WATCHING THE RISK FACTORS

WARIFA

ARTIFICIAL INTELLIGENCE AND THE PERSONALIZED PREVENTION AND MANAGEMENT OF CHRONIC CONDITIONS

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List of Abbreviations

Acronym	Definition
CE	Conformité Européenne
cMHAPP	Consumer Mobile Health Application Functional Framework
CSUQ	Computer System Usability Questionnaire
CVD	Cardiovascular Disease
eHealth	Electronic Health
EU	European Commission
GPS	Global Positioning System
H2020	Horizon 2020
HbA1c	Haemoglobin A1c
IPI	Interactive Photo Interface
ISO	International Organization for Standardization
IVDR	In Vitro Diagnostic Regulation
MAUQ	mHealth App Usability Questionnaire
MDCG	Medical Device Coordination Group
MDR	Minimum Daily Requirement
mHealth	mobile Health
NCD	Non-Communicable Disease
PSSUQ	Post-Study System Usability Questionnaire
QoL	Quality of Life
QUIS	Questionnaire for User Interaction Satisfaction
RCT	Randomized Controlled Trial
SMS	Short Message Service
SUS	System Usability Scale
WHO	World Health Organization

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1 INTRODUCTION

The aim of this document is to summarise the evidence about the usability, use and engagement, and behaviour change related to health apps, in order to set the foundations for the development of the WARIFA solution.

1.1 DEFINITIONS. MHEALTH AND HEALTH APPS

The WHO considers the use of mobile wireless technologies for public health, or mHealth, as an integral part of digital health, which in its turn includes both eHealth (cost-effective and secure use of information and communication technologies in support of health and health-related fields) and other, developing areas, like the use of advanced computing sciences [1]. Indeed, WHO's engagement in mHealth development and implementation includes specific initiatives for the prevention and management of non-communicable diseases, such as the joint initiative with the International Telecommunication Union "Be Healthy, Be Mobile" [2], as well as the development of guidelines for digital health interventions (see below).

According to EU's definition, Mobile Health (mHealth) is as "*a sub-segment of eHealth [which] covers medical and public health practice supported by mobile devices. It especially includes the use of mobile communication devices for health and well-being services and information purposes as well as mobile health applications*" [3] (see Figure 1).

In 2014, the European Commission published the Green Paper on mHealth, where it forecasts its applications on an ageing population as a way to improve the efficiency of the healthcare system, as well as to contribute to a more person-centred care [4]. Furthermore, emphasis is made on early detection of chronic conditions, as well as a shift towards prevention, in order to improve citizens' quality of life and life expectancy, by promoting healthy lifestyles.

WARIFA is aligned with these principles and objectives.

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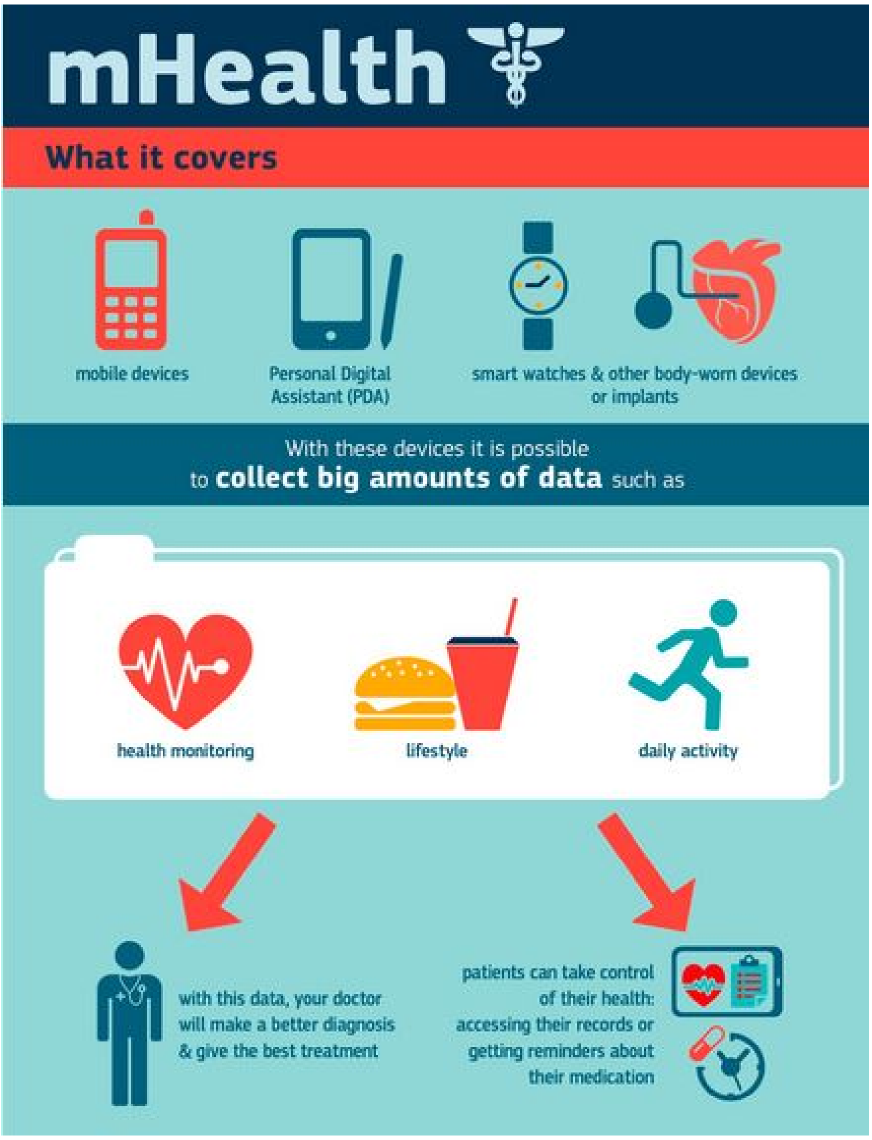

Figure 1 Areas covered by mHealth, according to the EU. Reproduced from [3].

2 HEALTH APP REQUIREMENTS

2.1 WHO GUIDELINES

In 2019, the WHO published an extensive guideline on digital interventions, based on a review of the existing evidence, that could be applicable to mHealth [5].

Targeted user communication for behaviour change is recommended under specific conditions, where sensitive content and data privacy can be adequately addressed, including clear instructions on how to opt out of receiving targeted communication. The main challenges identified in this context are a low demand for services, low adherence to treatments, loss of follow-up and lack of access to information.

