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Medication adherence supported by mHealth and NFC

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ABSTRACT

The present work proposes the use of modern ICT technologies such as smartphones, NFCs, internet, and web technologies, to help patients in carrying out their therapies. The implemented system provides a calendar with a reminder of the assumptions, ensures the drug identification through NFC, allows remote assistance from healthcare staff and family members to check and manage the therapy in real-time. The system also provides centralized information on the patient's therapeutic situation, helpful in choosing new compatible therapies.

1. Introduction

Therapeutic adherence is the measure by which a patient follows the doctor's directions and recommendations. According to the report "Adherence to long-term therapies: evidence for action" [1] issued in 2003 by the World Health Organization (WHO), only 50% of patients suffering from chronic diseases correctly follow the prescribed therapies in developed countries, a percentage that drops in the other countries.

Even the Italian Medicines Agency (AIFA) reveals worrying data: in 2013, only 55.1% of patients suffering from hypertension took continuous antihypertensive treatment [2]; almost 50% of patients treated with antidepressants stopped treatment in the first three months of therapy and over 70% in the first six months; in 2012 the percentage of patients adherent to antidiabetic treatments was 62.1%, while for asthma and chronic obstructive pulmonary was only 14.3% (data obtained from observational studies and the administrative databases of the ASL). In addition to being a danger to patients, non-observance of care is a significant economic burden on the health system. Many studies have been carried out in recent years to analyze the problem and propose solutions.

First of all, we distinguish two cases of non-adherence: intentional and unintentional. A patient may decide not to follow the therapeutic indications for many reasons: distrust in the doctor, fear of side effects, lack of understanding of the importance of the therapy, etc.

Often, however, the incorrect medication intake is not intentional. As highlighted in Ref. [3], the drugs themselves can mislead the patient: the same drug can occur in many similar packages but with different dosages and modes of administration (see Fig. 1a), or completely different drugs can have almost identical name (Fig. 1b) or packaging (Fig. 1c–e). All this shows that the problem relating to therapeutic adherence includes not only the missed drug intake, but, even more dangerously, the error in therapy, from the dosage and method of administration to the incorrect identification of the drug to take.

The main cause, however, remains distraction; especially in long-term therapies, repeating the same gestures several times a day reduces due attention, often leaving the patient with the doubt of having taken or not the drug and consequently with two possible choices, both potentially dangerous: skipping the dose or doubling it. The frequency of error increases significantly in visually impaired people, or elderly people: AIFA has established a particular study group, the "Geriatrics Working Group" (GWG), whose investigation [4] reveals that 50% of over 65s take between 5 and 9 drugs a day and 11% more than 10 drugs, resulting in a drastic decline in adherence to treatment.

This work aims to remedy these problems operating in the context of Ambient Assisted Living (AAL). To this aim, the technologies we used are smartphone and Near Field Communication (NFC). High connectivity capacity, increasing performances and vast diffusion makes smartphones the basis of mHealth (mobile health), mobile devices in medicine and, public health. The easiness of use of the NFC technology makes the solution proposed suitable for elderly and people with disabilities. The proposed solution can give support to the objective of active aging. A patient able to intake drugs in autonomously, can have

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support from the app developed as a reminder of drug intaking. Besides, with the simple operation of approaching the smartphone to the drug box, the tracing is performed allowing the drug intake monitoring by himself (with a minimum of digital knowledge) or by his familiar or caregivers.

One of the national authorities' problems in this COVID 19 pandemic period is the maintenance of acute disease care facilities. The massive impact on long-term care became the focus when the high number of deaths in nursing homes was reported. Proximity medicine with the support of telemedicine technologies is a possible solution to the problem. The methodology proposed in this work gives support to this solution.

The paper is organized as follows. Section 2 presents recent studies on medication adherence and commercial apps for a smartphone. The guidelines and the architecture of the system are proposed in Section 3. Section 4 presents the proposed assistance system with details on user client, assistant client and administration interface. Section 5 and 6 show some preliminary results and draw the conclusions.

2. Related works

2.1. mHealth impact on medication adherence

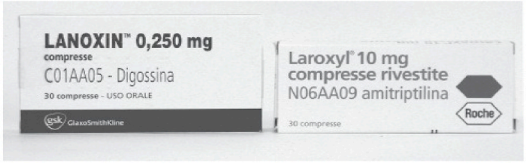
Recent works [5–14] studied the use of mHealth instruments. They tried to measure the user acceptability of utilizing mobile technologies in mHealth and investigated the mHealth tool's impact on medication adherence.

The study reported in Ref. [5] highlights the importance of considering diverse experiences when engaging patients in mHealth for medication adherence. It shows that better outcomes are reached when their individualized medication adherence strategies are used. Through a focus group of 17 patients, this study explored the barriers to medication adherence, investigating the potential use of mHealth as a possible solution.

Badawy et al. reports in Ref. [6] a review to identify and assess the effects of computer and mobile technology interventions designed to facilitate medication adherence and disease management in individuals

(a) Same drug, similar packs, different dosages and methods of administration.

(b) Different drugs, similar names.



(d) Different drugs, similar packs.

(e) Different drugs, similar packs.

(f) Different drugs, similar packs.

Fig. 1. Possible causes of confusion due to the packaging of drugs. (Images from "Bollettino d'informazione sui farmaci" [3]).

with thalassemia. They suggest that new research is required to evidence the mobile technology's efficacy on adherence in people with thalassemia. A mHealth platform is presented in Ref. [7] that showed feasibility and efficacy for enhanced medication adherence within public health clinics and successfully included older age groups. Among the patients using the platform, an approximate 2:1 ratio of persons agreed to try the smartphone app versus the SMS text messages. Among the results shown in the survey reported in the paper, 85% of the 132 patients agrees that mobile apps could help them remember to take medications.

In [8] the authors tried to verify the impact of a customizable medication management mobile app on medication adherence and adherence-related beliefs in patients with type 2 diabetes. They verified that a six-month test period for using a mobile app does not affect therapeutic adherence. Further testing is needed to determine the benefit for patients.

