

UNIVERSITY OF MODENA AND REGGIO EMILIA

PhD Course in Clinical and Experimental Medicine

Curriculum: Public Health

Cycle XXXV

Director: Prof. Marco Vinceti

**MEDICAL SELF-TRIAGE DURING COVID-19 PANDEMIC:
DEVELOPMENT AND USABILITY OF THE
SMASS PATHFINDER COVIDGUIDE**

PhD candidate: Dr. Jacopo Demurtas

Supervisor: Prof. Elena Righi

Co-supervisor: Prof. Roberto D'Amico

Academic year 2021/2022

Index

Abstract.....	1
Sinossi.....	4
Definitions.....	7
General background.....	9
General aims.....	24
Methods	25
Results.....	37
General discussion.....	62
Conclusions.....	72
Appendixes.....	74
- SMASS AfyaGuide Algorithm.....	75
- Questionnaire on the usability of the AfyaGuide	82
References.....	89

Abstract

Background:

Covid-19 represented a big challenge for healthcare professionals, which were asked to strengthen their efforts to cope with the pandemic.

During its first phases, many apps were launched to tackle the surge of covid-19, among those the SMASS Pathfinder CovidGuide app, a class IIa CE registered medical device, that helps gather crucial information about a patient's clinical picture and document the patient's medical history in a structured manner.

The app is a conversational agent (CA) with a neural network artificial intelligence (AI) which asks specific questions about warning signs and supports users in finding a solution for their healthcare problem.

In this work it was evaluated whether a self-triage app for covid-19, namely the SMASS Pathfinder CovidGuide, could be used by people to assess their symptoms, if the indications given by the app would be or not followed by the app's users in different scenarios, which are the features of the potential users of such an app. Indirectly, this work is aimed at understanding if the use of the app would be useful to decrease the burden on primary care professionals.

Methods:

- An app was developed, based on the SMASS Pathfinder and on the indications given by a critical appraisal of the existing literature on Corona virus respiratory disease in early 2020
- Relevant literature on safety and efficacy of self-triage tools and symptom checkers in primary care from database inception to May 2022 was assessed through a systematic review
- The features of the population's that used the app in a 2-year period, ranging from its inception to April 19th 2022, in Germany, where the app was embedded in the primary emergency care system, Switzerland and Italy
- The app was readapted to a different context, namely the Kenyan country
- A pilot study on its acceptability and usability, the AfyaGuide pilot study, was developed

Main Results:

Only 3 studies were included in the systematic review and only one was done in the primary care setting. Apps evaluated were Drugs.com, FamilyDoctor, ADA and Omaolo. A meta-analysis was not possible. Two works were deemed to be at high risk of bias, whilst for the third one evaluation of risk of bias was not possible as it was presented as conference abstract.

The database exploration showed that, on a total number of 374179 consultations, the most frequent advice given was the indication to see the doctor today (38% of the consultations). About 62% of patients were females, 75% in the age range 14-49 years, main symptoms reported were viral syndrome not otherwise specified and throat symptoms complaints. 75.692 patients, 20% of cases, received indication for self-monitoring with safety net (ie. indications on what to do in case of symptoms' worsening).

The AfyaGuide pilot study carried out in Kenya, on a sample of 1617 users, showed good usability of the app and intention to comply with app's advice.

Conclusions:

Data retrieved so far depict the core features of the users of the CovidGuide app: women in age range 14-49 were the most represented category of users. Further exploration of factors influencing intention to comply with the app's advice may help to understand what brings people to use this kind of app and eventually follow the given advice.

In Europe and in Kenya, the app has shown so far a good usability and intention to comply (ItC) with the app's advice.

Moreover, the huge number of consultations ending with the indications for self-monitoring may be investigated to understand whether it is possible to use these tools to decrease healthcare professionals' burden and improve health coverage.

Keywords:

mHealth, Triage, Artificial Intelligence (AI), covid-19, Usability

Sinossi

Contesto

La covid-19 ha rappresentato una grande sfida per gli operatori sanitari, chiamati a intensificare i loro sforzi per far fronte alla pandemia.

Durante le prime fasi sono state lanciate molte applicazioni, tra cui l'app SMASS Pathfinder CovidGuide, un dispositivo medico di classe IIa CE che aiuta a raccogliere informazioni cruciali sul quadro clinico del paziente e a documentare la sua storia clinica in modo strutturato.

L'app è un agente conversazionale (CA) con intelligenza artificiale (AI) a rete neurale che pone domande specifiche sui segnali di allarme e supporta gli utenti nella ricerca di una soluzione per il loro problema sanitario.

In questo lavoro è stato valutato se la app per il self-triage SMASS Pathfinder CovidGuide, potesse essere utilizzata dalle persone per valutare i propri sintomi, se le indicazioni fornite dall'app potessero essere seguite o meno dagli utenti in diversi scenari, quali fossero le caratteristiche dei potenziali utenti di tale app.

Indirettamente lo studio si propone di valutare se l'uso dell'app possa rivelarsi utile per diminuire il carico sui professionisti delle cure primarie.

Metodi

- è stata sviluppata l'app, basandosi sullo SMASS Pathfinder e sulla valutazione critica della letteratura esistente sulla malattia respiratoria da Corona virus all'inizio del 2020
- è stata esplorata la letteratura con una revisione sistematica sulla sicurezza e l'efficacia degli strumenti di self-triage e di controllo dei sintomi nelle cure primarie
- sono state identificate le caratteristiche della popolazione che ha utilizzato l'App in un periodo di 2 anni, dal suo lancio al 19 aprile 2022, in Germania, in Svizzera e in Italia.
- la App è stata riadattata ad un contesto diverso, quello keniota
- è stato effettuato uno studio pilota sulla accettabilità e usabilità della app, lo studio pilota AfyaGuide

Principali risultati:

- Nella revisione sono stati inclusi solo 3 studi e solo uno effettuato nel contesto delle cure primarie. Sono state valutate le app Drugs.com, FamilyDoctor, ADA e Omaolo. Non è stato possibile effettuare una metanalisi. Due lavori sono stati considerati ad alto rischio di bias, mentre per il terzo non è stato possibile valutare il rischio di bias in quanto presentato come abstract.
- l'esplorazione del database ha mostrato che su un numero totale di 374.179 consultazioni, il consiglio più frequentemente fornito è stato l'indicazione di essere valutati dal medico il giorno stesso (38% delle consultazioni). Il 62% dei pazienti era di sesso femminile, il 75% nella fascia d'età 14-49 anni, i principali sintomi riportati erano sindrome virale non altrimenti specificata e disturbi alla gola. 75.692 pazienti, il 20% dei casi, hanno ricevuto indicazioni per l'automonitoraggio con rete di sicurezza (cioè indicazioni su cosa fare in caso di peggioramento dei sintomi).
- lo studio pilota in Kenya, effettuato su 1617 soggetti, ha mostrato una buona usabilità e disponibilità a seguire le indicazioni della app (ItC).

Conclusioni:

I dati raccolti descrivono le caratteristiche principali degli utenti di questa applicazione: le donne di età compresa tra i 14 e i 49 anni sono la categoria più rappresentata. Un'ulteriore esplorazione dei fattori che influenzano l'intenzione di seguire i consigli dell'app, può aiutare a capire cosa porti le persone a utilizzare questo tipo di app e a seguire i consigli forniti.

In Europa e in Kenya, l'applicazione ha mostrato finora una buona usabilità e intenzione di aderire ai consigli dell'applicazione.

Inoltre, l'enorme numero di consultazioni che si concludono con le indicazioni per l'automonitoraggio, può essere studiato per capire se sia possibile utilizzare questi strumenti per ridurre il carico degli operatori sanitari e migliorare la copertura sanitaria.

Parole chiave: mHealth, Triage, Intelligenza Artificiale (IA), covid-19, usabilità

Definitions

Symptom checkers: application or software tools that enable patients to input their symptoms and biodata to produce a set of differential diagnoses and clinical triage advice.

The diagnostic function of symptom checkers is to provide a list of differential diagnoses, ranked by likelihood[1].

Artificial intelligence enabled computerized decision support softwares – (CDSS): intelligent entities used to provide healthcare workers (HCPs) with indications for decision making or recommendation, general or linked to a specific disease or pattern (such as, clinical diagnosis or therapy planning).

Conversational Agents (CA): agents that interact with users via written or spoken natural language. CAs accept as input natural language as speech, text, or video; in addition, they may receive input from several different sensors. CAs are required to process the input and provide relevant advice or feedback in a form of text or speech or by manipulating a physical or a virtual body. Some CAs can take specific actions either in the real world or in the virtual world. Most CAs use natural-language processing to understand and generate speech, and some may also have engagement and personalization abilities [2]. In recent years the technology behind CAs has rapidly improved[3-5], enabling CAs to be applied in various contexts, ranging from customer service[6] to healthcare[7].

While human service encounters are limited by time and space constraints, CAs can support users at any time, place, and provide a comfortable and convenient user experience[8]. Furthermore, CAs provide convenient access to information or managing user requests, covering typical service tasks (e.g., searching for information or writing e-mails) and personal assistance (e.g., Siri or Alexa for everyday tasks)[9,10].

Chatbot:[11]

A chatbot is a typical example of an AI system and one of the most elementary and widespread examples of intelligent Human-Computer Interaction (HCI). It is a computer program, which responds like a smart entity when conversed with through

text or voice and understands one or more human languages by Natural Language Processing (NLP). In the lexicon, a chatbot is defined as “A computer program designed to simulate conversation with human users, especially over the Internet”. Chatbots are also known as smart bots, interactive agents, digital assistants, or artificial conversation entities.

Theories of Technology Acceptance

A set of theoretical models aimed at describing the characteristics that influence the adoption of a technology.

General Background

Primary Healthcare Crisis in Europe and beyond

Health care systems, in Europe and beyond, are facing a moment of great crisis, which mainly affects the universalist models and is particularly focused on territorial primary care [12].

Evidence of this is in the recent uprisings, riots and strikes that took place in Spain and England, where primary care workers manifested their anger and the preoccupation for their condition [12].

The main concern is represented by the exploitation of practitioners in systems that have increasingly limited resources and that tend towards quantity instead than service quality, as protested in Spain, where doctors complained about the short timeframes allowed for the clinical assessment of patients. In England, on the other hand, a tendency has emerged on the part of National Health Service workers to find innovative, more rewarding contract formulas, which are progressively and inexorably undermining the National health service (NHS) [12].

The NHS, from being a model, now dismembered and impoverished, is losing staff and resources. Even in Spain staff is reduced, and resources are scarce. The situation presented is also evident in other healthcare models, such as the Italian model, the German model - with fewer and fewer doctors - and the French model [13].

Italy

Italy itself is in crisis. Its health system is modeled in a similar way to the English one, therefore its weaknesses and strengths are the same.

In Italy, there are (2019 data) 6.16 doctors per 1,000 inhabitants and 4.05 nurses per 1,000 inhabitants. The nurse-doctor ratio is 1.5 nurses per doctor.

In 2018, 17.89% of doctors in Italy worked as General Practitioners (GPs), compared to 21.47% represented by the EU average. GPs are steadily decreasing due to planned but uncompensated retirements and retirements related to the unsustainability of the job itself, in 2019 there were 0.88 per 1000 inhabitants [13].

In 2019, general practitioners in Germany were 1.01 per 1,000 inhabitants.

In 2019, the number of doctors (4.39) and nurses (11.78) per 1,000 inhabitants in Germany was higher than the average of the EU in 2018, represented by 3.93 doctors and 8.16 nurses per 1,000 inhabitants. In Switzerland the total number of doctors and nurses was even higher, 4,45 and 17,96 per 1000 inhabitants, with significant differences between rural areas and the most important urban areas [14,15].

Today, especially in the northern regions Italians, GPs are asked to manage as many as 1,800 to 2,000 patients and completely uncovered areas are appearing, leaving many patients without primary care [16].

To cope with the shortage of professionals reported in the last years, Italy adopted the strategies of increasing the number of trainees [16], both in the primary care setting and in other settings.

Nevertheless, retirements are peaking—following the COVID-19 pandemic and increasing burnout—and low numbers of new doctors are entering the health service. The major Italian general practitioner (GP) association (FIMMG) reported that as of Jan 1, 2021, there were 40 769 GPs in the country, but with 3000 GPs esteemed to retire each year, 31% of these professionals will be out of primary health care by 2024 [17]. The DM71 [17], recently converted in DM77 propose and plan a new organization of the resources with new structures, networks, actors and pathways for the territorial healthcare [18], financed with the resources of the PNRR [19,20].

Germany

The German health care system is strongly characterized by the separation between the outpatient and inpatient care sectors. Health policy debates and reform attempts in recent decades have been focused on improving the networking of the sectors or overcoming the sector boundary [21]. To date, however, no breakthrough has been achieved. This characteristic of German health care is understandably a major problem, especially in the areas of acute and emergency care.

The first point of contact for patients is usually their general practitioner or a specialist. In Germany, there is basically a free choice of doctor (even for the 90% of patients with statutory health insurance). Outside office hours, the Associations of Statutory Health Insurance Physicians (regionally organized associations that carry out both demand planning and remuneration allocation for all physicians who provide care to

statutorily insured patients) guarantee an after-hours on-call service. These services are mainly provided in centralized emergency practices (staffed by physicians in private practice, usually located at hospitals) or by the mobile on-call service (home visits) [21]. However, patients in Germany are also free to visit a hospital emergency room. Until the middle of the last decade, there was a steady increase in the use of emergency departments, especially by patients with less urgent treatment needs, but this trend has been reversed— not least by professionalizing the on-call service structures and establishing structured triage on the telephone to improve patient steering. In addition to the telephone service, structured triage in Germany is now also available to patients via a website for self-assessment [21].

A recent study in Germany by Methelmann et al. revealed that the urgency of health problems is often misjudged by patients, and about 70% of patients assessed their complaints differently to health care professionals in terms of urgency and necessary action [22]. On the other hand, in many countries the number of patients using emergency departments has been rapidly growing over the past years, and many policies are oriented at reducing the use of emergency departments by patients with low urgency conditions. In Germany, the number of emergencies in hospitals has risen from 14.9 million cases in 2009 to 19.3 million cases in 2016 and stayed on that level until 2020 [23].

Switzerland

The Swiss healthcare system is the result of historically evolved organisation and structures. Although health care is the responsibility of the cantons, which also bear most of the public sector costs, the Health Insurance Act regulates important health policy issues at the national level. In addition, the Federal Council has the authority to take emergency measures, like in the case of the pandemic [24].

The health care system in Switzerland is one of the most expensive in the world, but at the same time it is of high quality [24].

Patients in Switzerland pay for comprehensive and rapidly available healthcare, with high financial out-of-pocket payments and standard premiums for compulsory basic insurance [24]. The crisis highlighted major deficits in digitalisation in the healthcare sector, for example with regard to care models, data traffic and the electronic patient dossier [25]. The shortage of GPs is a national issue that has been known for a long

time. The first drastic effects have been felt by the population: more and more people no longer have a family doctor and are turning to the emergency departments of the hospitals even for harmless complaints. Others do not react to medical warning signs, - so-called “red flags” [26,27].

Africa and Kenya

Kenya is a sub-Saharan African country (SSA). The disease burden in Africa is dominated by a small number of basic health problems, such as malaria, AIDS, tuberculosis, pneumonia, diarrhea and obstetrical complications [28,29]. The African region, notably the SSA, is characterized by peculiar features. Poor health indices are present in most country, with maternal and infant morbidity rates high, very low life expectancies [29].

Among those features, the puzzling fact is that family medicine is still to be developed or scarcely developed [30,31]. Several initiatives contributed to the development and establishment of family medicine in this district, with the learning communities representing an asset of paramount importance in the dissemination of the discipline [30,32].

In SSA, however, a lack of clarity on the scope and practice of FM among policymakers often led to the discipline not being fully integrated into health systems [33].

Development of FM, with adaptation to local contexts, has taken place in many SSA countries, albeit in different ways and stages of development. The Primafamed network showed that between 2008 and 2010, the developmental stage of FM training and the acknowledgement of the discipline in the different HS improved substantially for each of the participating universities [30].

In a survey on understanding FM in SSA, some key leaders saw FM as a specialized PHC physician. However, most saw African FPs mainly as hospital specialists, a combination of the four major clinical specialties or as stepping stones to later specialization, rather than a positive career option in its own right [34].

As in other African countries, Universal Health Coverage (UHC) has moved up the policy agenda in Kenya amidst rising evidence that structural adjustment policies, introduced in 1989, which included devolving health costs onto patients through ‘user fees’, had a hugely detrimental impact on poverty while pushing many into debt [35].

Since 1989, public healthcare in Kenya has been based on a cost-sharing system. The Kenyan government embraced UHC as a policy goal only in 2018, but already in 2013 it had scrapped fees at primary health care facilities and introduced free maternal care and free treatment for under-fives [36].

In many situations, African people are not able to reach out for a family doctor and in some cases, they are not able even to find a healthcare solution in their context.

For instance, a study by Wilunda et al. [37], reported that access to health services in South Sudan is hampered by a poorly functioning health system that is plagued by chronic problems such as a shortage of human resources, lack of health infrastructure and supplies, and weak management. This is mirrored in other African regions.

Healthcare policies in low-income countries are primarily focused on improving technology, expanding access and increasing the quality of health service delivery with less attention paid to patient demand and health-seeking behavior [38].

Patients will seek health care at the nearest primary healthcare facility when sick and eventually follow the advice received. When patients do not visit the nearest facility, it is assumed that high costs are preventing them from seeking care [38]. Leonard et al. suggest that this view of patient behavior, whether implicit or explicit, does not fit the real-world experience, and more should be done to explore and understand health seeking behaviors. Kenyans say that over decades of evisceration of the healthcare system, public healthcare has become “*healthcare for the poor*”, care for those without the means to buy private healthcare services. The deterioration of public healthcare exists in tension with state support for private health care, with the quality of healthcare one can access increasingly associated with class identity. Private healthcare markets are growing alongside middle classes with access to health insurance and credit [39].

Covid-19

In March 2020, the World Health Organization (WHO) declared the covid-19 outbreak a global pandemic. Covid-19 is caused by SARS-CoV-2, a variant of coronavirus [40]. Covid-19 pandemic represented a huge challenge, and a massive defeat for most primary care and healthcare systems. Professionals were unprepared, often misguided, there were no clear instructions and politicians [41] lack the leadership necessary to take timely and consistent decision [42].

In the so called “leadership vacuum” [41] healthcare professionals were left alone to face the pandemic, with casualties and an impressive increase in burnout, that often lead to abandon the profession or choosing an early retirement.

The covid-19 pandemic has forced the reorganization of health care services, and the implementation of contingency plans which impacted Primary Health Care (PHC) workers’ daily demands [43].

Covid-19 and lockdowns hit the population and impacted on people functioning [44,45], impairing social aspects of daily living, spreading fear and having devastating economic effects [46].

Recent reviews reported that covid-19’s impact was responsible of

Symptoms may be mild, with rhinorrhea, cold, and malaise, seldom with fever, to impressive and brutal respiratory failures, often accompanied by a thorough destruction of the interstitial architecture of lungs.

Covid-19 was responsible, from its start to May 2023, of over 766440796 confirmed cases and 6932591 deaths. Frail people, but not necessarily older people [47] are more affected. Among the known risk factors multimorbidity, organ failure, weaker immune defense, higher viral load, male sex, previous organ damage and many more were reported [48].

Triage

Remote triage and consultation may be of paramount importance in dealing with healthcare scenarios, representing economic and ecologic alternatives to face-to-face consultation. This was highlighted by the pandemic.

The word triage derives from the French *trier* and as the meaning of prioritizing.

Triage was introduced by Dominique Jean Larrey, a surgeon of the Napoleonic Imperial Ward, who introduced it in the military to give safe and effective care to those who were more severely blunt but with good chances to survive.

Larrey’s concept was both simple and revolutionary:

“...those dangerously wounded must be attended first entirely without regard to rank or distinction and those less severely wounded must wait until the gravely hurt have been operated and addressed. The slightly wounded can go to the hospital in the first and second line, especially officers because the officers have horses” [49]

With these simple words he established for the first time in the history the concepts of time to treat and point of care.

Derkx, in his papers regarding quality of telephone triage, states that it depends (mainly) on three factors: clinical skills, communicational skills plus the ability to evaluate the information gathered [50-54].

In the reported experiences, notably the study published on the BMJ [50] with the methodology of incognito standardized patients [55], the relevance of questions posed or not posed showed brutally [50].

A primary care professional dealing with patients in the out of hours setting, handling calls at the phone, may not remind or know the essential questions to be asked in a certain scenario and this may jeopardize the advice given, leading to unsafe triage.[50] Failing to ask the right questions at the right moment, may lead to mistake time to treat and point of care [50].

It must be considered that also on training interventions to improve telephone triage and consultation, findings are scarce with no evidence specifically coming from telephone consultation studies available, as reported by Vaona et al. [56].

Greenhalgh et al proposed a model for telephone/remote consultation during covid-19 [57,58], which, interestingly, respects the structure and indications provided by Derkx et al.

To identify an emergency, triage scores are codified. The scores may be used for both face to face and remote consultation.

Triage systems score help healthcare provider in assessing case and codify emergencies and urgencies allowing them to properly triage the urgent cases, to define the priority of interventions, and to determine point of care and time to treat.

There are two main scores for triage, widely used around the world, the Emergency Severity Index (ESI) and the Manchester Triage System (MTS) [59-61].

The Emergency Severity Index (ESI)

The Emergency Severity Index (ESI) was originally introduced by doctor Wuerz, Eitel and colleagues in 1998. It is a tool for use in emergency department (ED) triage. The ESI triage algorithm yields rapid, reproducible, and clinically relevant stratification of patients into five groups suggesting 5 levels of care [62], from level 1 (most urgent) to level 5 (least urgent) [63] .

The ESI provides a method for categorizing by both patients' acuity and resource needs. Practically, it follows the stream of an algorithm starting from ESI 1 - patient is probably dying and should be seen immediately to ESI 5 – not urgent case, no resources needed.

Resources are defined as laboratory tests, radiology, intravenous fluids, specialty consultation, a simple or complex procedure and intravenous/intramuscular/nebulized medications [59].

Each patient, after a brief but thorough assessment by an experienced triage nurse, is assigned a certain number category based on how many resources are expected to be used. This process includes presentation of the patient and vital signs. Levels 3 through 5 are focused on allocation of resources, whereas levels 1 and 2 are based on patient acuity levels. For example, a 20-year-old patient with abdominal pain, right lower quadrant abdominal tenderness, and nausea should be placed into ESI level 3 because 2 or more resources were necessary to treat him/ her. It can be expected that this patient will receive blood work, intravenous hydration, and possibly some radiological studies [62]. The ESI was initially implemented in two university teaching hospitals in 1999, and then it was further refined and implemented in five additional hospitals in 2000, based on feedback from the seven sites. Several research studies have been conducted to evaluate the reliability, validity, and ease of use of the ESI [63,64]. Among a sample of more than 3,000 hospitals, the ESI was the most commonly used triage system, and more patients were triaged using the ESI than any other triage acuity system in the United States [64].

The Manchester Triage System (MTS)

Mostly used in Europe, the MTS is a 5 colors triage score (red, orange, yellow, green, and blue), ranging from red – immediate care to blue-non urgent care) [65]. The Manchester Triage System (MTS) has a list of 52 pre-defined conditions or

presentation flowcharts that are combined with the main complaint reported by the patient and recorded on a form by a nurse [59].

The risk for hospital admission reported was five times greater in high-priority patients (classified as red or orange using the MTS) compared with low-priority patients and death during hospitalization was 5.5 times higher in high-priority patients.

MTS may apparently lead to the misclassification of patients with Acute Coronary Syndrome (ACS) with ST segment elevation.

The MTS demonstrated moderate validity compared with a referenced standard independent pediatric emergency care and had sensitivity for “very urgent” classification of 63%, meaning that 37% of patients who should have been seen within 10 min were not categorised as “urgent” and it seemed to be a good discriminator for the use of diagnostic tools in the emergency department.

