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Perspective on mHealth Concepts to Ensure Users' Empowerment–From Adverse Event Tracking for COVID-19 Vaccinations to Oncological Treatment

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ABSTRACT Mobile applications have increasingly entered the healthcare sector. Besides being daily companions, so-called mHealth applications have the potential to enable individuals to collect data, document issues, and share them with healthcare professionals to better adjust medical treatment, side effects, or quality of life. While patient empowerment should be a paramount goal, the setup of these applications in a reliable and communication-effective way is under discussion. In particular, including mHealth applications in the clinical practice routine is crucial to boost their development. Security concerns are of utmost importance as such applications deal with personal data. Considering the sensitive nature of many of the involved data, a trustworthy transfer protocol to the respective health care providers is essential to convince potential users. On the same grounds, healthcare providers, which represent another major stakeholder, might be skeptical of utilizing mHealth applications. This issue is often not prioritized by app developers, and there is a multitude of apps lacking clear and transparent data transfer concepts with a focus on both security and usability. In the following, we present and discuss two different approaches for managing and reporting sensitive clinical information and their secure inter-sectoral transfer. Both use cases are currently implemented into clinical practice, and their applicability is under constant evaluation. Besides, to empower inter-sectoral communication, both approaches have been developed in close collaboration with healthcare providers to maximize both communication and effectiveness of the mHealth applications. Based on our work, we conclude that while mHealth applications can be important in many aspects of improving health care, there are often significant limitations of mHealth-based communication, which can hamper its integration in clinical settings. To overcome these limitations, we show how to apply and re-elaborate on existing security and communication strategies. Finally, we highlight how these approaches can strengthen both patient and healthcare professionals' empowerment.

INDEX TERMS Data communication, device-to-device communication, mobile applications, patient monitoring, public healthcare.

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I. INTRODUCTION

Over the last two decades, mobile devices, like smartphones or tablets, have become more and more a critical part of our everyday lives. A large-scale study with approximately 2,500 participants found that the average subject uses mobile devices for about 160 minutes a day [1]. Such devices, in turn, can run various types of applications, ranging from simple to-do applications over messenger services up to digital health applications [2]–[4]. The market for mobile health (*mHealth*) applications is increasing, and more companies are entering the mHealth sector.

Nowadays, such mHealth applications ideally offer helpful information regarding diseases and available treatments for patients, provide fitness workouts or collect data from patients in various settings [5]–[7]. This empowers patients by providing more self-awareness and control of one's health status [8]–[11]. This concept has been utilized in different mHealth applications, supporting the digitalization of the relationship between patients and healthcare professionals [12]. In this direction, direct digital data collection is simplified, and collected data can also be valuable for clinical decision-making processes and empowerment through explainability [13]–[15]. Exemplarily, the mHealth application *Cangaru* [4] aims to support pregnant women by providing a calendar for clinical appointments, tracking symptoms, and a social network platform to share information and networking among users. Similarly, approaches like *Manage my Pain* [16], *imitoCam* [17], or *Track Your Stress* [18] have been introduced to collect patient data continuously. Moreover, mHealth applications have been applied to support medical ward rounds [2] or document patient treatment processes [19]. While these approaches separately involve patients and healthcare professionals, there is still room for improvement in strengthening patient-doctor and developers-doctor communication [20]. In accordance, healthcare providers frequently reported feeling unprepared in judging data coming from different applications, not knowing which one could be more reliable [21]. Also, to ensure clinician empowerment, healthcare providers should receive their application interfaces and secure access to their patient's data. Although mHealth applications supporting medical care are commonly acknowledged, there are still some open issues concerning their implementation. Healthcare providers recognize the relevance of this source of clinical data [20], [21]. However, concerns are frequently raised about these applications' clarity, transparency, and privacy issues [21]. The lack of safe and effective communication between the user and health care providers is frequently hampering these applications in the health care routine [22]. An adequate balance of usability and data security is of significant impact on the success of an app in this field. Low-security hurdles, such as login-free systems often coincide with easier usability. Vice versa, secure systems with, for instance, two-factor authentication may be secure but do not correlate with the sensitivity of the stored data [22]. In this context, it is of utmost importance to select an appropriate approach for each given scenario. On these grounds, we intend to discuss a comprehensive workflow on different approaches and give a perspective on possible strategies to integrate mHealth applications into clinical care routines. Our workflow addresses the main requirements of both healthcare professionals and patients (Table 1) to ensure effective and safe inter-sectorial communication [11], [23]–[29]. To address these issues and address concerns from patients and healthcare professionals, one must improve the digital patient-doctor communication and relationship. This can include adapting established clinical workflows to properly integrate mobile devices or enrolling sophisticated mHealth applications to support specific application scenarios.

In this perspective, we aim at giving an overview of communication protocols in mHealth applications featuring patient empowerment. Notably, we want to point out that there is a vast range of different communication protocols. In contrast, the rapid increase of mHealth applications leads to a growing number of insecure or overcomplicated approaches. To this end, we presented two approaches located on different ends on the range of communication protocols but, each focusing on empowerment and security. Our work can be summarized as follows:

- We discuss different approaches in user-healthcare professionals communication where the role of patient and doctor empowerment is crucial.
- We propose an online data transfer model currently built into the `CoCoV` mHealth application to collect adverse events reports after vaccination.