The study in Ref. [9] tested an app for enhancing adherence to oral anticancer medications. Findings suggest that facing difficulties in maintaining adherence and patients' perceived superiority of the app over their current methods facilitate adoption intention. The authors warn that cost, linguistic barrier and patients' perception of inadequacy could be an obstacle to the adoption of the app. One of the reasons for non-adherence is forgetfulness due to being busy, having complicated regimens or not getting used to dosage timings. The test has been applied to a limited number of patients (15) and caregivers (3). Carmody et al. in Ref. [10] show that great collaboration is needed between psychologists, health technologists and app developers to increment the user acceptability of the app for medication adherence.

The review on twenty-one studies, presented in Ref. [11], finds evidence that mHealth interventions improved medication adherence and blood pressure control among people with hypertension. However, most studies were small in sample size and short in study duration, and not all studies reported that the improvements were statistically significant.

In [12], 5881 medical adherence applications were identified by searching the Apple App Store and the Google Play Store. Among them, only 66 show evidence of health care professional involvement. The data analysis showed that patients could identify the benefits of a medication reminder by smartphone apps. However, the data also revealed concerns about increasing health-related anxiety and doubts about the sustainability of this technology over time.

Ahmed et al. present in Ref. [13] a systematic review of available medication adherence apps on app repositories. The results demonstrate a concerning lack of stakeholders' involvement in app development. More collaboration is required to ensure the development of high-quality adherence apps with clinical trials investigating their effectiveness. In Ref. [14], Haase et al. studied in detail five applications (RxNetwork, Mango Health, MyMeds, C3HealthLink, and HuCare) among the 225 commercial applications for medical adherence that have been identified. The authors concluded that mobile applications have outstanding features to improve medication adherence helping patients to take medication as prescribed.

Wen et al. in Ref. [15] presented a study to understand the perception that a consumer has on mobile devices for health monitoring. They conclude that in many cases the apps and wearable devices fail to give users credible guidance, so many users stop wearing the devices.

An in-depth review of the available smartphone apps for postnatal care is presented in Ref. [16]. The authors state that postnatal mobile applications constitute a promising strategy for maximizing maternal and newborn health.

Mobile apps may have a great potential to support patients in healthcare; in particular, Luna-Perejon et al. in Ref. [17] developed and tested a mobile app to encourage smoking cessation, with good results on user acceptability of the app.

Chu-Ya Huang et al. [18] faced the medication non-adherence caused by forgetting and delays using personalized medication systems that send SMS to the user to remind the medication intake in Taiwan. Over 1000 patients have been involved with good results in the number of patients who forgot medications, although only short-term medication adherence was investigated.

In summary, the presented works show that mobile health has great potential in addressing different issues in healthcare. A significant advantage of smartphone use as a support to health care is cost-effectiveness and simplicity to use. Several studies have used smartphones to support health care in specific fields, such as: thalassemia, diabetes, anticancer medications, hypertension, health monitoring, postnatal care, smoking cessation, and so on. In many studies consumers' perceptions and attitudes were investigated through a questionnaire survey. They evidence a positive impact of smartphone applications for healthcare; the use of an app seems preferable over SMS for long-term medication adherence, and more attention should be paid to patient needs in the integration of the app with all actors of the treatment. In many cases, a test with a higher number of cases and a more extended study duration was needed.

2.2. Commercial apps for medication adherence

NFC is an extension of Radio Frequency Identification (RFID) technology, and it is implemented natively in a growing number of mobile devices. NFC allows, simply by bringing them closer to the tags, exchanging information, and automating operations based on the read content. The NFC performs wireless communication between the reader and the tag at a frequency of 13.56 MHz and a maximum speed of 424 kbps. The substantial difference with the RFID is that the communication range is reduced, typically less than 4 cm; this implies the user's explicit will to interact with the tag, as in the case of payments or contactless identification. Furthermore, NFC communication can also be established between two readers by providing two-way communication, typically used to create a simple connection among two devices, such as smartphones and television or two smartphones.

The involvement of the end-user through his smartphone and NFC technology has recently been proposed in many different applications, ranging from food traceability [19] to recharge of electric vehicles [20], due to its ease of use. Many applications are available for smartphones addressed to medication adherence, but few of them have features that go beyond the functions of an electronic diary. They offer good monitoring of drug intakes schedule, sometimes even offering storage of vital sign measurements, such as heart rate, blood pressure, and blood glucose; some also offer the possibility to easily share such information, for example to send it to the doctor. Advanced features, such as support for web services, access to drug databases, saving data to the cloud, integrated ordering services linked to pharmacies, can also be found. Finally, the use of automatic verification systems of the identity of drugs, is almost totally absent, entrusted at most to the presence of images with which the user can visually compare. A brief list of commercial apps is the following:

- Whatpills [21], one of the few based on NFC technology, used to manage medication just by tapping medicines in which a tag is inserted with the smartphone. The data are not stored in a cloud database, and monitoring service for assistants is not considered.
- MediSafe [22] gives support to patients managing complex medication therapies,. It can synchronize data in real-time with other devices, such as family members, in order to allow them to assist the user and be notified in case of intake omission. It is also characterized by great care in the realization of the interface to simplify understanding and use.
- myHealthbox [23] instead is a service accessible via the web and through mobile applications, which does not offer intake scheduling but creates a massive international database of information on drugs and, more generally on health products, allowing not only to have all drug data at hand but also by providing real-time safety warnings, for

example in the case of finding new side effects or withdrawing lots from the market unsafe.

- Med Helper [24] is a free app for scheduling, with good results from the point of view of clarity and simplicity of use. Alarms can be set to notify when medications need to be taken or when prescriptions are getting low and need refilling. Limited interaction with caregivers is needed to keep track of and schedule prescriptions.
- Pill Reminder [25] is a free app that is almost exclusively limited to the scheduling and notification of appointments, with good results from the point of view of clarity and simplicity of use;
- Pill Manager [26] is a pill scheduling reminder. The users can preview medication schedules, and manage the ordering of medicines to registered pharmacies.
- Dosecast [27] offers flexible scheduling of intakes, allows you to access to a drug database.
- Care4today [28] is intended as a health and wellness app. The medication reminder is based on a database containing pill images where the patient can quickly find and add his medications. Beyond a medication or medical appointment reminder, it can track personal health measurements and all medical self-reported data.
- Mydiabeteshome [29] is a medication reminder, and health data logger addressed to patients with diabetes.
- Mytherapy [30] is a medication reminder that also provides access to a family member for teamwork.
- Mango Health [31] is a medication reminder.

A summary of the commercial apps' features is reported in Table 1, compared to the proposed system called "Pharm NFC".