ESI vs MTS

The performance of the two triage systems in emergency care has been evaluated by different systematic reviews and meta-analysis [59,60].

Comparison of the Emergency Severity Index (ESI) with the MTS revealed that both tools were predictive of admission to the emergency department. However, the ESI was a better predictor of admission than the MTS. Mortality was associated with urgency category for both triage systems (van der Wulp et al., 2009).

The comparison of ESI and MTS revealed that both tools were predictive of admission to the emergency department, with ESI being a better predictor of admission than the MTS.

Van der Wulp et al. reported that sub-triage into orange and yellow categories was a serious problem with the MTS, especially in older patients, whilst similar sensitivities and specificities for hospital admission and the prediction of mortality were found for both scoring systems [66,67].

ICU admission was reported in five evaluations in adults (two performed by ESI, three MTS), Overall, sensitivity for ICU admission was moderate to good, ranging from 0.58 (95% CI 0.48 to 0.68) to 0.88 (95% CI 0.70 to 0.96) in adults.

In Storm Versloot et al. simulation study, a similar validity in both the ESI and the MTS was reported, but the ESI had a higher rate of sub-triage (i.e. classification of more-severe cases as less urgent) than the MTS, thus the MTS undertriaged a smaller proportion of patients compared with the ESI (8.3% vs 13.5%) at the cost of a larger proportion of overtriage [68,69].

Both systems seem to be reliable in most cases, however they may undertriage some conditions like ACS and some patients' categories.

Artificial Intelligence

Artificial Intelligence (AI) is concerned to both understanding and building intelligent entities (IEs) [70] able to compute how to act effectively and safely withing the surrounding environment [71,72]. Artificial intelligence is constantly evolving and is transforming the way we think about healthcare, also supporting healthcare professionals in decision-making [73,74].

From relatively simple models, useful for data mining [75,76], AI was developed in neural networks[77] and convolutional neural networks [78-80], mostly used in imaging technologies and diagnostics for their huge possibilities of detecting patterns and pathologies, for instance in cardiovascular medicine and in respiratory medicine [81,82,78].

Indeed, the domain of clinical decision support strategies is evolving by partially incorporating traditional Clinical Decision Support Systems (CDSSs) or replacing them with intelligent, learning and supporting algorithms, namely, AI-enabled Clinical Decision Support Systems (AI-CDSSs).

Artificial Intelligence enabled Computerised decision support softwares - CDSS

In CDSSs, the AI is mainly represented by a neural network[77], where we have an input layer and one or more output. Based on the input, the CDSSs guides the user to the output through several hidden layers. To date we are not yet sure of what happens in the hidden layers of a neural network.

AI-CDSSs, based on a variety of machine learning and natural language processing methods[83], are defined heterogeneously as intelligent entities used to provide healthcare workers (HCPs) with indications for decision making or recommendation, general or linked to a specific disease or pattern (such as, clinical diagnosis or therapy planning).

These definitions derive from those provided by the authors of trials or systematic reviews in the field.

Bates [84] defined AI-CDSS as computer-based systems providing “passive or active referential information as well as reminders, alerts and guidelines”.

Bright et al [85] describe AI-CDSS as electronic systems designed to aid directly in clinical decision making, in which characteristics of individual patients are used to generate patient-specific assessment or recommendations presented to clinicians for consideration. Another definition, from Payne [86], classified those tools as computer applications designed to aid clinicians in making diagnostic and therapeutic decisions in patient care.

Haynes [87] and colleagues suggest that as AI-CDSS we may define information systems aimed to support clinical decision-making linking patient-specific information in electronic health records (EHR) with evidence-based knowledge to generate case specific guidance messages through a rule or algorithm-based software.

This definition was adopted also in Moja et al [88].

The integration of AI-CDSSs in healthcare is evolving, engendering new opportunities of continued innovation in diagnostics [89-91], therapeutics [92,93], and healthcare management [94-96]. AI-CDSSs are virtual intelligent entities capable of learning from real-world use and experience while improving performance through the ability to adapt to needs and context [97].

Despite the growing enthusiasm for the promising role of AI-CDSSs in healthcare, their adoption is influenced by human and technological factors [98]. Among the human-related factors, we can include beliefs, digital literacy, and education [99], along with the net benefit perceived by users and organizations [98].

Many professionals, clients, and patients, see the use of CDSS as something to fear, a threat. Many as a huge opportunity. A realistic assessment of the needed human skills for successful implementing these innovative devices in healthcare settings is required, especially in times of professional shortage and lack of resources affecting all the most important healthcare systems.

Certainly, such tools to be used must prove their security and reliability.

Along with these, technological factors are involved in this complex process: transparency, time-related efficiency, ease/complexity of use, clinical environment interaction adaptability capability, a respectful way of knowledge and information delivery, and a rigorous process of acquiring and elaborating scientific evidence [83].

However, despite the many aforementioned advantages of AI, much remains to explore on its impact into healthcare processes dynamics (for instance in the patient-doctor relationship), to avoid facilitating its erosion [100].

Several models were proposed to describe what influences people in using a new technology, with different constructs and perspectives. Among those models, of relevance is the Unified Theory of Acceptance and Use of Technology (UTAUT), that may help understand factors underlying the use of digital devices such as AI-CDSS in healthcare.

The Unified Theory of Acceptance and Use of Technology

From its debut in 1986 (Davis) the theory of technology adoption was revised and modified many times, employed in different setting – commercial and not commercial - and for different purposes. Among the models and theories for technology adoption, the Unified Theory of Acceptance and Use of Tecnology (UTAUT) is one of the most used and represents a central tenet in digital services development and distribution. Born to be used in an organizational context, it moves from Davis experiences [101-103] and was further developed by Davis and Venkatesh in more complex models, which consider various factors that may impact on technology acceptance and use [104,105]. The theoretical model of UTAUT suggests that behavioral intention impacts deeply on the actual use of technology. In the model, the perceived likelihood that somebody will adopt the technology depends on the direct effect of four key constructs, namely performance expectancy, effort expectancy, social influence, and facilitating conditions [105].

Performance expectancy is defined as *"the degree to which an individual believes that using the system will help him or her to attain gains in job performance"* [105].

Effort expectancy is defined as *"the degree of ease associated with the use of the system"* [105]. Effort Expectancy is constructed from perceived ease of use and complexity

Social Influence is defined as *"the degree to which an individual perceives that important others believe he or she should use the new system"*

Facilitating conditions is defined as *"the degree to which an individual believes that an organisation's and technical infrastructure exists to support the use of the system"* [105].

The effect of predictors is moderated by age, gender, experience and voluntariness of use [105]. The moderation effects of age, gender, experience and voluntariness of use define the strength of predictors on intention. Age moderates the effect of all four predictors. Gender effects the relationships between effort expectancy, performance expectancy and social influence. Experience moderates the strength of the relationships between effort expectancy, social influence and facilitating conditions. Voluntariness of use has a moderating effect only on the relationship between social influence and behavioral intention [105].

By introducing three new constructs and altering some relationships, for instance removing the voluntariness as a moderator in the original model to adapt it to the consumer technology use context, the authors developed the UTAUT2 [106,107]. The goal of the theory was to represent an overarching framework for examining technology acceptance. The extension was designed to give a higher precision in explaining user behaviour [108]

This model postulates that the use of technology by individuals is influenced widely by the effect of hedonic motive, cost/perceived value and habit, moderated by age, gender and experience [106,107].

Hedonic motivation is defined *"as the fun or pleasure derived from using technology, and it has been shown to play an important role in determining technology acceptance and use"* [107]. Enjoyment of the user experience was reported to have an impact and represented a strong predictor of consumer technology use [109,110]. Price value is defined as *"consumers' trade-off between the perceived benefits of the applications and the monetary cost for using them"*[107] (Venkatesh, Thong & Xu, 2012). A positive relationship between perceived value and intention to use indicates that a user perceives the benefits of technology use as higher and more important than the associated monetary costs. Habit is defined as *"the extent to which people tend to perform behaviors automatically"* [107].

The extended version of UTAUT resulted in several theoretical contributions. The model explains 74 % of the variance in behavioral intention and 52 % of the variance in technology use, which suggests that the model has high predictive validity when applied to the consumer segment. The supported effects of price value, hedonic

motivation and habit indicate three significant drivers of consumers' intention to use or actual use of technology [107].

Symptom checkers and self-triage tools

Recently, covid-19 pandemic enhanced the development and use of a specific kind of CDSS [7,111-113], symptom-checkers, which may help patients understand the point of care and time to treat in several clinical conditions. These entities, by combining AI knowledge reasoning techniques and the functional models of clinical decision support system [114], represent a paradigm shift [115].

During the pandemic, many apps were launched, to help patients assess symptoms that could be the presentation of a covid-19 and generate indications for those patients regarding the right point of care and time to treat [116].

These apps, called symptom checkers or self-triage tools, are applications helping patients with a first level triage. They may be conversational agents, apps simulating a conversation model with a chatbot and sometimes they may have an embedded artificial intelligence.

From their launch and during the last decades, symptom-checkers and self-triage tools seem to show a promising role, notably in conditions of health care professional shortage, lack of resources and organizational problems [117-119].

These tools are based on algorithms, often powered with an artificial intelligence (AI) in one of its simplest presentations, the neural network.

In a neural network organization, customers or patients may give inputs to the tool which are converted in an output that, in the case of self-triage tools and symptom checkers, is represented by the indication on time to treat and point of care, namely a definition of the urgency of the intervention, and seldom management instruction for the cases deemed to be less urgent. Neural networks models are characterized by machine learning processes with the need of data to feed the intelligence and make the tool learn how to deal with different scenarios [77].

Covid-19 outbreak enhanced their use and their diffusion, and during the pandemic the use of this tools increased, leaving nevertheless concerns on their safety, efficacy, and accuracy [116].

Since the seminal paper from Semigran [1], in which several self-triage were compared based on their proficiency in solving simulated clinical case scenarios, there have been several works on symptom checkers, mostly addressing their usability, rarely investigating their safety and accuracy [120,119].

Self-triage tools could prove themselves useful and economics tools to ensure care provision [119].

New Public Management and Universal Health Coverage

The political drive towards the privatization of services is intense and inexhaustible on the spread of the New Public Management, with the risk that the citizens with less money could be the ones to pay the price if no corrective measures are taken: this would lead to a reduction in the accessibility of the system and, consequently, to a reduction of its equity, in Europe and in other continents.

The current social, political and leadership crisis has accelerated the process, further catalysed by the Covid-19 pandemic, which has disclosed all the contradictions and weaknesses of the various healthcare systems [41].

The digitalization of processes and the digital sharing of information could represent a tool to lighten the load on systems, but still many concerns remain, linked to the low digital literacy of the actors involved as well as to the real implementation capacities of political and administrative leaderships [12]. In this scenario, telemedicine strategies for monitoring patients [121], simplifying the communication among professionals[122], providing effective remote consultations [122] and aiming at improving communication and outputs could prove useful and valuable.

In conditions of professionals' shortage, lack of resources and poor infrastructures, it is mandatory to afford inequities and difficulties in the access to healthcare services, delivering new ways of care, tackling challenges eventually through telemedicine strategies, striving to guarantee universal health coverage (UHC) [123].

General Aims

In this work the applicability and the performance of a self-triage App for covid-19, namely the SMASS Pathfinder CovidGuide was investigated.

Applicability and performance were evaluated by:

- Exploring the main features of the potential users
- Assessing the ability of people to use the App to evaluate their symptoms.
- Assessing the attitude of users to follow the indications given by the app in different scenarios.

Methods

To do this, several projects were carried out, testing the app use in different geographical and sociodemographic contexts, and their methodologies are reported below.

Development of CovidGuide

- an app was developed, based on the SMASS Pathfinder and on the indications given by a critical appraisal of the existing literature on Corona virus respiratory disease in early 2020. In February 2020, a multidisciplinary team of doctors, epidemiologists, computer engineers, methodologists, psychologists and patient experts, based in Switzerland, Germany and Italy, was recruited to plan, design and develop the CovidGuide web-app.[124] The algorithm was first produced by the Italian team CONSTANTINE (Covid Neural Self Triage App – National Telemedicine Interdisciplinary Network). The clinical prediction rules for the diagnosis of covid-19 disease were outlined by analysing data available from Chinese and Italian studies, concerning the clinical presentation of covid-19 [124]. Relevant experience of primary care emergency professionals involved in the first wave and working in Northern Italy were also considered.

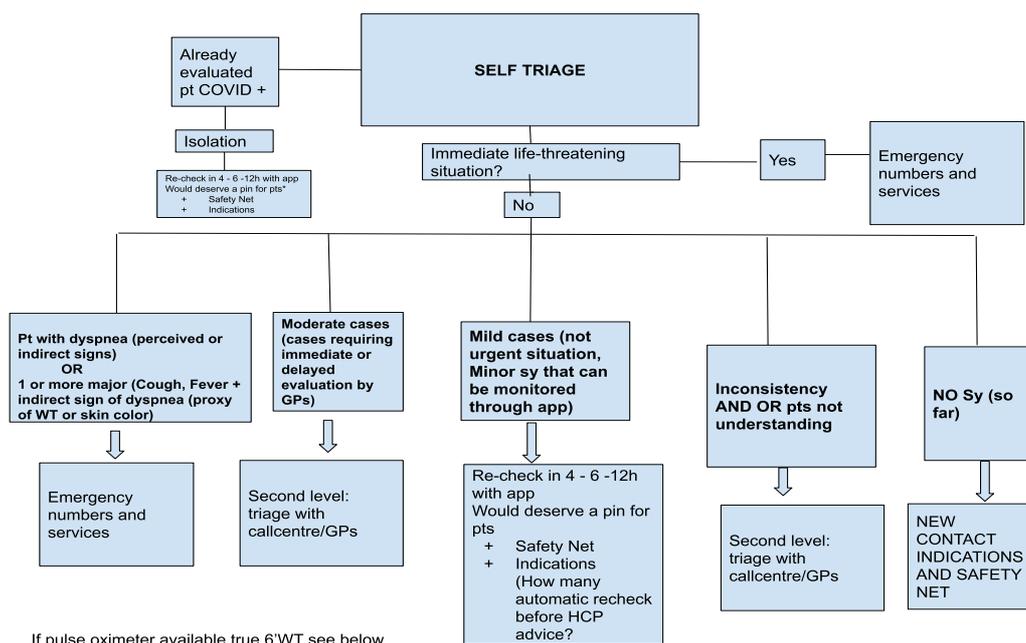


Figure 1: Original draft of the CovidGuide proposed algorithm

On this basis, the different scenarios of the self-triage web-app were defined (Figure 1).

Covid-Guide was based on the software SMASS, which had already been used for structured triage in Germany and Switzerland. SMASS (Swiss Medical Assessment) is a computerised decisional support software of Swiss origin, used in the German emergency-urgency system since 2019 under the name SmED (Strukturierte medizinische Ersteinschätzung in Deutschland).[125] The CDSS is integrated into the German healthcare system, used when the single emergency number 116117 is contacted for urgent health reasons.[126]

CovidGuide was launched as a web-app on 9 April 2020, available in German, French, English and Italian (Figure 2).



Figure 2: Frontpage of the SMASS Pathfinder CovidGuide web app

It is a conversational agent, notably a chatbot. The chatbot is equipped with social cues (Figure 3), including a human 2D avatar, gender, and greeting the users (“Hello and welcome, ...”).

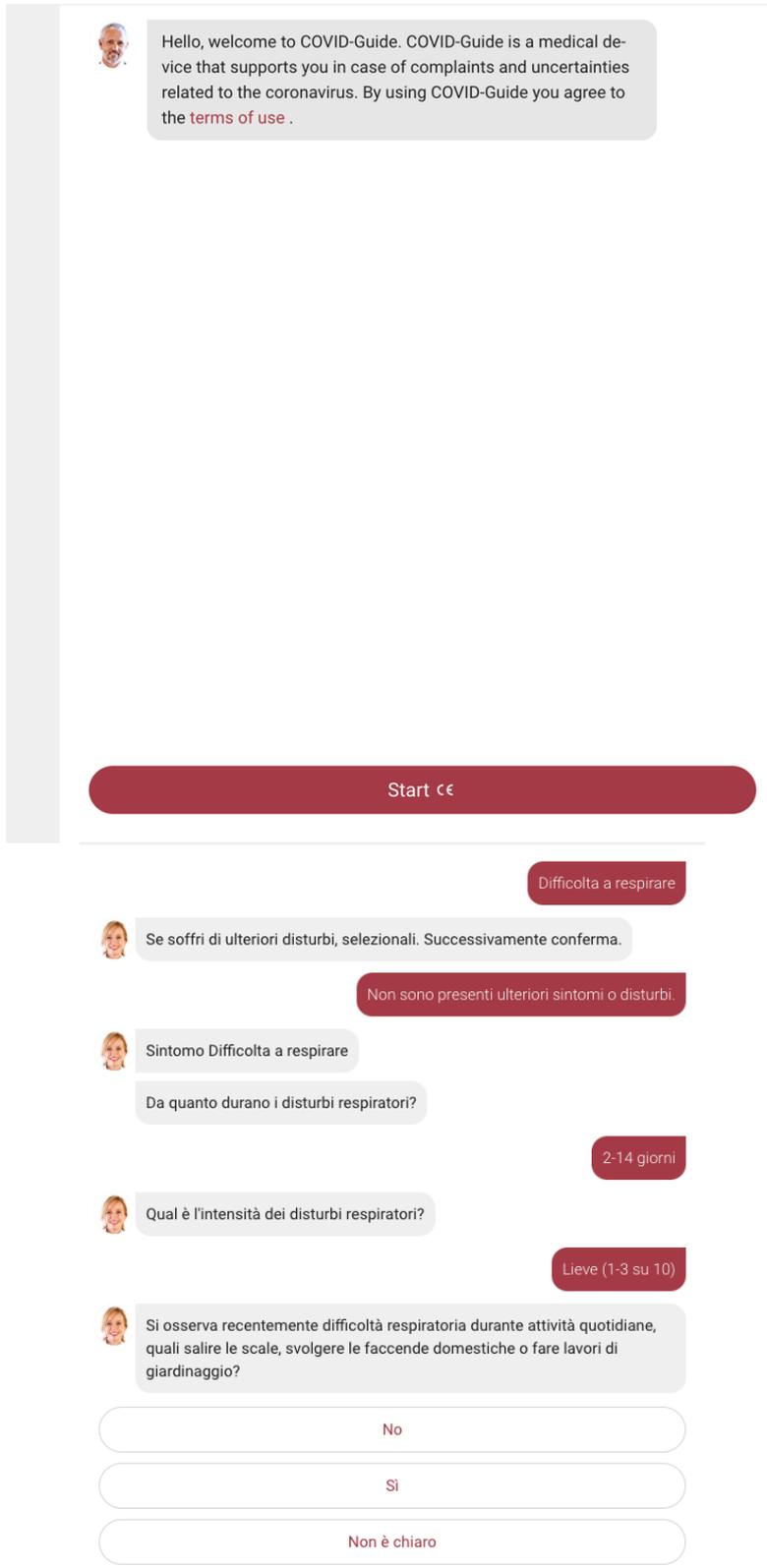


Figure 3: The chatbot interface

It provides counseling regarding the need to go to a covid-19 testing center or hospital. The SMASS Pathfinder CovidGuide asks specific questions about warning signs in MTS [59] (Red, Orange, Yellow, Green and Blue Flags) and makes a suggestion about the optimal time-to-treat (e.g. emergency, immediate or non-urgent treatment) and point-of-care (e.g. ambulance service, emergency room, doctor's office, pharmacy, telemedicine or self-treatment/self-monitoring). Also, if the user has described symptoms unrelated to potential covid-19 infection, corresponding recommendations are provided (e.g., advising to go to the emergency room because of a potential poisoning, referral to emergency in case of neck stiffness). The chatbot asks various questions regarding a potential covid-19 infection during the counseling, including current symptoms, age, and gender. Answers are predefined, and users can select them via predefined buttons or, in some cases, search functions. In the end, the chatbots recommend what the users should do (e.g., get tested or seek treatment for covid-19), including recommendations besides covid-19 (e.g., identifying poisoning and recommending seeking immediate medical help).[127] The software is medically based on an evidence-based knowledge and technologically on an artificial neural network. Through the interaction with its artificial intelligence, it is possible to obtain an initial assessment of any combination of symptoms reported by the patient and subsequent referral to the most appropriate health service. Main symptoms are encoded in International Classification of Primary Care's Reasons for Encounter (RFE), according to the 2-R version [128], considering those most frequent and important in covid-19-like scenarios, as reported in Table 1.

Table 1: Most common inputted reasons for encounter (RFE)/scenarios coded in ICPC-2R	
Classification coding ICPC 2R	Clinical Scenario
A03	Fever
A29	Cold/Flu
A77	Viral disease non otherwise specified
A98	Health main/preventive medicine
D10	Vomiting
D11	Diarrhoea
N01	Headache
R02	Shortness of breath/dyspnea
R05	Cough
R21	Throat symptom/Complaint

The servers of SMASS Pathfinder CovidGuide are certified according to ISO27001.

The SMASS Pathfinder CovidGuide is a medical device according to the current EU directives. This means that in4medicine AG and the Software meet strict requirements in terms of quality management and certification. CovidGuide is free of charge. It provides indications differentiated per country on what to do in case of symptoms and urgency (Figure 4), constantly updated on the directives given by each country authority. It represents one of the apps available for symptom checking and self-triage for covid-19 in primary care.



Recommendation

How fast?

Immediate medical treatment

The medical treatment can not be postponed. The treatment has to be immediate.

Where?

Emergency department

The medical treatment should be done in the emergency Department. Please contact the hospital before hand.

Reasons

- The chin can no longer be moved toward the chest. This may be caused by harmless conditions (e.g., stiff neck/torticollis). However, more serious diseases should also be considered. For example, if there is a severe feeling of illness, high fever, headache, and rash, meningitis should be considered.
- The sore throat/throat and shortness of breath may be related (e.g., if there is inflammation, swelling in the throat/throat).
- The difficulty breathing occurred within seconds/minutes. The cause should be clarified quickly (e.g., pulmonary embolism, allergy, inhalation of a toxin or foreign body, collapse of the lung/pneumothorax).

Figure 4: Possible output advice given by the app

Systematic Review on safety and effectiveness of self-triage tools

- Relevant literature was retrieved through a Prospero recorded systematic review on the safety and efficacy of self-triage tools and symptom checkers in primary care. The review was based on a Prospero recorded protocol (CRD42021277509). Medline through PubMed, Embase, Cinhal, Lilac and the Cochrane Central were searched from inception to May 2022. The PRISMA (Preferred Items Review for Systematic Reviews and Meta-Analyses) checklist in its latest version [129] and the MOOSE (Meta-analyses Of Observational Studies in Epidemiology) [130] were respected in this work. These two models are renowned methodological guidelines to develop a systematic review and set the standards for the review that was performed. The search strategy included studies where the self-triage tools were compared to the standards of care, identified, based on current literature, in telephone triage or face to face consultation provided by a health care professional, notably a nurse or a physician. No restrictions of language were applied. All types of peer reviewed studies having at least abstract in English were considered eligible. Observational studies describing/reporting the use of self-triage tools or symptom checkers; RCT or non-randomized studies having as intervention the use of self-triage tools or symptom checkers; letters, conference abstracts, peer reviewed original articles were deemed to be eligible. Book chapters, Cross sectional studies, Qualitative reviews (no quantitative data reported) publications for which no abstract or full text is available and studies that merely describe services without providing any quantitative or qualitative outcome data, conceptual papers and projections of possible future developments were excluded. The search strategy used is shown in Table 2.

