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# Mobile Health in Adherence to Oral Anticancer Drugs

## A Scoping Review

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In oncology, adherence to oral antineoplastic medication is a key element of treatment, on which the success of any therapeutic intervention depends. Given their widespread use in clinical practice, it is important to identify tools that can facilitate the monitoring and self-management of the patient at home, to avoid the consequences of employing ineffective treatment. One of the tools available today to take action on this phenomenon is mobile health technology. The aim of this review is to describe published studies relating to the use of mobile health to promote adherence to oral antineoplastic medication. This scoping review was conducted using the framework proposed by Arksey and O'Malley, adapted according to Levac et al. Of 1320 articles identified, only seven met the eligibility criteria and therefore were included in the review. All seven articles involved the use of digital means to measure adherence to treatment, patient satisfaction, acceptability and feasibility of the digital means used, and presence of symptoms, but not the effectiveness of the digital instrument used. In conclusion, the use of digital means to assist adherence of cancer patients to oral antineoplastic medication is widely recognized, but its effectiveness in clinical practice is poorly supported by the nature of the published studies.

**KEY WORDS:** App, Medication adherence, mHealth, OAM, Oncology patient, SMS

In oncology, more and more often, practitioners resort to the use of drugs in oral antineoplastic medication (OAM).[1] There are more than 50 oral antineoplastic agents on the market, and within the next decade they will represent 25% of all prescribed treatments in cancer patients.[2,3] Administration of OAM is carried out for a variable period of time depending on the primary tumor and the location and the severity of the disease.

Adherence to medication is a key element of this treatment, and since the success of any intervention depends on it, it is considered today as one of the most important problems of clinical practice[4] and an important indicator of response to the treatment itself.[5] Adherence of the patient to the prescribed medication, in fact, leads to greater probability of successful treatment, to fewer diagnostic procedures, fewer hospitalizations, and lower risk of mortality and morbidity.[4]

Despite its importance, the literature reports rates of adherence to OAM as lower than 80%, often greatly influenced by a number of exogenous determinants (clinical condition, therapy, healthcare system, socioeconomic system) and endogenous determinants (related to the patient).[4,6]

Nonadherence is manifested primarily in omitting or delaying taking the drug and in taking different doses than those prescribed and can be motivated by the will of the subject (intentional) or not (unintentional) in following the treatment plan.[5,7] Intervention therefore requires different modes: for intentional nonadherence, it is possible to use therapeutic education to increase the patient's awareness of treatment; for unintentional nonadherence, the creation of strategies is often used to enable the patient to remember to take the tablets.[8] In both cases, it is necessary to use tools that enable monitoring of patient self-management, including the most recent instruments developed through telemedicine and telemonitoring. The objective of these innovations is precisely to intervene, through the use of recent technological advances, in patient behavior in relation to the drug, in order to prevent the consequences of inefficient management of treatment.[8]

The digital boom that has brought approximately three-quarters of the planet to own a smartphone with powerful capabilities and features,[9] has in fact led to one of the most important innovations in the health field today, represented by "mobile health" (mHealth). This was defined by the Center for Global eHealth, World Health Organization, as "the healthcare practice supported by mobile devices such as mobile phones, patient monitoring devices, personal digital assistants (PDAs), and other wireless devices."[10] This

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practice has many advantages in terms of improved clinical outcomes; cost efficiency through better use of human, technical, and economic resources; and increased acceptability by patients.[10]

Another beneficial aspect is the reduction of disparities in access to health services, favored by the rapid increase in the adoption of smartphones among racial and ethnic minorities and the impressive spread of connectivity in extra-urban areas,[11,12] but hampered by differences in digital literacy (technical skills are needed to understand device functionality).[13,14]

For these reasons, the last 10 years have seen a rapid proliferation of different mHealth proposals around the world, with more than 500 projects presented in the single year 2011,[15] increasingly focused on developing healthcare apps dedicated especially to pain management,[16] diabetes,[17] lifestyles,[18] and cancer.[19]

In particular, studies conducted to evaluate the efficacy of mHealth on nontherapeutic adherence reported an increase in levels of satisfaction of the users regarding the healthcare received[20–24] and an improvement in clinical outcomes due to a greater understanding of the barriers to adherence[25,26] and strategies to be used to overcome them.[8] For example, sending text messages has been shown to be useful in improving adherence to antiretroviral treatments with a consequent reduction in viral load in patients with AIDS.[8]

Despite the importance of adherence to OAM, literature reviews on the impact of digital means include studies conducted in patients with various chronic diseases[27,28] but not cancer.