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The use of digital tracking combined with decision support and targeted user communication is recommended only in settings where the health system can support the implementation of these intervention components in an integrated manner and where potential concerns about data privacy and transmitting sensitive content to users can be addressed. The health system challenges identified in this context are insufficient continuity of care; data quality and reliability; delayed provision of care and poor adherence to guidelines.

Implementation recommendations of the eHealth Strategy Toolkit [5] affect infrastructure, health workforce, governance, financial resources, interoperability and standards, as well as policy and regulations. The transversal implementation framework comprises:

To Involve stakeholders in programme design and implementation.

- To assess how programmes can be efficiently integrated with the rest of the health system.
- To secure data confidentiality and informed consent.
- To ensure that health workers have adequate training, supervision, support and incentives.
- To ensure access to network connectivity and electricity.
- To ensure that health workers have access to functioning digital devices.

The implementation considerations should also be guided by the Principles for Digital Development [6], including the aspects shown in Table 1:

Table 1 Principles for Digital Development [6].

1)	Design with the User.
2)	Understand the Existing Ecosystem.
3)	Design for Scale.
4)	Build for sustainability.
5)	Be Data Driven.
6)	Use Open Standards, Open Data, Open Source and Open Innovation.
7)	Reuse and Improve.
8)	Address Privacy & Security.
9)	Be collaborative.

2.2 EU RECOMMENDATIONS

In order to guarantee their privacy and safety, Health Apps need to fulfil certain requirements. Indeed, in the EU, they are considered medical devices and, as such, need to follow corresponding rules. The most recent regulation on medical devices in Europe, Regulation EU 2017/745, took effect on the 26th May 2021.

Within the countries of the European Economic Area, CE marking applies, which indicates conformity with corresponding EU requirements [7]. According to their associated risk, medical devices are classified into class I, IIa, IIb and III (low, medium, medium/high and high risk, respectively). Examples of class I include adhesive bandages, wheelchairs or tongue depressors. A specific subtype are those non-sterile devices used for measurements (as a weighing machine) that require specific certifications despite its low-risk classification. Class IIa includes medium risk devices such as catheters, hearing aids and ultrasound equipment. Class IIb devices include surgical lasers and insulin infusion pumps for example. Lastly, class III are high risk devices such as pacemakers,

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orthopaedic implants or coronary stents. Also, closed-loop insulin infusion systems are in this class. The higher the risk, the more controls are required for market approval.

If we, a priori, try to define the class WARIFA would fall into, we must take several issues into consideration. The use of artificial intelligence that will be part of the WARIFA solution, with medical intention (including diagnosis, disease risk estimation, behaviour change and disease prevention), poses a novel problem for medical device regulation. If the software model built can retrain and evolve constantly and automatically, how can its safety and effectiveness be assessed? To tackle this situation, a robust WARIFA solution would only be available after completion of the initial AI training. Then, it could be launched as a closed and stable app. In future updates, with new data helping develop an improved model, the new version of WARIFA could be assessed again in terms of safety and efficacy and certified again as a new closed app that for the end-user would come as an update of their previous app.

In this regard, it is key for the regulating body to examine the clinical evidence backing the safety and effectiveness of the software. There is evidence of positive clinical outcomes behind the basis of the WARIFA solution, although it leaves vast gaps of knowledge. Nonetheless, if we consider the forefront nature of WARIFA, it is natural that these gaps exist. Therefore, a rigorous post-market strategy is paramount to ensure safety and effectiveness. Beside these specific items, general safety requirements must be assessed.

General safety requirements include at least clinical evaluation and/or performance evaluation. The former means that manufacturers are expected to produce a clinical evaluation report. Evaluation of relevant scientific literature, critical evaluation of results of all available investigations and considerations of currently available alternative treatment options must be made. However, clinical investigation is scarce for artificial intelligence medical devices and alternative treatment options are problematic as other developers' models and data often constitute a trade secret. Therefore, developers usually must perform their own clinical investigation study. The latter, performance evaluation, must include the validation of an analyte associated to a clinical condition, the ability of the medical device to correctly detect and measure that analyte and thirdly the ability of the device to yield results that relate to a particular clinical condition for the intended use. All these evaluations will be covered as part of the WARIFA validation.

Given all this information, 3 factors will condition if there is sufficient clinical evidence. Their intended use, evaluation of side-effects, interferences or cross-reactions of the device and the risk-benefit ratio that emerges. Considering this, WARIFA would generally fit into class IIa or IIb. However, given the multiple potential uses expected from WARIFA, this is a tough guess. The risk associated to the WARIFA solution will vary depending on the specific purpose and user at hand. Patients with diseases such as type 1 diabetes that rely on the WARIFA recommendations to adjust lifestyle and insulin treatment might be exposed to a class III risk whereas a healthy individual assessing their long-term risk of cardiovascular diseases and how to lessen it, would probably be exposed to no more than a class I or IIa risk.

The most recent regulation on medical devices in Europe, Regulation EU 2017/745, took effect on the 26th May 2021. The European Commission on its website has *the Guidance-MDCG endorsed documents and other guidance* of 2019 [8], it contemplates the regulation 2017/745 that is to be applied starting on May 26, 2021. Also, the guide *Manual on borderline and Classification in the Community Regulatory Framework for Medical Device* [9] on page 77 develops the regulation on Software and Mobile Applications. The Apps included within the framework of medical devices must comply with the objective of influencing the health of people (patients) and avoid handling population data or not being compatible with regulation for medical devices.

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The new European rule 2017/745 includes the establishment of a medical device database, whose aim is to improve transparency in the process, both for citizens and for health care providers. EUDAMED will be composed of six modules related to: actor registration, unique device identification (UDI) and device registration, notified bodies and certificates, clinical investigations and performance studies, vigilance and market surveillance [10].

To facilitate information on medical or health software, the EU published in March 2021 an Infographic according to the definition of MDCG 2019-11 [8] and Article 103 of Regulation 2017/745 to recognize whether a given software is considered a medical device [11].