Table 2: The search strategy designed and used for the review

```
((("Primary Health Care"[Mesh]) OR ("Pediatrics"[Mesh])) OR ("Primary Healthcare"[Title/Abstract] OR "Primary Care"[Title/Abstract] OR pediatric*[Title/Abstract])) AND (((("Triage"[Mesh]) OR "Diagnostic Self Evaluation"[Mesh]) OR "Diagnosis, Differential"[Mesh]) OR (Triage*[Title/Abstract] OR "Diagnostic Self Evaluation"[Title/Abstract] OR "Diagnostic Self Evaluations"[Title/Abstract] OR "Self Evaluation"[Title/Abstract] OR "Self Evaluations"[Title/Abstract] OR "Subjective Health Complaint"[Title/Abstract] OR "Subjective Health Complaints"[Title/Abstract] OR "Subjective Health"[Title/Abstract] OR "Subjective Healths"[Title/Abstract] OR "Self-Appraisal"[Title/Abstract] OR "Self Appraisal"[Title/Abstract] OR "Self-Appraisals"[Title/Abstract] OR "Self Appraisals"[Title/Abstract] OR "Self-Evaluation"[Title/Abstract] OR "Self Evaluation"[Title/Abstract] OR "Self-Evaluations" [Title/Abstract] OR "Self Evaluations"[Title/Abstract] OR "Self-Referral" [Title/Abstract] OR "Self-Assessment"[Title/Abstract] OR "Self Assessment"[Title/Abstract] OR "Differential Diagnosis"[Title/Abstract] OR "Differential Diagnoses"[Title/Abstract])) AND ((("Telephone"[Mesh:NoExp] OR ("Telemedicine"[Mesh]) OR ("Mobile Health"[Title/Abstract] OR "mHealth"[Title/Abstract] OR Telehealth[Title/Abstract] OR "eHealth"[Title/Abstract] OR telemedicine[Title/Abstract] OR telephone[Title/Abstract] OR "symptom checker"[Title/Abstract] OR "symptoms checker"[Title/Abstract] OR "Symptom checkers" [Title/Abstract] OR "Symptoms checkers"[Title/Abstract])) OR (telephone[Title/Abstract]))
```

The review was carried out using Rayyan, a tool for systematic reviews powered with an artificial intelligence [131]. Two investigators screened the records found. In case of disagreement, a third reviewer, was asked to decide whether the study could be included or not. Quality assessment of studies included was done following the ROBINS-I form by two independent reviewers. Controversies were solved by the judgment of a third reviewer, JD.

Features of users

- The features of the population's that used the app in a 2-year period, ranging from its inception to April 19th, 2022, in Germany, where the app was embedded in the primary emergency care system, Switzerland and Italy, were identified. Data were cleaned from demo and simulations. Descriptive statistics, including time series, were calculated using STATA 16 SE and R.
- Univariate and bivariate analyses were performed and absolute and relative frequencies for each variable recorded were extracted. Main symptom for consultations were reported in international classification of primary care (ICPC-2R) [128].
- Analyses were performed and reported also separately for each country where the app was used, notably Germany, Switzerland, and Italy.

AfyaGuide and the Pilot Study in Kenya



Afya Guide Kenya

The SMASS Afya Guide is an online application whose goal is to assist the public to carry out self-assessment for flu-like symptoms and to guide the user on the appropriate measures to take based on responses to the questions posed by the application. It can be used by both the general public and medical professionals as a rapid screening assessment of health related to flu-like symptoms. The main expected impact from this tool is to promote accessibility to quality and timely healthcare services to users outside of a physical health facility thus reducing overload on outpatient services in facilities.

Fig. 5: Welcome page of the AfyaGuide

- The CovidGuideapp was readapted to a different context, namely the Kenyan one, translated to Swahili and a pilot study on this readaptation's acceptability and usability, the AfyaGuide pilot study, was carried out.

- The study was done by online consultation mediated by a scout in individuals who accessed healthcare centers for treatment because they were experiencing covid-19 and influenza-like illnesses (ILIs).
- Study population: The pilot study aimed to assess consumer experience with the online AfyaGuide Triage solution and the subsequent health seeking behavior of at least 1,537 Keyan adults experiencing influenza and influenza-like illnesses. Inclusion and exclusion criteria were:
 - **Inclusion criteria**
 - Adults aged over 18 years who consent to participate in AfyaGuide triage solution.
 - Accept to be followed up to provide feedback on actions taken following the advice provided by the online triage solution.
 - **Exclusion criteria**
 - Individuals who were not experiencing any illnesses were excluded from the study analysis.
 - Individuals experiencing other illnesses, rather than covid-19 or influenza like illnesses were excluded from the study analysis.
 - Individuals unable to use the app were excluded from the study analysis.
- **Sample size**

- To determine the sample size, Fischer's formula ($n = \frac{Z^2 PQ}{e^2}$) [132] was used, with a confidence level 95% (1.96) and estimated Prevalence of influenza-like illness in the population at anytime (P) = 0.5 (50%) and margin of Error) = 2.5%

$$n = \frac{Z^2 PQ}{e^2} = \frac{1.96^2 * 0.5(1-0.5)}{0.025^2} = n = 1,537$$

The covid-19 guide survey assumed a proportion of responders of 50% with 95% confidence and 2.5% margin of error, based on a previous study in Sub-Saharan Africa [133]. The study done in Sub-Saharan Africa from Abu was used as reference to calculate the sample size [133], since no other study was performed before this one on AfyaGuide regarding telemedicine self-triage solutions.

- **Sample allocation**

All participants from all the 47 Kenyan counties with smartphones and able to access the internet were considered eligible for the pilot. An enumeration list of all eligible participants was obtained from Safaricom and other mobile phone providers. The sample was distributed among 7 counties. Participants were selected randomly using a table of random numbers/digitally. The study was conducted across 7 facilities ie hospitals spread across 4 counties: Nairobi, Mombasa, Nakuru and Kisumu. A study scout was stationed at each of the enrolling sites. Eligible and consented participants accessed the module through a web portal link, provided via SMS, the questionnaire was available either in English or Swahili. If patients were not able to use the app, due to their digital literacy or experience, they were excluded from the study. Only quantitative data were collected. A participant self-administered the questionnaire provided through the chatbot and were given recommendation regarding their symptoms. Participants provided a feedback based on a questionnaire linked to their assessment in terms of:

1. Humanness (i.e. sensation of having a human feel in the interaction with the tool provided)
2. Social presence (i.e. how social/human does the guide appear when chatting)
3. Trust (in the decision of the system/assessment)
4. Persuasiveness
5. Service satisfaction
6. Usefulness
7. Usability
8. Confirmation
9. Attitude towards compliance
10. Subjective norm
11. Behavioral Intention to Comply
12. Hypochondria
13. Perceived Health Treat

Users feedback was given on a Likert scale on the questionnaire for feedback (see appendix) [127].

Ethical considerations

The systematic review that was carried out, being based on previous studies and papers, did not need the approval of an Ethical Committee. Systematic reviewers use publicly accessible documents as evidence and are seldom required to seek an institutional ethics approval before starting a systematic review [134].

Also, for the descriptive analysis, as in many other studies on database made in primary care and emergency departments and based on patients' data with a retrospective or cross-sectional design, made during covid-19, ethical approval was not required due to the retrospective nature of the work and the entailed use of anonymized collected data [47]. Data analysis consent was obtained by the in4medicine company.

For the pilot market research project that was held in Kenya, ethical approval was asked and obtained from the Ethical Committee of the University of Nairobi.

Results

Systematic Review on safety and effectiveness of self-triage tools Results

The search yielded, after duplicates were removed, 6575 records. 6562 papers were excluded after title and abstract screening, and only 13 studies were deemed to be eligible for full text screening. At full text screening, only 3 studies were included, but, unfortunately, only one of those was made in the primary healthcare setting (see figure 6 - Prisma Flowchart). Due to the differences in population, intervention, comparison and outcome, a meta-analysis of data was not possible, and only a qualitative synthesis of data from the included studies was possible.

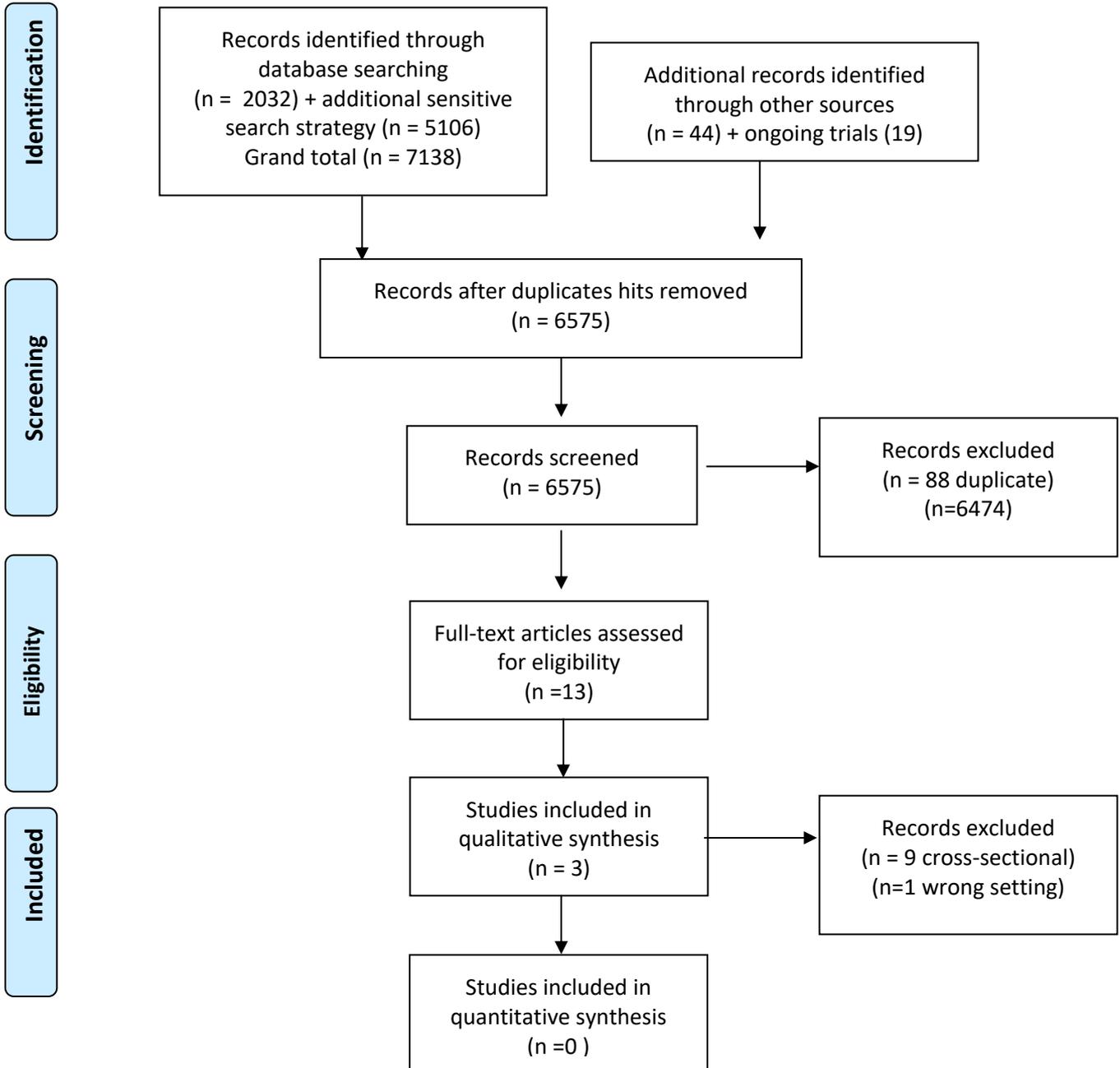


Figure 6: Prisma Flowchart

Studies characteristics and quality assessment

Included studies characteristics are reported in Table 3.

The applications used and considered in the studies included were the symptom-checkers from the website Drugs.com and FamilyDoctor [135], ADA© [136] and Omaolo© [137].

Table 3: Included studies' main characteristics								
Author, year	Tool (intervention)	Comparison	Population	Setting	Number of patients enrolled	Mean Age of Participants	F (%)	Year
Yu, 2020[135]	FamilyDoctor, Drugs.com	Triage Nurses	Inpatients emergency walk in center	Emergency	100	55,4; 56,6	58%, 55%	2016
Cotte 2022[136]	ADA	Physicians	Inpatients emergency walk in center	Emergency	378	46	43%	2020
Koskela, 2022[137]	Omaolo	Nurses	Primary Healthcare Patients	Primary Care	825	NR	NR	2019-2020
<i>Legend: F (female participants); NR: not reported</i>								

The results reported by Yu [135], Cotte [136] and Koskela [137], are shown in Table 3 and 4.

Table 4: Triage Summary of findings of included studies – Triage Quality						
Author, year	Tool	Comparison	Outcome	ES	95% CI LL	95% CI UL
Yu, 2020	Drugs.com	Triage Nurse	Sensitivity (%)	70	59	80
Yu, 2020	Drugs.com	Triage Nurse	Specificity (%)	90	68	99
Yu, 2020	Drugs.com	Triage Nurse	ICC (emergency status assignment)	0,85	0,8	0,89
Yu, 2020	Drugs.com	Triage Nurse	ICC (recommendation assignment)	0,73	0,6	0,82
Yu, 2020	Drugs.com	Triage Nurse	PPV (%)	97	88	100
Yu, 2020	Drugs.com	Triage Nurse	NPV (%)	43	28	59
Yu, 2020	Drugs.com	Triage Nurse	Overtriaged (%)	2	0,24	7
Yu, 2020	Drugs.com	Triage Nurse	Undertriaged (%)	24	16	34
Yu, 2020	Drugs.com	Triage Nurse	Accurately triaged (%)	74	64	82
Yu, 2020	FamilyDoctor	Triage Nurse	Sensitivity (%)	44	59	80
Yu, 2020	FamilyDoctor	Triage Nurse	Specificity (%)	75	68	99
Yu, 2020	FamilyDoctor	Triage Nurse	ICC (emergency status assignment)	0,86	0,82	0,9
Yu, 2020	FamilyDoctor	Triage Nurse	ICC (recommendation assignment)	0,75	0,63	0,83
Yu, 2020	FamilyDoctor	Triage Nurse	PPV (%)	88	73	96
Yu, 2020	FamilyDoctor	Triage Nurse	NPV (%)	25	15	38
Yu, 2020	FamilyDoctor	Triage Nurse	Overtriaged (%)	5	1,6	11
Yu, 2020	FamilyDoctor	Triage Nurse	Undertriaged (%)	45	35	55
Yu, 2020	FamilyDoctor	Triage Nurse	Accurately triaged (%)	50	40	60
Cotte, 2022	ADA	Physicians	AHS	20	-	-
Cotte, 2022	ADA	Physicians	Overtriaged (%)	57,1	-	-
Cotte, 2022	ADA	Physicians	Undertriaged (%)	8,9	-	-
Cotte, 2022	ADA	Physicians	Safe assessment	94,7	-	-
Cotte, 2022	ADA	Physicians	Exact match (MTS)	33,9	-	-
Koskela, 2022	Omaolo	Nurse	Exact match (%)	52,6	-	-
Koskela, 2022	Omaolo	Nurse	Overtriaged (%)	66,6	-	-
Koskela, 2022	Omaolo	Nurse	Safe assessment (%)	98,6	-	-

Legend: ES: effect size; CI: confidence interval; LL: lower limit; UL: upper limit; ICC: intraclass correlation coefficient; PPV: positive predictive value; NPV: negative predictive value; AHS: hazardous avoidable situation; MTS: Manchester Triage System

In Yu [135], each symptom checker was tested with 100 Accident and Emergency (A&D) charts, with an equal distribution between the five triage categories. A total of 51 charts were used to test both checkers, with two different sets of 49 charts used to test only one checker, making up a total of 149 charts sampled. Among the cases sampled for Drugs.com, the mean age was 56.6 years, with 42% being male.

Among the cases sampled for FamilyDoctor, the mean age was 55.4 years, with 45% being male. There was no significant difference in the average age of sampled cases between the two checkers.

Drugs.com was more accurate than FamilyDoctor (74% CI 64-82 vs 50% CI 40-60) and had a lower under-triage rate, 24%. All ICCs for the independent assignments of emergency statuses exhibited adequate agreements (>0.7). Drugs.com performed better than FamilyDoctor in overall sensitivity, specificity, negative and positive predictive value. Drugs.com outperformed FamilyDoctor in every category, and both symptom checkers performed better for non-emergency cases than for the emergency ones.

Cotte's analysis [136] indicated undertriage in 34/378 cases, 8.9% of the enrolled population of which 59% (20/34) were potential Avoidable Hazardous Situations.

It showed also a huge percentage of cases overtriaged (57.1%), 216 cases. A safe assessment was reached according to authors in 358/374 cases, whilst an exact match between physician panel was provided in 128 cases. Cotte's analysis on triage[136], even if impaired by the sampling, due to covid-19 pandemic outbreak, presented interesting results. Compared with usual hospital triage, 91% (344/378) of the participants were triaged identically or more conservatively by the app.

The app provided safe advice for 94.7% (358/378) of the patients when compared with the stand-alone MTS assessment, which served as the gold standard in this study. This includes identical or more conservative advice (344/378, 91%) and cases defined as safe by the physician panel (14/378, 3.7% no potential AHS).

The work was revised and modified due to covid-19 outbreak which made impossible for the authors to continue with the project.

All studies included were considered at serious risk of bias in Robins-I [138,139] (see Figure 6 and 7).

Koskela's study was reported as a conference abstract, thus it was not possible to properly assess the study itself [137]. In Yu's study [135] bias was due to the risk of selective reporting, whilst Cotte's study was mostly impaired by deviation from the intended intervention and missing data due to covid-19 outbreak, as stated by the authors [136]

		Risk of bias domains							
		D1	D2	D3	D4	D5	D6	D7	Overall
Study	Yu 2020	?	+	+	X	-	-	X	X
	Cotte 2022	?	+	+	X	X	+	X	X
	Koskela 2022	?	?	?	?	?	?	?	

Domains:
D1: Bias due to confounding.
D2: Bias due to selection of participants.
D3: Bias in classification of interventions.
D4: Bias due to deviations from intended interventions.
D5: Bias due to missing data.
D6: Bias in measurement of outcomes.
D7: Bias in selection of the reported result.

Judgement
X Serious
- Moderate
+ Low
? No information
Not applicable

Figure 7: Risk of bias in the three studies – traffic lights

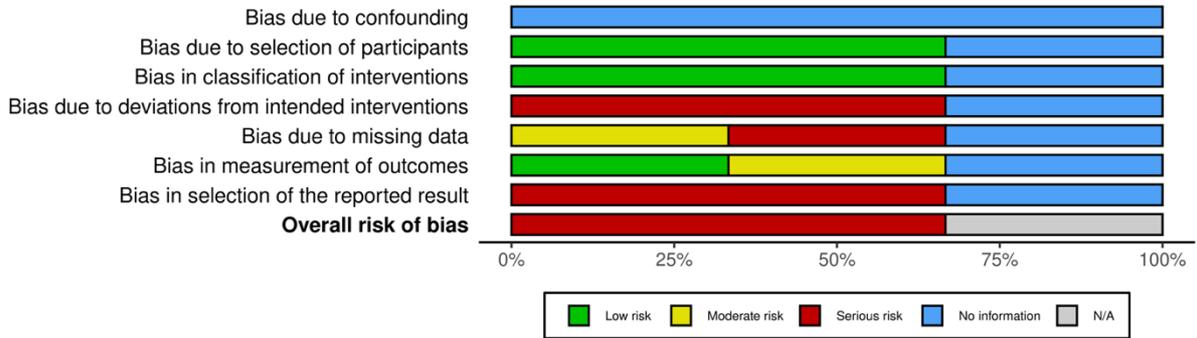


Figure 8: Risk of bias in the three studies – summary plot

Features of SMASS Pathfinder CovidGuide users

On a total number of 374179 consultations, coming from 10 countries, namely Germany, Switzerland, Italy, Austria, Holland, France, Belgium, England, Ireland, and other unspecified countries, 62% patients were females, 75% in the age range 14-49 years.

The main symptoms reported were viral syndrome not otherwise specified and throat symptoms complaints. The most frequent advice given was the indication to see the doctor today (38% of the consultations). 75692 patients, 20% of cases, received indications for self-monitoring with safety net (i.e. indications on what to do in case of symptoms' worsening).

The triage indications are reported in the table below.

Table 5: Time to treat and point of care suggested by the app in Europe and other countries

		Point of care								
Time to Treat		Ambulance	Callcentre	Doctor	Hospital	Pharmacy	Selfcare	Unclear	Null	Total
		Emergency	10057	0	0	7863	0	0	0	0
	Immediately	0	0	36129	55464	0	0	0	0	91773
	Later	0	5943	8858	0	18097	75001	45	0	102664
	Today	0	10922	137731	0	0	691	0	0	149310
	Null	0	0	0	0	0	0	0	412	412
	Total	10057	17401	188968	63507	18097	75692	45	412	374179

Italy

The app was not promoted in Italy. Therefore, it was used less than in other countries. It was proposed to the Ministry of Health as self-triage tool in a tender promoted by the Ministry itself, but did not meet the interest of the public, that was oriented to contact tracing tools.

In Italy the total number of in app consultations was 972. Most frequent age range of triage-handlers was 14-49 years (65,63%), with a slight prevalence of female users, 55,45%.

Most of the consultations were held in the months of April 2020 (235), August and October 2020 (111 and 106 respectively), as shown in Table 6 and Figure 9.

Table 6: Number of accesses to the app in Italy from inception to extraction date, organized per month

		Month											
		Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
Year	2020	0	0	0	235	46	8	33	111	93	106	74	23
	2021	37	17	16	10	4	4	9	6	8	17	15	22
	2022	24	20	25	9								

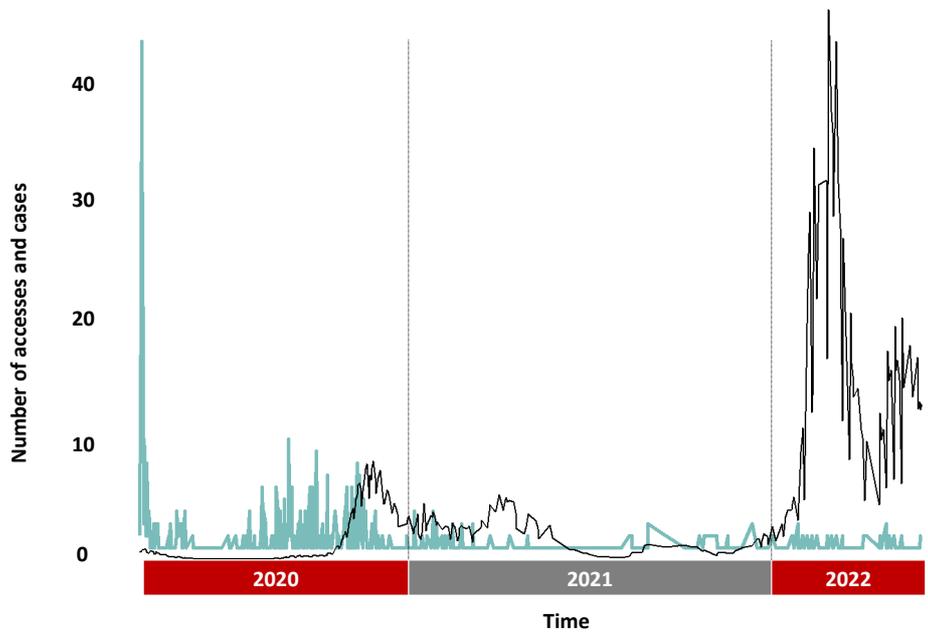


Figure 9: Time series of covid-19 cases and use of CovidGuide in Italy

Distribution of main symptoms inputted (Table 7) is reported below. The main symptom is the first presented by the user of the app, coded in ICPC 2-R.

