGNOME E NOME | |
| SESSO | |
| ETÀ | |

## CONDIZIONI PREESISTENTI

| | | | |
|---|---|---|---|
| DATA | | FIRMA PAZIENTE | |

CODICE PER PSEUDONIMIZZAZIONE PAZIENTE: ........................................................

## SCHEDA TERAPIE Pagina ........... di ...........

| | |
|---|---|
| MEDICINALE | |
| TEMPISTICA DI ASSUNZIONE | |
| DOSAGGIO | |
| NOTE | |

| | |
|---|---|
| MEDICINALE | |
| TEMPISTICA DI ASSUNZIONE | |
| DOSAGGIO | |
| NOTE | |

**SPERIMENTATORE: .........................**

| | | | |
|---|---|---|---|
| DATA | | FIRMA PAZIENTE | |

CODICE PER PSEUDONIMIZZAZIONE PAZIENTE: ........................................................

**Morisky Medication Adherence Scale 8**

| | Sì | No |
|---|---|---|
| 1. Qualche volta si dimentica di prendere le pillole? | ☐ | ☐ |
| 2. Nelle ultime due settimane, ci sono stati dei giorni in cui non ha preso le medicine? | ☐ | ☐ |
| 3. Ha mai ridotto o smesso di prendere le medicine senza dirlo al suo medico perché si sentiva male quando le prendeva? | ☐ | ☐ |
| 4. Quando viaggia o esce di casa, si dimentica di portare con sé i farmaci? | ☐ | ☐ |
| 5. Ieri ha preso tutte le sue medicine? | ☐ | ☐ |
| 6. Quando sente che i suoi sintomi sono sotto controllo, a volte smette di prendere le sue medicine? | ☐ | ☐ |
| 7. L'assunzione quotidiana dei farmaci è un vero e proprio disagio per alcune persone. Si sente mai infastidito o sente di avere delle difficoltà nell'attenersi al piano di trattamento? | ☐ | ☐ |
| 8. Quanto spesso le capita di avere difficoltà a ricordarsi di prendere tutti i suoi farmaci? | ☐ Mai<br>☐ Raramente<br>☐ Qualche volta<br>☐ Spesso<br>☐ Sempre | |

**IT-eHEALS**

| | 1 - Decisamente in disaccordo | 2 | 3 | 4 | 5 - Decisamente d'accordo |
|---|---|---|---|---|---|
| So come trovare su Internet informazioni utili sulla salute | ☐ | ☐ | ☐ | ☐ | ☐ |
| So come usare Internet per rispondere alle domande riguardo alla mia salute | ☐ | ☐ | ☐ | ☐ | ☐ |
| So quali informazioni sulla salute sono disponibili in Internet | ☐ | ☐ | ☐ | ☐ | ☐ |
| So dove trovare su Internet informazioni utili sulla salute | ☐ | ☐ | ☐ | ☐ | ☐ |
| So come usare le informazioni sulla salute che trovo su Internet in modo che mi possano essere d'aiuto | ☐ | ☐ | ☐ | ☐ | ☐ |
| Ho le capacità che mi servono per valutare le informazioni sulla salute che trovo su Internet | ☐ | ☐ | ☐ | ☐ | ☐ |
| Posso distinguere la bassa o alta qualità delle informazioni sulla salute che trovo su Internet | ☐ | ☐ | ☐ | ☐ | ☐ |
| Mi sento sicuro nell'usare informazioni che trovo su Internet per prendere decisioni riguardo alla mia salute | ☐ | ☐ | ☐ | ☐ | ☐ |

**SPERIMENTATORE: .........................**

**Dichiarazione Inserimento Terapie**

Io sottoscritto/a ……………………………………………………………………………………
nato/a a …………………… il ………………………… residente a ..……………………………
via …………………………………………………………………………………….... n. ……… ;

**DICHIARO**

1. di aver inserito le mie terapie, così come presentate nella Scheda Terapie da me compilata, all'interno del database cloud attraverso l'apposita interfaccia web;
2. che le terapie inserite nel database cloud combacino perfettamente in tempistiche, metodologia di somministrazione e dosaggio con quanto prescrittomi dal mio medico curante e dichiarato nella Scheda Terapie;
3. di aver avuto l'opportunità di porre domande chiarificatrici e di aver avuto risposte soddisfacenti;
4. di aver avuto tutto il tempo necessario per eseguire le operazioni di inserimento di cui sopra;
5. di non aver avuto alcuna coercizione nell'esecuzione di questo compito;
6. di essere consapevole che devo ricevere una copia del presente modulo.

| ______________________________ | __/__/____ | ________ | ____________________ |
|---|---|---|---|
| Nome per esteso del soggetto | Data | Ora | Firma |
| ______________________________ | __/__/____ | ________ | ____________________ |
| Nome per esteso dell'operatore | Data | Ora | Firma |

Codice Pseudonimizzazione Paziente ____________________________________________________________________