2.3. mHealth and NFC for medication adherence

A lof of research in the AAL area has highlighted the potential of mobile health and NFC. Dohr et al. in Ref. [32] analyze how the combination of NFC technology and active remote monitoring can bring benefits in implmenting an effective system of AAL. In Ref. [33], Engel et al. explored how mobile devices and NFC can be used to implement medical assistance systems, suggesting the decentralization of functions and information to involve the patient more in his care and improving the self-sufficiency. A strong emphasis is placed on creating applications with a clear, immediate and simple to use interface and flow. The work in Ref. [34] by Morak et al. is based on a so-called smart blister, a typical blister for medicines to which an electronic circuitry has been added, capable of detecting, storing, and then transmitting via NFC the instant in which a pill is extracted. The system cannot be used with a standard box of pills. The system presented in Ref. [35] by M. Vergara et al., also based on NFC technology, is addressed to enable patients to get prescriptions from home: tables with explanatory images are provided, approaching the phone to the NFC tag equipped image, activates the related function.

In [36], Tsuruoka et al. present a patient-pharmacist communication system enabling pharmacists to monitor home-bound patients' prescription drug compliance remotely. The studies presented in Refs. [37–39] focus on the construction of systems based on centralized databases, with detailed information on medicinal products as well as on the clinical situation of patients, and on the implementation of applications for consulting them in order to avoid complications due to adverse drug reactions, due to allergies and intolerances or negative interactions between multiple therapies carried out simultaneously.

The projects carried out in Refs. [40–42], addressed to visually impaired people, are aimed to develop "talking" packs of drugs, using identification through NFC, to convey the appropriate information, such as the name of the drug, expiry date, dosage and timing of administration, through audio messages generated by the device's voice synthesizer.

In [43], Ukalkar et al. use a cloud-based NFC health care system to authenticate patients and doctorgiving correct medicine to a patient. Similarly, in Ref. [44], the NFC is used to identify the patient in the hospital and access the patient's health information stored in the health server. In Ref. [45], Jiang et al. propose a mobile health solution to improve medication adherence. A nine-month real-world trial shows the effectiveness of the proposed solution.

In summary, the state-of-the-art papers and commercial applications focus on a smartphone app used to remind the drug assumption, or to order drugs to the pharmacy or to consult the database of existing drugs, or the focus on the use of NFC for the patient identification in the hospitals to avoid incorrect drugs assumption.

Aside from the possible positive impacts of mHealth, some open issues must be faced:

- Privacy. This issue is even more relevant in this period of pandemic crisis. The necessity of a fast and efficient response to the crisis is often in contrast with privacy such as contact tracing, vaccination passport, vaccination obligation.
- Trust and Security on data transmission and storage. Not experts on ICT technologies, especially older adults, may be more vulnerable to cyber-attacks due to a lack of awareness. In addition to software and hardware security procedures, familiars and caregivers's support is required to monitor this additional vulnerability.
- Lack of human relationship. As fundamental as choosing the correct diagnosis and treatment of the disease of the psychological treatment derived from the human relationship between doctor and patient. The mHealth must be a support and not a replacement to the human relation.

The aim of the present work, novel for state of the art, is to create a user assistance system that can respond to the previously evidenced problems, in particular: it reminds for drug intakes (or more generally for therapeutic adherence); it verifies the correctness of the drug intake using the NFC technology; it is a centralized system of the patient's therapeutic condition and provides a complete clinical review of

Table 1
Features of commercial apps.

	Use of smartphone	Intake reminder	Record of weight, pressure, …	Cloud database	Remote monitoring for assistant	Drug database	Pharmacy drug order	Automatic drug identification	NFC
Whatpills	X	X						X	X
Medisafe	X	X	X	X	X	X			
myHealthbox	X			X		X			
Med Helper	X	X			X				
Pill Reminder	X	X							
Pill Manager	X	X	X				X		
Dosecast	X	X				X			
Care4today	X	X		X					
Mydiabeteshome	X	X	X	X					
Mytherapy	X	X	X	X	X				
Mango Health	X	X	X						
Pharm NFC	X	X		X	X			X	X

ongoing care. It allows external monitoring of the state of adherence to the therapiesto intervene in case of need. Furthermore, the system must be as user-friendly and convenient as possible, to extend the use to persons not expert in information technologies like older adults. The The authors in Ref. [46], have presenting the idea of inserting an NFC in the drug box. A preliminary version of the app was presented in Ref. [47]. The present work shows the complete system's development, presents an updated state of the art of mHealth and NFC for medication adherence, a complete description of the interaction between user, drugs, and assistants and new experimental results.

3. Proposed approach

From the analysis of the state of the art, as well as the opportunities offered by technology, we defined the critical guidelines that the system we propose must follow:

- *Decentralization of assistance functions*: providing the user with the means and systems to carry out autonomously and self-sufficiently his life at home environment.
- *mHealth*: Maintaining contact with the assistance staff through mobile communication devices guarantees the patient autonomy and awareness of being followed, giving him greater security. Through dedicated web services, the assistance staff can carry out active monitoring and direct intervention in managing the patient's therapeutic regime.
- *Centralization of information*: the implementation of a web service allows creating centralized information of the patient's clinical situation, anytime and anywhere. This can avoid harmful situations due to its fragmentation, as episodes of adverse drug reactions due to intolerances or allergies or negative interactions between multiple therapies carried out simultaneously.
- *Simplicity of use*: the simplicity of use must be a fundamental point of its development. This translates into the care of both the graphic interface and the flow of use of the application. However, this simplification must not be achieved by hiding the information from the user but organizing it in such a way as to present it only when necessary.
- *Relevance of NFC technology*: the immediacy in NFC technology's use of NFC technology is one of the main factors that can help realize the simplicity of use desired in the previous point. As already pointed out, the ability to automate device operations based on the content read allows creating new ways to interact with the application. The NFC technology, thus, should be a constituent part of the interaction interface.
- *low cost*: the system does not require specific high-cost hardware. The app should be installed on a NFC-enabled smartphone. The NFC tags can simply be placed in the regular pillbox and reused when the box is empty.

