Chapter 12
Mobile Apps

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12.1 Operating Systems

Two major operating systems are important for mobile apps: iOS (Apple) and Android (Google), a total market share of 99% (iOS 54% and Android 45% in May 2018, measured in USA). (Mobile Operating System Market Share United States Of AmericalStatCounter Global Stats [21]) These two operating systems are not compatible, which means that programming for both requires a different approach. Developing native iOS apps is done using the programming language Objective-C or Swift, and native Android apps are developed in Java or Kotlin. As these languages, and more importantly the operating system-specific frameworks, are fairly different, hybrid app development has become increasingly popular. Hybrid apps are essentially "web apps" (mobile web pages) that are wrapped in a native binary (the file that is downloaded from the App Store or Google Play) and can access native device features such as the camera or the accelerometer. The main advantage is that the app only needs to be developed and maintained once. Potential disadvantages are a lack of native look and feel (which is important from a usability perspective), and a lack of access to features that are not available in the hybrid framework (such as health- and research-frameworks as explained in Chap. 1). A hybrid framework that is very popular at the time of writing is Ionic (www.ionicframework.com), which is open source and available free of charge. Alternatives that can sometimes even offer a native look and feel for the app's graphical user interface (e.g. Titanium Appcelerator) often come at a price.

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12.2 Collecting Health Data

Apple HealthKit and Google Fit are operating system-specific frameworks for users to collect and organize health data on their mobile device. With the addition of ResearchKit in 2015, Apple created an innovative open-source approach towards easily collecting data from large cohorts that give informed consent and provide data completely from the app. Successful applications have been described in Parkinson, asthma and spine disease [4, 5, 35]. An Android alternative for ResearchKit is the open-source initiative ResearchStack.org. Such frameworks open completely new ways to acquire scientific data, but require a shift in thinking from the researcher's perspective from classic data collection methods to digital tools and correlated new opportunities (e.g. finger tapping task for Parkinson patients in a mobile app or uploading videos of walking patterns for deep learning applications).

12.3 Mobile Clinical Decision Support Systems

From the perspective of applications, mobile devices are excellent tools to implement decision support systems. A systematic review of the literature was performed to assess the current evidence on this topic. MEDLINE has been searched using the PubMed website and medical subject headings (MeSH) in combination with free text search. The combination ("Decision Support Systems, Clinical"[Mesh]) AND "Computers, Handheld"[Mesh], ("Decision Support Systems, Clinical"[Mesh]) AND smartphone and ("Decision Support Systems, Clinical"[Mesh]) AND "Cell Phones"[Mesh] revealed a total of 183 hits after removing duplicates. These were screened based on title and abstract. The inclusion criteria were: English, mobile, clinical decision support system, patient-related outcome parameters (including caregiver or guideline adherence), and focus on implementing guidelines. Exclusion criteria were: no abstract, no outcome parameters, case study, focus on telemonitoring, or focus on (implementation) strategy. From this screening, 30 articles were included for full text screening. After full text screening, 7 articles were included for a qualitative synthesis of the literature on clinical decision support systems (mCDSS). Reasons for excluding articles based on full text screening are given in Table 12.1. An evidence table summarizing the included studies is presented in Table 12.2.

Samore (2005) performed a randomized clinical trial (RCT) in 12 rural communities represented by a total of 334 general physicians using a Palm OS based mCDSS with a cradle-based database synchronisation. The primary outcome was antimicrobial usage in acute respiratory tract infection. In the mCDSS group there was a 9% decrease in (false positive) prescriptions compared to a 1% decrease in the control group ($p = 0.03$) [27].

Sintchenko (2005) performed a prospective trial with historical cohorts amongst an unspecified number (at least 12) of intensive care unit physicians and residents,

Table 12.1 Exclusion reasons after full tekst screening

Reference	Reason for exclusion
Alexander, 2008 [1]	Focus on clinical alerts and triggers
Bochicchio, 2006 [3]	Focus on e-learning, knowledge tool for residents
Charani, 2013 [6]	Strategic paper on app uptake
Chin, 2006 [7]	Focus on usability without specific suggestions
Clauson, 2008 [8]	PDA vs online database, no interactive CDSS
Cricelli, 2006 [9]	Infomercial without scientific evaluation
Di Pietro, 2012 [10]	Qualitative study on usability
Divall, 2013 [11]	Review
Etchells, 2011 [12]	Focus on alerts
Garrett, 2008 [13]	Focus on implementation strategy
Gupta, 2016 [14]	Focus on uptake and usage statistics
Johansson, 2010 [15]	Focus on nurses' usability/perception
Lapinsky, 2004 [16]	Knowledge access, no interactive CDSS
Lapoint, 2013 [17]	Focus on drug reference alerts (comparing different apps)
Laporta, 2012 [18]	Not mobile (Windows 7)
Leung, 2003 [20]	Focus on mobile info database, no interactive guideline
Payne, 2013 [22]	Implementation strategy, no interactive guideline
Ray, 2006 [23]	No interactive guideline
Rubin, 2006 [26]	Overlap with Samore (2005)
Snooks, 2010 [30]	Focus on trial design
Stephens, 2010 [32]	Focus on PDA use by students
Van Belle, 2012 [33]	Focus on mathematical model
Yu, 2007 [34]	Focus on PDA/app usage by residents