**CONFIGURAZIONE MEDICO VIRTUALE**

1. Al primo accesso ti è stato chiesto di impostare il codice univoco sul dispositivo Amazon Alexa. Quanto è stato complesso?

| Per niente | Poco | Abbastanza | Molto | Moltissimo |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

2. Al primo accesso ti è stato chiesto di configurare vocalmente le terapie. Quanto è stato complesso?

| Per niente | Poco | Abbastanza | Molto | Moltissimo |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

**UTILIZZO MEDICO VIRTUALE**

3. Ti è capitato di non ricevere i promemoria per una data terapia?

____________________________________________________________________________________

____________________________________________________________________________________

4. Hai trovato delle difficoltà nel comunicare con il Medico Virtuale?

____________________________________________________________________________________

____________________________________________________________________________________

5. Hai trovato utile la funzione del doppio promemoria?

____________________________________________________________________________________

____________________________________________________________________________________

6. Ritieni che il tempo a disposizione per prendere il medicinale sia adeguato?

____________________________________________________________________________________

____________________________________________________________________________________

7. Ti è capitato di utilizzare altre funzioni del Medico Virtuale oltre al rispondere alle notifiche (i.e. controllare aderenza)?

☐ Sì ☐ No

8.a. Se SÌ, quali e perché?

____________________________________________________________________________________

____________________________________________________________________________________

8.b. Se NO, perché?

____________________________________________________________________________________

____________________________________________________________________________________

Codice Pseudonimizzazione Paziente ____________________________________________________________

9. Quali sono gli aspetti del Medico Virtuale che hai trovato più utili o interessanti?

________________________________________________________________________________

________________________________________________________________________________

10. Quali sono gli aspetti del Medico Virtuale che hai trovato meno utili o di disturbo?

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________________________________________________________________________________

11. Quanto è stato intrusivo l'utilizzo del Medico Virtuale nelle tue normali attività giornaliere?

________________________________________________________________________________

________________________________________________________________________________

12. Complessivamente, su una scala da completamente insoddisfatto a completamente soddisfatto, quanto sei soddisfatto della settimana di utilizzo del Medico Virtuale?

| Completamente insoddisfatto | Leggermente insoddisfatto | Indifferente | Abbastanza soddisfatto | Completamente soddisfatto |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

**UTILIZZO AMAZON ALEXA**

13. Prima di questo test utilizzavi già un dispositivo Amazon Alexa?

________________________________________________________________________________

________________________________________________________________________________

14. In generale, saresti interessato/a ad utilizzare nella tua vita quotidiana Alexa monitorare la tua aderenza?

________________________________________________________________________________

________________________________________________________________________________

14.a. Se NO, perché? Preferisci utilizzare altri strumenti? (ad esempio smartphone, calendario fisico)

________________________________________________________________________________

________________________________________________________________________________

15. In generale, saresti interessato/a ad utilizzare nella tua vita quotidiana Alexa per altro oltre il monitoraggio dell'aderenza?

________________________________________________________________________________

________________________________________________________________________________

15.b Se NO, perché?

________________________________________________________________________________

________________________________________________________________________________

Codice Pseudonimizzazione Paziente ____________________________________________________________

**PERCEZIONE ADERENZA**

16. Su una scala da molto bassa a molto alta, come pensi fosse la tua aderenza prima dell'esperimento?

| Molto bassa | Bassa | Media | Alta | Molto alta |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | ☐ |

17. Pensi che la tua aderenza sia rimasta uguale, migliorata o peggiorata durante l'esperimento?

☐ Migliorata

☐ Rimasta uguale

☐ Peggiorata

☐ Altro ____________________________________________________________

18. Hai dei consigli o suggerimenti da darci su come migliorare la Skill?

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Codice Pseudonimizzazione Paziente ____________________________________________

## System Usability Scale (IT-SUS)

18. Rispondi alle seguenti domande su una scala da 1 (molto in disaccordo) a 5 (molto d'accordo).

| | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| Penso che mi piacerebbe utilizzare questo sistema frequentemente. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Ho trovato il sistema complesso senza che ce ne fosse bisogno. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Ho trovato il sistema molto semplice da usare. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Penso che avrei bisogno del supporto di una persona già in grado di utilizzare il sistema. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Ho trovato le varie funzionalità del sistema ben integrate | ☐ | ☐ | ☐ | ☐ | ☐ |
| Ho trovato incoerenze tra le varie funzionalità del sistema. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Penso che la maggior parte delle persone potrebbero imparare ad usare il sistema facilmente. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Ho trovato il sistema molto macchinoso da utilizzare. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Ho avuto molta confidenza con il sistema durante l'uso. | ☐ | ☐ | ☐ | ☐ | ☐ |
| Ho avuto bisogno di imparare molti processi prima di riuscire ad utilizzare al meglio il sistema. | ☐ | ☐ | ☐ | ☐ | ☐ |

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# Ringraziamenti

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