Keeping in mind these general guidelines, we created a system called "Pharm NFC" that can provide new functionality without changing the current doctor-pharmacist-patient relationships. No ad hoc device and no interference with the usual medicine methods must be introduced; the only change required is to insert NFC labels on the packages. Considering that the application is dedicated to people with a high number of prescriptions and long-term care, its use must be reduced to a few simple operations; the NFC gives a significant contribution in this sense. Currently, the use of NFC is wide-spreading to trace goods from clothing to food, see Ref. [19] and reference therein, but according to Ref. [48], the Future-proof Pharma Labels Market is experiencing a compound annual growth rate of 16%, driven by the fight against counterfeiting, but also by the increasing adoption of smart technologies and mitigation of non-adherence. So, we can expect drug packages to be equipped with NFC in the near future.

To reduce complex patient involvement, the only operation required to the patient is to record the successful intake. The phase of inserting data about prescriptions, which in the other apps often constitutes the last stumbling block in the simplification process, must therefore be entrusted to who assists the patient. Furthermore, the monitoring activity by the assistants will have to be as least invasive as possible.

The structure of the assistance system implemented is represented in Fig. 2. The system consists of:

- An Android app, called "user client", intended for the person who needs assistance; it provides the reminder functions of drug intakes, the safe identification of drugs by reading the NFC tags affixed on the packages and finally the recording and communication to a central server of the events of successful or missed intake.
- A second Android application, called "assistant client", intended for assistance staff (doctors, family members, …), through which it is possible to remotely manage the patient's medical prescriptions, interacting with the related user clients, and at the same time supervising the continuation of the therapy.
- A central server, the primary depository of information, makes it available and thus guarantees the assistance functions performed by the Android applications.
- An administration interface, created on a web platform, through which the user accounts of the system can be managed.

Each assistant can follow multiple users through its application, and to each user can be associated multiple assistants: a register keeps track of the actions performed by each of them to be able to go back to the author.Besides, assistants can take on different roles distinguished by the degree of operation: a role dedicated to medical personnel and a role designed for the patient's family, which allows to follow the correct continuation of therapy without being able to modify it.

4. User interface and android applications

4.1. User client

The user client's basic operation is the following: at the scheduled time for taking a drug, the application alerts the patient by means of a sound signal and updates the information on the screen (reminder function). The patient approaches the smartphone to the drug box and the application checks the correspondence of the medicine (identification function) by reading the NFC tag. The app registers the successful assumption (registration function), which must be carried out within a defined time interval. The happened or the missed assumption is communicated to the central server and made available to the assistance staff, who can verify it through their application. It is also possible to send text messages automatically from the patient's smartphone to the assistant smartphone in case of failure to take a drug.

To highlight the simplicity of use of the system, Fig. 3 shows the typical flow of use of the user client for the registration of an assumption at the arrival of the prescribed time.

The steps requiring user intervention are highlighted in red in Fig. 3, while the others correspond to automated operations. The sequence of images in Fig. 4 shows the application running in the case corresponding to the steps in the diagram of Fig. 3:

a. At the time indicated in the prescription the alarm is issued. The application warns the user through a main screen update.
b. The user scans the NFC tag corresponding to the indicated drug.
c. The registration screen is automatically opened. The user presses the button to record the successful recruitment
d. A message confirms successful registration.

The user can take the drug before; otherwise, the alarm is issued; it is possible to take it later when the alarm stopped, in this case step (a) is skipped.

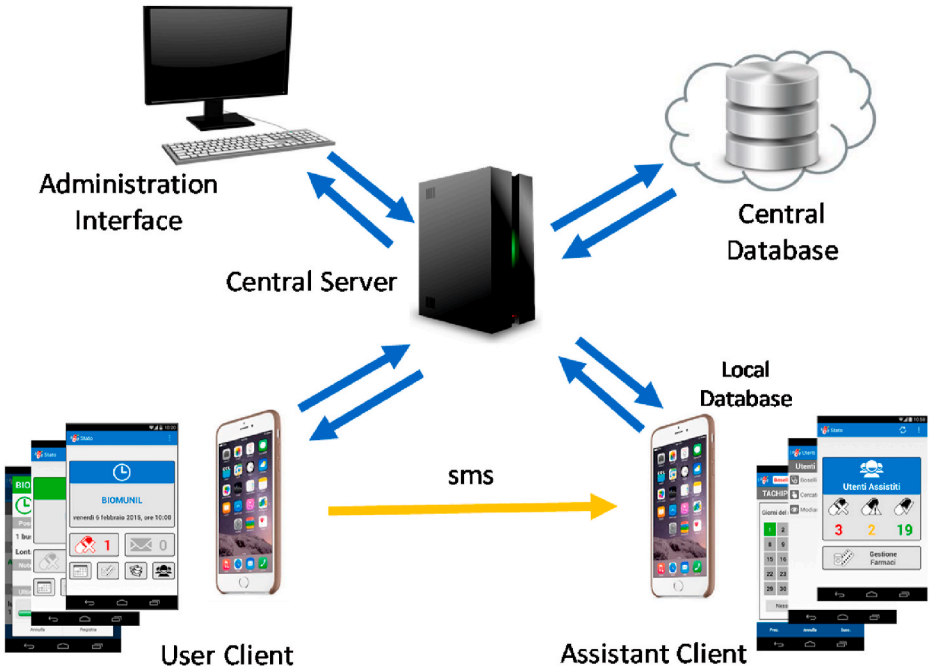


Fig. 2. Architecture of the assistance system.

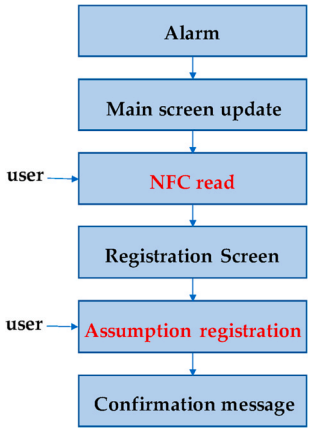


Fig. 3. Flowchart of the user client.

The key points are steps b and c. The action (b) of approaching the smartphone to the tag placed where the drug is maintained (the original drug box or drug dispenser filled by the user daily or weekly) implies that the user has the pills in his hand. The smartphone identifies and shows to the user that the drug and the time of assumption are correct. This identification is a key point of the proposed system. The action (c) of pressing the button for few seconds implies intaking the drug.

A simple reminder does not guarantee these aspects. Sometimes the user does not hear the alarm or is busy when the alarm is issued, and he postpones the intake. Later, if the user doubts having or not taken the drug, he can approach the smartphone, and the smartphone shows that he has already taken the drug and when or that he is late.