Table 7: Main symptom RFE inputted - Italy			
Classification coding ICPC 2R	Clinical Scenario	Frequencies	%
A03	Fever	121	13,53
A29	Cold/Flu	30	3,36
A77	Viral disease non otherwise specified	286	31,99
A98	Health main/preventive medicine	4	0,45
D10	Vomiting	5	0,56
D11	Diarrhoea	23	2,57
N01	Headache	81	9,06
R02	Shortness of breath/dyspnoea	41	4,59
R05	Cough	137	15,32
R21	Throat symptom/Complaint	166	18,57

Only the 10,7% of assessments received the indication to call the emergency service for an ambulance or to reach the nearest hospital. Self-monitoring was the advice given in the 20,26% of cases. The most frequent indication given was to seek care by a general practitioner or call a doctor for advice in the day of assessment, output for the 42,90% of consultations, as reported in the Table 8 and Figures 10 and 11.

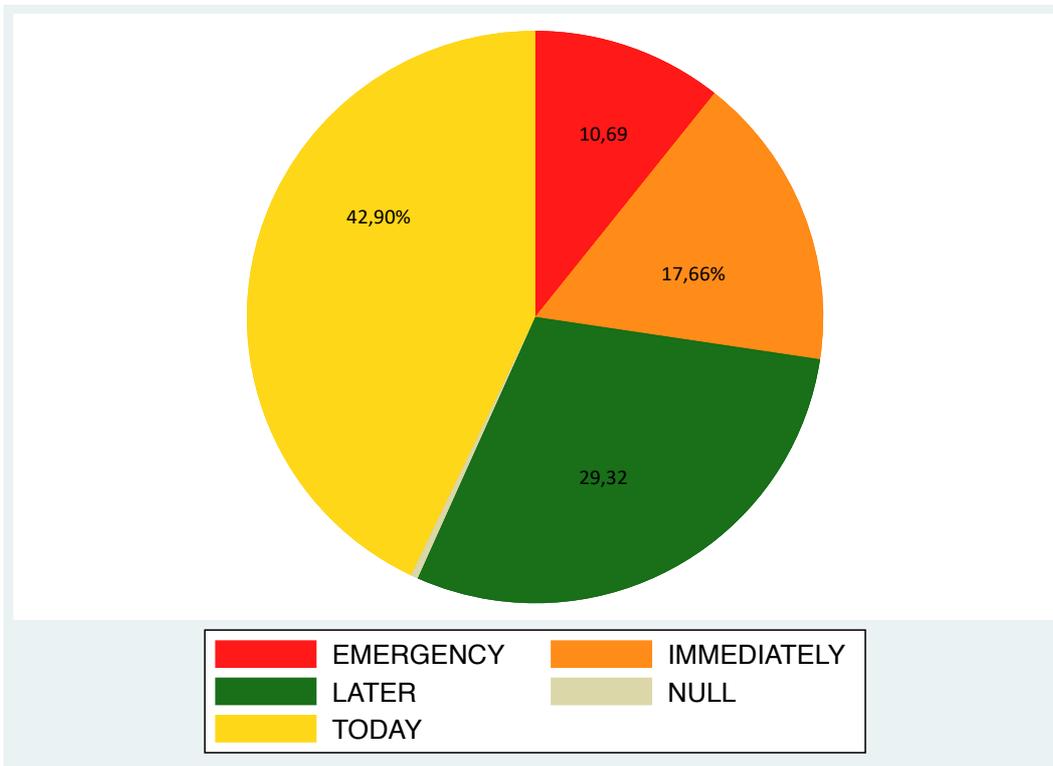


Figure 10: Distribution per suggested time to treat in Italy

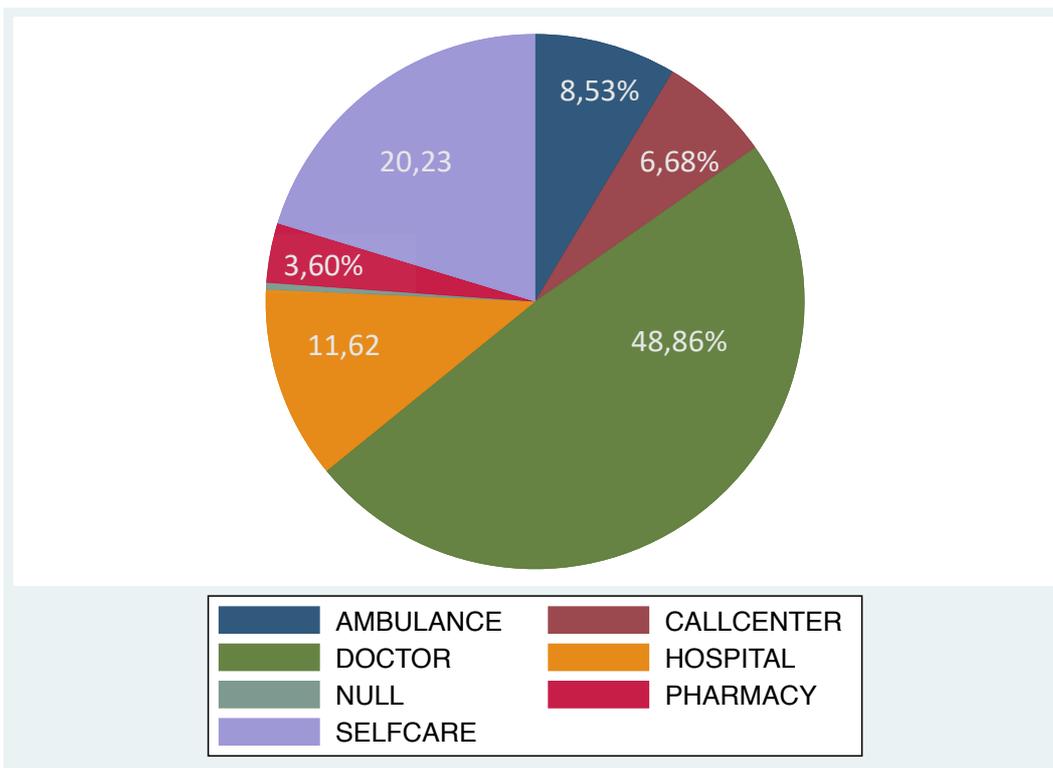


Figure 11: Distribution per suggested point of care in Italy

Table 8: Time to treat and point of care suggested by the app in Italy									
		Point of care							
Time to Treat		Ambulance	Callcentre	Doctor	Hospital	Pharmacy	Selfcare	Null	Total
	Emergency	83	0	0	21	0	0	0	104
	Immediately	0	0	70	92	0	0	0	162
	Later	0	31	29	0	35	190	0	285
	Today	0	34	376	0	0	7	0	417
	Null	0	0	0	0	0	0	4	4
	Total	83	65	475	113	35	197	4	972

Germany

In Germany, Total number of app consultations were 357693. Of those, the 62,74% were held by female users, whilst the 37,26% by male users, as reported in Figure 12. Most represented age range was 14-49 years (74,98%) followed by the 50-65 years, as reported in the following table.

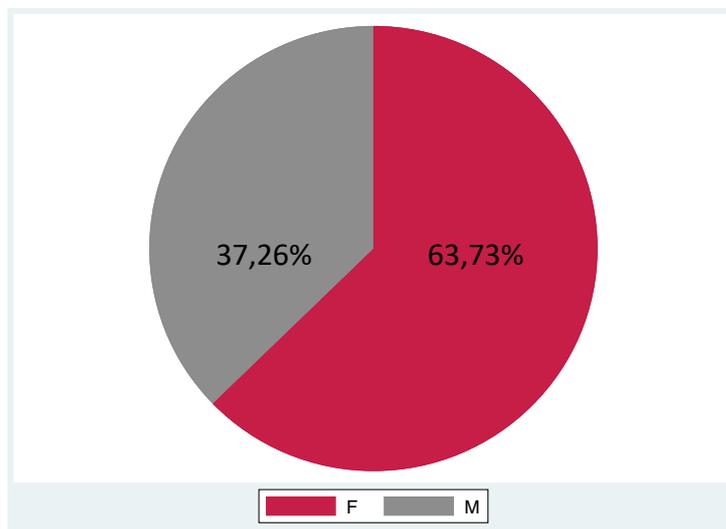


Figure 12: Distribution of users per sex in Germany

Table 9: Distribution per age range and sex of app users in Germany			
Age range	F (%)	M (%)	Total (%)
1-4 w	35 (0,009)	31 (0,008)	66 (0,017)
5-8 w	17 (0,004)	22 (0,006)	39 (0,01)
3-12 m	265 (0,07)	253 (0,07)	518 (1,4)
1-3 y	2,140 (0,60)	2,358 (0,66)	4,498 (1,26)
4-8 y	3,589 (1,00)	3,571 (0,99)	7,160 (1,99)
9-13 y	3,638 (1,01)	3,776 (1,05)	7,414 (2,06)
14-49 y	174,328 (48,74)	93,872 (26,24)	268,200 (74,98%)
50-65 y	34,911 (9,76)	23,642 (6,61)	58,553 (16,37)
66-80 y	4,840 (1,35)	5,051 (1,41)	9,891 (2,76)
> 80 y	639 (0,18)	715 (0,2%)	1,354 (0,38)
Total	224,402 (62,74)	133,291 (37,26)	357,693 (100)

Most of self-triage consultations took place in 2020, notably in the months of October and November, 68382 and 52913 in app consultations. In 2021 consultations held were 72481 and in the first months of 2022, 34174, as shown in the table and figure below.

Table 10: Number of accesses to the app in Germany from inception to extraction date, organized per month.													
		Month											
		Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
Year	2020	0	0	0	4493	11610	7447	14180	24139	33153	68382	52913	34721
	2021	14951	8806	12197	8181	3142	1545	2168	2463	3559	4183	9098	2748
	2022	7789	8889	12198	5298								

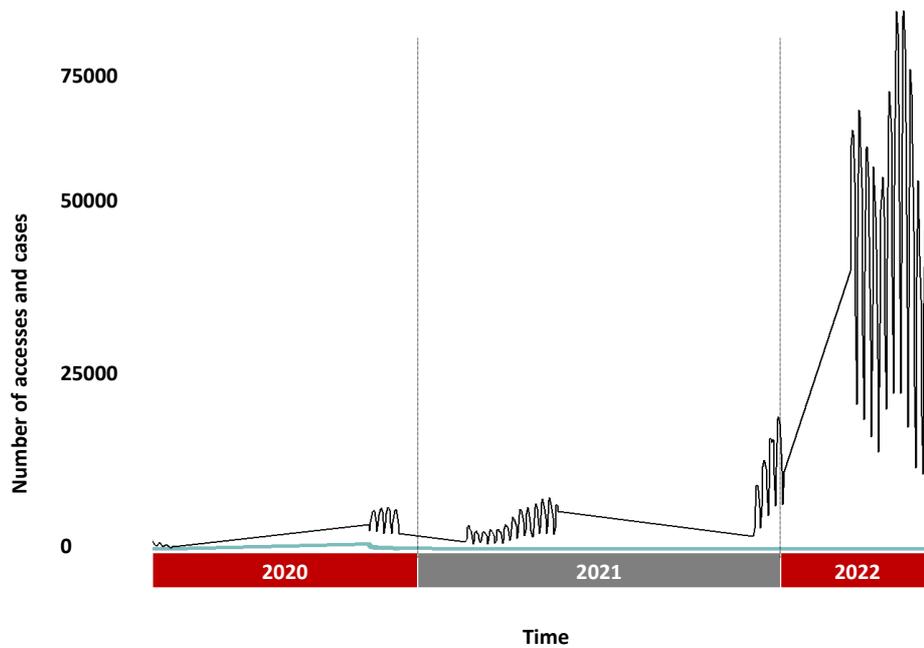


Figure 13: Time series of covid-19 cases and use of CovidGuide in Germany

Main symptom count mean, with reference to the ones presented by the user on the tool, was 2,23 with SD 1,16 and symptom count ranging from 1 to 9 symptoms.

Main symptom most frequently presented by the user of the tool was the ICPC-2R code A77 (viral syndrome not otherwise specified) – 32,68%, followed by the R21 (throat symptom complaints) 24,78% and R05 (cough) 13,05%, accounting for the 70,55% of the examined population (complete list and frequencies are shown in table below).

Table 11: Main symptom RFE inputted - Germany

Classification coding ICPC 2R	Clinical Scenario	Absolute frequencies	Relative frequencies (%)
A03	Fever	28050	8,02
A29	Cold/Flu	8424	2,41
A77	Viral disease non otherwise specified	114295	32,68
A98	Health main/preventive medicine	4032	1,15
D10	Vomiting	4718	1,35
D11	Diarrhoea	6878	1,97
N01	Headache	34971	10
R02	Shortness of breath/dyspnoea	15949	4,56
R05	Cough	45790	13,09
R21	Throat symptom/Complaint	86681	24,78

Only the 5,58% of users already had a covid-19 confirmed test. The 0,61% had already recovered from covid-19.

7,69% of users reported an occupational risk (working in a health facility with direct patient contact or working in a nursing home with direct patient contact), 27533 users. Risk factors (high blood pressure, excessive cholesterol level or smoking), asked for in 322791 consultations, were reported in 77432 subjects, whilst diseases such as diabetes, tumor, immunosuppression, respiratory or other chronic diseases) when asked for by the app, were reported respectively in 8030, 3307 and 8098 users.

The question regarding respiratory diseases was asked to 332202 users. Among respiratory diseases, asthma was the one most frequently reported (28187 users)

Polypharmacotherapy, thus defined as assuming more than 5 different drugs, was reported in 21,23% of the responders to the question regarding drug assumption (9819 total users)

The time to treat and point of care were indicated on a total number of 357652 consultations as described in table 12 and figures 14 and 15.

The most frequent indication given was to seek care by a doctor in the same day of the consultation (38,5%), the number of emergencies detected and referred to the hospital or the emergency service were respectively 7618 and 9401, the 4,75% of the total sample.

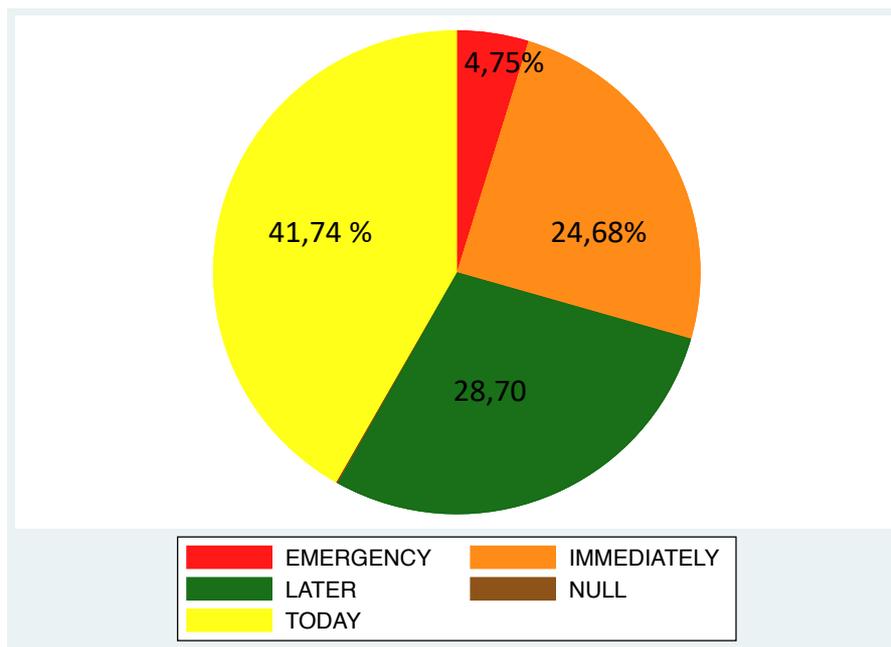


Figure 14: Distribution per suggested time to treat in Germany.

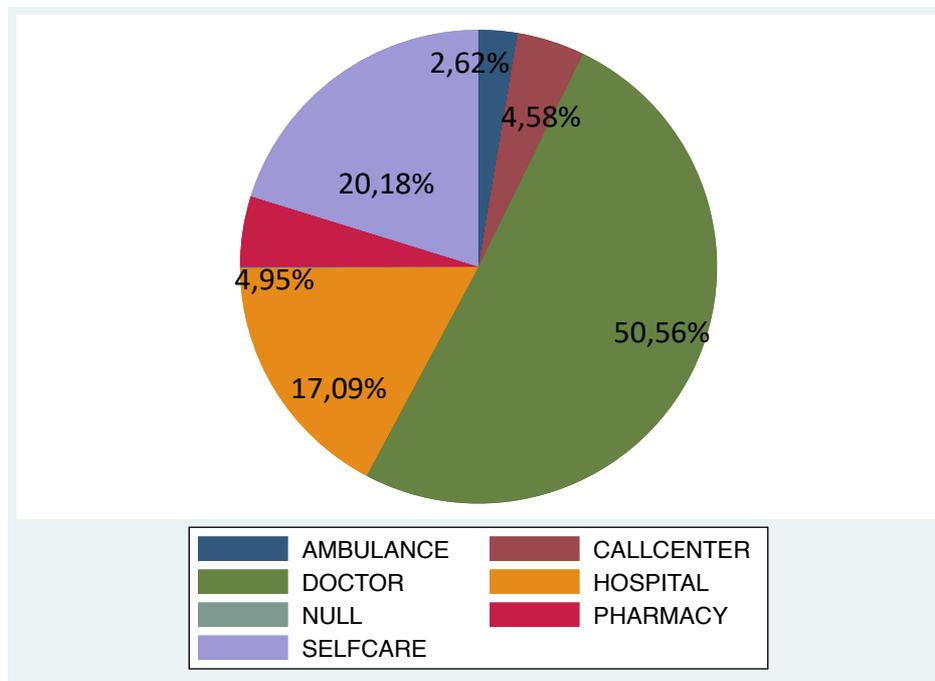


Figure 15: Distribution per suggested point of care in Germany

Table 12: Time to treat and point of care suggested by the app in Germany									
		Point of care							
Time to Treat		Ambulance	Callcentre	Doctor	Hospital	Pharmacy	Selfcare	Null	Total
	Emergency	9401	0	0	7618	0	0	0	17019
	Immediately	0	0	34736	53539	0	0	0	88275
	Later	0	5492	8363	0	17270	71539	0	102664
	Today	0	10922	137731	0	0	657	0	149310
	Null	0	0	0	0	0	0	384	384
	Total	9401	16414	180830	61157	17270	72196	384	357652

Interestingly, an indication for self-monitoring was given in the 20,18% of consultations.

Switzerland

In Switzerland, the self-triage tool was used by 14932 subjects. Most of the consultation were held by female users or for female patients, 56,12% (fig.16). The age range most represented was 14-49 years, followed by 50-65 years, accounting respectively for the 73,90 and the 17,91% of cases (table 13).

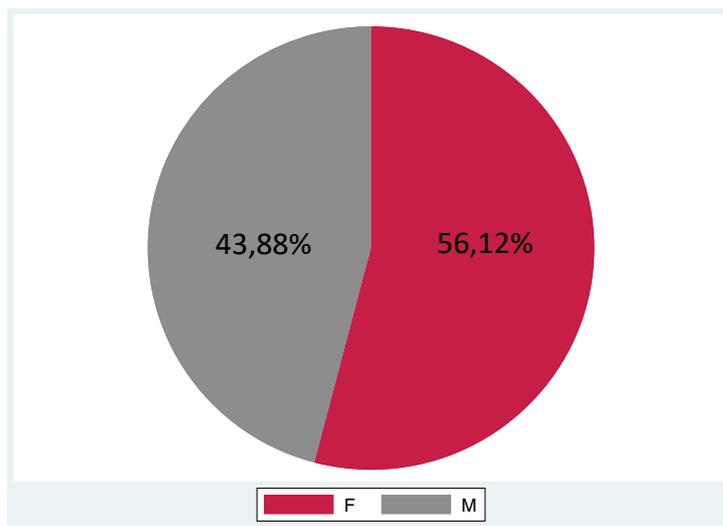


Figure 16: Distribution per sex in Switzerland

Age range	F (%)	M (%)	Total (%)
1-4 w	29 (0,19)	8 (0,05)	37 (0,24)
5-8 w	4 (0,03)	1 (0,01)	5 (0,04)
3-12 m	9 (0,06)	7 (0,04)	16 (0,1)
1-3 y	38 (0,25)	20 (0,13)	58 (0,38)
4-8 y	78 (0,52)	79 (0,53)	157 (1,05)
9-13 y	107 (0,72)	80 (0,53)	187 (1,25)
14-49 y	6541 (43,80)	4584 (30,10)	11035 (73,90)
50-65 y	1372 (9,19)	1303 (8,72)	2675 (17,91)
66-80 y	256 (1,71)	425 (2,84)	681 (4,55)
> 80 y	36 (0,24)	45 (0,30)	81 (0,54)
Total	8380 (56,12)	6552 (43,88)	14932 (100)

Most of the consultations took place in the months of April 2020 (4406), October and November 2020 (1496 and 1135 respectively) as shown below in Table 14 and Figure 17.

Table 14: Number of accesses to the app in Switzerland from inception to extraction date, organized per month.

	Year	Month											
		Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
	2020	0	0	0	4406	460	828	829	1067	893	1496	1135	818
	2021	365	213	301	172	98	43	41	75	134	99	221	265
	2022	282	222	377	92								

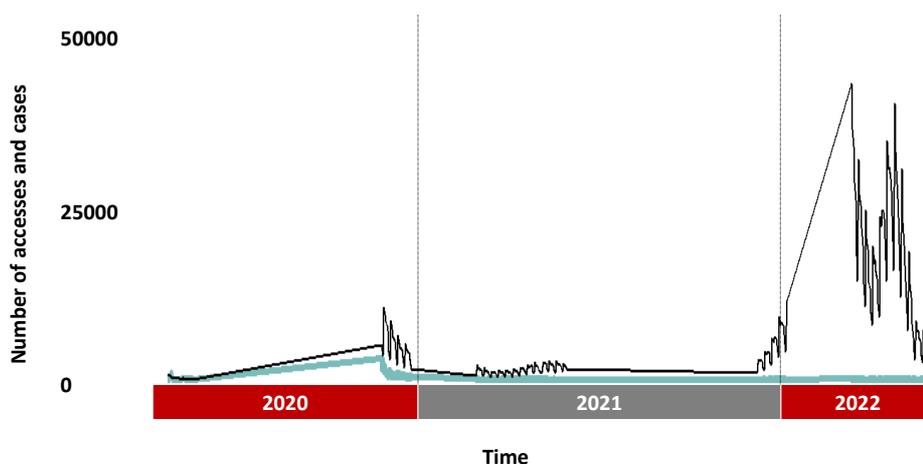


Figure 17: Time series of covid-19 cases and use of CovidGuide in Switzerland

Users of the app presented a mean of 2.01 symptoms, SD 1,06 and symptom count ranging from 1 to 8 symptoms.

As in Italy and in Germany, main symptom inputted was A77 – viral syndrome not otherwise specified (28,35%), followed by R21 throat complaints (25,25%) and cough (17,38%) as shown in Table 15.

Table 15: Main symptom RFE inputted – Switzerland

Classification coding ICPC 2R	Clinical Scenario	Frequencies	%
A03	Fever	893	6,17
A29	Cold/Flu	450	3,11
A77	Viral disease non otherwise specified	4106	28,35
A98	Health main/preventive medicine	93	0,64
D10	Vomiting	179	1,24
D11	Diarrhoea	266	1,84
N01	Headache	1574	10,87
R02	Shortness of breath/dyspnoea	748	5,16
R05	Cough	2517	17,38
R21	Throat symptom/Complaint	3657	25,25

Polypharmacotherapy was reported in 13,44% of cases.

Only 9,89% of app users reported an occupational risk.

Risk factors, where asked, were reported by 19,80% of users.

Among respiratory disease, the most frequently reported was asthma.

Loss of smell/taste, which seemed to be one of the most common findings, at least during the first waves, was reported only in 7,24% of the cases in which the question was asked.

On the total population studied, only 3,22% already had covid-19 confirmed by a test.

Fear of suffering of corona virus disease was reported by 49,38% of the app users.

In 14928 cases it was possible to give advice regarding time to treat and point of care, as shown in Table 16 and Figures 18 and 19.