Therefore, the aim of this review is to describe published studies on the use of mHealth to foster adherence to oral antineoplastic treatments. In view of the limited knowledge of the use of "mobile health" for adherence to oral treatments in oncology, the scoping review is appropriate for the study rationale.[29] This review mode is, in fact, defined as "studies with the aim to map rapidly the key concepts underpinning a research area and the main sources and types of evidence available, and can be undertaken alone as projects in their own right, especially where an area is complex or has not been comprehensively reviewed before."[30]

## METHODS

A scoping review was conducted in accordance with the framework proposed by Arksey and O'Malley,[30] adapted in accordance with the recommendations of Levac et al,[29] which involves six stages: (1) definition of the research question (background); (2) identification of relevant studies; (3) selection of the studies; (4) extraction of the data; and (5) collection, synthesis of the results, and reports. The optional step concerning the consultation with the parties concerned (6) was not carried out.

### Identification of Studies

An expanded search through PubMed was used, employing free text words and thesaurus descriptors (MeSH) combined with each other using the Boolean operators AND and OR (Table 1).

A string of free words only was then reproposed on Web of Science, Scopus, and CINAHL, combining them first with a single item with the OR operator, and then together with AND (Tables 2 and 3).

A search was also performed in the Cochrane Library, on multidisciplinary search engines such as Google Scholar, in journal indexes and in references in primary and secondary studies.

## ELIGIBILITY CRITERIA

The articles included were studies that aimed, primarily or secondarily, to evaluate the effectiveness of mHealth interventions on adherence to oral antineoplastic treatment in cancer patients.

It was decided not to narrow the search field to a single disease, treatment, or intervention, in order to gather as much information as possible. In addition to primary studies, items were included that related to research topics pursuing the same goal, in order to evaluate current research on the topic of interest. As well as adherence to treatment, they also took into account the acceptability and feasibility of the intervention in question and satisfaction with it. They included all relevant articles published up to January 2018. There were no restrictions associated with the language or year of publication.

**Table 1.** PubMed Research Proposal String

| |
|---|
| ((((("mHealth" OR "mobile health" OR m-health OR mobile-health OR "mobile phone*" OR "cell phone*" OR cellphone* OR cell-phone* OR "cellular phone*" OR smartphone* OR tablet* OR ipad OR iPhone OR blackberry OR android OR ios OR "windows phone*" OR text OR "text messag*" OR "short message service" OR SMS OR "Mobile phone application" OR "Mobile app" OR "Phone app" OR "mobile device*")) OR ("Smartphone"[MeSH] OR "Mobile Health Units"[MeSH] OR "Cell Phone Use"[MeSH] OR "Telemedicine"[MeSH] OR "Mobile Applications"[MeSH] OR "Cell Phone"[MeSH]))) AND ((((((("Medication Adherence"[MeSH] OR "Patient Compliance"[MeSH]) OR "Self Administration"[MeSH]) OR "Administration, Oral"[MeSH]) OR "Capsules"[MeSH])) OR ((adherence OR compliance OR "madherence" OR "mobile adherence" OR m-adherence OR nonadherence OR noncompliance OR non-adherence OR non-compliance OR persistence OR concordance) AND (medication* OR "oral drug*" OR capsule* OR pill*)))) AND ((((oncolog* OR neoplas* OR cancer OR cancer* OR tumo* OR tumou* OR carcino* or malignan*))) OR "Neoplasms"[MeSH]) |



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**Table 2.** Search String With Clear Words Combined to Single Argument

| |
|---|
| "mHealth" OR "mobile health" OR m-health OR mobile-health OR "mobile phone*" OR "cell phone*" OR cellphone* OR cell-phone* OR "cellular phone*" OR smartphone* OR tablet* OR ipad OR iPhone OR blackberry OR android OR ios OR "windows phone*" OR text OR "text messag*" OR "short message service" OR SMS OR "Mobile phone application" OR "Mobile app" OR "Phone app" OR "mobile device*" |
| adherence OR compliance OR "madherence" OR "mobile adherence" OR m-adherence OR nonadherence OR noncompliance OR non-adherence OR non-compliance OR persistence OR concordance |
| medication* OR "oral drug*" OR capsule* OR pill* |
| oncolog* OR neoplas* OR cancer OR cancer* OR tumo* OR carcino* or malignan* |

### Selection of Studies

From the total number of items collected, duplicates were eliminated through the use of a reference manager (EndNote X8; Clarivate Analytics, Philadelphia, PA).