using a Pocket PC platform with HL7-compatible web-based database synchronisation. The primary outcome was antibiotic use and patient outcome on the ICU. Use of the mCDSS resulted in a 17.5% decrease in defined daily doses per 1000 patient days ($p = 0.04$) and a 13% decreased length of stay on the intensive care unit ($p = 0.02$) [28].

Berner (2006) performed a RCT amongst 68 internal medicine residents using a Palm OS based mCDSS. The primary outcome was NSAID-related gastrointestinal risk assessment in drug prescriptions. The study compares the ratio of unsafe prescriptions in the mCDSS group (0.23) to the control group (0.45), which is statistically significant ($p < 0.05$). However, the same rates at baseline are 0.27 and 0.29 for the mCDSS and control group respectively. Apparently in the control group the number of unsafe prescriptions increased compared to baseline, therefore clinically relevant conclusions are hard to draw from these data [2].

Lee (2009) performed a RCT amongst 20 nurses with a total of 1874 patient encounters, using a Palm OS based mCDSS. The primary outcome was the proportion of obesity-related diagnoses. The mCDSS led to a more than 10% increase in (true positive) diagnoses compared to the control group ($p < 0.001$) [19].

Table 12.2 Evidence table for mCDSS studies

Reference	Population	Study design	Technical platform	Primary outcome	Results
Samore, 2005 [27]	12 rural communities (334 GPs)	RCT	Palm OS, cradle-based database sync	Antimicrobial usage in acute respiratory tract infection	9% decrease in prescription in CDSS arm vs 1% increase in CG ($p = 0.03$)
Sintchenko, 2005 [28]	ICU physicians (n =?)	Prospective trial with historical controls	Pocket PC with web-based syncing, HL7-compatible	Antibiotic use and patient outcome in ICU	17.5% decrease in DDD/1000 patient days ($p = 0.04$) and 13% decreased LOS ($p = 0.02$)
Berner, 2006 [2]	68 internal medicine residents	RCT	Palm OS	NSAID-related GI risk assessment in prescribing	Decrease in ratio of unsafe prescriptions[a]
Lee, 2009 {Lee:2009iy}	20 nurses (1874 pt encounters)	RCT	Palm OS	Proportion of obesity-related diagnoses	>10% increase in (true positive) diagnoses compared to CG ($p < 0.001$)
Roy, 2009 [25]	20 emergency departments (1645 pt)	Cluster RCT	Palm OS	Pulmonary embolism diagnosis	19.3% increase in correct diagnosis compared to CG ($p = 0.023$)
Snooks, 2014 [29]	Paramedics[b]	Cluster RCT	Tablet PC (forming part of EPR)	Fall emergency referrals in elderly population	9.6% referrals vs. 5.0% in CG (OR 2.04; CI95: 1.12–3.72)
Spat, 2016 {Spat:2016kd}	30 patients with type 2 diabetes mellitus	Open, noncontrolled intervention study	iOS, Android	Glucose serum levels	Decrease in hypoglycemia compared to a historic CG (1.3% vs 3.0%, $p = 0.01$)

CG control group, *CI95* 95% confidence interval, *DDD* defined daily doses, *EPR* electronic patient record, *GI* gastrointestinal, *ICU* intensive care unit, *LOS* length of stay, *NSAID* non-steroid anti-inflammatory drugs, *OR* Odds ratio, *pt* patients, *RCT* randomized controlled trial

[a]The study compares the ratio of unsafe prescriptions in the intervention group (0.23) to the control group (0.45), which is statistically significant ($p < 0.05$). However, the same rates at baseline are 0.27 and 0.29 for the intervention and control group respectively. Apparently in the control group the number of unsafe prescriptions increased compared to baseline, therefore clinically relevant conclusions are hard to draw from these data

[b]17 out of 42 paramedics used the mCDSS for 54 out of 436 (12.4%) of the participants

Roy (2009) performed a cluster RCT in 20 emergency departments with a total of 1645 patients, using a Palm OS based mCDSS. The primary outcome was pulmonary embolism diagnosis, and use of the mCDSS led to a 19.3% increase in correct diagnosis compared to the control group (95% CI: 2.9–35.6%; p = 0.023) [25].