TABLE 1. Comparison of mHealth application requirements for patients and healthcare professionals.

Application requirements

Patients	**Healthcare professionals**
- Customization of personal information (e.g. age, gender, risk factors)	- Access patient data upon request
- Documentation of treatment information (e.g. dates of vaccination or medication)	- Attach adverse events to medical record
- Documentation of adverse events	
- Data sharing with healthcare professionals in a secure and self-determined manner	- Review adverse events
- Revoke access to private medical data	- Aggregate data for research purposes and statistical analyses
- Delete personal data	
- User-friendly interface is suitable also for older patients	
- Transparency about data collection and security	

- Alternatively, we demonstrate communication via a direct visual data transfer implemented in the mHealth application NEMO to track and prevent patients' side effects during oncological treatments.

II. METHODS

A. TECHNICAL DETAILS

Both mHealth applications were implemented using state-of-the-art web technologies. We used NativeScript for the mobile clients and Electron for the NEMO desktop healthcare professional (HCP) client. The CoCoV server application, in turn, is developed using TypeScript. User interfaces were designed with the latest HTML5 and CSS versions.

B. EVALUATION DIMENSIONS

Considering these prior illustrated applications and implementing the two mHealth applications, we documented various dimensions grouped into categories, allowing us to compare both approaches. For example, *Data* groups dimensions concerning the actual data exchanged between patient and healthcare professional. This category deals with data encoding and decoding, or whether submitted data can be changed again after submitting it (i.e., correct an answer). The *Structure* group defines dimensions, such as extensibility or interoperability of the data structure. The *Communication* category focuses on the interaction between the involved parties, like the transport protocol it uses (i.e., WiFi), if the communication is synchronous or asynchronous or the number of participants involved in communication. *Security* deals with dimensions related to authentication or authorization within the mHealth application. Finally, *Client* groups dimensions are related to integrating 3rd party clients, like existing hospital information systems. Note that some dimensions directly follow from others. For example, if data is encoded in a proprietary format, a specifically tailored HCP client application is required to review or visualize collected data. Likewise, other dimensions may mutually exclude each other. Data structures cannot be extensible but still fully implement interoperability standards, like HL7 FHIR (Health Level 7, Fast Healthcare Interoperability Resources, https://www.hl7.org/fhir/) or OpenEHR (Open Electronic Health Record, https://www.openehr.org/).

III. RESULTS

Designing and developing mobile applications that work with personal medical data requires security aspects and stakeholders' empowerment. In this context, current mHealth applications (e.g. fitness trackers, calendars) consider more self-record of data while still lacking secure communication transfer required to implement clinical assets. On these grounds, we developed two transfer approaches that ensure secure data transfer between users and healthcare providers.

In the following, we present the fundamental concepts of these two approaches. The significant difference between these approaches is the communication protocol. One approach uses flexible communication via the internet. The other approach aims to maximize security via strict offline and face-to-face data transfer.

A. ONLINE DATA TRANSFER

The *online data transfer* approach aims at anonymously collecting sensible data. To increase the transfer data's validity, access is restricted to registered devices and predefined end-points without requiring user accounts or login credentials with passwords, tickets, etc. The communication between client and server is divided into two significant steps: the initialization and data transmission (see Figure 1). A secret keyword (bearer authentication) is sent from client to server for client registration during initialization. Before submission to the server, the predefined keyword is securely encrypted via a hash function (using, for instance, bcrypt [30]). This keyword is known by both the server and client applications. For registration, the encrypted keyword is then sent from the mobile device to the corresponding server via secure HTTPS. The server validates the received hash of the keyword. If this validation process is successful, the client will be registered to the server; otherwise, the request is rejected. The secure hash function is designed to map the keyword to a large variety of different hashes. This hash allows the server to identify, and for instance, ban devices sending the same hash frequently [31]. Consequently, this avoids malicious data via sniffed hashes due to man-in-the-middle attacks. For valid requests, the server creates a unique random ID and sends it to the pending client. This ID is saved by the client and used for any further communication. For this communication, verification of IDs acts on the one hand as access control. On the other hand, this anonymously allows record-linkage of data. By linking sequential data to one single user (in an anonymous fashion), one can analyze the progression of, e.g., the tracked disease. Consequently, transferred information contains 1) the assigned ID and 2) the recorded data. Similar to the identification of malicious hashes, unusually frequent submissions with the same ID enable fraud detection. As a further data protection layer, the communication can only be done via the secured transfer protocol HTTPS.