The publications were initially subjected to screening conducted by two independent researchers, to evaluate their potential to meet the eligibility criteria. The titles were evaluated first, and then the abstracts. In cases of discrepancy, the results were discussed by the researchers to reach an acceptable degree of correlation. After screening of the abstracts, the full texts of the selected publications were retrieved and analyzed.

The reliability of the researchers' selection was checked in the second screening phase (evaluation abstract) by calculating Cohen's $\kappa$ coefficient, which proved to be equal to 0.61 (moderate concordance/good).

## DATA EXTRACTION

The following characteristics of each article were then considered: type of study, setting, sample size, type of intervention, and outcome. These data were then identified within the article and summarized (see Table, Supplemental Digital Content 1, http://links.lww.com/CIN/A65, which included a summary of features and content of the studies included in the review).

## RESULTS

The results of the research process and selection of studies are presented according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines for systematic reviews.[31] From 1320 articles identified, 172 duplicates were eliminated, and of the remaining 1148, only seven met the eligibility criteria and therefore were included in the review (Figure 1), of which three are study protocols.

Most of the studies were conducted or proposed in the United States and consist of a qualitative pilot study,[32] a longitudinal study with pre and posttest,[33] a prospective study for the validation of a nonpharmacological intervention,[34] and four randomized controlled trials (RCTs).[3,35–37] Of the RCTs, one was multicenter, and one used a mixed-methods approach (see Table, Supplemental Digital Content 1, http://links.lww.com/CIN/A65, which included a summary of features and content of the studies included in the review).

All studies involved a digital intervention (see Table, Supplemental Digital Content 2, http://links.lww.com/CIN/A66, which included a description of the proposed intervention) used to measure, directly or indirectly, adherence to treatment, patient satisfaction with the intervention, its acceptability and feasibility, as well as the symptoms and their severity (see Table, Supplemental Digital Content 1, http://links.lww.com/CIN/A65, which included a summary of features and content of the studies included in the review). The available results of the individual studies are shown in a Supplemental Digital Content 3 (http://links.lww.com/CIN/A67).

## DISCUSSION

The objective of this review was to describe published studies on the use of mHealth to encourage adherence to oral antineoplastic treatments.

Eligible articles had been published in one indexed journal (*JMIR Research Protocols*[35,36]) and in four journals with different impact factors (IFs) (*BMJ Open*, IF: 2.376[34]; *JMIR mHealth and uHealth*, IF: 4.301[32]; *Oncology Nursing Forum*, IF: 1.785[33,37]; and *Telemedicine and e-Health*, IF: 1.996[3]).

**Table 3.** Search String With Free Words

| |
|---|
| (("mHealth" OR "mobile health" OR m-health OR mobile-health OR "mobile phone*" OR "cell phone*" OR cellphone* OR cell-phone* OR "cellular phone*" OR smartphone* OR tablet* OR ipad OR iPhone OR blackberry OR android OR ios OR "windows phone*" OR text OR "text messag*" OR "short message service" OR SMS OR "Mobile phone application" OR "Mobile app" OR "Phone app" OR "mobile device*") AND ((adherence OR compliance OR "madherence" OR "mobile adherence" OR m-adherence OR nonadherence OR noncompliance OR non-adherence OR non-compliance OR persistence OR concordance) AND (medication* OR "oral drug*" OR capsule* OR pill*)) AND (oncolog* OR neoplas* OR cancer OR cancer* OR tumo* OR carcino* or malignan*)) |