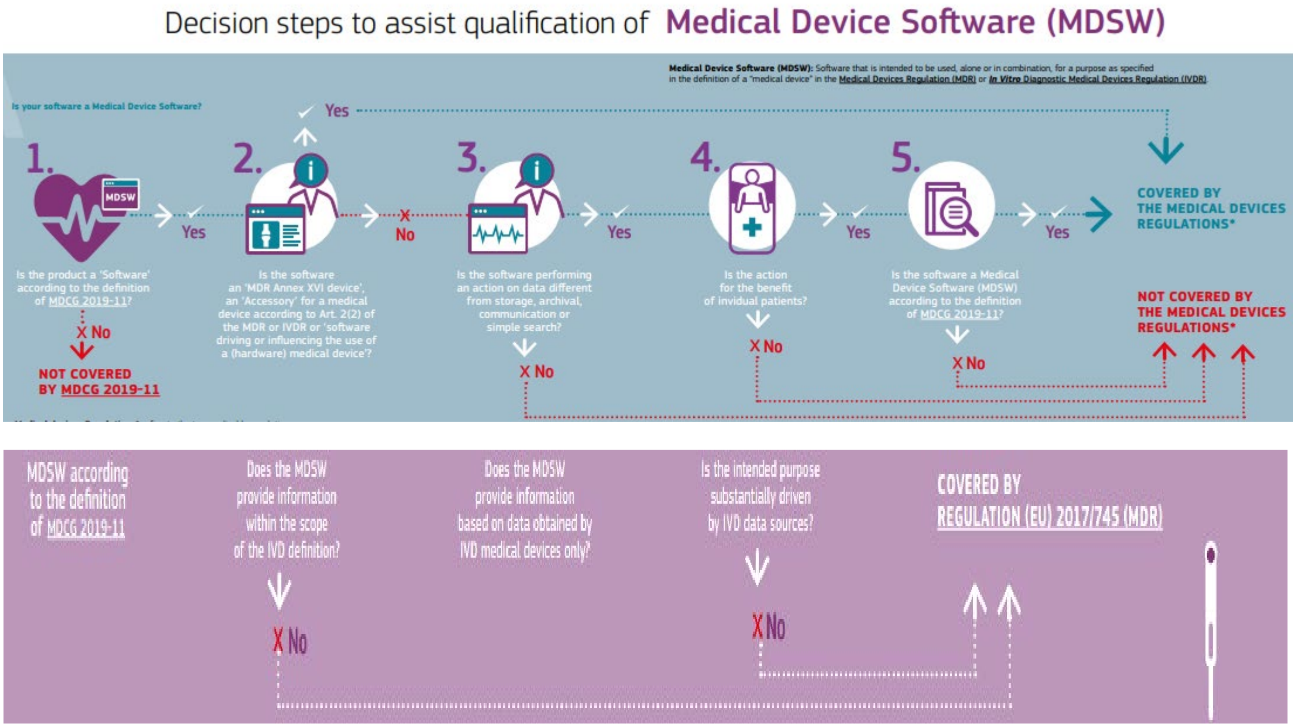

Figure 2. EU Infographic (March 2021) for medical devices assessment according to the definition of the Medical Device Coordination Group 2019-11 [8].

Following the infographic in Figure 2, the WARIFA solution is Software according to the MDCG-2019 11, it is not a "MDR Annex XVI device" nor "Accessory" for another medical device according to Art. 2(2) of the "MDR" or "IVDR" and in some instances it could be a software driving the use of a hardware medical device, is performing actions on data different from storage, archival, communication or search, those actions are for the benefit of individual patients/people at risk of disease and is a Medical Device Software according to the definition of MDCG 2019-11. Therefore, all the regulations above-mentioned apply.

2.3 Evaluation and Certification

Before the recent European rule took effect, there had been many attempts to standardize the assessment of health app quality. Indeed, both public and patient led organizations have developed certification programmes, as reviewed within the European [H2020] Innovation and Knowledge mHealth-hub [12], in deliverable 2.1: Health app assessment frameworks [13]. The aim of these frameworks is to increase confidence of citizens and health care providers in the use of health apps.

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After achieving a set of pre-established requirements during the assessment process, the health apps are given a quality seal or certification, which in turn increases user confidence.

In the countries involved in WARIFA, only Spain is reported to have assessment frameworks for health apps, namely:

- The Safety and Quality Strategy in Mobile Health Apps, by the Andalusian Agency for Healthcare Quality.
- The Accreditation Service and TICSS guarantee certification, by TIC Salut Social Foundation, Catalonia.
- The iSYS score, by the iSYS Foundation, Catalonia.

In Norway, different assessment frameworks have been considered[1], but so far no decision has been made. Other EU countries, such as Germany, Portugal, Belgium and the Netherlands also have government-initiated frameworks. The ISO 82304-2 'Health software – Quality and reliability of health and wellness apps' [14] and the Consumer Mobile Health Application Functional Framework (cMHAPP) are early, ongoing international efforts. The European Commission established the Working Group on mHealth Assessment Guidelines, as a starting point to establish common ground, who published a report [15].

Most of these assessment frameworks, however, are developed and maintained at national or regional level, often in the national language and on a voluntary basis, which limits their adoption and the integration of health apps in the health care system.

2.4 Certification criteria

The domains evaluated by the different assessment frameworks include privacy, transparency, safety, reliability, validity, interoperability, technical stability, effectiveness, accessibility, scalability, (technical) security and usability/user experience [13].

2.4.1 Privacy

Protection of personal data is increasingly addressed in mHealth and assessment frameworks, especially after the enforcement of the European General Data Protection Regulation. User consent is also now established, although less attention is paid regarding how personal data are accessed, kept and transmitted. Furthermore, user tracking and third-party involvement still need to be tackled.

2.4.2 Transparency

Although transparency about data collection is generally addressed, there is less information about the developer and distributor of the app, and their potential interests. In addition, as a user, it is usually hard to access information about the algorithms in the app or how the provided information is used in these algorithms and assessment frameworks usually do not take this into consideration as al quality feature.

2.4.3 Safety

[1] Available in Norwegian from: https://www.helsedirektoratet.no/tema/velferdsteknologi/rapporter-og-utredninger/Tryggere%20helseapper.pdf/_/attachment/inline/e3f6f78d-e56c-4c75-ba64-7bb37be4442c:396f6ade6ba977a71f41167532bfe7b52f5fc011/Tryggere%20helseapper.pdf

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This domain considers the assurance that the use of the app does not cause harm. Despite its relevance when dealing with people's health, some frameworks do not make clear reference to safety, although increasing attention is being paid to content quality and validity, which are some of the main pillars of safety.

2.4.4 Reliability

Reliability is a measure of reproducibility and consistency, which, in the case of health apps, can have an impact on safety, too. Most of the assessment networks do not consider it at all.

2.4.5 Validity

This term refers to the information present in the application, as reviewed by experts, as well as the health data which serves as a basis for the mHealth solution. Validity favours consistency and reliability of the data presented to the user, which should be in accordance with guidelines and current scientific evidence. However, few of the assessment networks delve into this relevant aspect [16]. Indeed, ideally, the design of the initial app content should be based on current international guidelines and should also be periodically updated as new evidence is available. Furthermore, clinical validation studies should also be used to assess health apps [17], though randomised controlled trials are still scarce in this context. Finally, validity assessment should also be applied to data obtained through external (wearable) sources.