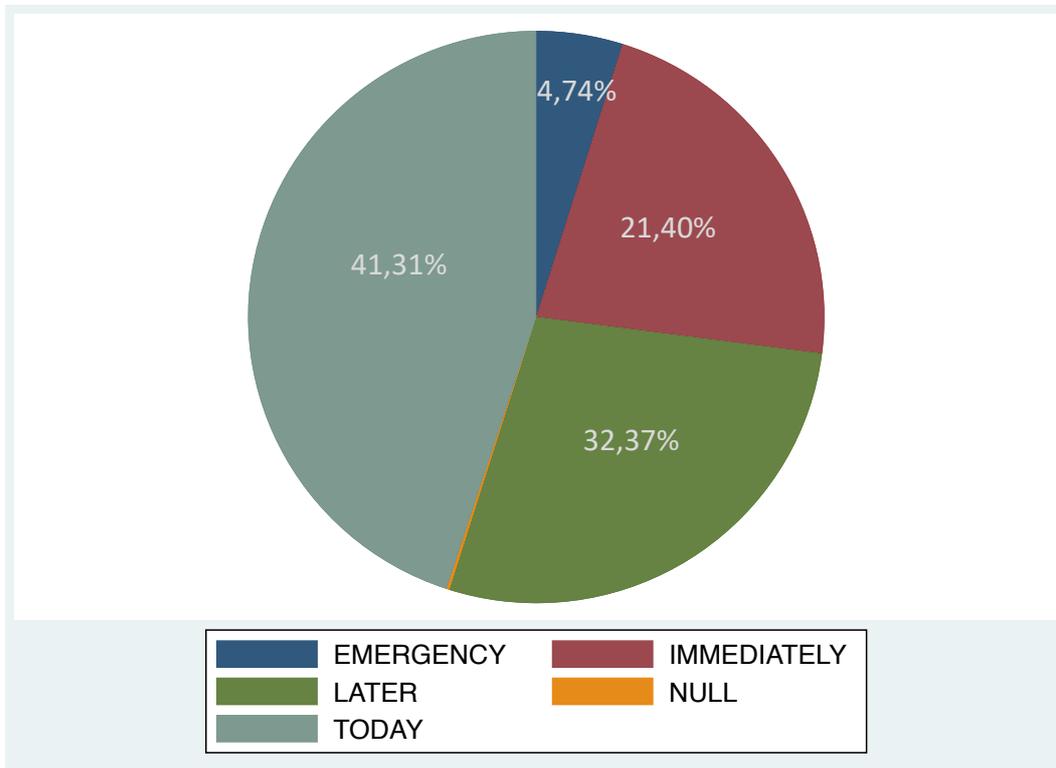


Figure 18: Distribution per suggested time to treat in Switzerland.

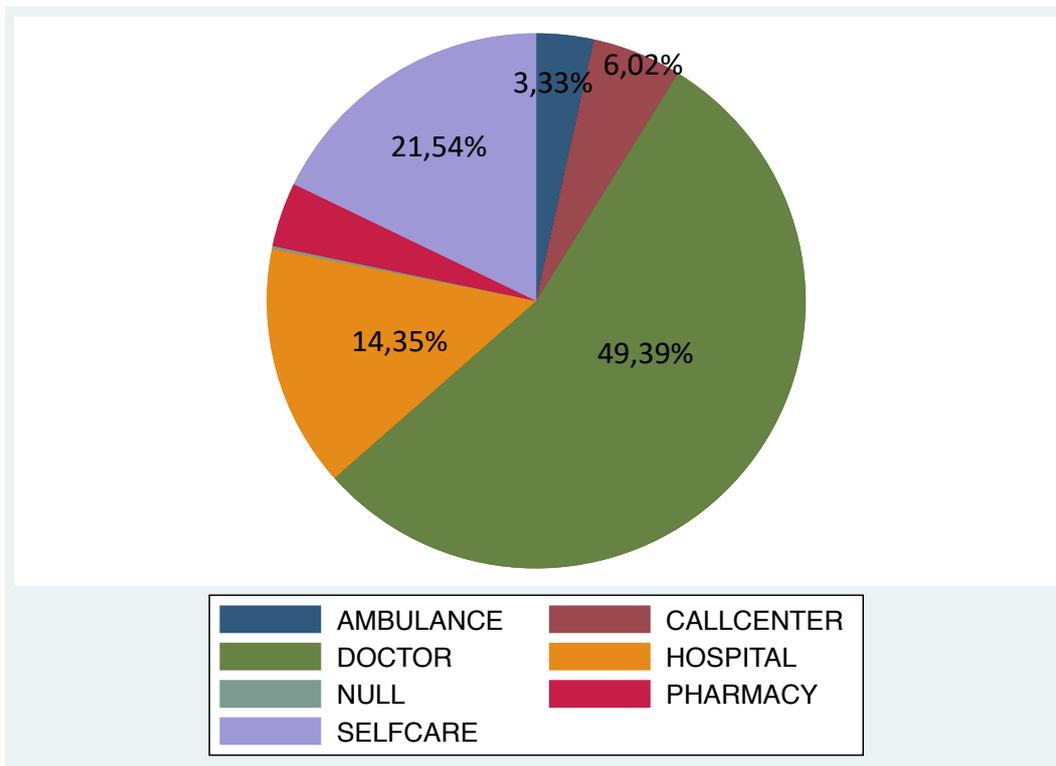


Figure 19: Distribution per suggested point of care in Switzerland

Table 16: Time to treat and point of care suggested by the app in Switzerland									
		Point of care							
Time to Treat		Ambulance	Callcentre	Doctor	Hospital	Pharmacy	Selfcare	Null	Total
	Emergency	497	0	0	211	0	0	0	708
	Immediately	0	0	1264	1932	0	0	0	3196
	Later	0	407	461	0	0	3189	0	4833
	Today	0	492	5649	0	0	27	0	6168
	Null	0	0	0	0	0	0	23	23
	Total	497	899	7374	2143	776	3216	23	14,928

As shown in Table 16, the main indication given was to seek care from a doctor during the day of the assessment – suggestion given by the app in 5649 cases (37,84%). Emergencies (call an ambulance - reach the hospital) were identified in 707 cases, 4,73% of the population assessed. Self-care/self-monitoring was suggested in 21,54% of cases.

A total of 1617 participants completed the survey. The 60,2% were female users, with a mean age of 30,2 years (a similar age range was identified in male users, as reported in Table 17).

Table 17: Kenyan users per age, sex, and location

	Female	Male	Overall
	N=974 (60.2%)	N=643 (39,8%)	N=1617
Age			
Mean (SD)	30.2 (10.2)	30.9 (11.3)	30.5 (10.7)
Median [Min, Max]	27.0 [18.0, 70.0]	27.0 [18.0, 87.0]	27.0 [18.0, 87,0]
County			
Kisumu	289 (29.7%)	163 (25.4%)	453 (28.0%)
Mombasa	270 (27.7%)	169 (26.3%)	439 (27.1%)
Nairobi	197 (20.2%)	164 (25.5%)	361 (22.3%)
Nakuru	216 (22.2%)	145 (22.6%)	361 (22.3%)
Facility			
Bahati Sub-County Hospital	139 (14.3%)	104 (16.2%)	243 (15.0%)
Jaramogi Oginga Odinga Teaching and Referral Hospital	160 (16.4%)	71 (11.1%)	231 (14.3%)
Kisumu County Referral Hospital	129 (13.2%)	92 (14.3%)	222 (13.7%)
Mama Lucy Kibaki Hospital	196 (20.1%)	164 (25.5%)	360 (22.3%)
Mbagathi County Hospital	1 (0.1%)	0 (0%)	1 (0.1%)
Nakuru Level 6 Hospital	77 (7.9%)	41 (6.4%)	118 (7.3%)
Port Reitz Hospital	270 (27.7%)	169 (26.3%)	439 (27.1%)

80% of the surveyed users reported that they do not work in the medical sector, only 207 subjects reported an involvement in the medical sector.

The 54% of the surveyed population reported higher education.

Main symptom identified and assessed by the app was cough (79,4%), followed by Cold or Flu (75,9%), headache (54,5%) and fever (53,1%) as shown in table 18.

Table 18: Main symptom assessed by the AfyaGuide app

Symptom	N
Fever	858 (53,1%)
Cough	1284 (79,4%)
Breathing problems	508 (31,4%)
Throat pain	769 (47,6%)
Cold or Flu	1227 (75,9%)
Headache	880 (54,4%)
Nausea or vomiting	204 (12,6%)
Diarrhoea	77 (4,8%)
General body weakness	726 (44,9%)
Loss of smell and taste	458 (28,3%)

An interesting sample was the one of users vaccinated against covid-19, 1096/1617 users (39% 2 doses, 9% booster).

Table 19: Vaccination status of app users

Vaccination	N (%)
Vaccination against covid-19	1096 (67,8%)
2 doses	630 (39,0%)
booster	145 (9,0%)

App identified an emergency scenario in only 7 cases- , and the most common indication given was to go to the pharmacy to seek treatment in the same day of the evaluation (838 users).

A relevant quote of the sample was suggested to self-monitor their symptoms, about 23%, as reported in Table 20 and chart (Figures 20 and 21).

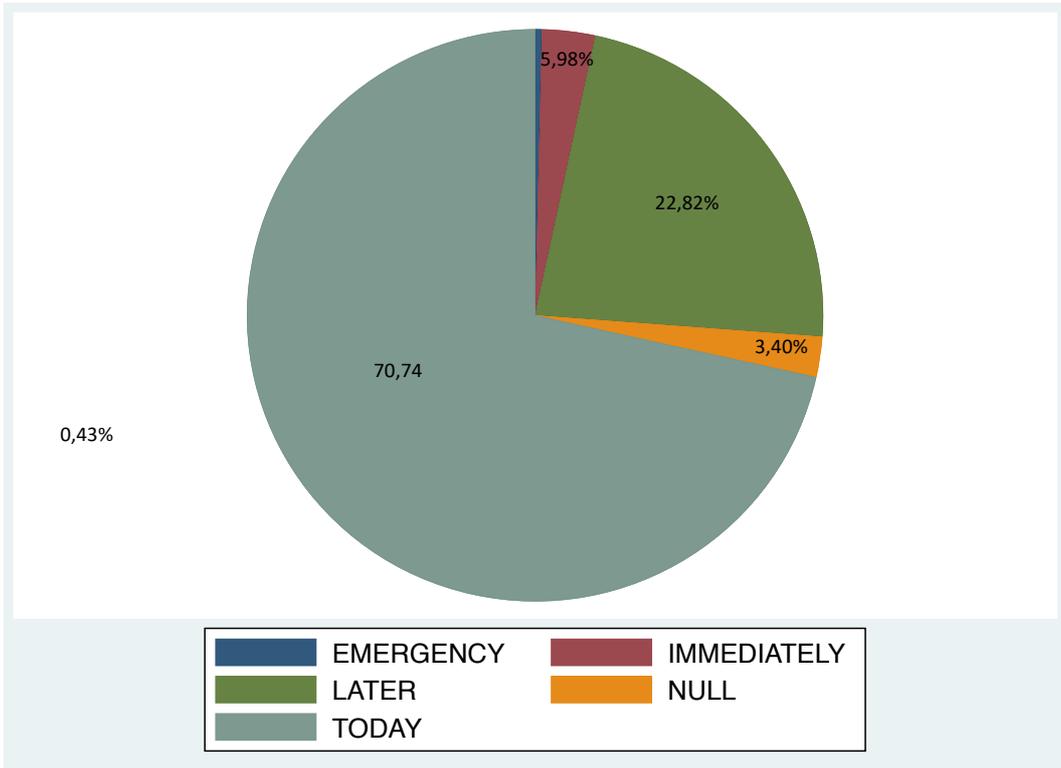


Figure 20: Time to treat suggested in Kenya

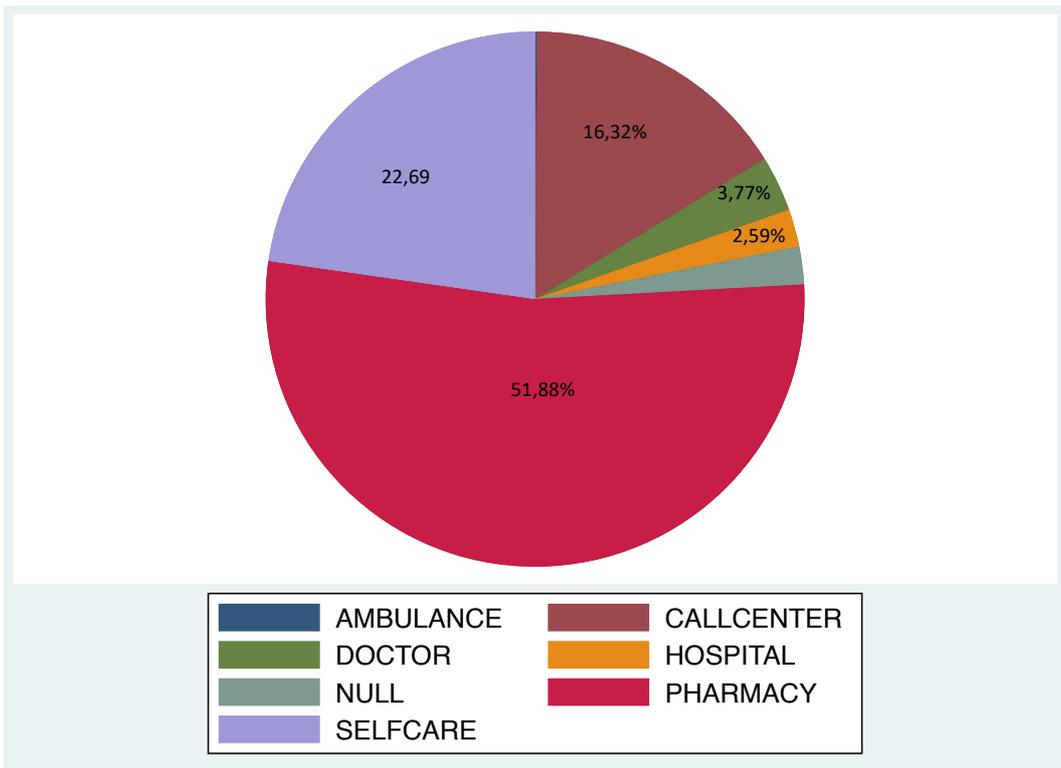


Figure 21: Point of care suggested in Kenya

Table 20: Time to treat and point of care suggested by the app in Kenya									
		Point of care							
Time to Treat		Ambulance	Callcentre	Doctor	Hospital	Pharmacy	Selfcare	Null	Total
	Emergency	2	0	0	5	0	0	0	7
	Immediately	0	0	18	37	0	0	0	55
	Later	0	1	0	0	1	367	0	369
	Today	0	263	43	0	838	0	0	1144
	Null	0	0	0	0	0	0	42	42
	Total	2	264	61	42	839	367	42	1617

Usability and intention to comply

The filling of the questionnaire required a mean of 3,2 minutes.

Users of the app in Kenya were mostly satisfied with the app assessment and reported a 72% service satisfaction.

Regarding persuasiveness assessment, 69% of the respondents indicated that the AfyaGuide had an impact on their thinking and reconsidered their previous thoughts and beliefs on covid-19.

71% of the population evaluated reported that they would trust the advice given by the app, with full confidence in the platform's suggestions.

Humanness and social presence were rated respectively by 76% and 74% of population.

Humanness, the sensation of getting a human feel from the interaction with the tools, was reported by 76% of participants, 74% indicated that the platform was committed and 75% that covid-19 module was accessible.

Social presence, i.e. how social/human is the guide perceived while running the self-triage, was positively rated. 71%-74% of the users reported a sense of either human contact while using the AfyaGuide, a sense of human personality or a sense of human sensitivity.

71% of participants indicated that the tool was very thorough and 71% reported full confidence in its decision and advice.

69% reported that the app made them reconsider their previous thoughts and feeling regarding covid-19.

72% reported that they were satisfied with the way the app treated them.

Usefulness and usability were satisfactory and 68% of users surveyed indicated that the platform was easy to interact with.

Interestingly, 47% of users reported that the indication given was different from what they expected.

68% of respondents indicate that they would follow the indications given, whilst 58% reported that they would be compliant to the existing covid-19 rules.

A health threat from covid-19 was present in 57% of the surveyed population, hypochondria related to flu or cold was reported by 54% of the respondents.

Intention to comply: even if the ratings for the app advice, trust, persuasiveness and usability were good, and 68% of respondents indicated that they would follow thoroughly the indications given by the app, 67% of respondents indicated that despite the indications given by AfyaGuide they would still seek care by the hospital.

General discussion

In the present study the usability of a tool for self-triage, namely the SMASS Pathfinder CovidGuide, focused on covid-19 and influenza like illnesses (ILIs) scenarios, was investigated.

To do this the literature for relevant papers on the topic was searched and a new app was developed, the SMASS Pathfinder CovidGuide, translated to Swahili and converted for the African setting in the AfyaGuide, used in the market pilot study carried out in Kenya.

Efficacy and Safety of symptom checkers for self-triage in primary care: systematic review

Unfortunately, studies reported in literature were mostly performed in the emergency department, had a cross-sectional design, and were not deemed to be eligible in the systematic review run. Even this information is still relevant, because the lack of trials and observational studies in a context as primary care, must be solved. In the studies included different results in terms of under-triage were available, thus determining differences in the reported safety and accuracy of the examined self-triage tools.

Yu's paper described the use of Drugs.com and FamilyDoctor [135] – considered also in Semigran's work [1] - compared to the triage indications given for the same records by a triage nurse (with no specific triage skill). As also considered for telephone triage, the lack of skills on triage may lead to different indications given in terms of time to treat and point of care and likely different outcomes [140-144].

Both Drugs.com and FamilyDoctor performed suboptimally, reaching an overall triage accuracy of 74% and 50% respectively.

According to the audit study performed by Semigran et al. in 2015, the overall triage accuracies of Drugs.com and FamilyDoctor were 60% and 54% [1].

In Yu's study, the percentage of accurately triaged records was 74% with the webapp Drugs.com and 50% for FamilyDoctor. Yu suggested that the difference between their data and Semigran's was due to the use of clinical vignettes in Semigran [1,135], since the two methodologies were otherwise similar.

Cotte's study [136], which was methodologically sound, ended unfortunately with a reduced sample compared to the pre-established sample size and thus the indications given by the study were impaired.

Koskela's project is presented in form of abstract and its findings are not fully disclosed [137].

Nevertheless, it provides interesting findings in terms of safety of the tool Omaolo©, considering a 99,8% of safety of triage reported, a 52,6% of exact matches between nurses and self-triage tool and the trend toward overtriage (66,6%).

Other reviews, from Chambers [120] and Wallace [145], investigate the self-triage tools and included studies that were excluded due to the specificity of the protocol that was followed. The consistency of this review is perhaps its main strength. It was decided to keep only observational studies and trials comparing real life self-triage to the standard of care, namely face to face consultation or telephone triage. Only three studies done in primary care/primary emergency care were found and considered eligible, limiting the findings to keep the consistency with the pre-established protocol.

Also, methodologically, both Yu's and Cotte's papers could be excluded, if not considering emergency care part of primary care.

Studies reported their results differently, leaving no chance to meta-analyze the data.

Moreover, Yu's study [135] reported on the records of patients, taking in consideration the Accident and Emergency Department Charts reports, not direct self-triage.

Another limitation may be due to the search strategy, which did not comprehend some terms, notably the words for community care. This may have led to missing some hits which could have proven useful.

Further studies are needed, considering the current status of literature, with not enough studies or trials even regarding the gold standard indicated as comparison, i.e. telephone triage and face to face consultation, where literature has shown differences based also on the rating scores used (ETI, MTS) [59].

A thorough revision of the protocol, or a new one, more inclusive and less specific, that considers eligible also non prospective cross-sectional studies, could help investigate the use of symptom-checkers in the setting of primary care, where symptom checkers and self-triage tools could be a game-changer, if proven to be safe and effective.

Features of SMASS Pathfinder CovidGuide users

The CovidGuide tool seemed to show a good usability, considering the total number of consultations held in-app as a proxy.

In all countries where the app was used, the data on the features of users, symptoms inputted, suggested distribution of time to treat and point of care app's output were similar. In the three countries examined most of the consultations were made by female users, in age range 14-49 years, and main symptom to start the selftriage was the ICPC code A77, Viral Disease non otherwise specified.

The percentage of cases that were deemed to configure an emergency were, respectively, of 10,7% in Italy, 4,75% in Germany, and 4,73% in Switzerland. The results, in terms of detection of emergency cases, if proven to be consistent with patients' outcomes, could be of utmost importance, especially in conditions of physicians' shortage and lack of resources. Percentages of the indication more frequently given, namely, to see a doctor during the same day of the consultation, probably depicting a tendency towards overtriage, were of the 42,9% for the Italian population examined whilst of the 38,5% for German and 37,84% for Swiss population.

Overall, the most interesting data retrieved, the one that could open a research path itself, is the one on self-care/self-monitoring.

In over 20% of cases the self-triage app, regardless of the country where triage was held, gave indications on safety net and suggested patients to manage their symptoms by themselves. Considering the current and impairing situation of healthcare services, if the output suggested results to be safe and reliable, this could mean a huge reduction of the burden on emergency and out of hours care.

In the time-series provided, the use of the app seems to match with the pandemic's pikes. A trend towards its use during the first year of the pandemic is particularly evident.

This first approach may be useful to define a model of the customer of such tools. Based on data gathered, the customer is more frequently a female user, using it for subjects from 14 to 60 years of age.

In Chambers's [120] systematic review, the included studies revealed that younger and more highly educated users are more likely to use these services while older and less educated patients were more likely to opt for telephone or face-to-face contact. This probably matches with the presented findings. Also, in the UTAUT model, age and sex represent

factors that may impact positively or negatively on the use of a certain technology, affecting performance and effort expectancy, social influence and facilitating condition in the UTAUT and hedonic motivation, price value and habit in the UTAUT 2 [105,107].

Gender itself exerts a relevant effect on the relationships between effort expectancy, performance expectancy and social influence in the UTAUT model, whilst age may impact on the effect of all four predictors of the UTAUT model [105]. Moreover personal factors such as gender and age may moderate the effect that hedonic motivation, price value and habit have on intention and use of a technology [107].

Since the seminal paper of Semigran, the renowned audit study stressing several symptom checkers for triage indications and evaluating diagnostic and triage accuracy, symptom tools were deemed to be inferior to expert panel assessment, whilst they seemed to be superior to the mere search of terms on a search engine, like Google or others. The authors argue that probably the symptom checkers would have had as a mean of comparison nurse/lay led telephonic triage [1].

Considering the systematic review from Chambers, symptom-checkers' use left the concern regarding their safety and efficacy.

The work from Michel et al. [146-148] on covid-19 triage performed at the Inselspital in Bern seems to show also future applicability for the online forward triage tools.

The data retrieved from the SMASS database and pertaining to the German, Swiss and Italian setting, showed the profile of the potential users of a conversational agent for self-triage, at least during the pandemic. The app was used mostly by younger patients/caregivers and female users. This seems to be consistent with the findings of literature reviews, highlighted in Chambers [120] and Wallace [145].

The tool provided outputs that we were not able, to date, to match with real patients' outcome, which will be investigated at least in the settings where the app is embedded in the healthcare system, namely Germany's regions.

The usability and the barriers and facilitators to the use of the app may be investigated with different methodological approaches. In this kind of evaluation, a mixed method approach is often chosen and preferred, as in the recent experiences from Michels et al. [146-148].

The health seeking behaviors of users must be considered and investigated further, to understand which solutions we may propose to guarantee access to care and universal health coverage.

A qualitative approach, starting from generative questions, to understand and explore the acceptability, usability, and perceived benefits of using a self-triage tool like the CovidGuide,

could be relevant for its further developments and complementary to the methodologies used so far.

It should involve different categories of users and stakeholders, for instance citizens, patients, patient-caregivers, healthcare professionals, healthcare workers.