B. FACE-TO-FACE DATA TRANSFER

Alternatively to the previously described online data transfer approach (see Figure 1), we developed another communication protocol that strictly communicates offline. There is decreasing trust of users in the technical validity of mHealth applications, data transfer, and the control over these interfaces [32]. Moreover, clinical IT infrastructure is sensible and, thus, presumed to be highly secure. Consequently, wireless and even cable-based connections of unknown devices to computers in the hospital network are mostly blocked as those interfaces are prone to be attacked [33], [34]. Face-to-face authentication and authorization processes in person are the significant aspects of this protocol. This protocol is based on an adjacent client-host system without cable or standard

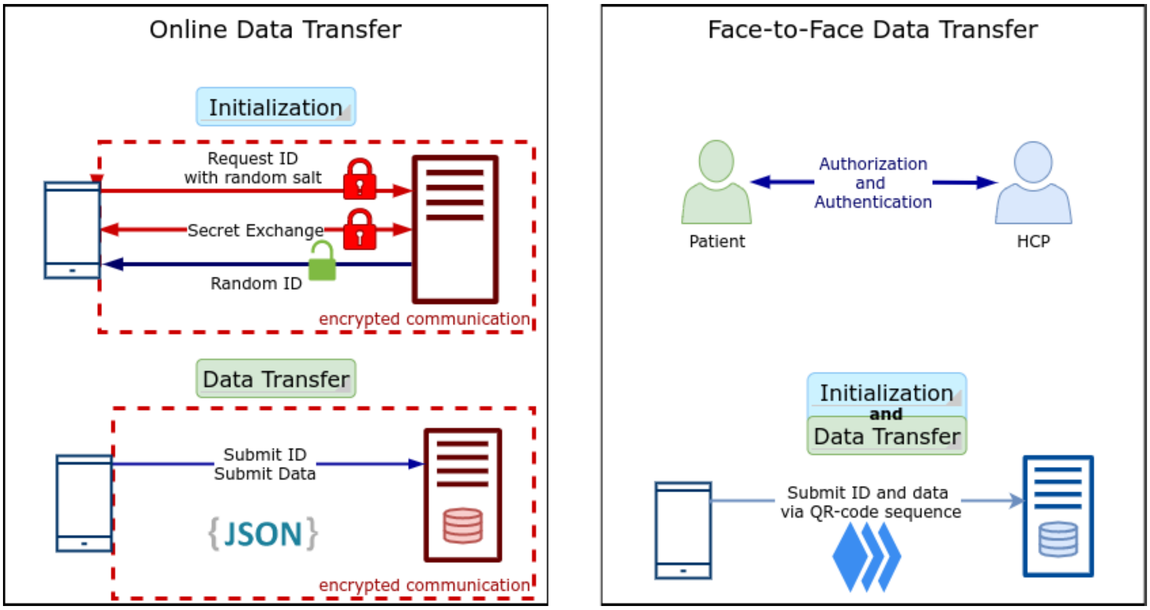


FIGURE 1. Data transfer approaches. For Online Data Transfer (left), initialization is necessary before establishing secure data transfer. Authorization and authentication are done by secure and encrypted communication. A secret exchange can be validated and results in a randomly generated valid ID using an encrypted cryptographic salt. This ID can be used in further data transfer communication to assign data to a pseudonym. Authorization and authentication in face-to-face data communication (right) are done between patients and healthcare professionals (HCP). Initialization and data submission are made by a local system and a sequence of QR-codes to transfer data. Here, the HCP has to assign data of a generated ID to the corresponding person.

wireless protocols. The mobile client application creates and stores data. To this end, information is stored locally on the smartphone instead of being transmitted via an internet or cable connection. For data transmission, QR-Code sequences are created and displayed. The host application captures these QR-Codes via a camera interface. Thereby, the user has complete control over who will receive the data. For encoding, the amount of data is reduced as much as possible and then transferred to a QR-Code representation. If the information exceeds the single QR-Code storage capacity, sequences of QR-Codes are used. Altogether, the face-to-face data transfer protocol comprises a short header in the QR-Code, which contains a version number to ensure consistent decoding of the data and a user-specific ID. The body contains compressed encodings of the specific data. Specific characters separate different entries (e.g. ";"), while the end of the data is characterized by another (e.g. " "). Ensuring patient empowerment, the transmission must be initiated on the mobile client by creating a QR-code. Then, the latter is transferred to the corresponding desktop application. Placing the smartphone display in front of the desktop camera starts the transfer. The sequence of QR-Codes is repeatedly displayed until all QR-Codes are captured. Depending on the header data, the host application identifies the number of required scans. The incoming data is checked for uniqueness and reports back to the users as soon as each QR-Code is scanned successfully to prevent data loss. The data transfer's capacity can be specified by the complexity of the QR-Code, error correction, and display time of one code within the sequence. The upper limit using QR-Codes (maximum capacity is 23,648 bits [35]) and, for instance, a camera with 60 frames per second and smartphone with equal frame rate, is $23,648$ bits $\times 60 = 1.418.880$ (approximately 177 *kByte*) per second. The data is then automatically assigned to the user via the corresponding ID on the host application.

C. USE CASE A: CoCoV

The COVID-19 pandemic showed the need to support the healthcare sector in providing digital solutions. A central topic is an evaluation of the safety and efficacy of the new vaccines. Especially the assessment of potential adverse events is currently of enormous interest. In this context, most of the symptoms are mild and would not lead the vaccinated subjects to contact their doctors. Nevertheless, getting a complete overview of the symptomatic landscape would critically help determine the benefit of the COVID-19 vaccination effort. This could help fine-tune adverse events and the efficacy of the available vaccines in different subgroups (e.g. elderly, young, chronic diseases affected) and different vaccines. Thus, a digital interactive application where users can record their symptoms, including a safe and anonymous transfer to a central server, is in demand. Also, applying such mHealth techniques in the context of, e.g. vaccination, is beneficial for research and allows to collect a large sample of the population quickly. Following this need, we conceptualized and developed a mHealth application called `CoCoV` (Figure 4).