2.4.6 Interoperability

Interoperability is a key aspect for integration of mHealth into the different information systems, including the health care system. Several levels of interoperability should be addressed, namely foundational, structural, semantic and organisational. In the European context, semantic interoperability affects, not only data formats, but national languages, too. Indeed, the use of harmonised standards for data sharing is crucial.

2.4.7 Technical stability

This term refers to the capacity of the app to maintain a certain level of performance over time. Although most of the assessment frameworks do not include this domain, technical testing should also be part of the quality criteria of an app. To ensure that the app maintains its level of performance this testing should be done assuming sudden increases in the number of users and data.

2.4.8 Effectiveness

Effectiveness is assessed by ensuring that the app achieves what it claims to achieve, which, in the case of health apps, is often a health outcome. Thus, in this context, this term is closely linked to safety, too.

2.4.9 Accessibility

This is an underdeveloped issue in the assessment of health apps, which is closely related to usability. Adaptations are often limited to text or image readability or size. However, in the context of mHealth, it is especially relevant to address both physical and cognitive disabilities, as well as a wide range of digital health literacy.

2.4.10 Security

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This term refers to technical aspects, such as network and communication protocols, though it is closely related to privacy and reliability domains.

2.4.11 Usability/user experience

This domain is addressed in about half of the assessment frameworks. More detail about related criteria and direct application to mHealth follows.

3 HEALTH APPS: USABILITY

Although evidence-based content of Health Apps is necessary, if the technology itself is difficult, the end-user might not find any benefit from its application, or the latter might even be negative for the expected outcomes, regardless of its theoretical relevance. Thus, ease of use (usability) should also be closely monitored in the development and validation of mHealth tools.

According to the ISO (International Organization for Standardization), usability is defined as: "*the extent to which a system, product or service can be used by specified users to achieve specified goals with effectiveness, efficiency and satisfaction in a specified context of use*" [18]. In this context, effectiveness is defined as "*accuracy and completeness with which users achieve specified goals*", efficiency, as "*resources used in relation to the results achieved*" and satisfaction "*includes the extent to which the users experience that results from actual use meets the user's needs and expectations*".

Another, extensively accepted definition of usability is that established by Nielsen [19], which includes 5 dimensions, namely: learnability, efficiency, memorability, error management and satisfaction (see their definitions in Table 2).

Table 2 Definition of the five dimensions of usability extracted from [20].

Learnability	Ease of learning the functionality and the behaviour of the system.
Efficiency	Level of attainable productivity of the user after he has learned the system.
Memorability	Ease of remembering the system functionality, so that the casual user can return to the system after a period of non-use, without needing to learn again how to use it.
Few errors	Capability of the system to support users in making less errors during the use of the system, and in case they make errors, to let them easily recover.
Satisfaction	Measure of how pleasant the design is to use.

The main limitation in the assessment of these attributes of mHealth usability is the lack of standardisation, as highlighted by a systematic review [20].

3.1 USABILITY CRITERIA: SCALES

Several usability scales have been developed, but no standardised system is available yet. A systematic review analysed 15 existing scales, covering three to four of the attributes defined by Nielsen, learnability, efficiency, and satisfaction being the most frequently assessed (by all 15, 12 and 12 scales, respectively) and memorability only covered by one [20].

The authors concluded that usability is often misunderstood and only partially assessed but that, despite their weaknesses, efforts should be made to include the strongest measures of usability in research, in order to improve the implementation of eHealth. Four of the tools assessed were selected as the strongest available options at the time, based on generalisability, attribute coverage

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and quality criteria: System Usability Scale SUS [21], Questionnaire for User Interaction Satisfaction QUIS [22], the Post-Study System Usability Questionnaire PSSUQ [23] and the Computer System Usability Questionnaire CSUQ [24]. SUS scored highest in quality (7 out of 10 points), based on questionnaire validity, reliability, user-centeredness, sample size and feasibility [20]. More recently, the mHealth App Usability Questionnaire (MAUQ) was specifically developed for this purpose [25].

3.1.1 System Usability Scale

SUS was developed by John Brooke [21] to cover the need for general measures, which could quickly evaluate the usability of computational systems. This was done acknowledging that context specificity is relevant but lacking in such a general tool. On the other hand, comparability across systems is allowed.

SUS is a high-quality tool designed for the assessment of user-perceived usability of a digital product. It includes three attributes defined by the ISO (effectivity, efficiency and satisfaction), though only two of the five defined by Nielsen (learnability and satisfaction [20]). Presented as a 10-item, 5-point, Likert scale, it can be easily completed by the end-user of a technological solution, after having tried the latter. It is broadly used and has been translated to several languages [20], though validation is lacking for most of these versions. Regarding languages that are relevant to WARIFA, the Spanish version was recently validated [26]. To our knowledge, neither Norwegian nor Romanian versions are available, though both Swedish [27] and Danish [28] are. Other languages to which SUS has been translated and validated include Chinese, French, German [29] and Portuguese [30]. Figure 3 shows the SUS questionnaire as published by Brooke in 1996.

SUS is robust and reliable and correlates well with other measures of usability. It is free to use, as long as the source is acknowledged. Both the questionnaire itself and the scoring instructions are available [31]. This tool is particularly relevant for the comparison of different technologies intended for the same purpose, since it is method-independent. Indeed, designed more than 25 years ago, it has been applied to hardware, software, websites, operating systems, etc [32].

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System Usability Scale

	Strongly disagree				Strongly agree
1. I think that I would like to use this system frequently	1	2	3	4	5
2. I found the system unnecessarily complex	1	2	3	4	5
3. I thought the system was easy to use	1	2	3	4	5
4. I think that I would need the support of a technical person to be able to use this system	1	2	3	4	5
5. I found the various functions in this system were well integrated	1	2	3	4	5
6. I thought there was too much inconsistency in this system	1	2	3	4	5
7. I would imagine that most people would learn to use this system very quickly	1	2	3	4	5
8. I found the system very cumbersome to use	1	2	3	4	5
9. I felt very confident using the system	1	2	3	4	5
10. I needed to learn a lot of things before I could get going with this system	1	2	3	4	5

Figure 3 SUS questionnaire, from Brooke 1996 [21].

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3.1.2 mHealth App Usability Questionnaire (MAUQ)

Unlike SUS, which is applicable to a wide range of technologies, this questionnaire was specifically developed to assess the usability of Health apps. Through the thorough review of 38 existing questionnaires, which had been applied in the assessment of app usability, a total of 312 items were collected and skimmed down to 53 statements, with the involvement of seven usability experts. Further refinement led to the reduction of the questionnaire to 21 and 19 items, for the interactive and standalone apps, respectively.