Snooks (2014) performed a cluster RCT amongst paramedics. A total of 17 out of 42 paramedics used the mCDSS for 54 out of 436 (12.4%) of the participants. The mCDSS was presented on a tablet PC forming part of the electronic patient record. The primary outcome was fall emergency referrals in the elderly population. The mCDSS led to 9.6% referrals compared to 5.0% in the control group (odds ratio 2.04; 95% CI: 1.12–3.72) [29].

Spat (2016) performed an open, noncontrolled intervention study in 30 patients with type 2 diabetes mellitus in which a mCDSS for insulin dosing was provided to an interdisciplinary team of engineers, physicians and nurses. The mCDSS was a mobile app developed for both iOS and Android. The primary outcome was glucose serum levels. In comparison with a historic control group, there was a statistically significant decrease in hypoglycaemia (1.3% vs 3.0%; p = 0.01) [31].

Based on the available scientific literature it is safe to say that there is level I evidence that mCDSS can be beneficial in guideline implementation for diagnostic and therapeutic purposes. Adoption of mobile devices capable of data connectivity has increased throughout the years and availability should be not a problem nowadays, in particular in combination with a so-called “bring your own device” strategy.

Most of the excluded articles after full text screening were concerned with app usage, implementation strategy and usability issues. Recurring concerns on implementation are good institutional support, good wireless data connectivity and sufficient technology skills by the end user [6, 13, 22]. A validated rating scale (Attitudes toward Handheld Decision Support Software Scale (H-DSS)) could be used to assess physician attitudes about handheld decision support systems ([23] but no recent articles mentioned the use of this tool. Another application of mCDSS is the opportunity to alert healthcare workers of relevant information immediately when it becomes available. In a prospective study by Etchells, the provision of real-time clinical alerts and decision support for critical laboratory abnormalities did not improve clinical management or decrease adverse events [12]. [12] A different study evaluating opioid prescribing in pharmacopoeietic apps found that multiple programs fail to prominently display drug safety information. This may be an impediment to safe prescribing and may represent a missed opportunity to improve prescribing practices (Lapoint et al. 2013) [17].

A methodological challenge for future studies will be to evaluate outcome at a patient level. Many CDSS studies measure outcome on a healthcare provider level, whether that is correct diagnosis, drug usage or guideline adherence. Indirectly such

outcome parameters should be translatable to improved patient outcome, but this has not been measured directly. Obviously in a clinical setting where many parameters influence patient outcome, isolating the influence of the mCDSS is difficult and may require rather large study cohorts.

For the future, more complex models underlying mCDSS can be implemented. For example, Apple's CoreML technology allows for applying machine learning models in iOS apps. Using the "coremltools" converter, or "turicreate" for modelling, Python-based models can be easily converted to CoreML-format for implementation in a mobile app. XCode 10 even allows to create machine learning models directly from within the development environment.

12.4 Software as a Medical Device

In May 2020, the new medical device regulations (MDR 2017/745 of the European Parliament) will become the standard for medical devices, including software applications such as mobile apps. The new Regulations contain a series of important improvements to modernise the current system. Among them are: (Regulatory framework – Growth – European Commission [24])

- stricter ex-ante control for high-risk devices *via* a new pre-market scrutiny mechanism with the involvement of a pool of experts at EU level
- the reinforcement of the criteria for designation and processes for oversight of Notified Bodies
- the inclusion of certain aesthetic devices which present the same characteristics and risk profile as analogous medical devices under the scope of these Regulations
- the introduction of a new risk classification system for *in vitro* diagnostic medical devices in line with international guidance
- improved transparency through the establishment of a comprehensive EU database on medical devices and of a device traceability system based on Unique Device Identification
- the introduction of an "implant card" containing information about implanted medical devices for a patient
- the reinforcement of the rules on clinical evidence, including an EU-wide coordinated procedure for authorisation of multi-centre clinical investigations
- the strengthening of post-market surveillance requirements for manufacturers
- improved coordination mechanisms between EU countries in the fields of vigilance and market surveillance

Mobile apps that are considered as a medical device will still need CE (Conformité Européenne) marking, but cannot be registered as a risk class 1 device anymore. As a consequence, self-certification will not be possible, and a notified body is required – a far more expensive necessity.

12.5 Conclusion

Overall, these are exciting times for mCDSS applications. There is level 1 evidence for their effectiveness, and new opportunities both for collecting data and implementing machine learning models in a mobile app create new horizons for scientific research and improving quality of health and healthcare.

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