`CoCoV` helps individuals document adverse events after vaccinations (i.e., COVID-19 vaccination) by providing a diary feature and implementing the online data transfer approach. This will optimize patients' self-management and help them better recall these adverse events in a direct

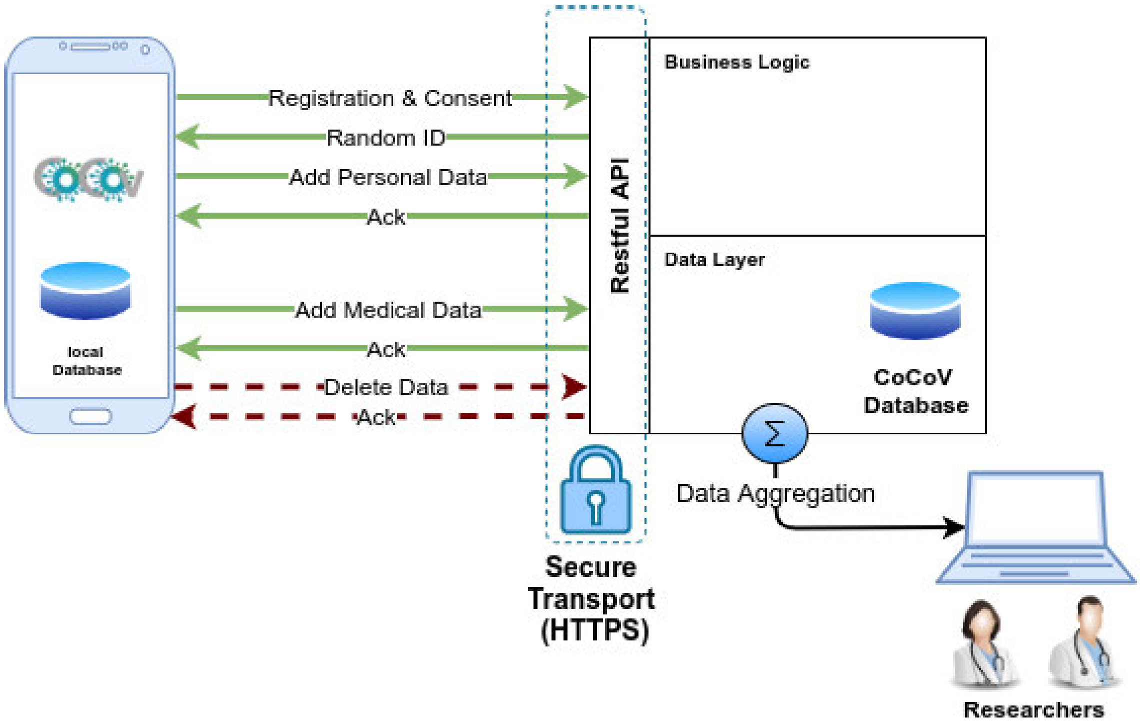


FIGURE 2. **Workflow of the CoCoV mHealth application. Communication between CoCoV and the server backend is encrypted and secured by a secure sockets layer. Communication endpoints are defined by a REST API (Representational State Transfer Application Programming Interface). Acknowledgment packages (Ack) close successful communication. Researchers can use aggregated data.**

meeting with healthcare professionals. To document individual events, an established questionnaire tackling main vaccination symptoms was adapted in close collaboration with involved healthcare professionals and included in the application (Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials) [36]. The vaccinated subjects' answers are stored in the application in a diary to allow for a well-documented overview. The overall goal was to increase semantic interoperability and thus to improve patient-doctor communication.

In addition to the self-documentary features, CoCoV allows individuals to submit meta-information concerning their vaccination (i.e., date, manufacturer) and personal information, like their age or gender and includes a reminder functionality. Whenever adverse events are noticed, individuals can document the information within a daily report and upload data immediately to a server. Obviously, for this communication, CoCoV requires an internet connection. CoCoV follows our described *Online Data Transfer* approach. To respect privacy as well as to increase security, uploaded data is anonymized with a random ID. This ID is generated by the server application and sent back to the client when the individual digitally signs the consent. This ID is then automatically stored within the smartphone client and is sent with any future communication to the server. ID and recorded data are sent via a JSON-object. Via ID-based record linkage, received JSON-objects can be linked to protocol sequential events of individual users. The application flow of this communication protocol is illustrated in Figure 2.

As an extension of this approach, patient-doctor communication can be improved. An API endpoint can be used by ID exchange with the healthcare professional querying to retrieve recorded data.

D. USE CASE B: NEMO

Our second use case addresses the documentation of adverse events during oncological treatments by implementing the *face-to-face data transfer* approach. Precise documentation of adverse events is of utmost importance to assure tolerability and treatment success, particularly when patients do not see their treating physicians daily. In contrast to vaccination, these therapies are prolonged in time and need to be followed up in a more personalized fashion. This allows for the use of a direct data transfer from face-to-face. On the other side, providing a mHealth application for a cancer therapy scenario requires other concepts. The incidence of developing a tumor disease increases with age and is highest from the age of 70 [37]. Here, the application should be designed to address the requirements of older people. This includes adequately adapted user interfaces [27], [38], big fonts, auditory feedback [39], [40], or additional input methods (i.e., voice input) which support their demands [26]. On these grounds, we developed the mHealth application called NEMO (Figure 5).