The development and validation process, involving 128 participants, demonstrated good internal validity and reliability of the tool, with strong correlation with SUS and PSSUQ [25]. Psychometric analysis revealed three domains within the questionnaire, named: ease of use and satisfaction, system information arrangement and usefulness, akin to ISO definitions of satisfaction, efficiency and effectiveness, respectively.

Furthermore, four versions of the MAUQ were developed in relation to the target user of the app (patient or health care provider) and the type of app (standalone or interactive with the health care system), which are available through an open-access website [33]. The most relevant to the WARIFA solution would probably be the version for standalone apps for patients, shown in Figure 4.

Despite its novelty, this tool has already been incorporated in the assessment of mHealth apps focused on non-communicable chronic diseases, such as breast cancer [34], and their risk factors, i.e. alcohol consumption [35] and hypertension [36].

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mHealth App Usability Questionnaire (MAUQ)
for Standalone mHealth Apps Used by Patients

#	Statements	N/A		1	2	3	4	5	6	7	
1.	The app was easy to use.	☐	DISAGREE	☐	☐	☐	☐	☐	☐	☐	AGREE
2.	It was easy for me to learn to use the app.	☐	DISAGREE	☐	☐	☐	☐	☐	☐	☐	AGREE
3.	The navigation was consistent when moving between screens.	☐	DISAGREE	☐	☐	☐	☐	☐	☐	☐	AGREE
4.	The interface of the app allowed me to use all the functions (such as entering information, responding to reminders, viewing information) offered by the app.	☐	DISAGREE	☐	☐	☐	☐	☐	☐	☐	AGREE
5.	Whenever I made a mistake using the app, I could recover easily and quickly.	☐	DISAGREE	☐	☐	☐	☐	☐	☐	☐	AGREE
6.	I like the interface of the app.	☐	DISAGREE	☐	☐	☐	☐	☐	☐	☐	AGREE
7.	The information in the app was well organized, so I could easily find the information I needed.	☐	DISAGREE	☐	☐	☐	☐	☐	☐	☐	AGREE
8.	The app adequately acknowledged and provided information to let me know the progress of my action.	☐	DISAGREE	☐	☐	☐	☐	☐	☐	☐	AGREE
9.	I feel comfortable using this app in social settings.	☐	DISAGREE	☐	☐	☐	☐	☐	☐	☐	AGREE
10.	The amount of time involved in using this app has been fitting for me.	☐	DISAGREE	☐	☐	☐	☐	☐	☐	☐	AGREE
11.	I would use this app again.	☐	DISAGREE	☐	☐	☐	☐	☐	☐	☐	AGREE
12.	Overall, I am satisfied with this app.	☐	DISAGREE	☐	☐	☐	☐	☐	☐	☐	AGREE
13.	The app would be useful for my health and well-being.	☐	DISAGREE	☐	☐	☐	☐	☐	☐	☐	AGREE
14.	The app improved my access to healthcare services.	☐	DISAGREE	☐	☐	☐	☐	☐	☐	☐	AGREE
15.	The app helped me manage my health effectively.	☐	DISAGREE	☐	☐	☐	☐	☐	☐	☐	AGREE
16.	This app has all the functions and capabilities I expected it to have.	☐	DISAGREE	☐	☐	☐	☐	☐	☐	☐	AGREE
17.	I could use the app even when the Internet connection was poor or not available.	☐	DISAGREE	☐	☐	☐	☐	☐	☐	☐	AGREE
18.	This mHealth app provides an acceptable way to receive healthcare services, such as accessing educational materials, tracking my own activities, and performing self-assessment.	☐	DISAGREE	☐	☐	☐	☐	☐	☐	☐	AGREE

Figure 4 Example of mHealth App Usability Questionnaire for standalone apps targeted to patients. Extracted from Zhou et al 2019 [25].

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3.2 App features associated with higher usability

In order to identify the features associated with higher app usability, engagement and behaviour change, a literature search was performed in Medline and Embase, using the following terms: Mobile applications/(mobile OR portable OR tablet OR smartphone OR health) App OR (smartphone-based) AND Motivation OR continuous use OR success OR failure OR sustained use OR adherence OR compliance OR engagement OR utilisation OR uptake OR motivation OR health management OR health behaviour OR lifestyle change. Only randomised controlled trials and systematic reviews were included. The following inclusion criteria were applied: apps used on mobile devices (mainly phones and tablets), by healthy people and/or patients with chronic conditions and having functions that are described in detail. Studies should report on apps that require (at least in part) manual input by the user, monitor and display objective health parameters, provide personalised output and report outcomes with a causal relation to app functions (i.e., there is an explanation on how a certain app function affects the outcome). For randomised controlled trials the study period had to be at least 6 months.

The following exclusion criteria were applied: studies focusing on cost-effectiveness or acute conditions, studies that report only outcomes without any causal relation to app functionalities (i.e., there is no explanation on how a certain app functionality affects the outcome), studies without a detailed description of the app used in the trial and economic studies were excluded. Randomised controlled trials of less than 6 months duration were excluded. Also, studies reporting the following conditions were excluded as they are not in line with the Warifa concept of chronic conditions: Acute illness, infectious diseases (e.g., HIV or TBC), complex psychiatric disorders, (e.g. psychoses) and pregnancy-related gynaecological conditions. Furthermore, studies merely investigating drug adherence were excluded.

The articles were distributed and reviewed by 5 reviewers (TS, KL, AD, MA, AW).

The lack of standardisation and understanding of the term usability limits the conclusions that can be drawn from the publications where it is evaluated. Some authors use validated questionnaires, whereas others use ad-hoc developed questionnaires, or semi-structured interviews and qualitative research. mHealth technology is under continuous and fast development, whereas the tools for validation and assessment need more time. Table 3 and table 4 summarise the findings of systematic reviews and randomised controlled trials identified, showing the list of features associated with higher usability in Health Apps. Briefly, the interface should be simple and intuitive, tasks should also be kept simple, minimising manual input. Furthermore, assistance (as needed) to start with the app and in-app educational content available on demand will also increase usability. Personalisation at different levels is key, both for usability and engagement with the app.

3.2.1 Nutrition (healthy diet) Apps and Usability

Dietary interventions are central in the prevention of NCDs. Thus, mHealth applications aimed at improving dietary lifestyles are highly relevant. Nevertheless, recommendations should be evidence based, which is not always the case, and this might lead to changes in behaviour which have no impact or even pose a risk on health. Hence, the need for evaluation, certification and regulation of health apps focused on diet, too.

