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REVIEW ARTICLE

Integrating smart phone applications in the management of cirrhotic patients: A scoping review

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Abstract

Background and Aim: Chronic liver disease and cirrhosis is a significant cause of healthcare utilization and patient morbidity and mortality worldwide. Smartphone applications have high uptake in most communities and therefore have great potential to provide remote support solutions to this patient population. The aim of this scoping review was therefore to provide a comprehensive overview using narrative synthesis on the use of smartphone-application-based digital interventions in cirrhotic populations.

Materials and Methods: PRISMA guidelines were followed, with two independent researchers identifying 10 relevant studies. Patients studied were predominantly those with decompensated cirrhosis, and hepatic encephalopathy was the most common complication studied.

Results: Smartphones were the most common platform used, but training periods, prior to commencement of the study, were rarely offered. Patient engagement rates with the technology were reported only in three studies, but all reported high (>50%) rates of engagement. Only one study examined the clinical effects of their digital intervention, with a 38% reduction in readmission rate reported.

Conclusion: Overall, the use of smartphone apps in cirrhosis is in an early phase of development and evaluation but preliminary studies suggest significant potential as an adjunct to routine medical care. Further high-quality studies of well-designed digital interventions are needed to advance this promising early experience.

Introduction

Liver disease affects over 6 million Australians[1] and remains a major contributor to both morbidity and mortality. Data from the Australian Institute of Health and Welfare reveals that liver cirrhosis was the 11th leading cause of premature death in Australia between 2010 and 2021.[2] Between 2008 and 2016, hospitalization rates due to liver cirrhosis increased in Australia, from 8.50 to 11.21 per 10 000.[3] In addition, patients with cirrhosis are at increased risk of readmission, with approximately half of discharged cirrhotic patients readmitted within 3 months.[4] Ascites, the most common decompensating event in this population,[5] carries significant morbidity, with the 5-year survival reducing from 80% to 30% following onset of this complication.[6] The medical management of ascites is restricted to dietary salt restriction, diuresis, and paracentesis.

The chronic and debilitating nature of liver cirrhosis and its impact on the quality of life of affected populations highlight the critical need for remote support solutions in the community. A promising solution is the use of smartphone applications (apps), which has been shown to be highly acceptable among the cirrhotic population.[4] Patients who had recently been admitted to hospital or who had established decompensated liver disease have shown greater willingness to engage with smartphone app technology.[4] Several smartphone apps have been developed and studied in the cirrhotic population, the most popular being the "EncephalAp". EncephalApp has demonstrated the ability to screen for minimal hepatic encephalopathy (HE),[7] prevent encephalopathy-related readmissions,[8] and diagnose covert encephalopathy.[9]

However, there is a lack of research on the effectiveness of smartphone apps in improving the management of ascites, despite its high prevalence in the cirrhotic population, with only one study identified.[10]

Aims and research questions

The aim of this scoping review was to provide a comprehensive overview of available data using narrative synthesis with regard to the use of smartphone-application-based digital interventions in the cirrhotic population. We sought to examine the factors that contribute to successful implementation, user engagement,

feasibility and accessibility, and potential future directions. Specifically, we aimed to address the following questions:

1. What are the clinical characteristics of the participants in the studies of digital interventions for cirrhosis?
2. What are the features of the digital interventions, including the tools used and how information was presented?
3. How do patients engage with the digital interventions?
4. What are the clinical effects of the digital interventions on the cirrhotic population?

Methodology

The following inclusion and exclusion criteria were agreed upon, to best address the research questions.

Inclusion criteria. The study population should comprise adults with underlying liver disease;
2. They should have been suffering from chronic liver disease (CLD) with a follow-up of at least 1 month;
3. The intervention being investigated had to include a digital application that is interactive, facilitating communication between the patients and/or caregivers and the clinicians;
4. The intervention needed to report clinically significant data, such as effects on encephalopathy or ascites.

Exclusion criteria. Studies on pediatric populations;
2. Acute liver diseases with duration of follow-up less than 1 month;
3. Non-interactive applications, that is, simple delivery of educational content;
4. Publications in abstract form.

Study design. All study designs (protocols, theses, and reports) were considered in this review. Only full-text articles were included. The sources of evidence for this scoping review were Medline, Psychinfo, Scopus, and Web of Science. The final search results are shown in Table 1.

Selection of studies and data extraction. We followed the PRISMA guidelines to ensure a rigorous study selection process (Fig 1). Two independent researchers, with expertise in clinical gastroenterology and digital health, respectively, reviewed the articles for eligibility, and any conflicts or discrepancies were resolved through mutual consensus. Out of the 2823 records identified, 1828 articles underwent screening, and after the initial screening process, 1748 studies were excluded for not meeting the inclusion criteria. Additionally, 70 studies were excluded as they were not full-text articles. Finally, 10 studies met the inclusion criteria.