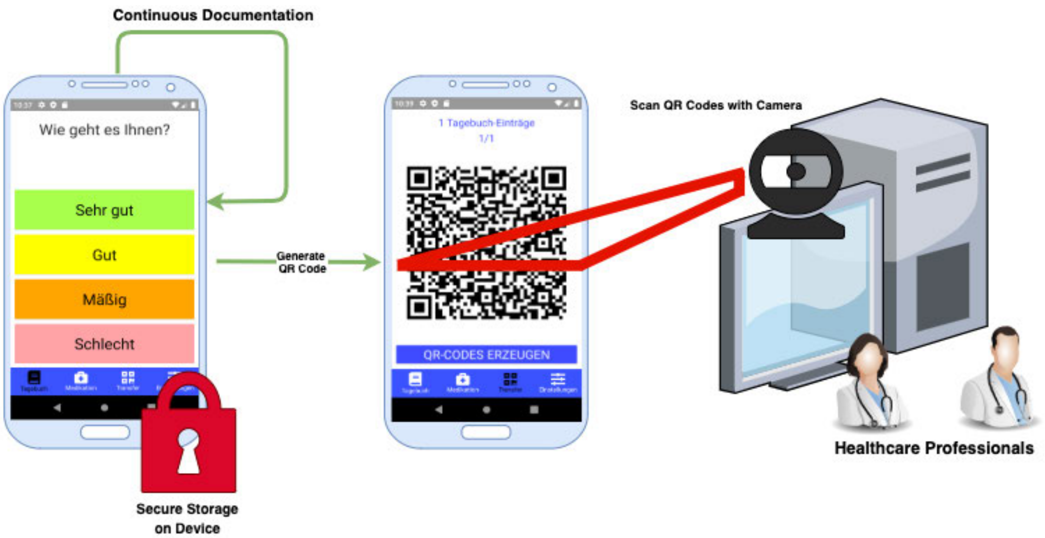


FIGURE 3. **Workflow of the NEMO mHealth application. Data is stored locally on the smartphone. For transmission to the NEMO desktop application, data is encoded in (sequences of) QR-codes. The desktop application then processes this data via a camera-interface. The message protocol comprises a header with version number and patient ID and the body with the data derived from the questionnaire for adverse events.**

NEMO helps cancer patients to track adverse events associated with oncological treatment. Users can track the adverse events of their treatment via a standardized questionnaire. This questionnaire is based on the Common Terminology Criteria for Adverse Events (CTCAE V5.0) by the National Cancer Institute (NCI) [41]. We defined a simplified questionnaire in close cooperation with healthcare professionals to obtain a patient-comprehensible phrasing. The goal was to build a common ground for patients and clinicians by mapping the different answers from the NEMO questionnaire to the clinical applied CTCAE scoring that the patients answer routinely (e.g. daily). The acquired data is only stored locally on the mobile device, and the mHealth application does not communicate with external servers. Instead, the user can transfer the entered data to the assigned physician over the regular appointments. The NEMO communication follows our face-to-face protocol. For transfer, the smartphone's collected data is encoded as a sequence of QR-Codes that are repeatedly displayed on the mobile device. A dedicated protocol encodes a header with the version number for the protocol (to ensure compatibility), the total number of QR-Codes to transmit all data, a user-ID, and the body with daily entries without personal information as comma-separated values. Different entries are separated via a swung dash. The sequence of QR-Codes is scanned until all required information is transmitted. With current settings, the protocols allow for 650 characters per QR-Code. Even if this is not the theoretical maximum, it also provides for smooth detection with low-quality cameras. After successful transmission, the desktop application assigns the received information to the corresponding patient by matching the transmitted ID. This procedure is illustrated in Figure 3.

Such a face-to-face meeting, in turn, also acts as an *authentication* and *authorization* process. On the one hand, the healthcare professional identifies the patient by direct contact. The respective electronic health record may then be accessed. On the other hand, the patient authorizes the healthcare professional to access the mobile device's data by showing the respective QR-Codes.

E. COMPARISON AND HIGHLIGHTS

Given that the presented two approaches may serve as a blueprint to adapt to future new mHealth applications, we summarize critical characteristics (Table 2).