A literature search was performed for publications (systematic reviews, meta-analyses and randomised clinical trials) in the last 5 years including the terms “mobile app” and “Nutrition/diet” and “usability/easy use”. Their results are summarised in Table 4. The use of most of the apps promoting a healthy diet is associated with weight loss and behaviour changes (regarding eating or physical activity), i.e., they are effective. We can assume that people who download and use these health apps have intrinsic motivation to do so, such as a need to improve their eating patterns, to lose

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weight, or to increase physical activity, either through a decision of their own or due to the recommendation by a health care provider.

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Table 3 Features associated with higher usability in Health Apps.

Author (Year) [Ref]	Aim of the app	Usability criteria	Features associated with higher usability	Comments
Angelini et al. (2019) [37]	Diabetes management.	User perception.	Photographs. Automatic recording (GPS tracking, heart rate monitor, pedometers) of physical activities appears to be more useful than manual recording.	Systematic review Photographs of meals increase user understanding and healthcare professionals can monitor eating habits. Some apps use image processing to analyse consumed carbs.
Fu et al. (2017) [38]	Diabetes self-management.	Usability scales.	Manual data entry restricted usability. Interactive features (Realtime feedback) beneficial for glycaemic control. Combination of app with other components improved glycaemic control.	Systematic review Majority of included studies of less than 6 months duration. Many interventions had several additional components (e.g., interaction with social forum or health care professionals).

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Table 4 Features associated with higher usability in Nutrition Health Apps.

Author (Year) [Ref]	Aim of the app	Usability criteria	Features associated with higher usability	Comments
Alfonsi et al. (2020) [39]	Carbohydrate counting in type 1 diabetes.	Usability (qualitative interview). Acceptability (E-Scale). Effectiveness. Satisfaction. Engagement.	Simplicity. Clear graphs. Clear instructions.	Randomised controlled trial The efficacy and acceptability of an app for counting carbohydrates through images is studied in young people.
Kosa et al. (2019) [40]	Dietary management in chronic kidney disease.	Ease of use (qualitative).	Food icons.	Systematic review Food icons were helpful in monitoring dietary intake.
Liu et al. (2016) [41]	Measure amount of food in the diet.	Ease of use (qualitative). Efficiency (response time).	Interactive photo interface.	Randomised controlled trial Three free visual aids were compared: Interactive Photo Interface, Sketch Based Interface, and control (Life Size Photographs) for the estimation of food intake in college students.
Liu et al. (2020) [42]	Measurement of food portion size.	Usability scale.	No difference between the options.	Randomised controlled trial Three different ways of measuring portion sizes of food were compared. Keyboard-based (weight, volume or home measurements), photo-based and gesture-based (gestures or finger movements on the screen to describe volume).
Liu et al. (2020) [43]	Measurement food portion size (for the elderly).	Usability scale. Precision. Effectiveness efficiency. User perception.	Voice only function.	Randomised controlled trial Two forms of food registration were used: user voice only and voice, buttons and touch screen. In adults aged 60-90 years.
Mauch et al. (2021) [44]	Healthy meal planner.	Usability scale. Engagement (self-reported).	Effort-saving features. Less manual input. Customisation. Efficiency.	Randomised controlled trial comparing 5 different, commercially available, healthy meal planner.

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3.3 Accessibility issues

Despite technology being ever more present each day, smartphones and internet connection are not available in all regions of the globe. Besides, the costs associated to them can be a barrier for many potential users. Other accessibility issues include language, health and digital literacy, and awareness of the existence of mHealth solutions that are safe and efficient. Also, law and local regulations impose a barrier in some places. To address all this, different paths can be explored [17].

Education and awareness are a first step to improve health and digital literacy along with awareness of digital solutions for health. This can include clinicians receiving digital health training and also planning on integration of health apps with current workflow of clinicians and integration of apps with the electronic patient history. Also, potential users should receive updated information and education on available health apps. Other solutions to enhance awareness must be designed. This can be achieved in several ways, one of them would be by means of “app labels” (similar to nutrition labels for food) that are validated to be a mark of trustworthiness of a given app.

Payment models must be considered. If wearables are needed or apps become more and more complex in the future, it is to be expected that prices associated increase.

The apps themselves should, in their design, be usable by functionally diverse users, with different physical and cognitive abilities. Finally, a support structure should be considered. As app complexity increases, specific support might be needed to help patients and clinicians stay updated with new versions of apps, technical incidences or best uses and indications of a given app.

4 HEALTH APPS: USE AND ENGAGEMENT

The terms use and usability have a certain degree of overlap in the published literature. However, in this section, we focus on the actual engagement in app use. Although there is a growing body of evidence that health apps may be effective in promoting self-management of chronic diseases, observational, real-world studies suggest a low percent of user retention (between 0.5 and 29% at 6 weeks or more), i.e. a high degree of attrition [45]. Indeed, a recent systematic review and meta-analysis showed an average 49% drop-out rate in real-world, observational studies, vs 40% in randomised controlled trials [46].

4.1 Criteria for use and engagement

Engagement criteria vary from study to study and include number of logins, frequency of use, data entry, duration of use, task completion or self-reported use.

The definition of attrition also varies among studies, ranging from single time log-in to use of the app once or twice. In addition, the definition of the total number of participants (i.e., the denominator in the fraction: drop-outs/total) may also vary, including all participants in the trial (those randomised, as recommended for intention to treat analysis) or only those downloading the app or logging in [46].

4.2 Features associated with use and engagement

Several, participant-dependent features are associated with reduced attrition [46–48], such as age (more engagement in the younger), health literacy and postgraduate education, but also poorer self-perceived health, healthy eating at baseline and engagement in multiple interventions. In addition,

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drop-out rate is lower for apps addressing chronic metabolic diseases than those used for non-metabolic diseases [46]. Features of mHealth itself, associated with higher engagement, are summarised in Table 5.

Briefly, understanding the potential users and including personalisation to participants' needs (digital and health literacy, accessibility) and preferences (data input and output, interface features), as well as addressing privacy and credibility concerns are crucial. In addition, users prefer the app to be low-maintenance, i.e. to be low cost or free, consume little energy and device storage capacity, be available despite internet unavailability and require as little manual data entry as possible. Behaviour change techniques (e.g., goal-setting, feedback, personalisation), gamification and social interaction also increase engagement.