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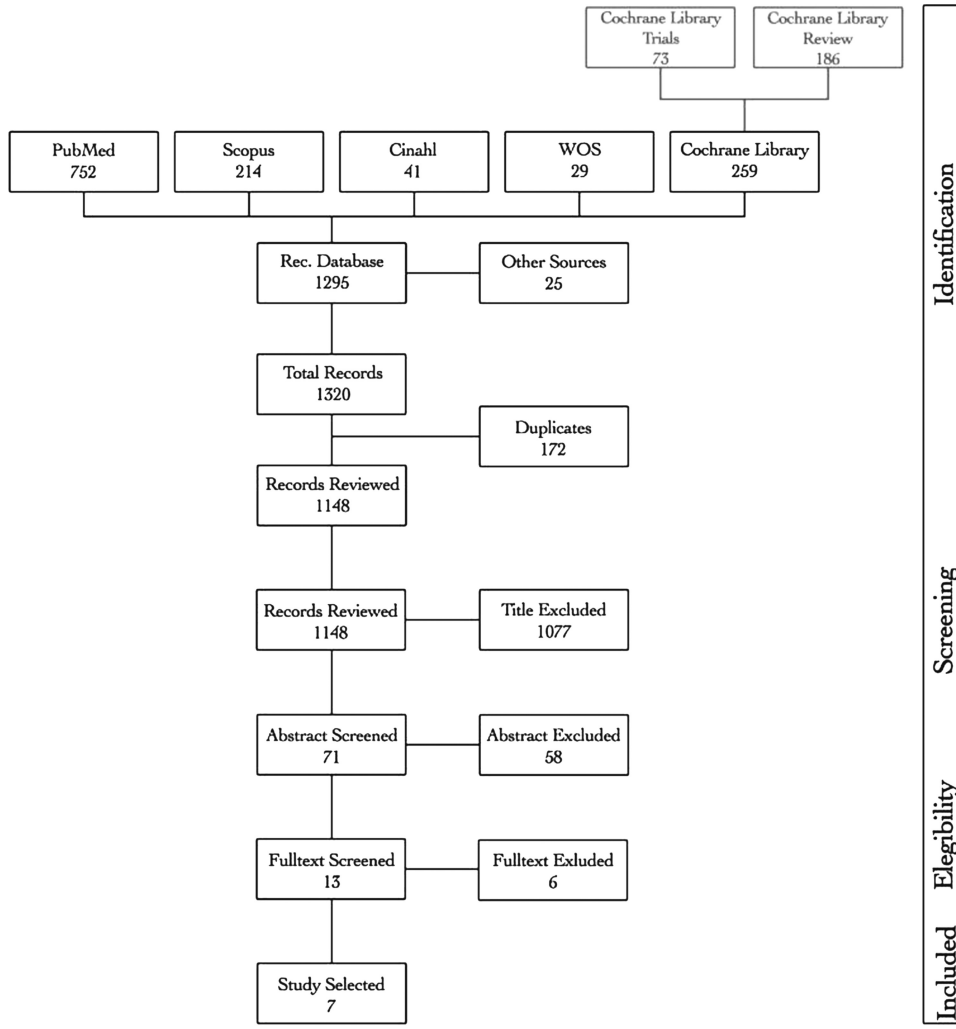


**FIGURE 1.** PRISMA statement.

The IF or journal IF (JIF) is a bibliometric index used to measure "the relative importance of a journal to its field."[38] This index is calculated through the ratio between the total number of citations to the articles (the numerator) and the total number of articles published (the denominator) within specific time periods.[39] Today JIF is increasingly applied not only to access journals, but also to assess and to predict the performance of documents and associated authors within journals.[40]

The eligible articles were published in the period from 2014 to 2018 (Figure 2).

The very recent time range is due to the fact that Web devices were introduced by the World Health Organization in the health sector in 2011 under the term "mHealth."[10] The use of digital interventions is supported by the widespread dissemination of mobile devices around the world,[41] so much so that, in the month of November 2018, Web devices generated 37.08% of European Internet traffic and 70.10% of American (38.67% in the North and 31.43% in the South).[42] In the US, 95% of the population owns a mobile phone; about a third live in a house where there are more than three; and

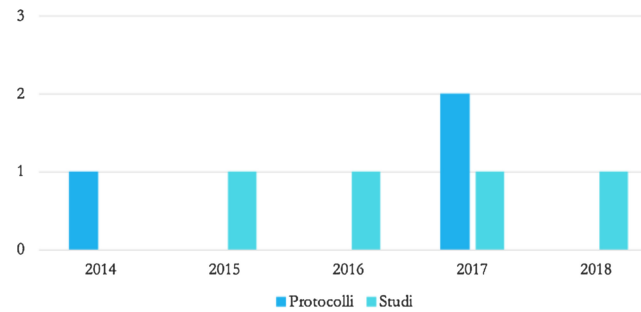


**FIGURE 2.** Breakdown by year of publication of studies and protocols identified.



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77% are smartphones.[43] Added to this are the major healthcare costs faced by the US annually for patients with chronic conditions.[44] These two aspects are a sufficient explanation for the almost entirely US distribution of the studies presented in this review.