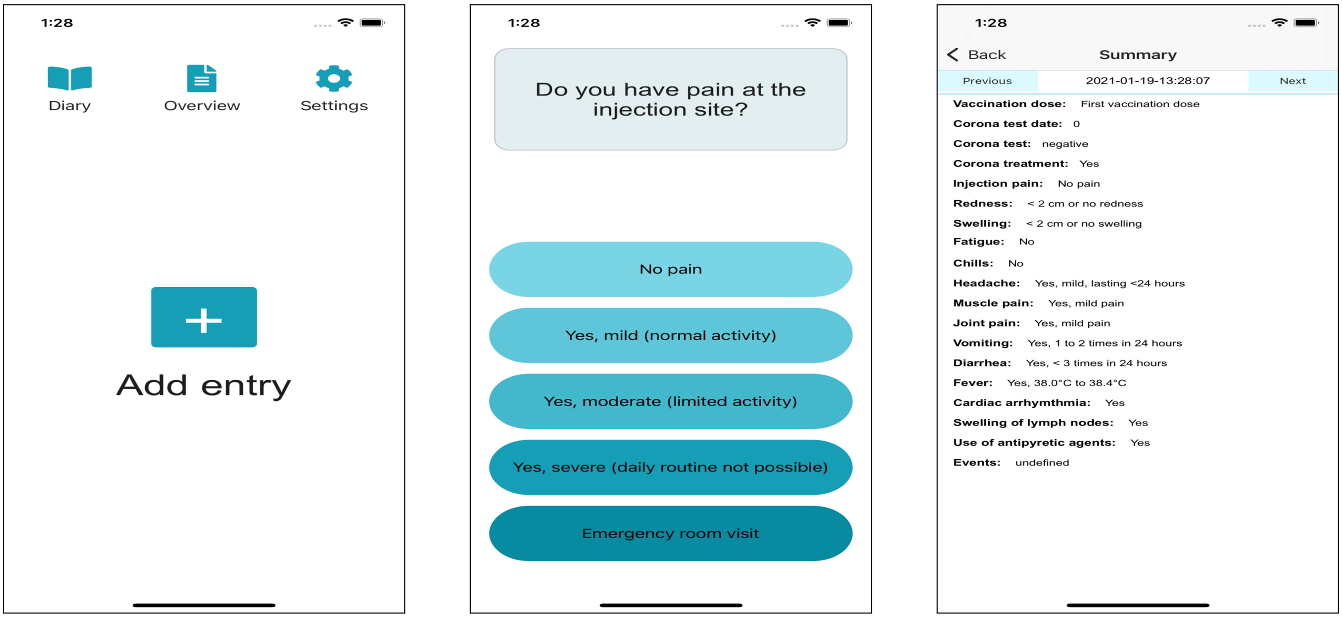
TABLE 2. **Comparing Settings with Different Categories.**

Category	Dimension	Approach A	Approach B
Data	Transmission	◐	○
	Encoding	◐	●
	Size Limit	○	●
	Update after Submission	●	○
Structure	Extendability	●	◐
	Interoperability	◐	◐
	Transformation	●	○
	Flexibility	●	○
Comm.	Synchron	◐	●
	Asynchron	●	○
	Multiple Parties	●	○
Security	Authentication	◐	○
	Authorization	◐	○
	Secure Submission	◐	●
	Patient Empowerment	◐	●
Client	Patient Client	●	●
	HCP Client	◐	●
	HIS Integration	◐	◐

○: Not Important; ◐: Quite Important; ●: Very Important;

a: SETTING A (ONLINE DATA TRANSFER)

The mHealth application can be used for a variety of different scenarios. For example, educational material concerning diseases or treatments may be provided, or self-reported



(a) Homeview of the application. Here, new diary entries can be created, the user-diary, a short summary and the settings can be accessed.

(b) Example question of the questionnaire. On top, the question is displayed. Below are different possible answers according to the scaling of the toxicity grading scale for healthy adult, and adolescent volunteers enrolled in preventive vaccine clinical trials.

(c) Summary of the Data Collection. The summary lists the answers of the questionnaire for one particular entry.

FIGURE 4. Screenshots of the CoCoV mHealth application.

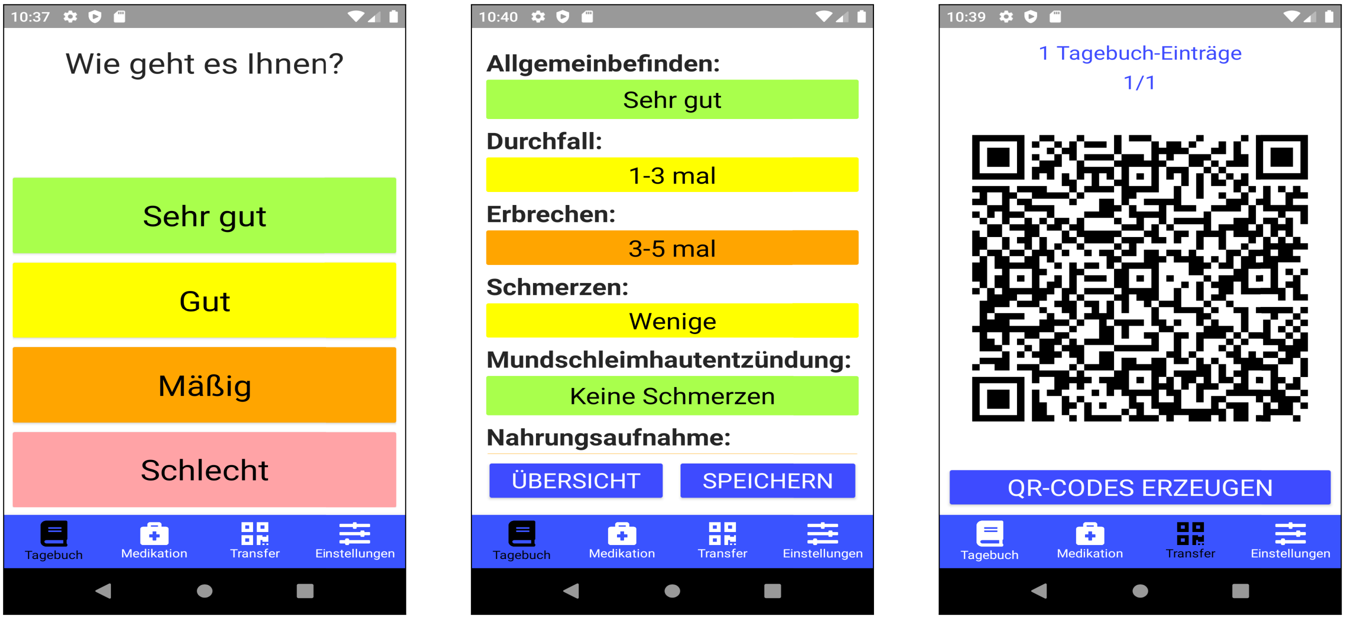
data can be collected. These features, however, require an Internet connection as the content could be updated frequently. Furthermore, an authentication mechanism is needed as sensitive data must be stored on a server to make it available across the platform for different users. Depending on the features, multiple parties might be involved or various protocols used.