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Table 5 Features associated with higher use and engagement in Health Apps

Author (Year) [Ref]	Aim of the app	Engagement criteria	Features associated with higher use/engagement	Comments
Agarwal et al. (2019) [49]	BlueStar: Type 2 diabetes self-management Users could report glucose readings, exercise, food intake. App delivered customized, evidence-based messages. Data transferred to user's clinician.	Entries in app.	Blood glucose tracking feature. Intervention usability evaluated by an adapted version of the Mobile App Rating Scale. A qualitative part of this study found that the health care provider was an important source of support in app adoption.	Multicentre pragmatic randomised controlled trial. High variability in usage by site; Higher use might be linked to better implementation of the intervention (more time spent). Study participants could not use their own phone.
Coorey et al. (2018) [50]	Self-management of cardiovascular disease.	App usage frequency, duration, data registration or responsiveness of the user to daily tasks. Self-reported preferences.	Healthy eating and exercise goal setting. Recognition of achievements. Memory and psychological tasks. Enable user editing of self-entered numeric data, reminders and appointments. Motivational messages with: - Opt-out option. - User-created and system-generated content. - Content responsive to user input to app. Game-based design techniques. Enable textual data to be entered with numeric data. Ensure graphical data displays are viewable on a smartphone. Tailor content of cardiac rehabilitation-related apps to stage of recovery. Offer team-based competition options. Remove requirement for daily data entry. Provide in-app 'how to' guides.	Systematic review Often low participant numbers, dropouts and short exposure duration.

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Gong et al. (2020) [51] **Complemented by Baptista et al. (2020)** [52]	Self-management of type 2 diabetes.	QoL scale. HbA1c. User-reported opinions.	There was a dose-response relationship between the number of chats and the change in the QoL scores. Compared with people who completed chats less than 7 times, those who completed more than 24 chats with Laura during program access had a significantly greater improvement in QoL scores. The "My Diabetes Coach" app incorporated interactive voice recognition and an embodied conversational agent, Laura, with human-like characteristics who used a very conversational style of speech to provide people with T2DM with personalized coaching and support on a range of essential diabetes self-management activities in their home environment. The process evaluation that received response from 66 out of 93 participants at 6 months showed that more than 80% of them considered Laura as a helpful, friendly and competent assistant and 72% described Laura as trustworthy. Different self-management styles (of users) were identified affecting app experiences. Interactive voice recognition did not offer any obvious advantages. Benefits of personalization and tailoring.	Randomised controlled trial Qualitative study reporting user experiences. "My Diabetes Coach" Programme including an app with an embodied conversational agent (Laura) providing gamification and human-like features.
Meyerowitz-Katz et al. (2020) [46]	Chronic disease self-management.	Drop-out rate.	Varying and tailored messaging. Self-management skills. Allowing contact with health care provider. Guidance/support.	Systematic review Wide range of diseases. Heterogeneity.

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Monteiro-Guerra et al. (2020) [53]	Physical activity coaching.	Not specified.	Authors highlight 3 aspects they consider key to engagement and behaviour change: - Tailoring. - Based on behaviour change theories. - Gamification.	Scoping review. Theoretical review. No quantification of association/causality.
Szinay et al. (2020) [48]	Promotion of healthy behaviours (smoking, alcohol, physical activity, diet).	Number of logins Frequency of use Other relevant measure tracking user engagement.	Psychological capability: - User guidance. - Health information. - Statistical information on progress. Memory, attention and decision processes: - Well-designed reminders. - Less cognitive load, including automatization of data collection. - Coping games. Behavioural regulation: - Self-monitoring. - Established routines. - Safety netting. Physical opportunity: - Availability, accessibility and low cost. - Interactive and positive tone in messages. - Personalization to needs. Social opportunity: - Health professional support. - Community networking. - Competition. Automatic motivation: - Feedback. - Rewards. Reflective motivation:	Systematic review Authors provide a list of recommendations built on the identified factors to guide app developers, health app portal developers and policy makers.

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			- Goal setting.	
Wang et al. 2021 [54]	Health issues in general (not otherwise specified).	Mobile app acceptance and use.	Social Dimension: - Social networking increases interest and promotes users' staying power. - Source credibility: published by credible mass media, recommendation by healthcare professionals, support from healthcare institutions. - Legal supervision. App design: - Accuracy, timeliness, and relevance. -Core function: reminders, notifications, encouragement, follow-up and goal setting. - Personalization. - Gamification. - Clean and simple interface. - Efficiency. - Perceived usefulness. - Security and privacy. - Cost.	Systematic review
Wei et al. (2020) [54]	Healthy lifestyle promotion, chronic disease prevention.	User feedback.	Personalization: - Self-assessment, feedback and customisation. Reinforcement: - Rewards and reminders. Communication: - With peers and health care professionals. Navigation: - Ease of use, automation, guidance. Credibility: - No advertisements, evidence-based, privacy, data protection. Message presentation:	Most included articles were qualitative and mixed methods studies.

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			- Simple, specific, positive, non-judgemental, gamification. Interface aesthetics: - Attention-grabbing, simplicity and consistency.	
Wu et al. 2021 [55]	Management of depression and anxiety.	Duration of use and completion of interventions.	Unexpected negative association between Persuasive System Design features (such primary task support, e.g., self-monitoring and personalisation) and engagement, as measured by completion rate.	Systematic review Heterogeneity. No association between engagement and effect on symptoms.

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5 HEALTH APPS: BEHAVIOUR CHANGE

Although usability and engagement are desirable, the final aim of health apps is in fact to lead to lifestyle changes in their users. The WARIFA solution will be designed to reduce risk behaviours associated with the development of non-communicable chronic diseases, i.e., to promote healthy eating and physical activity, as well as avoidance of tobacco, alcohol and sun exposure. In addition, tools will be developed to reduce the burden of therapy for people with type 1 diabetes and help them reduce the risk of complications from the disease.

Table 6 lists the features associated with behaviour change with the use of Health Apps. As the ultimate goal of behaviour change is improved health outcomes, this table also includes studies reporting health outcomes. According to a systematic review of 52 randomised controlled trials, the evidence for an effectiveness on behaviour change is varied. Regarding healthy eating, for example, there is significant evidence of efficacy in food choice (increasing vegetables and reducing salt), but not in apps focused on control or restriction. Regarding physical activity, there is evidence of a change in the number of daily steps, when this is monitored, and a reduction of sedentary time, but not on moderate-high intensity physical activity [56].

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Table 6 Features associated with behaviour change and health outcomes with the use of Health Apps.