Furthermore, even if he is in vacation far from the user, a familiar can verify in real time the hour of drug intake or the missing intake.

It is not possible to modify the drugs or the prescriptions inserted: these operations are carried out remotely by the assistants, who modify, through their client, the data on the central server. The user client will periodically synchronize these changes with its local database. This mechanism, based on data stored locally and synchronized with remote ones, ensures the app's operation even in case of temporary impossibility of communication with the central server.

The user can also monitor its previous missed assumptions, visualize the list of its prescriptions and scheduled assumptions, and visualize messages from the caregivers.

The graphic interface has been chosen with the aim of simplicity of use. The main application screen is shown in Fig. 5: in addition to links to reach the other parts (icons below, starting from the left: calendar, medication list, message archive, list of assistants), here are highlighted the priority information to be presented to the user:

- The scheduled time for the following assumption (Fig. 5a) or the time interval's expiration if the assumption time interval is already in progress (Fig. 5b).
- The counter in the middle on the left indicates the number of missed assumptions that the user has not yet seen; pressing the icon gives detailed information on the missed therapeutic appointment.
- The center-right counter indicates the number of unread messages. The messages are generated in case of changes to drugs or prescriptions, occurred after synchronization with the central server.

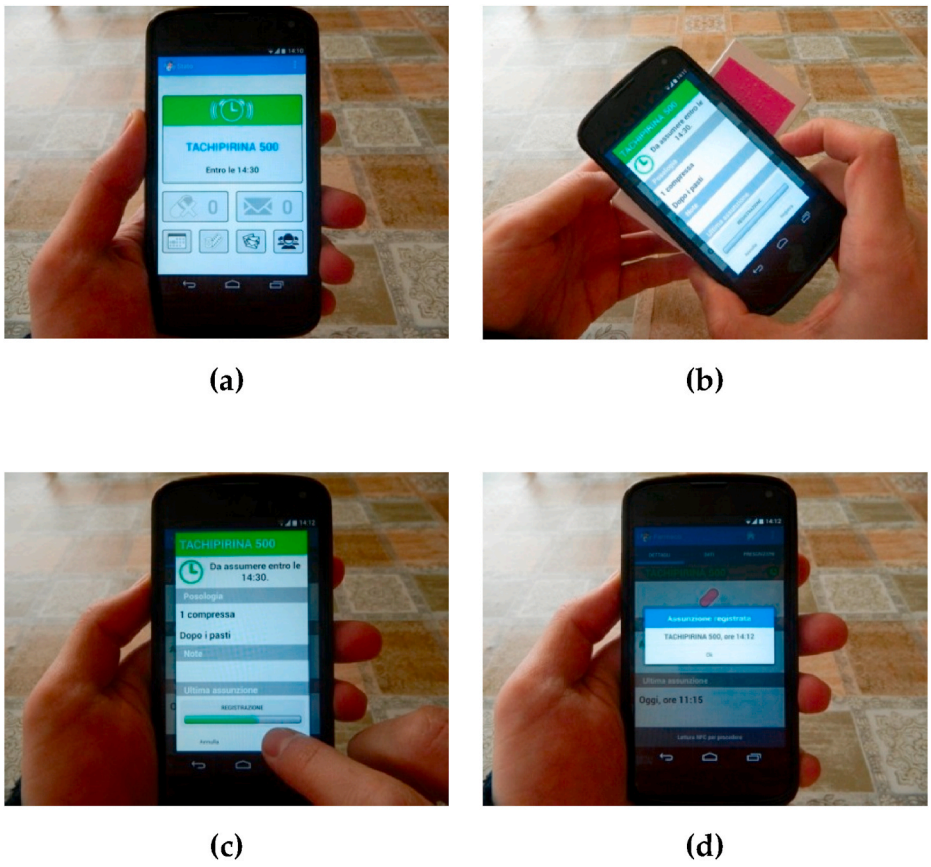


Fig. 4. Typical use of the user client: (a) assumption notification and time window of assumption, (b) NFC read and automatic opening of registration window, (c) registration of drug assumption, (d) confirmation message.

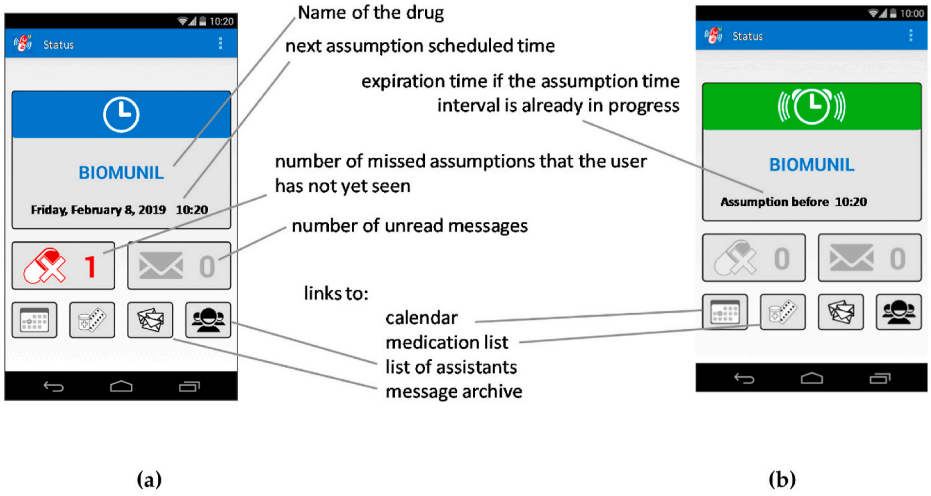


Fig. 5. Two examples of the screenshots of the user client.

The NFC technology has been used to simplify navigation within the application. The only way to access the screen that provides the recording function of the successful taking (Fig. 6) is by reading the NFC tag associated with the relative drug. This mechanism ensures the simultaneous verification of the drug's identity and it allows the user to navigate immediately within the application, simplifying its use. By accessing this screen the user is informed through a differentiated graphic if the intake of this drug is on time (Fig. 6a), if it is out of time (Fig. 6b) or if there is no prescription associated with the drug (Fig. 6c). According to the case, information, such as the dosage, the last time the drug was taken or when the next intake is expected, chages. In any case it is possible to record the successful intake of the drug through the prolonged pressure of a button until a progress bar (in the bottom) is filled to prevent this operation from happening accidentally.