The potential of mHealth in the management of chronic patients has led many researchers to use digital monitoring of oral treatments prescribed for various diseases such as HIV, tuberculosis, diabetes mellitus, cardiovascular diseases, and chronic lung diseases.[8] This explains the high number of articles identified in the first phase of the review process (N = 1130). However, only a small number of these (n = 7) considered the problem of adherence in cancer patients and were therefore eligible for the purposes of this scoping review. In this regard, it should be borne in mind that the use of antineoplastic drugs in oral formulation is relatively recent: Capecitabine was the first oral drug marketed for the treatment of cancer patients after approval by the US Food and Drug Administration in April 1998.[45]

Reminders in the form of notifications within an app or by text message are the interventions proposed in the studies to promote adherence to oral antineoplastic drugs. In the studies for which results are available, such interventions have been helpful in prompting patients to remember to take this treatment, so that their use has been recommended not only for those who are being treated with oral medications, but also for oncologists, family members, and friends, as a form of remote monitoring. Patients, in fact, say they not only need to have contact with people suffering from the same condition[36] but also need the support of well-trained professionals,[32] social support,[3(p497)] and family to serve as a support network. The literature confirms the need for patients to have someone they trust (family/caregiver) to help them to remember to take medication and healthcare professionals on whom to rely constantly.[46] Nurses too, as reported in the study by Pereira-Salgado et al,[32] recognized the potential of mHealth interventions in facilitating a therapeutic relationship with patients, in agreement with the literature studies. It is known, in fact, how Medicine 2.0, implemented through digital means for medical purposes, is able to improve the shared management of the disease between patients and caregivers.[47,48]

Although well received by patients or by operators, observed data do not support the efficacy of digital interventions in improving adherence to antineoplastic treatment. In a multicenter RCT, Spoelstra et al[3(p504)] even show that, at the fourth week of observation, the adherence levels are higher in the control group compared to the experimental group (p504). This lack of effect could be supported by patients' ability to implement simple functional strategies for remembering to take the treatment, such as alarm clocks, the date on the blister pack, or placing the drug in view,[46] which therefore make the digital reminder only an unessential addition.

## LIMITATIONS

This review did not evaluate the quality of the evidence. In addition, the low number of studies and the presence of study protocols with no results made comparisons between the data difficult. Our review, however, expands current knowledge regarding the impact of mHealth on adherence to treatment of chronic diseases, offering an overview of the implications of its use as part of the patient's management of cancer.

### Implications for Nursing Informatics Practice and Nursing Clinical Practice

The use of mHealth has the potential to provide tailor-made assistance for the user, to guarantee a degree of customization otherwise difficult to achieve[49] and to improve patient satisfaction levels regarding the nursing care received.[20–24,50,51]

Especially in the field of oncology, the potential of mHealth is enormous, offering the possibility of providing rapid, continuous, and easy access to both educational resources and strategies for self-management of physical symptoms,[52,53] access to peer support (social function),[54] and monitoring therapeutic treatment at a distance.[55] Patients themselves recognize the usefulness of mobile phones as reminders for taking drugs.[56]

The potential of the combination "adherence digitization" or "mobile adherence" (mAdherence) is also recognized by health professionals, and primarily by nurses, who underline a series of advantages, which include, in addition to the increase in adherence rates to the treatment, a more efficient form of continuity of care and the improvement of communication between health workers and patients.[57]

## CONCLUSION

The objective of this review was to describe published studies on the use of mHealth in encouraging adherence to oral antineoplastic treatments. The use of digital means in facilitating the adherence of oncology patients to oral antineoplastic treatments is strongly recognized in the literature; despite this, its effectiveness in clinical oncology practice is poorly supported by the nature of the studies published to date and, above all, by their results.

The extent of knowledge to date remains very limited. For this purpose, future evaluations should focus on determining how the instruments of mHealth can be used to identify barriers to adherence and to deliver high-quality digital personalized healthcare to cancer patients. To do this, it is necessary to start by identifying digital interventions designed on the basis of the actual needs of the cancer patient treated with OAM.



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