Author (Year) [Ref]	Aim of the app	Behaviour change or health outcomes	Features associated with behaviour change	Comments
Fitzgerald et al. (2017) [57]	Health issues in general (not otherwise specified).	Behaviour change in general.	Key features; education, personalisation and networking. Most effective: range of strategies as cognitive behavioural therapy, goal setting, real time feedback. Collection of data, personalisation, use of data in social networking to reinforce desired behaviour. Less effective: little involvement by professionals can result in limited use, inflexibility, irrelevant content, poor customization capacity.	Systematic review. Discussion of behaviour change theories.
Fu et al. (2017) [38]	Diabetes self-management.	HbA1c.	Manual data entry restricted usability. Interactive features (Realtime feedback) beneficial for glycaemic control. Combination of app with other components improved glycaemic control.	Systematic review Majority of included studies of less than 6 months duration. Many interventions had several additional components (e.g., interaction with social forum or health care professionals).
Hosseinpour et al. (2019) [58]	Increase physical activity.	Physical activity.	Feedback: list types of feedback found. Feedback positively affected users' physical activity. Some studies found negative effect for instance if the avatar was sad (they stopped checking). Goal setting: various effects, too high goals could result in lack of motivation, while goals also had a good effect on physical activity. Reward: badges, butterflies, trophies, ribbons, stars, electronic postcards, encouraging messages, and collectable points. Social sharing: Sharing with strangers in segregated groups appeared to have mixed effects".	Systematic review guided by theoretical framework.

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			Competition: Conflicting results.	
Iribarren et al. (2021) [59]	Promote health and/or manage disease. Any disease could be included, but the majority of studies was investigating on chronic or lifestyle related diseases.	A variety of health outcomes including behaviour change.	Interactive communication. Reminders. Gamification. Journaling ("diary").	Systematic review Logistic regression showed a slight positive effect (not significant) on health outcomes for these features. No data on app usage.
Li et al. (2020) [60]	Self-management of hypertension.	Medication adherence Outcomes mostly related to blood pressure control.	Medication reminders. Interaction with health care professionals. Multiple app functions.	Systematic review Trials with a tailored frequency of reminders, a patient-doctor interactive loop, and multifaceted functions showed a larger overall effect on blood pressure, compared with trials with a fixed frequency of reminders, a noninteractive loop, and a single function. Not all studies used apps.
Peiris et al. (2019) [61]	Smoking cessation.	Number of quitters.	Participants suggested: - Improve functionality. - Greater customization of messages. - Integration with existing social platforms. - Gamification features.	Pilot randomised controlled trial.
Stuckey et al. (2017) [62]	Increase physical activity.	Step count. Energy expenditure. Self-reported change in physical activity.	No conclusive evidence supporting a specific behavioural theory or change technique superior to others. App features evaluated: - Feedback. - Motivational cuing. - Goal setting. - Information and education.	Systematic review Some studies included interactions with health care professionals.

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			- Reminders. - Rewards. - Social support. - Gamification. Behavioural change theories evaluated: - Five A's model. - Learning theory / operant conditioning. - Self-determination theory. - Social cognitive theory. - Social influence theory. - Theory of reasoned action. - Transtheoretical model (stages of change).	
Tong et al. (2021) [63]	Improve lifestyle behaviour.	Various lifestyle-related behaviours, e.g., physical activity, diet, smoking and alcohol consumption.	Automatically captured data acquisition was associated with higher effectiveness than user-reported data (but similar effectiveness in systems that used both). Interventions mostly personalized their content and rarely personalized other features such as intervention timing, dosage, or delivery. Personalization algorithms were scarcely specified or described in detail.	Systematic review Other modalities included in some studies (websites, emails or interaction with health care professionals).
Villinger et al. (2019) [64]	Improve dietary behaviours (patients and healthy citizens).	Body mass index, clinical parameters (e.g., blood lipids) and nutrition behaviours (Healthy Eating Index, total caloric intake, meal types, specific foods or nutrients…).	Positive effects on obesity indices, blood pressure, lipids and nutrition behaviours. No significant effect of specific or number of behaviour change techniques. The inclusion of additional treatment components besides the app or the number or type of BCTs implemented did not moderate the observed effectiveness.	Systematic review Overall pooled effect size was positive and significant. Effects are likely small but reliable. Long-term (> 6months), effects were generally small and non-significant.

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6 CONCLUSIONS

Health Apps have the potential of improving health behaviours and relevant health outcomes. However, in order to achieve this, they have to be appealing to end-users, lead to their engagement and promote evidence-based interventions. Although different criteria are used to assess both usability and user engagement, some (mostly weak) recommendations can be made to app developers, based on published evidence (see Table 7).

To be usable, an app has to be effective, efficient and satisfactory to the user, but interaction with it has to be simple, too. The interface should be intuitive, but also flexible, customizable, adaptable to the (changing) needs of the end user. And even if the app is easy to use, support should be available to the user, and it should be quick and simple.

To be engaging, an app has to be satisfactory, rewarding and entertaining. User-centredness and personalisation are again central, as are privacy and credibility. The app should run smoothly, without big resource demands from the user. Finally, using behaviour change techniques, gamification and social interaction may also increase engagement.

Less evidence is available on the features that lead to behaviour change and improved health outcomes, but they seem to be based on the same principles as for engagement, emphasizing appropriate behaviour change techniques.

Table 7 Recommendations for Health App development for optimal usability and engagement

User-centredness	App development should involve end-users at early stages of the design process.
Beliefs	Negative beliefs about the behaviour to be changed should be addressed from the beginning.
Human support	Even if the app is easy to use, human support from health providers, caregivers or family is valuable.
Customised simplicity	Comfortable and intuitive screen layouts and menus, minimizing manual data entry, avoiding long multi-step tasks, assistance in proportion to the learning-curve stage of the user and making useful educational content being available to the user at any time.
User characteristics	Considering age, gender, baseline health, culture, desire of empowerment, disease stage, health literacy, digital literacy and other user-related factors that can influence engagement.
Accessibility issues	Enhancing education, awareness, ease of payment and support structures for users and providers. Personalisation to different degrees of physical and cognitive capabilities.
Privacy	Transparency and choice of data use/sharing.
Credibility	Prescription by health care professionals and support by scientific organisations improve user confidence. Validation methods should be described.
Technical issues	If possible, avoiding need for internet connection, high usage of battery or storage capacity, conflicting operating systems, slow running apps and costs associated with app use. When external hardware is needed for app functions, it should be minimized and kept as simple and comfortable as possible.
Gamification	A wide range of features have been proposed, especially those that enhance mechanisms based on behaviour change theories. This includes: challenges, leader-boards, level-up systems, reward mechanics, avatars…
Social interaction	Facilitating social interaction. It can be implemented in different ways ranging from allowing in-app interaction with family and friends to full integration with existing social media platforms or health care professionals.
Tailoring model and behaviour change theory	Increasing evidence suggests using feedback, goal-setting, user targeting, adaptation, user education, context awareness, self-learning, incentives, predictive analytics and/or personalisation. The tailoring model of the app should be based upon behaviour change theories, which also are diverse and not fully explored. Most apps use a small array of behaviour change techniques to increase engagement, and probably different users will interact better with different behaviour change techniques.

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