The main screen and the navigation through NFC are designed to simplify the use of the application. Visiting the remaining parts, the user can acquire a complete knowledge of the information concerning their therapy. For example, Fig. 7 shows some screens relating to: (a) the list of drugs, (b) the monthly calendar of the assumption taken or to be taken in the future, and (c) the daily calendar of the assumptions.

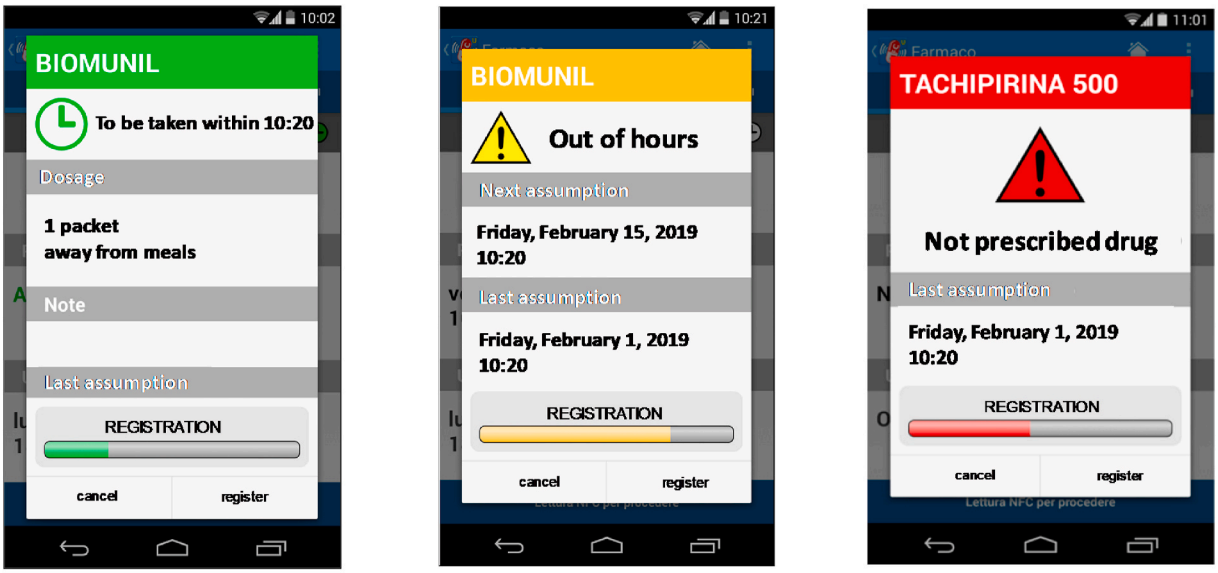


Fig. 6. Window of drug assumption (a) on time, (b) out of time, (c) without prescription.

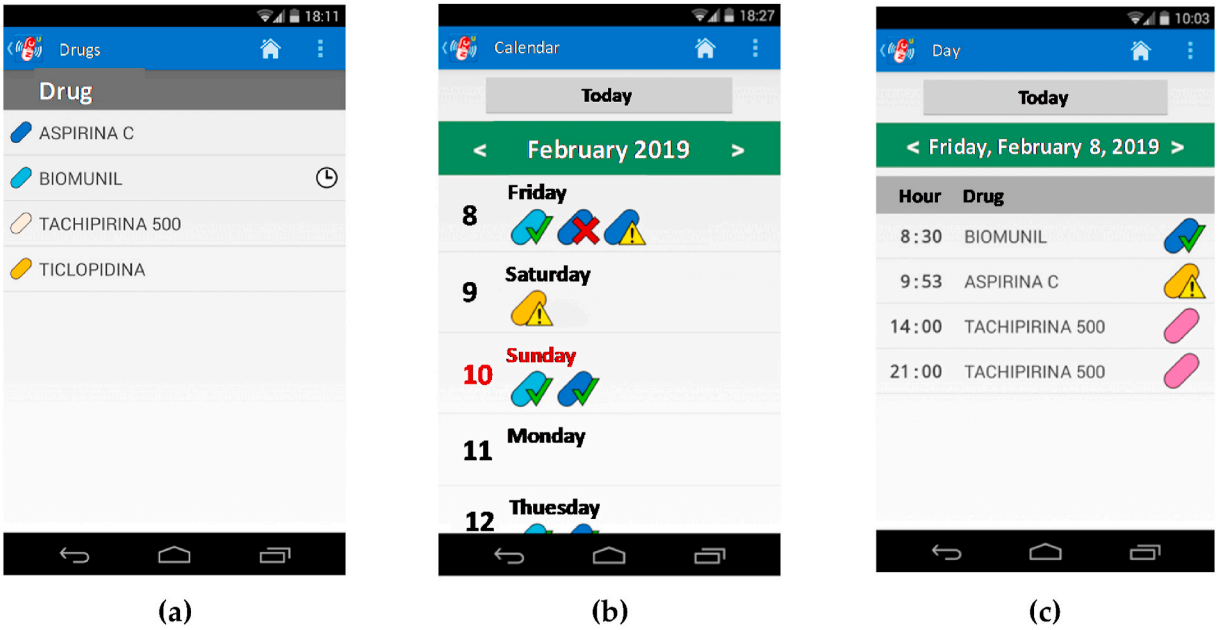


Fig. 7. Some screens of the user client (a) the list of drugs, (b) the monthly calendar of the assumptions and (c) the daily calendar of assumptions.

Each drug is represented by a different colored icon, as shown in Fig. 7a. The appointments of the assumptions, (past or planned) are indicated. It is shown on the calendar (cf. Fig. 7b and c) by the icon of the related drug, with a symbol that specifies the state, following the legend shown in Fig. 8.

In this case, the philosophy is to use a graphical interface providing in easly and immediately the main information. More detailed information can be accessed selecting the specific drug, such as the type of medicine, the active ingredient, the pharmaceutical firm, the manufacturing company and the associated requirements. Similarly, the assumption's details, such as the regular dosage, are shown by selecting an appointment from the calendar.

4.2. *Assistant client*

Through this client, the assistants can supervise the continuation of assisted patient therapies. The graphical interface is designed to present general information first and then go down through the navigation more and more in detail.