Users could be asked to answer to the question:

"What is the experience of covid-19 self-triage use of citizens, patients, patient-caregivers, healthcare professionals and caregivers?"

By listening to the voice of key informants, the results of such a study could enable the improvement of digital triage systems, with the production, based on the experience of figures from different categories, of increasingly effective and patient/customer-friendly tools for triage.

Brendel's study provided relevant information on the role of social presence on the intention to comply [127]. Social presence, represented in the CovidGuide by the name, avatar, gender difference and initial greetings, was perceived as important and may influence users' intention to comply [127]. Nevertheless, CovidGuide was not equipped with other common elements, such as using emoticons [149], a human-like name [150], or frequent self-reference [151] (e.g., "I am..."), things that may have impaired the perceived social presence. Furthermore, the CA provided quick reply buttons (i.e., a selection of predefined answers) for users [127] that may harm the perception of humanness of the app, making it seem more robotic and distant [152].

Development, Acceptability and Usability of Afya Guide's COVID - 19 and Influenza-Like Illness (ILI) in Kenya

In the AfyaGuide pilot study, the usability and acceptability of a remote solution for symptom-checking and self-triage were investigated in the SSA setting, notably in Africa. Most of the participants received the indication to go to the pharmacy to seek care, meaning that most of the cases were low-urgency cases, that did not need a major healthcare effort.

The information gathered may be important to understand health seeking behaviors and the factors influencing the intention to use and eventually comply with the indications given by symptom checkers and self-triage tools. Moreover, this experience will help designing and developing more complete tools to allow the triage of tropical and infectious diseases in the Kenyan context.

The app showed overall a good usability and intention to comply by its users. Nevertheless, some aspects are to be further investigated. Notably, the pilot showed that, even if the users were persuaded and said that they would follow the advice given by the app (68%), 67% of them would anyway seek care in the hospital, if given the opportunity. This introduced a mismatch between the answers to the survey and the health seeking behavior of patients. As stated by Leonard et al., understanding what drives patients, considered as active elements with their own health seeking behavior [38], even with a different methodological approach, likely a qualitative one, would prove useful.

The results of the pilot study performed in 4 counties seem to show a promising role for self-triage tools in the Kenyan and most widely in the SSA context. Health seeking behaviors should be further analyzed and understood to learn how to introduce in a meaningful and viable way these tools in the SAA area. Notably, factors influencing intention to comply should be re-evaluated with a different study design, avoiding patients from being already in a healthcare center to understand whether they would really adhere to the app's recommendations. A qualitative methodological approach should also be used to explore the patterns emerging from their narratives. Lastly, the interaction between healthcare professionals (HCP) and users in the hospital setting should be minimized during the interaction with the app, and study eventually performed in the community setting, to avoid biasing conditions.

Limitations

This study presents several limitations, that need to be considered.

In the systematic review, as previously reported, some hits may have been missed due to the search strategy and, considering the papers that were retrieved, a meta-analysis was not possible.

The evaluation carried out on the CovidGuide usability in Europe has several flaws.

The data that were analyzed are based on the questions made by the app and gathered in the database, so it was not possible to produce more complex models. For instance, only age ranges as stated by the app were available, variables were different depending on the triage held by the tool, so different questions may have been posed to different subjects.

Moreover, it is possible that the questions regarding risk factors have been posed to the same subjects, thus impairing the understanding of the impact of the risk factors in the triage of subjects.

Triage was done mostly for female subjects in young age, 62,74%, but it is not possible to be sure that the triage was done by the same subjects using the self-triage. It may be that the app was used by caregivers of infants, of children, of older people or of people with disability or cognitive impairment.

Another aspect to consider is the role of the null or unclear consultations found in the database. Null identifies conditions in which the user was unable to correctly complete the triage, whilst unclear represents a safety netting mechanism, in case of inconsistency in the answers given by the patient/user to the self-triage tool. In these cases, the app advice is not given, and the patient is asked to seek care through a different mechanism.

Overall, nevertheless, the number of situations in which the app was not able to assess the patient conditions, is small, representing the 0,12% of in-app consultations.

The pilot study held in Kenya had also several limitations.

First, a relevant bias was introduced by the Ethic Committee's decision that the triage with the app should be done in face-to-face consultations with healthcare personnel.

Study participants were individuals who accessed healthcare centers for treatment. The recommendation to stay at home and self-monitor symptoms was not adhered to. Moreover, it is not possible to exclude a white coat effect, because participants were approached by healthcare professionals to be enrolled in the study.

Second, due to the tools used, some participants had to be excluded. Some had smartphones or connection problems. Thus, those data were excluded from the analysis.

The digital literacy was important to use the tool and to understand it, so participants with lower education were limited in participation in the study, introducing a relevant bias in the study.

Digital divide posed several challenges to the use of the app, as patients in areas with poor connectivity were limited in their access to the platform.

Some participants highlighted that the triage was long, but this consideration, even if understandable, must be neglected. The length of the questionnaire is directly linked to the questionnaire's safety and accuracy. Many questions were asked to correctly define time to treat and point of care for each user.

Implications for practice

The results of this study seem to show that, self-monitoring with safety netting advice is a relatively common advice. The percentage of people receiving the indication for self-monitoring is certainly relevant – around 20% of each population studied - and the resources that would be employed for people with minor conditions could be allocated for different services, whilst medical professional and healthcare professionals could be relieved from the burden of those patients that do not need face-to-face contact and can be monitored through the app.

In both Europe and Africa, researchers and stakeholders are striving to extend and scale up medical applications so that everyday complaints can be assessed, beyond covid-19 and starting in Africa from tropical diseases, with the aim of providing patients with a medically sound app for self-assessment.

The introduction of a digital health self-triage tool, using standardized protocols, plays a crucial role in the healthcare space in Kenya by providing alternatives to the need for patient-provider face-to-face consultations with health care workers that results in overcrowding of the limited medical facilities. Reducing the number of visits to health care facilities saves patients time and money and could deter unnecessary prescribing of medications, including antibiotics, leading to avoidable adverse drug reactions including Anti-Microbial Resistance (AMR). In addition, patients with severe symptoms requiring immediate medical attention could be directed to seek the appropriate emergency care.

Based on the results of the CovidGuide, affected persons can take specific measures: the spectrum of advice ranges from simple self-treatment, through the recommendation of a prompt contact with a doctor, to an immediate or emergency visit to a doctor or health facility.

The focus goes beyond the mere clarification of possible signs of a covid-19 infection, as patients with related symptoms may need to see a doctor urgently even during a pandemic.

Further research is needed to better understand the role of symptom checkers and self-triage tools. These tools could probably triage in a safe and effective way, relieving the healthcare professional from the burden of those calls which would need mostly advice on self-care.

The healthcare systems will need to find different solutions to cope with the burden of care, which will be even worse in the years to come, with the so called silver-tsunami on us [153]. Among the possible solutions, there will be room for safe and effective self-triage tools. Several experiences, made in other settings, showed a good rate of triage safety, still with a certain risk of undertriage. These tools may be effective if used appropriately, with safety netting advice and good detection of time to treat and point of care. The gap of knowledge in this field could open a race to find possible AI-assisted self-triage solutions, especially in these times of crisis where the healthcare professionals' shortage is spreading and impairing care all over the world.

Future developments

Based on the current findings, further studies, notably on situational factors and their impact on the intention to comply, through a collaboration among In4Medicine, the Aqua Institut and the university of Gottingen[127] and Dresden, will be performed.

The model on which the study will be based is shown in figure 26.

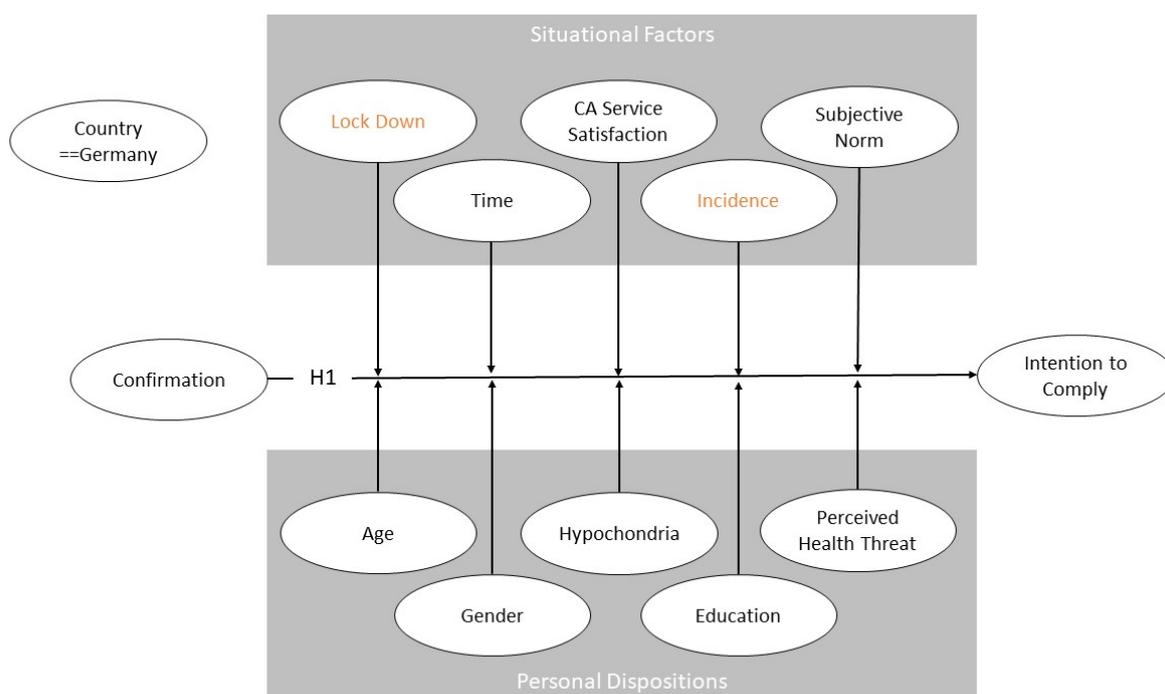


Fig. 26 The model for the study on situational factors, personal dispositions, and their impact on ItC

Exploratory factor analysis (EFA) and confirmatory factor analysis (CFA) will be used to describe what factors impact on intention to comply in the sample of 613 patients in Germany, as done by Brendel's group in the study on intention to comply and social presence [127] and in the previous experiences in the setting of out of hours care [154,155].

Conclusions

The main findings from the present work depict the core features of the user of a self-triage tool, designed and produced to afford the covid-19 outbreak by assessing its user's symptoms and referring them to the appropriate service: a female user, of young age, at least for the CovidGuide experience. This may drive towards a targeted intervention on this category or an attempt to make the application more viable for a broader public. In these terms, enhancing the performance expectancy on these tools, reducing the effort expectancy, and working on their systemic adoption, could improve the use of these technologies. Hedonic motivation seems to drive users more than performance expectancy, thus a modification of the app, adding more social cues, improving the graphics and simplifying the user experience – regardless of age and gender – could prove itself relevant for app's adoption.

The data regarding self-monitoring/self-treatment, which represent the indication for about 20% of the population assessed, independently from the country in which the triage was done, are of utmost importance and need, in our opinion, further studies, to define whether the indication given by our tool matched with the choice of treatment of the users and their outcome.

This will require a new study, and could be done in Germany, in the regions where the self-triage tool was embedded in the healthcare system and notably linked to the emergency care service. Qualitative methodologies could be preferred to investigate compliance with the advice of the app, as completing the recommendations of a counseling covid-19 self-triage tool is paramount to its effectiveness. If users do not comply, the healthcare infrastructure (including testing centers) can be overloaded by covid-19 free individuals, while individuals needing testing and subsequent treatment are not attending. Besides providing information, conversational agents (CAs) can also display a human-like design and elicit a perception of social presence. The findings from Brendel et al. support the positive effect of social presence for users' compliance with the recommendations of the CovidGuide, through its impact on trust in the app, a key driver for users' intention to comply [127]. On the other hand, no support for a similar effect of a CA's perceived persuasiveness was found [127].

In the African experience previously discussed, intention to comply was biased or impaired by the fact that self-triage was used in the healthcare centers, leading users to seek care

into the hospital even if the app advice, which they reported they would follow, recommended self-monitoring or a different point of care.

Considering the role of social presence described, future development of self-triage tools will probably focus on 3D virtual assistant with AI [156], in mixed or augmented reality [157], humanoids that will guide the patient/user through the step of triage and learn in the meanwhile how to deal with the different scenarios.

These systems could be powered with 5G or 6G [158] to allow the emergency services to be alerted in real time while the user is still assessing his/her symptoms.

The recent “exploit” of chatGPT [159-161] urges professionals to deal with new and “invasive” technologies which may prove themselves useful in healthcare. It is mandatory to accept this challenge and try to adapt to a transforming scenario, perhaps exploiting the new technologies, integrating them in our current healthcare models to ensure better care to our patients.

Appendix:

- 1 The algorithm of AfyaGuide
- 2 The usability questionnaire

Adapted SMASS Covid Afya Guide Questionnaire

	Patient Information	Kindly check
1.	Biological Sex	
	Is the affected person female or male?	
	• Female	
	• Male	
2.	Age (Age-Group)	
	How old is the person?	
	• 1-4 weeks of age	
	• 5-8 weeks of age	
	• 3-12 months of age	
	• 1-3 years of age	
	• 4-8 years of age	
	• 9-13 years of age	
	• 14-49 years of age	
	• 50-65 years of age	
	• 66-80 years of age	
	• More than 80 years of age	
3.	Pregnancy/breastfeeding	
	Is the person pregnant or breastfeeding?	
	• No pregnancy	
	• Pregnancy unclear	
	• Pregnancy	
	• Postpartum period/breastfeeding	
4.	Week of pregnancy	
	Which week of pregnancy?	
	• 0-13 weeks	
	• 14-27 weeks	
	• 28-42 weeks	

5.	Childbirth	
	How long has it been since the birth?	
	• Less than 6 weeks (postpartum period)	
	• More than 6 weeks	
6.	Underlying Conditions	
	• Hypertension	
	• Obesity	
	• Asthma	
	• Cardiovascular disease	
	• Renal disease	
	• Chronic Obstructive Pulmonary Disease (COPD)	
	• Diabetes mellitus	

Main COVID 19 Symptoms	
Question	Answer
Is there a temperature/fever?	Yes
	No
Are there any cough symptoms?	Yes
	No
Is the person experiencing breathing problems?	Yes
	No
Is there pain in the throat and/or pharynx?	Yes

	No
Is there a cold or flu?	Yes
	No
Is there a headache?	Yes
	No
Is there nausea or vomiting?	Yes
	No
Has the person experienced diarrhoea?	Yes
	No

Nonspecific symptoms



Reassure

Mild flu-like Symptoms:
 Fever, cough, sore throat, malaise, headache, muscle pain, nausea,
 vomiting, diarrhea, loss of taste and smell



Community Care with critical assessment of progression – if at the extremes of age, pregnant or lactating and with underlying chronic conditions observe for 12 – 24 hours and refer immediately to next level if symptoms worsen!!

Refer



If

Moderate COVID 19 Symptoms: above plus shortness of breath or difficulty breathing - if at the extremes of age, pregnant or lactating and with underlying chronic conditions observe for 12 – 24 hours and refer immediately to next level if symptoms worsen!

progresses



Refer

Home or in designated non-health facilities: if at the extremes of age, pregnant or lactating and with underlying chronic conditions observe for 12 – 24 hours and refer immediately to next level if symptoms worsens!



If progresses

Severe COVID-19 Symptoms: altered mental state, shortness of breath, **SpO2 < 94%**, respiratory rate **> 30/min**, systolic blood pressure **< 90 mm Hg** or other signs of shock or complications as well as co morbidities or **age > 60 years³**



Refer

Inpatient Admission and Care at Designated Hospital



Designated Hospitals (including Tertiary)

- Full clinical assessment and management. Perform blood test (e.g., CBC and chemistry profile) and chest X ray/CT scan, if available
- Test for COVID 19 (prioritize high risk patients, including unstable cases and those anticipated to need aerosol generating procedures) c
- Monitor severity of illness and complications (e.g., respiratory failure, ARDS, septic shock) Criteria for referral to ICU may include:
 - Impending respiratory failure, life threatening organ dysfunction or shock
 - Patient needs intensive monitoring
 - Patient needs intensive therapies (e.g., mechanical ventilation)

Presence of specific complications



Referred for assessment and further management by specialists

General internal medicine
Pediatrics and adolescent medicine
Gynecology and obstetrics
Surgery
Cardiac and thoracic vascular surgery
Ophthalmology
Oto-Rhino-Laryngology
Anesthesiology
Neurosurgery
Neurology
Orthopedic surgery and traumatology of the musculoskeletal system
Pneumology
Psychiatry and psychotherapy
Urology
Allergology and clinical immunology
Dermatology and venereology
Endocrinology and Diabetology

Electrical derivation of body signals (e.g. ECG, EEG)
Diagnostic procedure
Pharmacotherapy and prescription
Preventive vaccination and medication
Observation, health education, counseling and diet
Incision, drainage, irrigation, aspiration, and removal of body fluids.
Excision, tissue removal, biopsy, destruction, debridement and cauterization.
Instrumentation, catheterization, intubation and dilatation
Repair - sew or join
Bandaging or splints
Placement or removal of a prosthesis
Local injection and infiltration
Dressings, pressure, compression and tamponade
Therapeutic counselling
Interventions due to childbirth
Other special treatment and therapeutic and preventive interventions
Corona test

	<input type="checkbox"/> Strongly disagree <input type="checkbox"/> Disagree <input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Neither agree or disagree <input type="checkbox"/> Somewhat agree <input type="checkbox"/> Agree <input type="checkbox"/> Strongly agree
	<p>c. I felt a sense of human sensitivity using the Covidguide.</p> <input type="checkbox"/> Strongly disagree <input type="checkbox"/> Disagree <input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Neither agree or disagree <input type="checkbox"/> Somewhat agree <input type="checkbox"/> Agree <input type="checkbox"/> Strongly agree
Trust (in the decision of the system/the assessment)	<p>a. I perceive Covidguide to be very thorough.</p> <input type="checkbox"/> Strongly disagree <input type="checkbox"/> Disagree <input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Neither agree or disagree <input type="checkbox"/> Somewhat agree <input type="checkbox"/> Agree <input type="checkbox"/> Strongly agree
	<p>b. I have full confidence in the Covidguide's decisions.</p> <input type="checkbox"/> Strongly disagree <input type="checkbox"/> Disagree <input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Neither agree or disagree <input type="checkbox"/> Somewhat agree <input type="checkbox"/> Agree <input type="checkbox"/> Strongly agree
	<p>c. All in all, I have full confidence in the Covidguide.</p> <input type="checkbox"/> Strongly disagree <input type="checkbox"/> Disagree <input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Neither agree or disagree <input type="checkbox"/> Somewhat agree <input type="checkbox"/> Agree <input type="checkbox"/> Strongly agree
Persuasiveness	<p>a. The Covidguide has had an impact on my thinking about Covid-19.</p> <input type="checkbox"/> Strongly disagree <input type="checkbox"/> Disagree <input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Neither agree or disagree <input type="checkbox"/> Somewhat agree <input type="checkbox"/> Agree <input type="checkbox"/> Strongly agree
	<p>b. The Covidguide is relevant to me personally.</p> <input type="checkbox"/> Strongly disagree <input type="checkbox"/> Disagree <input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Neither agree or disagree <input type="checkbox"/> Somewhat agree <input type="checkbox"/> Agree <input type="checkbox"/> Strongly agree

	<p>c. The Covidguide makes me rethink my previous thoughts on Covid-19.</p> <p><input type="checkbox"/> Strongly disagree <input type="checkbox"/> Disagree <input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Neither agree or disagree</p> <p><input type="checkbox"/> Somewhat agree <input type="checkbox"/> Agree <input type="checkbox"/> Strongly agree</p>
Perception of the service	
Please rate how much you agree with the following statements.	
Service Satisfaction	<p>a. I am very pleased with the overall interaction with Covidguide.</p> <p><input type="checkbox"/> Strongly disagree <input type="checkbox"/> Disagree <input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Neither agree or disagree</p> <p><input type="checkbox"/> Somewhat agree <input type="checkbox"/> Agree <input type="checkbox"/> Strongly agree</p>
	<p>b. I am very happy with how the Covidguide treated me.</p> <p><input type="checkbox"/> Strongly disagree <input type="checkbox"/> Disagree <input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Neither agree or disagree</p> <p><input type="checkbox"/> Somewhat agree <input type="checkbox"/> Agree <input type="checkbox"/> Strongly agree</p>
Usefulness	<p>a. I find the Covidguide useful to support me regarding my Covid-19 concern</p> <p><input type="checkbox"/> Strongly disagree <input type="checkbox"/> Disagree <input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Neither agree or disagree</p> <p><input type="checkbox"/> Somewhat agree <input type="checkbox"/> Agree <input type="checkbox"/> Strongly agree</p>
	<p>b. Using the Covidguide makes it easier for me to complete my Covid-19 request.</p> <p><input type="checkbox"/> Strongly disagree <input type="checkbox"/> Disagree <input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Neither agree or disagree</p> <p><input type="checkbox"/> Somewhat agree <input type="checkbox"/> Agree <input type="checkbox"/> Strongly agree</p>
Usability	<p>a. I find it easy to interact with the Covidguide.</p> <p><input type="checkbox"/> Strongly disagree <input type="checkbox"/> Disagree <input type="checkbox"/> Somewhat disagree</p> <p><input type="checkbox"/> Somewhat agree <input type="checkbox"/> Agree <input type="checkbox"/> Strongly agree</p>

	<input type="checkbox"/> Neither agree or disagree
	<p>b. I find the Covidguide easy to use.</p> <input type="checkbox"/> Strongly disagree <input type="checkbox"/> Disagree <input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Neither agree or disagree <input type="checkbox"/> Somewhat agree <input type="checkbox"/> Agree <input type="checkbox"/> Strongly agree
Perception of the recommendation for action	
Please rate how much you agree with the following statements.	
Confirmation	<p>a. The Covidguide recommendation confirmed what I had expected.</p> <input type="checkbox"/> Strongly disagree <input type="checkbox"/> Disagree <input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Neither agree or disagree <input type="checkbox"/> Somewhat agree <input type="checkbox"/> Agree <input type="checkbox"/> Strongly agree
	<p>b. The Covidguide recommendation was different than I expected.</p> <input type="checkbox"/> Strongly disagree <input type="checkbox"/> Disagree <input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Neither agree or disagree <input type="checkbox"/> Somewhat agree <input type="checkbox"/> Agree <input type="checkbox"/> Strongly agree
	<p>c. Overall, the expectations I had about the Covidguide recommendation were confirmed.</p> <input type="checkbox"/> Strongly disagree <input type="checkbox"/> Disagree <input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Neither agree or disagree <input type="checkbox"/> Somewhat agree <input type="checkbox"/> Agree <input type="checkbox"/> Strongly agree
Attitude towards Compliance	<p>a. I follow the covidguide's recommended action exactly.</p> <input type="checkbox"/> Strongly disagree <input type="checkbox"/> Disagree <input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Neither agree or disagree <input type="checkbox"/> Somewhat agree <input type="checkbox"/> Agree <input type="checkbox"/> Strongly agree
	<p>b. I do not plan to follow the covidguide's recommendations for action.</p>