b: SETTING B (FACE-TO-FACE DATA TRANSFER)

The mHealth application is mainly used as a diary for the doctor (i.e., patients document their current health status for the clinician). If data is collected, it is stored securely directly on the mobile device and not primarily transferred to a server. The main focus lies in putting the user in total control of their data. This setting can be applied in clinical scenarios where a frequently scheduled consultation with healthcare professionals is recommended. In this context, data is stored most likely in a proprietary format (as it must not be shared with other parties), or an explicit authentication process is omitted for simplicity.

IV. DISCUSSION

Over the last decade, the market for mHealth applications has continuously grown, and various applications have emerged. mHealth applications can have a significant impact aiming to empower patients further. Numerous studies found that individuals are willing to share their medical data with respective healthcare providers to get a more suitable treatment [42], [43]. Here we presented two strategies to ensure fast and secure communication between patients and healthcare providers based on established concepts, thereby providing intra-sectoral empowerment of involved parties. From a general context, digital approaches are an emerging source for fast and secure data collection in clinical care [44], [45]. However, they still have to tackle more barriers than social media communications or banking accounts. mHealth applications for collecting data may be significantly cheaper than traditional approaches (i.e., paper-based questionnaires). In this context, Pavlović and colleagues [14] estimates that approximately 50% of costs related to data collection procedures in clinical scenarios can be reduced when using smart mobile devices instead of paper. Furthermore, the time needed to collect data would decrease [46] while simultaneously increasing the quality and density of data [47]. Finally, data collection procedures using mobile devices are always available as such devices are daily companions [1]. Overall, healthcare professionals [24] and patients [25] demand the use of mHealth applications. A study revealed that a significant amount of reviewed mHealth applications are of poor quality, lack data security concepts, or transparency [23]. In this context, Zhou and colleagues [48] found that downloaded and installed patients do not use mHealth applications because of security concerns, loss of interest, or hidden costs. Also, participants reported that entering a large amount of



(a) Example question of the NEMO questionnaire (in German) and its respective answers. Colouring for good readability and auditory feedback optimize NEMO for the elderly.

(b) Summary of the Data Collection. The summary of a given diary entry again is colour-optimised to provide an easy-to-understand recap of the entered data.

(c) QR-Code transmission. For data transfer, the local data is encoded as (series of) QR-Codes. These codes can then be scanned via the corresponding desktop application.

FIGURE 5. Screenshots of the NEMO mHealth application.

data on smartphones may be cumbersome and scare them off. For these reasons, we decided to propose and compare two approaches to address these issues. Our applications are meant to be inserted in different clinical scenarios meeting the diverse needs of users and healthcare staff. Their usability and feasibility are currently tested in clinical studies (see ClinicalTrials.gov: NCT04493450 [7] and NCT04686409). The present perspective aims at analyzing and proposing strategies on how to include mHealth applications into clinical settings, ensuring patients and healthcare providers empowerment. As case studies, we presented two applications developed for tracking adverse events occurring during specific treatments. In both contexts, we presented key features connected with safe communication among users and the requirements of these two applications, which are fulfilled to be successfully introduced into clinical use. The CoCoV application is designed to document such events after a COVID-19 vaccination, whereas the NEMO application tracks adverse events during oncological treatment.

The CoCoV application is designed as a personal diary of symptoms, allowing aggregated analyses of the documented data. In contrast, the NEMO application was established to simplify and improve patient-doctor communication and the patient diary. Given the different features of these applications, we developed two different communication strategies. The *online data transfer* approach of the CoCoV application aims at collecting anonymized data at a central server. Relying on JSON structures sent to RESTful endpoints allows for integrating established medical standards, such as HL7 FHIR. Further, these RESTful endpoints allow for the development of easy-to-maintain software applications for healthcare professionals. No additional hardware is required in this context, resulting in an easy integration into existing clinical IT infrastructures. Finally, using a centralized server application also enables researchers to download the data. However, developers have to keep interoperability, informed consents, and data governance in mind. Although CoCoV submits data to a central server, it does not offer authentication. This application is mainly used to collect adverse events in an anonymous setting to get a general overview in an accumulated fashion without linking data to specific users. Instead, data collected is assigned to an automatically generated random ID than an actual username, making it impossible to trace data back to a particular person or device. However, changing the mobile device or reinstalling the application resets all data for this specific user. Omitting the login and user authentication process made the application more accessible. Note that while this may be suitable in our use case, it may not work out for other application scenarios. In this case, it would be possible to easily extend the application with an authentication module or additional features.