Fig. 9a shows the main application screen: here, starting from the left, the number of missed, out of time and correct assumptions for all the followed users is reported; assumptions occurred since these data were checked. The same values are presented in detail for each of them, pressing the user list (Fig. 9b). The roles of the assistants are distinguished. According to the degree of operation granted, an assistant can assume for each of the followed users a different role, indicated by the icon close to the name, (cf. Fig. 9). This is according to the legend reported in the comments on Fig. 9b.

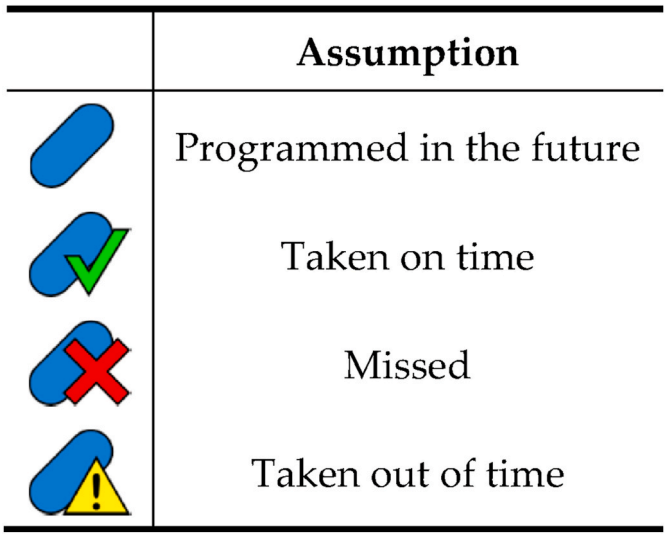


Fig. 8. Symbols that represent the state of the assumption.

The administrator, only one for each user and with greater authority (ideally the doctor), and the operators, optional and in an indefinite number, constitute the operational roles. The observers, also optional and in an indefinite number, are instead characterized by the total absence of operations, keeping only the supervision function of the state of the therapy. In this way family members can use the system to control and help the patient with their smartphone without interfering with the prescriptions' data, with the possibility of receiving text messages in case of missed medications of particular relevance.

As shown in Fig. 9b, detailed information is shown by selecting the assisted user's name: the associated drugs, the prescriptions and the calendar of the assumptions, both past and planned.

The assistant client also allows (except for observers) to remotely manage user therapy, modifying associated drugs and related prescriptions. The dosage of the prescriptions is inserted, indicating the dose, the schedules and the timing of the scheduled days, which can be daily, weekly, or monthly. As an example, Fig. 10 shows three screens relating to this operation.

Unlike the user client, the assistant client does not have an internal database but acts as an interface for the server's data. The changes made to these data will then be transferred to the user clients using periodic synchronization.

Finally, since the boxes of the drugs are not natively provided with NFC tags, up to now, through this application it is possible to write the tags so that they are associated with the relative drug. The NFC tag can be placed in the drug box or in a card that can be reused and placed inside the drug box as shown in Fig. 11. The tag writing and placement in the card are made once for all by the assistant, while the user moves the card to the new box when the previous box is empty.

4.3. Administration interface

The administration interface consists of a series of web pages through which it is possible to create and manage system users' accounts, defining their roles and associating users with their assistants. This interface is dedicated to a sort of "general administration" of the system, which is entrusted with the most properly bureaucratic tasks.

5. System analysis and discussion

The system has been tested and verified by the developers. Furthermore, it has been applied in few real situations with some middle aged users. The system's preliminary test has been carried out for two months with four users of different ages. This study recruited users who must take medications at home, from 25 years to 80 years old, with different basic knowledge of smartphones' use. The caregivers monitoring the users are familiar not living with the users.

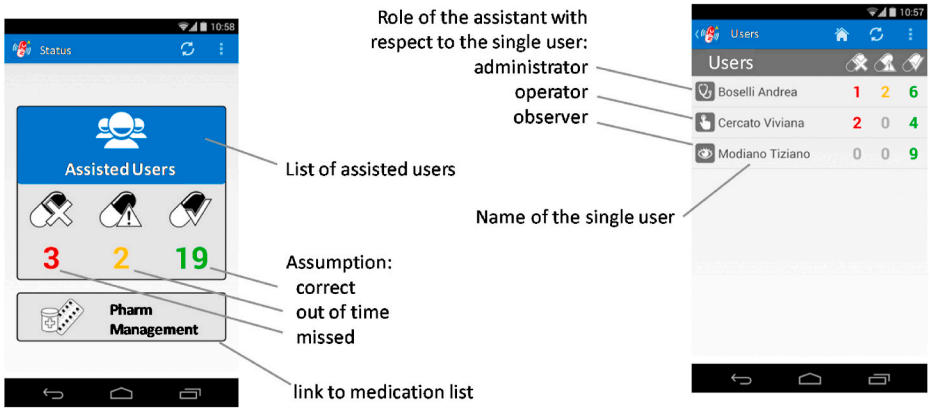
The assistant convinced the user to use the app. The users are conscious of the problem of respecting medication adherence. Sometimes they forgot to take the medication, sometimes they do not respect the correct timing, sometimes they are not sure to have taken the medication. They usually follow some practical methodology to trace the drug intake, for example user2 fills a box every week with the drugs, user1 writes on the drug box the date of intake and counts the number of pills in the drug box.

Table 2 reports the list of prescriptions for each user:

The NFC tag with the same image of the drug box has been placed by the assistant inside the drug box and reused in a new box when the previous box is empty.

The app has been installed on the smartphone of the user with the NFC reader. In the case of User1 (80 years old) it was necessary to change the smartphone since the previous one was an old smartphone without NFC. In the first phase, the app developers explained to the users and the caregivers the use of the app and programmed the NFC tags. The familiar, caregivers or family doctor can monitor the user's drug assumption through the assistant app accessing periodically the data on the database that is updated in real time.

The caregivers almost every day went to meet the users. At the end of the test, the app developers made a thirty minutes face to face interview to users and caregivers to collect their comments.



(a) (b)

Fig. 9. Assistant Client: (a) main screen, (b) list of assisted users.