	<input type="checkbox"/> Strongly disagree <input type="checkbox"/> Disagree <input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Neither agree or disagree <input type="checkbox"/> Somewhat agree <input type="checkbox"/> Agree <input type="checkbox"/> Strongly agree
	<p>c. I intend to follow the recommended action.</p> <input type="checkbox"/> Strongly disagree <input type="checkbox"/> Disagree <input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Neither agree or disagree <input type="checkbox"/> Somewhat agree <input type="checkbox"/> Agree <input type="checkbox"/> Strongly agree
Subjective Norm	<p>a. In general, I follow the COVID-19 rules that my friends and family think are right.</p> <input type="checkbox"/> Strongly disagree <input type="checkbox"/> Disagree <input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Neither agree or disagree <input type="checkbox"/> Somewhat agree <input type="checkbox"/> Agree <input type="checkbox"/> Strongly agree
	<p>b. People I care about think I should follow the official Covid 19 regulations.</p> <input type="checkbox"/> Strongly disagree <input type="checkbox"/> Disagree <input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Neither agree or disagree <input type="checkbox"/> Somewhat agree <input type="checkbox"/> Agree <input type="checkbox"/> Strongly agree
	<p>c. People who influence my behavior think I should follow the official Covid-19 rules.</p> <input type="checkbox"/> Strongly disagree <input type="checkbox"/> Disagree <input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Neither agree or disagree <input type="checkbox"/> Somewhat agree <input type="checkbox"/> Agree <input type="checkbox"/> Strongly agree
(Behavioral) Intention to Comply	<p>a. Regardless of the covidguide recommendation, I will still go to the doctor for confirmation.</p> <input type="checkbox"/> Strongly disagree <input type="checkbox"/> Disagree <input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Neither agree or disagree <input type="checkbox"/> Somewhat agree <input type="checkbox"/> Agree <input type="checkbox"/> Strongly agree
	<p>b. I follow the recommendation of the Covidguide (go to the doctor/do not go to the doctor)</p> <input type="checkbox"/> Strongly disagree <input type="checkbox"/> Disagree <input type="checkbox"/> Somewhat agree <input type="checkbox"/> Agree

	<input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Strongly agree <input type="checkbox"/> Neither agree or disagree
	<p>c. Regardless of the Covidguide recommendation, I will not be going to the doctor.</p> <input type="checkbox"/> Strongly disagree <input type="checkbox"/> Somewhat agree <input type="checkbox"/> Disagree <input type="checkbox"/> Agree <input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Strongly agree <input type="checkbox"/> Neither agree or disagree
Person-specific properties	
Please rate how much you agree with the following statements:	
Hypochondria	<p>a. In general, I am very susceptible to colds, flu and other infectious diseases.</p> <input type="checkbox"/> Strongly disagree <input type="checkbox"/> Somewhat agree <input type="checkbox"/> Disagree <input type="checkbox"/> Agree <input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Strongly agree <input type="checkbox"/> Neither agree or disagree
	<p>b. If a disease is "circulating," I will get it.</p> <input type="checkbox"/> Strongly disagree <input type="checkbox"/> Somewhat agree <input type="checkbox"/> Disagree <input type="checkbox"/> Agree <input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Strongly agree <input type="checkbox"/> Neither agree or disagree
	<p>c. I am more likely to catch a contagious disease than the people around me.</p> <input type="checkbox"/> Strongly disagree <input type="checkbox"/> Somewhat agree <input type="checkbox"/> Disagree <input type="checkbox"/> Agree <input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Strongly agree <input type="checkbox"/> Neither agree or disagree
Health Threat	<p>a. COVID disease is a serious threat to me.</p> <input type="checkbox"/> Strongly disagree <input type="checkbox"/> Somewhat agree <input type="checkbox"/> Disagree <input type="checkbox"/> Agree <input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Strongly agree <input type="checkbox"/> Neither agree or disagree
	<p>b. COVID disease is a serious threat to my health.</p>

	<input type="checkbox"/> Strongly disagree <input type="checkbox"/> Disagree <input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Neither agree or disagree <input type="checkbox"/> Somewhat agree <input type="checkbox"/> Agree <input type="checkbox"/> Strongly agree
	<p>c. COVID disease is a serious threat to my social environment.</p> <input type="checkbox"/> Strongly disagree <input type="checkbox"/> Disagree <input type="checkbox"/> Somewhat disagree <input type="checkbox"/> Neither agree or disagree <input type="checkbox"/> Somewhat agree <input type="checkbox"/> Agree <input type="checkbox"/> Strongly agree
Education	<p>What is the highest level of school you have completed or the highest degree you have received?</p> <input type="checkbox"/> No education <input type="checkbox"/> Below Primary <input type="checkbox"/> Primary <input type="checkbox"/> Secondary <input type="checkbox"/> Tertiary (Any education above secondary school)

References

1. Semigran H, Linder JA, Gidengil C, Mehrotra A (2015) The effectiveness of symptom checkers for self-diagnosis and triage: Beyond “googling” symptoms. *Journal of General Internal Medicine* 30:S271-S271
2. Allouch M, Azaria A, Azoulay R (2021) Conversational Agents: Goals, Technologies, Vision and Challenges. *Sensors (Basel)* 21 (24). doi:10.3390/s21248448
3. McTear M, Callejas Z, Griol D (2016) Conversational interfaces: Past and present. In: *The Conversational Interface*. Springer, pp 51-72
4. Berg MM Development of Natural Dialogue Systems.
5. McTear MF The rise of the conversational interface: A new kid on the block? In: *International workshop on future and emerging trends in language technology, 2016*. Springer, pp 38-49
6. Barrett M, Davidson E, Prabhu J, Vargo SL (2015) Service innovation in the digital age. *MIS quarterly* 39 (1):135-154
7. Laranjo L, Dunn AG, Tong HL, Kocaballi AB, Chen J, Bashir R, Surian D, Gallego B, Magrabi F, Lau AYS, Coiera E (2018) Conversational agents in healthcare: a systematic review. *J Am Med Inform Assoc* 25 (9):1248-1258. doi:10.1093/jamia/ocy072
8. Verhagen T, Van Nes J, Feldberg F, Van Dolen W (2014) Virtual customer service agents: Using social presence and personalization to shape online service encounters. *Journal of Computer-Mediated Communication* 19 (3):529-545
9. Burton NG, Gaskin J (2019) “Thank you, Siri”: politeness and intelligent digital assistants.
10. Danielescu A, Christian G A bot is not a polyglot: Designing personalities for multi-lingual conversational agents. In: *Extended Abstracts of the 2018 CHI Conference on Human Factors in Computing Systems, 2018*. pp 1-9
11. Adamopoulou E, Moussiades L An overview of chatbot technology. In: *IFIP International Conference on Artificial Intelligence Applications and Innovations, 2020*. Springer, pp 373-383
12. Demurtas J, Vaona A (2023) Comparison of primary care health systems in Europe: the role of the General Practitioner. 18° rapporto CREA Sanità:397-407
13. AGENAS (2022) Analisi comparata delle cure primarie in Europa, vol *Quaderno di Monitor 2022*.
14. Kringos DS, Boerma WG, Hutchinson A, Saltman RB, Organization WH (2015) Building primary care in a changing Europe: case studies. World Health Organization. Regional Office for Europe,
15. Statistics O (2021) Available via <https://stats.oecd.org>. Accessed,
16. Colombo A, Bassani G (2019) Lack of doctors, but for what System? Shortage of clinicians in Italy and Lombardy and reflections on structural constrains in training. *Igiene e sanità pubblica* 75 (5):385-402
17. Paterlini M (2022) Warnings over doctor shortages amid Italian health reforms. *The Lancet* 399 (10341):2093
18. Caldirola D (2022) Welfare comunitario e Case della Comunità: dal PNRR alla riforma dell'assistenza sanitaria territoriale. *JUS* 2022 (5):161-193
19. Calabria S, Piccinni C, Recchia G, Santoro E, Grigolo S, Martini N (2022) Applications of digital medicine to care pathways: taxonomy, methods, impact on patients, barriers to overcome. *Recenti Progressi in Medicina* 113 (2):105-113

20. Muzzi A, Panà A (2022) The "redisorganisation" of the Italian Healthcare Service. *Igiene e Sanita Pubblica* 78 (1):4-6
21. Blümel M, Spranger A, Achstetter K, Maresso A, Busse R (2020) Germany: Health system review.
22. Metelmann B, Brinkrolf P, Kliche M, Vollmer M, Hahnenkamp K, Metelmann C (2021) Emergency medical service, medical on-call service, or emergency department: Germans unsure whom to contact in acute medical events. *Medizinische Klinik, Intensivmedizin und Notfallmedizin* 117 (2):144-151
23. Schäfer I, Menzel A, Herrmann T, Willms G, Oltrogge JH, Lühmann D, Scherer M (2023) Compliance and patient satisfaction with treatment settings recommended by the medical on-call service 116117 in Germany using computer-assisted structured initial assessment: a cross-sectional observational study accompanying the demand intervention. *BMJ open* 13 (5):e070475
24. Sax A 1.1 Struktur und Aufbau des Gesundheitssystems Schweiz-Aufgabenverteilung, Stärken und Schwächen, Resultate im internationalen Vergleich.
25. Benstetter F, Blum J, Dorn F, Greß S, Heuer A, Jesberger C, Jochimsen B, Schmidt CM, Schreyögg J, Pimpertz J (2022) Lehren aus der Covid-19-Pandemie: Der Weg zu größerer Resilienz im deutschen Gesundheitssystem. *ifo Schnelldienst* 75 (03):03-30
26. Lagolio E, Rossiello I, Meer A, Noventa V, Vaona A (2022) Red Flags in Geriatric Medicine: Assessing Risk and Managing It in Primary Care. In: *The Role of Family Physicians in Older People Care*. Springer, pp 221-240
27. Haller N, Lareida J, Meer A (2020) Aargauer Ärzteschaft präsentiert Web-App "MedicalGuide". *Bulletin des médecins suisses* 101 (43):1401-1406
28. Heiby J (2014) The use of modern quality improvement approaches to strengthen African health systems: a 5-year agenda. *International Journal for Quality in Health Care* 26 (2):117-123
29. Adindu A (2010) Assessing and assuring quality of health care in Africa. *African Journal of Medical Sciences* 3 (1):31-36
30. Flinkenflögel M, Essuman A, Chege P, Ayankogbe O, De Maeseneer J (2014) Family medicine training in sub-Saharan Africa: South-South cooperation in the Primafamed project as strategy for development. *Family practice* 31 (4):427-436
31. De Maeseneer J (2013) Scaling up family medicine and primary health care in Africa: statement of the primafamed network, Victoria Falls, Zimbabwe. *African Journal of Primary Health Care and Family Medicine* 5 (1):1-3
32. De Maeseneer J (2017) Twenty years of Primafamed Network in Africa: Looking back at the future. *African Journal of Primary Health Care and Family Medicine* 9 (1):1-2
33. Flinkenflögel M, Sethlare V, Cubaka VK, Makasa M, Guyse A, De Maeseneer J (2020) A scoping review on family medicine in sub-Saharan Africa: Practice, positioning and impact in African health care systems. *Human resources for health* 18:1-18
34. Moosa S, Downing R, Mash B, Reid S, Pentz S, Essuman A (2013) Understanding of family medicine in Africa: a qualitative study of leaders' views. *British Journal of General Practice* 63 (608):e209-e216
35. Salari P, Di Giorgio L, Ilinca S, Chuma J (2019) The catastrophic and impoverishing effects of out-of-pocket healthcare payments in Kenya, 2018. *BMJ Global Health* 4 (6):e001809
36. Mbau R, Oliver K, Vassall A, Gilson L, Barasa E (2023) A qualitative evaluation of priority-setting by the Health Benefits Package Advisory Panel in Kenya. *Health policy and planning* 38 (1):49-60
37. Wilunda C, Scanagatta C, Putoto G, Takahashi R, Montalbetti F, Segafredo G, Betrán AP (2016) Barriers to institutional childbirth in Rumbek North County, South Sudan: a qualitative study. *PLoS One* 11 (12):e0168083

38. Leonard KL (2014) Active patients in rural African health care: implications for research and policy. *Health policy and planning* 29 (1):85-95
39. Muinde JVS, Prince RJ (2023) A new universalism? Universal health coverage and debates about rights, solidarity and inequality in Kenya. *Social Science & Medicine* 319:115258
40. Di Gennaro F, Pizzol D, Marotta C, Antunes M, Racalbutto V, Veronese N, Smith L (2020) Coronavirus diseases (COVID-19) current status and future perspectives: a narrative review. *International journal of environmental research and public health* 17 (8):2690
41. Editors (2020) Dying in a Leadership Vacuum. *N Engl J Med* 383 (15):1479-1480. doi:10.1056/NEJMe2029812
42. Mareiniss DP (2021) The Emperor Has No Clothes - Medical Journals and Experts Must Stand Up and Condemn the Federal Pandemic Response. *Am J Emerg Med* 45:666. doi:10.1016/j.ajem.2020.10.056
43. Conceição Outeirinho RB, Joana Costa-Gomes, Luís Alves, Ana Margarida Cruz, Ana Clavería, Antón Núñez-Torrón, Marina Jotic, Jacopo Demurtas, Tugba Çalıřkan, Victoria Tkachenko, Poliana Jorge (2021) The Covid-19 pandemic: Reorganization of health services and coping of health care workers in Primary Health Care. Paper presented at the 93rd EGPRN Conference, Halle ,
44. Solmi M, Estrade A, Thompson T, Agorastos A, Radua J, Cortese S, Dragioti E, Leisch F, Vancampfort D, Thygesen LC, Aschauer H, Schloegelhofer M, Akimova E, Schneeberger A, Huber CG, Hasler G, Conus P, Cuenod KQD, von Kanel R, Arrondo G, Fusar-Poli P, Gorwood P, Llorca PM, Krebs MO, Scanferla E, Kishimoto T, Rabbani G, Skonieczna-Zydecka K, Brambilla P, Favaro A, Takamiya A, Zocante L, Colizzi M, Bourgin J, Kaminski K, Moghadasin M, Seedat S, Matthews E, Wells J, Vassilopoulou E, Gadelha A, Su KP, Kwon JS, Kim M, Lee TY, Papsuev O, Mankova D, Boscutti A, Gerunda C, Saccon D, Righi E, Monaco F, Croatto G, Cereda G, Demurtas J, Brondino N, Veronese N, Enrico P, Politi P, Ciappolino V, Pfennig A, Bechdorf A, Meyer-Lindenberg A, Kahl KG, Domschke K, Bauer M, Koutsouleris N, Winter S, Borgwardt S, Bitter I, Balazs J, Czobor P, Unoka Z, Mavridis D, Tsamakias K, Bozikas VP, Tunvirachaisakul C, Maes M, Rungrirundorn T, Supasitthumrong T, Haque A, Brunoni AR, Costardi CG, Schuch FB, Polanczyk G, Luiz JM, Fonseca L, Aparicio LV, Valvassori SS, Nordentoft M, Vendsborg P, Hoffmann SH, Sehli J, Sartorius N, Heuss S, Guinart D, Hamilton J, Kane J, Rubio J, Sand M, Koyanagi A, Solanes A, Andreu-Bernabeu A, Caceres ASJ, Arango C, Diaz-Caneja CM, Hidalgo-Mazzei D, Vieta E, Gonzalez-Penas J, Fortea L, Parellada M, Fullana MA, Verdolini N, Farkova E, Janku K, Millan M, Honciuc M, Moniuszko-Malinowska A, Loniewski I, Samochowiec J, Kiszkiel L, Marlicz M, Sowa P, Marlicz W, Spies G, Stubbs B, Firth J, Sullivan S, Darcin AE, Aksu H, Dilbaz N, Noyan O, Kitazawa M, Kurokawa S, Tazawa Y, Anselmi A, Cracco C, Machado AI, Estrade N, De Leo D, Curtis J, Berk M, Ward P, Teasdale S, Rosenbaum S, Marx W, Horodnic AV, Oprea L, Alexinschi O, Ifteni P, Turliuc S, Ciuhodaru T, Bolos A, Matei V, Nieman DH, Sommer I, van Os J, van Amelsvoort T, Sun CF, Guu TW, Jiao C, Zhang J, Fan J, Zou L, Yu X, Chi X, de Timary P, van Winke R, Ng B, Pena E, Arellano R, Roman R, Sanchez T, Movina L, Morgado P, Brissos S, Aizberg O, Mosina A, Krinitski D, Mugisha J, Sadeghi-Bahmani D, Sadeghi M, Hadi S, Brand S, Errazuriz A, Crossley N, Ristic DI, Lopez-Jaramillo C, Efthymiou D, Kuttichira P, Kallivayalil RA, Javed A, Afridi MI, James B, Seb-Akahomen OJ, Fiedorowicz J, Carvalho AF, Daskalakis J, Yatham LN, Yang L, Okasha T, Dahdouh A, Gerdle B, Tiihonen J, Shin JI, Lee J, Mhalla A, Gaha L, Brahim T, Altynbekov K, Negay N, Nurmagambetova S, Jamei YA, Weiser M, Correll CU (2022) The collaborative outcomes study on health and functioning during infection times in adults (COH-FIT-Adults): Design and methods of an international online survey targeting physical and mental health effects of the COVID-19 pandemic. *J Affect Disord* 299:393-407. doi:10.1016/j.jad.2021.07.048

45. Solmi M, Estrade A, Thompson T, Agorastos A, Radua J, Cortese S, Dragioti E, Leisch F, Vancampfort D, Thygesen LC, Aschauer H, Schloegelhofer M, Akimova E, Schneeberger A, Huber CG, Hasler G, Conus P, Cuenod KQD, von Kanel R, Arrondo G, Fusar-Poli P, Gorwood P, Llorca PM, Krebs MO, Scanferla E, Kishimoto T, Rabbani G, Skonieczna-Zydecka K, Brambilla P, Favaro A, Takamiya A, Zoccante L, Colizzi M, Bourgin J, Kaminski K, Moghadasin M, Seedat S, Matthews E, Wells J, Vassilopoulou E, Gadelha A, Su KP, Kwon JS, Kim M, Lee TY, Papsuev O, Mankova D, Boscutti A, Gerunda C, Saccon D, Righi E, Monaco F, Croatto G, Cereda G, Demurtas J, Brondino N, Veronese N, Enrico P, Politi P, Ciappolino V, Pfennig A, Bechdolf A, Meyer-Lindenberg A, Kahl KG, Domschke K, Bauer M, Koutsouleris N, Winter S, Borgwardt S, Bitter I, Balazs J, Czobor P, Unoka Z, Mavridis D, Tsamakias K, Bozikas VP, Tunvirachaisakul C, Maes M, Rungnirundorn T, Supasitthumrong T, Haque A, Brunoni AR, Costardi CG, Schuch FB, Polanczyk G, Luiz JM, Fonseca L, Aparicio LV, Valvassori SS, Nordentoft M, Vendsborg P, Hoffmann SH, Sehli J, Sartorius N, Heuss S, Guinart D, Hamilton J, Kane J, Rubio J, Sand M, Koyanagi A, Solanes A, Andreu-Bernabeu A, Caceres ASJ, Arango C, Diaz-Caneja CM, Hidalgo-Mazzei D, Vieta E, Gonzalez-Penas J, Fortea L, Parellada M, Fullana MA, Verdolini N, Farkova E, Janku K, Millan M, Honciuc M, Moniuszko-Malinowska A, Loniewski I, Samochowiec J, Kiszkiel L, Marlicz M, Sowa P, Marlicz W, Spies G, Stubbs B, Firth J, Sullivan S, Darcin AE, Aksu H, Dilbaz N, Noyan O, Kitazawa M, Kurokawa S, Tazawa Y, Anselmi A, Cracco C, Machado AI, Estrade N, De Leo D, Curtis J, Berk M, Ward P, Teasdale S, Rosenbaum S, Marx W, Horodnic AV, Oprea L, Alexinschi O, Ifteni P, Turliuc S, Ciuhodaru T, Bolos A, Matei V, Nieman DH, Sommer I, van Os J, van Amelsvoort T, Sun CF, Guu TW, Jiao C, Zhang J, Fan J, Zou L, Yu X, Chi X, de Timary P, van Winke R, Ng B, Pena E, Arellano R, Roman R, Sanchez T, Movina L, Morgado P, Brissos S, Aizberg O, Mosina A, Krinitski D, Mugisha J, Sadeghi-Bahmani D, Sadeghi M, Hadi S, Brand S, Errazuriz A, Crossley N, Ristic DI, Lopez-Jaramillo C, Efthymiou D, Kuttichira P, Kallivayalil RA, Javed A, Afridi MI, James B, Seb-Akahomen OJ, Fiedorowicz J, Carvalho AF, Daskalakis J, Yatham LN, Yang L, Okasha T, Dahdouh A, Gerdle B, Tiihonen J, Shin JI, Lee J, Mhalla A, Gaha L, Brahim T, Altynbekov K, Negay N, Nurmagambetova S, Jamei YA, Weiser M, Correll CU (2022) Physical and mental health impact of COVID-19 on children, adolescents, and their families: The Collaborative Outcomes study on Health and Functioning during Infection Times - Children and Adolescents (COH-FIT-C&A). *J Affect Disord* 299:367-376. doi:10.1016/j.jad.2021.09.090
46. Maital S, Barzani E (2020) The global economic impact of COVID-19: A summary of research. Samuel Neaman Institute for National Policy Research 2020:1-12
47. Lagolio E, Demurtas J, Buzzetti R, Cortassa G, Bottone S, Spadafora L, Cocino C, Smith L, Benzing T, Polidori MC (2021) A rapid and feasible tool for clinical decision making in community-dwelling patients with COVID-19 and those admitted to emergency departments: The Braden-LDH-Horowitz Assessment—BLITZ. *Internal and Emergency Medicine*:1-6
48. Zhang J-j, Dong X, Liu G-h, Gao Y-d (2023) Risk and protective factors for COVID-19 morbidity, severity, and mortality. *Clinical Reviews in Allergy & Immunology* 64 (1):90-107
49. Skandalakis PN, Lainas P, Zoras O, Skandalakis JE, Mirilas P (2006) "To afford the wounded speedy assistance": Dominique Jean Larrey and Napoleon. *World J Surg* 30 (8):1392-1399. doi:10.1007/s00268-005-0436-8
50. Derkx HP, Rethans JJ, Muijtjens AM, Maiburg BH, Winkens R, van Rooij HG, Knottnerus JA (2008) Quality of clinical aspects of call handling at Dutch out of hours centres: cross sectional national study. *BMJ* 337:a1264. doi:10.1136/bmj.a1264
51. Derkx H, Rethans JJ, Maiburg B, Winkens R, Muijtjens A, Van Rooij H, Knottnerus A (2009) The quality of telephone triage on general practitioners' posts. *Huisarts en Wetenschap* 52 (7):326-331. doi:10.1007/bf03085669 LK - <http://sfx-39bic.hosted.exlibrisgroup.com/sfxbic3/?sid=EMBASE&sid=EMBASE&issn=00187070&id=doi:10.1>

[007%2Fbf03085669&atitle=The+quality+of+telephone+trriage+on+general+practitioners%27+post&stitle=Huisarts+Wet.&title=Huisarts+en+Wetenschap&volume=52&issue=7&spage=326&epage=331&aulast=Derkx&aufirst=Hay&aunit=H.&aufull=Derkx+H.&coden=HUWEA&isbn=&pages=326-331&date=2009&aunit1=H&aunitm=](#)