The NEMO application can be applied in scenarios where a personal consultation with healthcare professionals is recommended regularly particularly when the data obtained are important for further treatment decisions. This is suitable for long-term treatments, like chronic diseases. In the presented use case, NEMO aims at optimizing the treatment strategy by improving patient-doctor communication on side effects during chemotherapy. For this purpose, we integrated a *face-to-face data transfer* that guarantees maximum security and patient empowerment. The collected data can only be shared through direct contact by visual scanning a QR code. Besides, this approach in the described scenario has several advantages over other data transfer methods. Wireless techniques such as WiFi Direct, Bluetooth, or RFID are not available or usable for data transmission in each smartphone device or operating system [49]. The use of cables or USB transfer can be problematic in clinical practice, being often prohibited due to the risk of contamination (i. e. with viruses) [50]. Instead, the transfer via QR codes is more secure as the patient explicitly has control when and to whom he wants to transfer the data. Moreover, the transmission of data via a camera reduces the susceptibility of infecting the clinical infrastructure to a minimum. Note that the current version of NEMO is designed as a diary of the patient for the clinician. However, it does not include a timeline report of occurred symptoms. This concept was chosen to provide the clinician with a daily report about adverse events but not biasing the patients when summarizing the last weeks. The longitudinal data collected using NEMO allows the physician to track the documented adverse events since the previous treatment sessions. Additionally, the standardized and structured questionnaire provides optimized treatment by enabling semantic interoperability and improving patient-doctor communication [51]. The derived data can further be analyzed with novel machine learning methods [15], [52]–[55], which can aid the decision process towards personalized medicine [56]. Again, NEMO does not offer a digital authentication mechanism; however, involved parties are authorized in a personal consultation. The lack of authorization for NEMO was chosen because we considered sick participants who might require support from relatives to fill out the daily questionnaire. An overcomplicated authentication step would be a substantial obstacle for them to using the app. Since documentation is a crucial step in detecting side effects of the treatment as soon as possible, easing this process was the central focus of our NEMO app. However, for scenarios requiring these authorization features, the app design allows for fast integration of these. One could further secure the application by adding password authentication during startup. Although this approach has significant advantages concerning trustworthiness, reliability, and security, it also has drawbacks. For example, the healthcare professional requires additional hardware (i.e., a camera) and dedicated software to decode (read) and process the QR-codes.

Besides using case-specific features, one can integrate both applications into more extensive settings, such as hospital IT infrastructures. The integration of both approaches differs by design. The *online data transfer* approach allows integrating the collected data directly into an existing IT infrastructure (e.g. hospital information system (HIS)). In contrast, the *face-to-face* approach achieves the same on the HCP client application level. Depending on the applied strategy, minor adaptations may need to be implemented to comply with organization-wide standards, like HL7 FHIR. When using the *online data transfer* approach, such as CoCoV, these standards can be implemented in the mobile application to communicate with compatible infrastructure layers. In the *face-to-face* approach, the mobile client application is closely connected to the corresponding desktop application, which is essentially a consequence of the communication protocol. The protocol requires dedicated one-to-one communication between patients and healthcare professionals. Instead, in an extension, the integration must be moved to the HCP client application to keep the communication paradigm.

While we use cases to address communication and safety empowerment in mHealth applications in the present study, there are still open issues that have to be considered when using these digital approaches for health companions in general. For instance, applications with gamification might cause unintended side-effects, such as data manipulation by "cheating" or discouragement due to failure [57]. On the other hand, other approaches might take advantage of introducing healthy habits in games, such as exercises for rehabilitation after stroke [58]. In this case, a game is presented to motivate exercising without the drawback of inter-user competition. To prevent inaccessible healthcare, people with disabilities should not be excluded from using mHealth applications [59], [60]. Furthermore, mHealth applications cannot replace all tasks of general practitioners [61] and these should still be involved in the diagnosis and treatment, especially in case of emergencies. Consequently, besides their advantages, still, many mHealth approaches need a substantial improvement in their build-up and safety. This holds also for safety concerns in the integration of artificial intelligence approaches in medicine, where the first aim is to move out of online clouds in favor of local hardware options [62].

In conclusion, we presented and analyzed a controversial topic currently discussed in the digital medicine approach. While mHealth applications are more and more demanded and in use, they often lack protocol and safety requirements that would make them suitable to be introduced into clinical practice. Here, we proposed two alternative strategies to empower users of mHealth applications and ensure their integration in the clinical context. By introducing technical case studies, we showed how these two approaches can be implemented into different clinical scenarios. Altogether, this perspective work might serve as a basis to sustain future development of safely integrated mHealth applications in clinical settings.

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