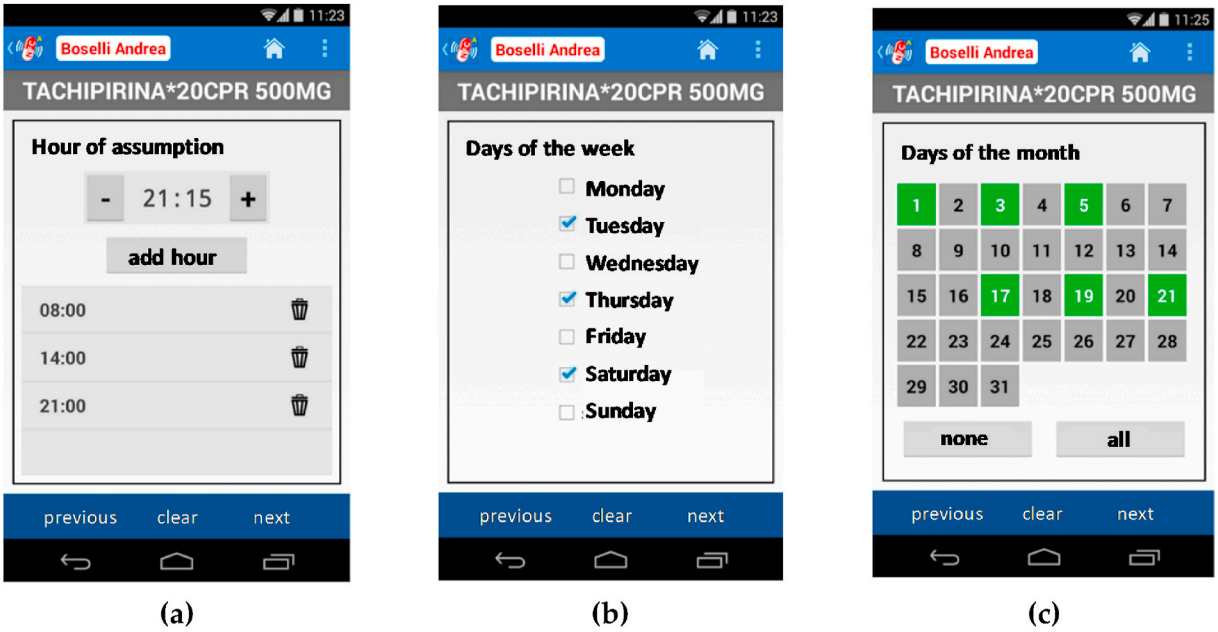


Fig. 10. Example of the screen for the insertion of the time schedule of a new prescription.

Fig. 11. NFC tag in the drug box.

Table 2
Preliminary test users.

User	Age	M/F	N. of drugs	Drug	Assumption time
User 1	80	F	5	A	morning before breakfast
				B	morning and evening
				C	after lunch
				D	evening
				E	after dinner
User2	58	M	3	A	morning before breakfast
				B	morning before breakfast
				C	morning before breakfast
User3	56	M	1	A	morning
User4	25	M	1	A	morning

First comments could be drawn from the application of the system, far from a statistical analysis of the results.

The motivation to use the app and smartphone should be firmly connected to the motivation of the older adults to stay in contact with the family (sons, daughters or grandchildren) or the assistant. Otherwise, the effort, even limited, to learn the system could be too high. Once overtaken this obstacle, in few days, the person gets used to the app, which is seen as a helpful reminder of drug intake.

From the point of view of the assistant, typically familiar with the use of smartphone and app, the system was seen as a helpful way to monitor the drug assumption of the elderly mother of father who still lives alone in an autonomous way, but needs some kind of support: sometimes forget the drug assumption or sometimes does not remember if he assumed or not the drug. The system is advantageous when the assistant must be away for some days and controls from the remote database the situation.

The trial test results indicate that the proposed system with NFC and mobile phones allows adherence monitoring only touching the medication blister with the mobile phone. This easy-to-use has been well accepted even by elderly users.

6. Conclusions and future works

The entire system has been developed to implement the following services: drug identification, taking reminders, information centralization and remote monitoring. The system does not require any disruption to the subjects' habits and is immediately useable, although exclusively through NFC technology.

The target that the monitoring activity is the least invasive and transparent to the user has been realized through the automatic sharing of data and not being present any form of direct interaction between the assistant and user. Perhaps in this way the application is too aseptic and without human contact, but it must be underlined that the system must be simply complemented and support the doctor-patient relationship.

The graphical interface and the flow of use have been developed following principles of clarity and simplicity, made up of older adults, often not accustomed to the world of information and technology.

However, a first testing phase has already confirmed that at least the potential of its features highlighting the importance and effectiveness in particular of two of them:

- The centralization of information: in this application, the creation of a central repository of information has made it possible to share among the various subjects, allowing to avoid that fragmentation of knowledge of the therapeutic situation of the patient, potentially harmful, and at the same time to monitor the effective compliance of the therapies. Starting from this point, the implementation of new functionalities becomes almost automatic. Integrating the stored information with everything that may be of interest from the medical point of view would allow to obtain an accurate patient history (pre-existing pathologies, allergies and intolerances to drugs) useful in emergencies.
- The use of NFC technology: the increasingly widespread use of mobile devices compatible with this technology and the simplicity and

immediacy were the reasons that led to focus on NFC as a fundamental mechanism in the use of the application. In addition to the identification function, the possibility of programming the software's behavior based on the context and the content read in the tag allows an even more immediate use and opens up new avenues of interaction.

The trial test consists of a minimal number of users. The test has no statistical relevance. Despite this, it has been helpful in the improvement of the developed system. Future work will be devoted to the application of the system to a more significant number of test users.

A possible improvement of the developed app could consist in voice instructions or voice commands (like Google Home or Amazon Alexa) to make the system accessible to patients with disability (e.g., vision problems). The user acceptability of vocal interface is much more critical with respect to actual the proposed system, and it must be accurately investigated.

Author contributions

Conceptualization, Simone Orcioni, Roberto Pellegrini, Ralf Seepold, Maksym Gaiduk, Natividad Martinez Madrid and Massimo Conti; Investigation, Roberto Pellegrini and Massimo Conti; Methodology, Massimo Conti; Software, Roberto Pellegrini; Supervision, Massimo Conti; Validation, Massimo Conti; Visualization, Roberto Pellegrini, Simone Orcioni and Massimo Conti; Writing – original draft, Simone Orcioni, Roberto Pellegrini and Massimo Conti; Writing – review & editing, Simone Orcioni, Ralf Seepold, Maksym Gaiduk, Natividad Martinez Madrid and Massimo Conti.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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