52. Derkx H, Rethans JJ, Maiburg B, Winkens R, Muijtjens A, Van Rooij H, Knottnerus A (2009) Quality of telephone triage in general practitioner posts in The Netherlands: Communication and reporting skills. *Huisarts en Wetenschap* 52 (9):455-460
53. Derkx H, Rethans JJ, Muijtjens A, Maiburg B, Winkens R, van Rooij H, Knottnerus A (2010) 'Quod scripsi, scripsi.' The quality of the report of telephone consultations at Dutch out-of-hours centres. *Qual Saf Health Care* 19 (6):e1. doi:10.1136/qshc.2008.027920
54. Derkx HP, Rethans JJ, Knottnerus JA, Ram PM (2007) Assessing communication skills of clinical call handlers working at an out-of-hours centre: development of the RICE rating scale. *Br J Gen Pract* 57 (538):383-387
55. Derkx H, Rethans JJ, Maiburg B, Winkens R, Knottnerus A (2009) New methodology for using incognito standardised patients for telephone consultation in primary care. *Med Educ* 43 (1):82-88. doi:10.1111/j.1365-2923.2008.03177.x
56. Vaona A, Pappas Y, Grewal RS, Ajaz M, Majeed A, Car J (2017) Training interventions for improving telephone consultation skills in clinicians. *Cochrane Database Syst Rev* 1 (1):CD010034. doi:10.1002/14651858.CD010034.pub2
57. Greenhalgh T, Koh GCH, Car J (2020) Covid-19: a remote assessment in primary care. *BMJ* 368:m1182. doi:10.1136/bmj.m1182
58. Greenhalgh T, Wherton J, Shaw S, Morrison C (2020) Video consultations for covid-19. *BMJ* 368:m998. doi:10.1136/bmj.m998
59. Zachariasse JM, van der Hagen V, Seiger N, Mackway-Jones K, van Veen M, Moll HA (2019) Performance of triage systems in emergency care: a systematic review and meta-analysis. *BMJ Open* 9 (5):e026471. doi:10.1136/bmjopen-2018-026471
60. Azeredo TR, Guedes HM, Rebelo de Almeida RA, Chianca TC, Martins JC (2015) Efficacy of the Manchester Triage System: a systematic review. *Int Emerg Nurs* 23 (2):47-52. doi:10.1016/j.ienj.2014.06.001
61. Mirhaghi A, Mazlom R, Heydari A, Ebrahimi M (2017) The reliability of the Manchester Triage System (MTS): a meta-analysis. *J Evid Based Med* 10 (2):129-135. doi:10.1111/jebm.12231
62. Shelton R (2009) The emergency severity index 5-level triage system. *Dimensions of Critical Care Nursing* 28 (1):9-12
63. Gilboy N, Tanabe P, Travers DA, Rosenau AM, Eitel DR (2005) Emergency severity index, version 4: implementation handbook. Rockville, MD: Agency for Healthcare Research and Quality 1
64. McHugh M, Tanabe P, McClelland M, Khare RK (2012) More patients are triaged using the Emergency Severity Index than any other triage acuity system in the United States. *Academic Emergency Medicine* 19 (1):106-109
65. Speake D, Teece S, Mackway-Jones K (2003) Detecting high-risk patients with chest pain. *Emergency Nurse (through 2013)* 11 (5):19
66. van der Wulp I, van Baar ME, Schrijvers AJ (2008) Reliability and validity of the Manchester Triage System in a general emergency department patient population in the Netherlands: results of a simulation study. *Emerg Med J* 25 (7):431-434. doi:10.1136/emj.2007.055228
67. van der Wulp I, Schrijvers AJ, van Stel HF (2009) Predicting admission and mortality with the Emergency Severity Index and the Manchester Triage System: a retrospective observational study. *Emerg Med J* 26 (7):506-509. doi:10.1136/emj.2008.063768

68. Storm-Versloot MN, Ubbink DT, Chin a Choi V, Luitse JS (2009) Observer agreement of the Manchester Triage System and the Emergency Severity Index: a simulation study. *Emerg Med J* 26 (8):556-560. doi:10.1136/emj.2008.059378
69. Storm-Versloot MN, Ubbink DT, Kappelhof J, Luitse JS (2011) Comparison of an informally structured triage system, the emergency severity index, and the manchester triage system to distinguish patient priority in the emergency department. *Acad Emerg Med* 18 (8):822-829. doi:10.1111/j.1553-2712.2011.01122.x
70. McCarthy J, Minsky ML, Rochester N, Shannon CE (2006) A proposal for the dartmouth summer research project on artificial intelligence, august 31, 1955. *AI magazine* 27 (4):12-12
71. Russell SJ, Norvig P (2003) *Artificial Intelligence: A Modern Approach* (Harlow. Pearson Education,
72. Scott IA, Cook D, Coiera EW, Richards B (2019) Machine learning in clinical practice: prospects and pitfalls. *Medical Journal of Australia* 211 (5):203-205. e201
73. Sutton RT, Pincock D, Baumgart DC, Sadowski DC, Fedorak RN, Kroeker KI (2020) An overview of clinical decision support systems: benefits, risks, and strategies for success. *NPJ digital medicine* 3 (1):1-10
74. Topol E (2019) *Deep medicine: how artificial intelligence can make healthcare human again*. Hachette UK,
75. Jiang F, Jiang Y, Zhi H, Dong Y, Li H, Ma S, Wang Y, Dong Q, Shen H, Wang Y (2017) Artificial intelligence in healthcare: past, present and future. *Stroke and vascular neurology* 2 (4)
76. Yoo I, Alafairet P, Marinov M, Pena-Hernandez K, Gopidi R, Chang J-F, Hua L (2012) Data mining in healthcare and biomedicine: a survey of the literature. *Journal of medical systems* 36:2431-2448
77. Lakshmanaprabu S, Mohanty SN, Krishnamoorthy S, Uthayakumar J, Shankar K (2019) Online clinical decision support system using optimal deep neural networks. *Applied Soft Computing* 81:105487
78. Bai Y, Li D, Duan Q, Chen X (2022) Analysis of high-resolution reconstruction of medical images based on deep convolutional neural networks in lung cancer diagnostics. *Computer Methods and Programs in Biomedicine* 217:106592
79. Ge R, Shen T, Zhou Y, Liu C, Zhang L, Yang B, Yan Y, Coatrieux J-L, Chen Y (2021) Convolutional squeeze-and-excitation network for ECG arrhythmia detection. *Artificial Intelligence in Medicine* 121:102181
80. Zhang C, Sun X, Dang K, Li K, Guo Xw, Chang J, Yu Zq, Huang Fy, Wu Ys, Liang Z (2019) Toward an expert level of lung cancer detection and classification using a deep convolutional neural network. *The oncologist* 24 (9):1159-1165
81. Nurmaini S, Partan RU, Bernolian N, Sapitri AI, Tutuko B, Rachmatullah MN, Darmawahyuni A, Firdaus F, Mose JC (2022) Deep Learning for Improving the Effectiveness of Routine Prenatal Screening for Major Congenital Heart Diseases. *Journal of Clinical Medicine* 11 (21):6454
82. Yang Z, Li P, Wang R (2022) Prediction of Metabolic Characteristics of Cardiovascular and Cerebrovascular Diseases Based on Convolutional Neural Network. *Computational and Mathematical Methods in Medicine* 2022
83. Shortliffe EH, Sepúlveda MJ (2018) Clinical decision support in the era of artificial intelligence. *Jama* 320 (21):2199-2200
84. Kaushal R, Shojania KG, Bates DW (2003) Effects of computerized physician order entry and clinical decision support systems on medication safety: a systematic review. *Archives of internal medicine* 163 (12):1409-1416

85. Bright TJ, Wong A, Dhurjati R, Bristow E, Bastian L, Coeytaux RR, Samsa G, Hasselblad V, Williams JW, Musty MD (2012) Effect of clinical decision-support systems: a systematic review. *Annals of internal medicine* 157 (1):29-43
86. Payne TH (2000) Computer decision support systems. *Chest* 118 (2):475-525
87. Jeffery R, Iserman E, Haynes R, Team CSR (2013) Can computerized clinical decision support systems improve diabetes management? A systematic review and meta-analysis. *Diabetic Medicine* 30 (6):739-745
88. Moja L, Kwag KH, Lytras T, Bertizzolo L, Brandt L, Pecoraro V, Rigon G, Vaona A, Ruggiero F, Mangia M (2014) Effectiveness of computerized decision support systems linked to electronic health records: a systematic review and meta-analysis. *American journal of public health* 104 (12):e12-e22
89. Faviez C, Chen X, Garcelon N, Neuraz A, Knebelmann B, Salomon R, Lyonnet S, Saunier S, Burgun A (2020) Diagnosis support systems for rare diseases: a scoping review. *Orphanet Journal of Rare Diseases* 15 (1):1-16
90. Wulff A, Montag S, Marschollek M, Jack T (2019) Clinical decision-support systems for detection of systemic inflammatory response syndrome, sepsis, and septic shock in critically ill patients: a systematic review. *Methods of information in medicine* 58 (S 02):e43-e57
91. Langerhuizen DW, Janssen SJ, Mallee WH, Van Den Bekerom MP, Ring D, Kerkhoffs GM, Jaarsma RL, Doornberg JN (2019) What are the applications and limitations of artificial intelligence for fracture detection and classification in orthopaedic trauma imaging? A systematic review. *Clinical orthopaedics and related research* 477 (11):2482
92. Roumeliotis N, Sniderman J, Adams-Webber T, Addo N, Anand V, Rochon P, Taddio A, Parshuram C (2019) Effect of electronic prescribing strategies on medication error and harm in hospital: a systematic review and meta-analysis. *Journal of general internal medicine* 34 (10):2210-2223
93. Rawson T, Moore L, Hernandez B, Charani E, Castro-Sanchez E, Herrero P, Hayhoe B, Hope W, Georgiou P, Holmes A (2017) A systematic review of clinical decision support systems for antimicrobial management: are we failing to investigate these interventions appropriately? *Clinical Microbiology and Infection* 23 (8):524-532
94. Yu K-H, Beam AL, Kohane IS (2018) Artificial intelligence in healthcare. *Nature biomedical engineering* 2 (10):719-731
95. Oluoch T, Santas X, Kwaro D, Were M, Biondich P, Bailey C, Abu-Hanna A, de Keizer N (2012) The effect of electronic medical record-based clinical decision support on HIV care in resource-constrained settings: a systematic review. *International journal of medical informatics* 81 (10):e83-e92
96. Carter J, Sandall J, Shennan AH, Tribe RM (2019) Mobile phone apps for clinical decision support in pregnancy: a scoping review. *BMC medical informatics and decision making* 19 (1):1-13
97. Food, Administration D (2019) Proposed regulatory framework for modifications to artificial intelligence/machine learning (AI/ML)-based software as a medical device (SaMD).
98. Yusof MM, Kuljis J, Papazafeiropoulou A, Stergioulas LK (2008) An evaluation framework for Health Information Systems: human, organization and technology-fit factors (HOT-fit). *International journal of medical informatics* 77 (6):386-398
99. Kilsdonk E, Peute L, Jaspers MW (2017) Factors influencing implementation success of guideline-based clinical decision support systems: a systematic review and gaps analysis. *International journal of medical informatics* 98:56-64
100. Topol EJ (2019) High-performance medicine: the convergence of human and artificial intelligence. *Nature medicine* 25 (1):44-56

101. Davis FD (1989) Perceived usefulness, perceived ease of use, and user acceptance of information technology. *MIS quarterly*:319-340
102. Davis FD (1993) User acceptance of information technology: system characteristics, user perceptions and behavioral impacts. *International journal of man-machine studies* 38 (3):475-487
103. Davis FD, Bagozzi RP, Warshaw PR (1989) User acceptance of computer technology: A comparison of two theoretical models. *Management science* 35 (8):982-1003
104. Venkatesh V, Davis FD (2000) A theoretical extension of the technology acceptance model: Four longitudinal field studies. *Management science* 46 (2):186-204
105. Venkatesh V, Morris MG, Davis GB, Davis FD (2003) User acceptance of information technology: Toward a unified view. *MIS quarterly*:425-478
106. Venkatesh V, Thong JY, Xu X (2016) Unified theory of acceptance and use of technology: A synthesis and the road ahead. *Journal of the association for Information Systems* 17 (5):328-376
107. Venkatesh V, Thong JY, Xu X (2012) Consumer acceptance and use of information technology: extending the unified theory of acceptance and use of technology. *MIS quarterly*:157-178
108. Alvesson M, Kärreman D (2007) Constructing mystery: Empirical matters in theory development. *Academy of management review* 32 (4):1265-1281
109. Van der Heijden H (2004) User acceptance of hedonic information systems. *MIS quarterly*:695-704
110. Brown SA, Venkatesh V (2005) Model of adoption of technology in households: A baseline model test and extension incorporating household life cycle. *MIS quarterly*:399-426
111. Whitelaw S, Mamas MA, Topol E, Van Spall HG (2020) Applications of digital technology in COVID-19 pandemic planning and response. *The Lancet Digital Health* 2 (8):e435-e440
112. Davalbhakta S, Advani S, Kumar S, Agarwal V, Bhojar S, Fedirko E, Misra DP, Goel A, Gupta L, Agarwal V (2020) A systematic review of smartphone applications available for corona virus disease 2019 (COVID19) and the assessment of their quality using the mobile application rating scale (MARS). *Journal of medical systems* 44 (9):1-15
113. Munsch N, Martin A, Gruarin S, Nateqi J, Abdarahmane I, Weingartner-Ortner R, Knapp B (2020) Diagnostic Accuracy of Web-Based COVID-19 Symptom Checkers: Comparison Study. *Journal of medical Internet research* 22 (10):e21299-e21299. doi:10.2196/21299
114. Salem H, Attiya G, El-Fishawy N (2015) A survey of multi-agent based intelligent decision support system for medical classification problems. *International Journal of Computer Applications* 123 (10)
115. Ji M, Genchev GZ, Huang H, Xu T, Lu H, Yu G (2021) Evaluation Framework for Successful Artificial Intelligence–Enabled Clinical Decision Support Systems: Mixed Methods Study. *Journal of medical Internet research* 23 (6):e25929
116. Miner AS, Laranjo L, Kocaballi AB (2020) Chatbots in the fight against the COVID-19 pandemic. *NPJ digital medicine* 3 (1):65
117. Poote AE, French DP, Dale J, Powell J (2014) A study of automated self-assessment in a primary care student health centre setting. *Journal of telemedicine and telecare* 20 (3):123-127
118. Verzantvoort NC, Teunis T, Verheij TJ, van der Velden AW (2018) Self-triage for acute primary care via a smartphone application: practical, safe and efficient? *PLoS One* 13 (6):e0199284
119. Pairon A, Philips H, Verhoeven V (2023) A scoping review on the use and usefulness of online symptom checkers and triage systems: How to proceed? *Frontiers in Medicine* 9:1040926
120. Chambers D, Cantrell AJ, Johnson M, Preston L, Baxter SK, Booth A, Turner J (2019) Digital and online symptom checkers and health assessment/triage services for urgent health problems: systematic review. *BMJ open* 9 (8):e027743-e027743. doi:10.1136/bmjopen-2018-027743

121. Alvarez P, Sianis A, Brown J, Ali A, Briasoulis A (2021) Chronic disease management in heart failure: focus on telemedicine and remote monitoring. *Reviews in Cardiovascular Medicine* 22 (2):403-413
122. Carrillo de Albornoz S, Sia K-L, Harris A (2022) The effectiveness of teleconsultations in primary care: systematic review. *Family Practice* 39 (1):168-182
123. Kluge HHP, Azzopardi-Muscat N, Novillo-Ortiz D (2022) Leveraging digital transformation for better health in Europe. *Bull World Health Organ* 100 (12):751-751A. doi:10.2471/BLT.22.289132
124. Demurtas J, Tonelli R, Celotto S, Veronese N, Lagolio E, Rossi F, Clini E, Righi E, Meer A (2021) [COVID-Guide: an app for covid-19 triage and self-assessment.]. *Recenti progressi in medicina* 112 (5):387-391. doi:10.1701/3608.35876
125. Graf von Stillfried D, Czihal T, Meer A (2019) Sachstandsbericht: Strukturierte medizinische Ersteinschätzung in Deutschland (SmED). *Notfall+ Rettungsmedizin* 22 (7):578-588
126. Roth C, Breckner A, Paulus J, Wensing M (2020) Implementation of a standardized initial assessment for demand management in outpatient emergency care in Germany: Early qualitative process evaluation. *JMIR formative research* 4 (9):e18456
127. Brendel AB, Greve M, Riquel J, Böhme M, Greulich RS (2022) " Is it COVID or a Cold?" An Investigation of the Role of Social Presence, Trust, and Persuasiveness for Users' Intention to Comply with COVID-19 Chatbots.
128. Colleges WOoN, Academies, Physicians AAoGPF (2005) ICPC-2-R: International Classification of Primary Care. Oxford University Press, USA,
129. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hrobjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D (2021) The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 372:n71. doi:10.1136/bmj.n71
130. Brooke BS, Schwartz TA, Pawlik TM (2021) MOOSE Reporting Guidelines for Meta-analyses of Observational Studies. *JAMA Surg* 156 (8):787-788. doi:10.1001/jamasurg.2021.0522
131. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A (2016) Rayyan-a web and mobile app for systematic reviews. *Syst Rev* 5 (1):210. doi:10.1186/s13643-016-0384-4
132. Pourhoseingholi MA, Vahedi M, Rahimzadeh M (2013) Sample size calculation in medical studies. *Gastroenterol Hepatol Bed Bench* 6 (1):14-17
133. Abu EK, Oloruntoba R, Osuagwu UL, Bhattarai D, Miner CA, Goson PC, Langsi R, Nwaeze O, Chikasirimobi TG, Ovenseri-Ogbomo GO (2021) Risk perception of COVID-19 among sub-Saharan Africans: a web-based comparative survey of local and diaspora residents. *BMC Public Health* 21 (1):1-13
134. Suri H (2020) Ethical considerations of conducting systematic reviews in educational research. *Systematic reviews in educational research: Methodology, perspectives and application*:41-54
135. Yu SWY, Ma A, Tsang VHM, Chung LSW, Leung S-C, Leung L-P (2020) Triage accuracy of online symptom checkers for Accident and Emergency Department patients. *Hong Kong Journal of Emergency Medicine* 27 (4):217-222
136. Cotte F, Mueller T, Gilbert S, Blumke B, Multmeier J, Hirsch MC, Wicks P, Wolanski J, Tutschkow D, Schade Brittinger C, Timmermann L, Jerrentrup A (2022) Safety of Triage Self-assessment Using a Symptom Assessment App for Walk-in Patients in the Emergency Care Setting: Observational Prospective Cross-sectional Study. *JMIR Mhealth Uhealth* 10 (3):e32340. doi:10.2196/32340
137. Koskela T, Liu V, Kaila M (2022) How Does Triage by an Electronic Symptom Checker Match with Triage by a Nurse? *Stud Health Technol Inform* 294:571-572. doi:10.3233/SHTI220528

138. McGuinness LA, Higgins JPT (2020) Risk-of-bias VISualization (robvis): An R package and Shiny web app for visualizing risk-of-bias assessments. *Research Synthesis Methods* n/a (n/a). doi:10.1002/jrsm.1411
139. Sterne JA, Hernan MA, Reeves BC, Savovic J, Berkman ND, Viswanathan M, Henry D, Altman DG, Ansari MT, Boutron I, Carpenter JR, Chan AW, Churchill R, Deeks JJ, Hrobjartsson A, Kirkham J, Juni P, Loke YK, Pigott TD, Ramsay CR, Regidor D, Rothstein HR, Sandhu L, Santaguida PL, Schunemann HJ, Shea B, Shrier I, Tugwell P, Turner L, Valentine JC, Waddington H, Waters E, Wells GA, Whiting PF, Higgins JP (2016) ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ* 355:i4919. doi:10.1136/bmj.i4919
140. Huibers L, Keizer E, Giesen P, Grol R, Wensing M (2012) Nurse telephone triage: good quality associated with appropriate decisions. *Fam Pract* 29 (5):547-552. doi:10.1093/fampra/cms005
141. Huibers L, Smits M, Renaud V, Giesen P, Wensing M (2011) Safety of telephone triage in out-of-hours care: a systematic review. *Scand J Prim Health Care* 29 (4):198-209. doi:10.3109/02813432.2011.629150
142. Giesen P, Ferwerda R, Tijssen R, Mokkink H, Drijver R, van den Bosch W, Grol R (2007) Safety of telephone triage in general practitioner cooperatives: do triage nurses correctly estimate urgency? *Qual Saf Health Care* 16 (3):181-184. doi:10.1136/qshc.2006.018846
143. Giesen P, Van der Wilden-van Lier E, Schers H, Schreuder J, Busser G (2002) Advice via the telephone and triage during regular hours of the general practitioner. *Huisarts en Wetenschap* 45 (6):299-302
144. Newbould J, Abel G, Ball S, Corbett J, Elliott M, Exley J, Martin A, Saunders C, Wilson E, Winpenny E (2017) Evaluation of telephone first approach to demand management in English general practice: observational study. *bmj* 358
145. Wallace W, Chan C, Chidambaram S, Hanna L, Iqbal FM, Acharya A, Normahani P, Ashrafian H, Markar SR, Sounderajah V, Darzi A (2022) The diagnostic and triage accuracy of digital and online symptom checker tools: a systematic review. *NPJ Digit Med* 5 (1):118. doi:10.1038/s41746-022-00667-w
146. Michel J, Kilb TS, Mettler A, Muller M, Hautz WE, Hautz SC, Sauter TC (2022) The Utility of an Online Forward Triage Tool During the SARS-CoV-2 Pandemic: Health Care Provider and Health Authority Perspectives. *Front Public Health* 10:845996. doi:10.3389/fpubh.2022.845996
147. Michel J, Mettler A, Muller M, Hautz WE, Sauter TC (2022) A Utility Framework for COVID-19 Online Forward Triage Tools: A Swiss Telehealth Case Study. *Int J Environ Res Public Health* 19 (9). doi:10.3390/ijerph19095184
148. Michel J, Mettler A, Stuber R, Muller M, Ricklin ME, Jent P, Hautz WE, Sauter TC (2022) Effects and utility of an online forward triage tool during the SARS-CoV-2 pandemic: a mixed method study and patient perspectives, Switzerland. *BMJ Open* 12 (7):e059765. doi:10.1136/bmjopen-2021-059765
149. Beattie A, Edwards AP, Edwards C (2020) A bot and a smile: Interpersonal impressions of chatbots and humans using emoji in computer-mediated communication. *Communication Studies* 71 (3):409-427
150. Araujo T (2018) Living up to the chatbot hype: The influence of anthropomorphic design cues and communicative agency framing on conversational agent and company perceptions. *Computers in Human Behavior* 85:183-189
151. Lee S, Choi J (2017) Enhancing user experience with conversational agent for movie recommendation: Effects of self-disclosure and reciprocity. *International Journal of Human-Computer Studies* 103:95-105

152. Diederich S, Brendel AB, Morana S, Kolbe L (2022) On the design of and interaction with conversational agents: An organizing and assessing review of human-computer interaction research. *Journal of the Association for Information Systems* 23 (1):96-138
153. Demurtas J, Mereu A, Veronese N, Maeseneer JD (2022) Family Doctors and the Silver Tsunami: Team up to Survive the Storm. In: *The Role of Family Physicians in Older People Care*. Springer, pp 1-13
154. Demurtas J, Marchetti P, Vaona A, Veronese N, Celotto S, Deilkås EC, Hofoss D, Bondevik GT (2020) Patient safety culture in Italian out-of-hours primary care service: a national cross-sectional survey study. *BJGP open* 4 (5)
155. Demurtas J, Marchetti P, Veronese N, Deilkås EC, Hofoss D, Bondevik GT, Vaona A (2020) La cultura della sicurezza del paziente in un Servizio di Continuità Assistenziale di cure primarie: una analisi descrittiva. *Recenti Progressi in Medicina* 111 (9):515-526
156. Karimova GZ, Goby VP (2020) The adaptation of anthropomorphism and archetypes for marketing artificial intelligence. *Journal of Consumer Marketing*
157. Farshid M, Paschen J, Eriksson T, Kietzmann J (2018) Go boldly!: Explore augmented reality (AR), virtual reality (VR), and mixed reality (MR) for business. *Business Horizons* 61 (5):657-663
158. Nayak S, Patgiri R (2020) A vision on intelligent medical service for emergency on 5G and 6G communication era. *EAI Endorsed Transactions on Internet of Things* 6 (22)
159. Doshi RH, Bajaj SS, Krumholz HM (2023) ChatGPT: Temptations of Progress. *Am J Bioeth*:1-3. doi:10.1080/15265161.2023.2180110
160. Cascella M, Montomoli J, Bellini V, Bignami E (2023) Evaluating the Feasibility of ChatGPT in Healthcare: An Analysis of Multiple Clinical and Research Scenarios. *J Med Syst* 47 (1):33. doi:10.1007/s10916-023-01925-4
161. Howard A, Hope W, Gerada A (2023) ChatGPT and antimicrobial advice: the end of the consulting infection doctor? *Lancet Infect Dis*. doi:10.1016/S1473-3099(23)00113-5