Table 1 Search results by database

Medline	1015
PsychInfo	52
Scopus	1142
WoS	614
Total	2823

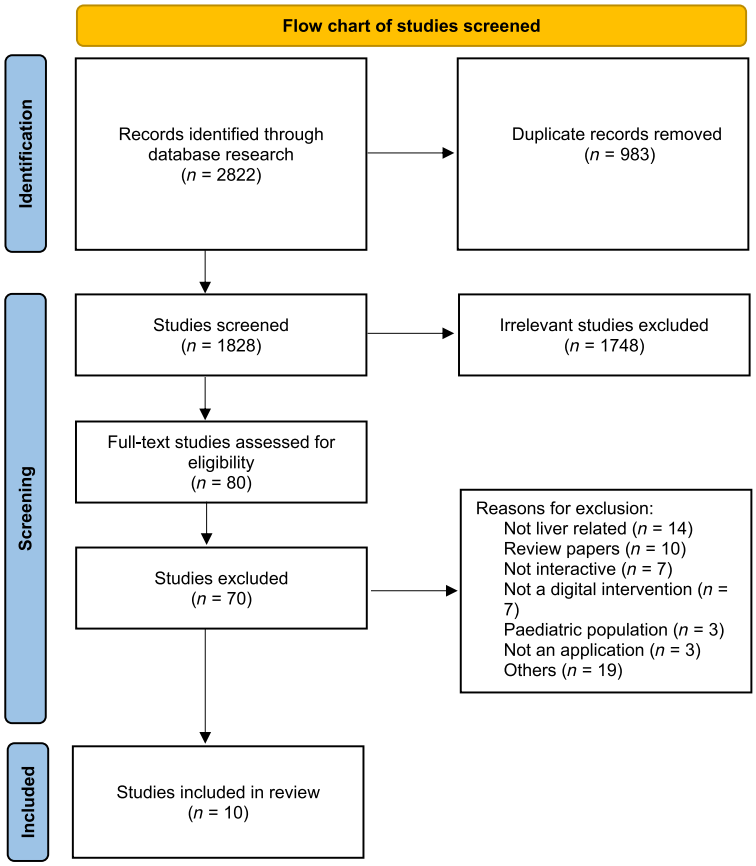
Data from these studies were extracted and analyzed to answer the review questions related to clinical characteristics of participants, features of the digital intervention, engagement with the digital intervention, and clinical effects of the digital intervention.

Results

Clinical and demographic characteristics. Table 2 summarizes the main characteristics of the included studies. The majority of the studies (70%) were conducted in the United States, and half of the studies were based on cohort design. The number of participants in the studies varied widely, from 20 in Kazankov *et al.*[11] to over 400 in the Bajaj *et al.*[12]. The median age of the participants was 56 years, and 60% of the studies had a control arm. More than half of the studies recruited their patients from outpatient clinics. The majority of participants had decompensated cirrhosis, with a mean MELD (Model for End-Stage Liver Disease) score of 13.4 across the studies. HE was the most common complication studied, with more than 70% of the studies investigating interventions for this complication. The underlying etiology of liver cirrhosis varied among the studies but was reflective of the overall trends in CLD epidemiology following the introduction of direct-acting antivirals for the treatment of hepatitis C. A decline in hepatitis C and an increase in metabolic-associated fatty liver disease (MAFLD) and alcohol,[11,12] were seen in more recent studies as the major causes of an underlying liver disease.

Features of digital intervention. The majority of studies opted to use smartphone as their digital applications, with iPads being used only in a minority of studies. Only two of the studies, Bloom *et al.*[13] and Ganapathy *et al.*,[8] provided their participants with a training period before commencement of the intervention. In Bloom *et al.*, the participants received help in downloading the app, registering for it, and were given Bluetooth scales. In the study of Ganapathy *et al.*, participants received more extensive training and education, including information on the app prompts, how to message the team via the app, and education on some of the serious complications of CLD such as gastrointestinal bleeding and HE, how to recognize them, and how to access emergency care. They were also given a brochure summarizing the information.

Descriptions of how the apps worked, from the patient perspective, were provided for the EncephalApp, CirrhoCareApp, and the app described by Bloom *et al.* Five of the studies included in this review were based on the Stroop EncephalApp, which has an "off" state with neutral stimuli and an "on" state with incongruent stimuli. The app provides a test of psychomotor speed and cognitive flexibility and evaluates the functioning of the anterior attention system with high sensitivity for the detection of cognitive impairment in minimal HE. The incongruent stimuli are presented in 9 of the 10 stimuli. In this portion, the subject must accurately touch the color of the word presented, which represents the name of the discordant color. In the easier "off" state, the subject views a neutral stimulus presented in red, green, or blue, one at a time, and must respond rapidly by touching the matching color of the stimulus to the colors displayed at the bottom of the screen.



From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

Figure 1 PRISMA flowchart of data extraction. *From*: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

In the Bloom *et al*. study,[13] patients were given Bluetooth scales that were connected to the mobile app. The data entry (weights) automatically got transferred from the scales to the mobile app and then to an electronic medical record.

The CirrhoCare app[11] was more complex as it required daily monitoring of the participants' heart rate, blood pressure, weight, % body water, cognitive function, self-reported well-being, and intake of food, fluids, and alcohol. The required devices to input this data provided to the enrolled participants included a wristwatch, a blood pressure cuff, and a weighing scale with bioimpedance to record the body water percentage. To assess cognitive function, the patients performed an animal recognition test, which was integrated into the app.

Engagement with digital intervention. Engagements rates were reported in only three studies, with all three reporting rates >50%. Bloom *et al*.[13] assessed engagement by measuring the number of times the study providers responded to the alerts and prompts, which was around 84%. Notably, engagement rates differed significantly among different provider groups (senior doctors, junior doctors, and nurses), with junior doctors having the highest rate (75%) and senior doctors having the lowest rate (37%).

Valizadeh *et al*.[14] evaluated engagement of the app under development through questions administered to their 73 cirrhotic patients. The participants rated the app based on entertainment, interest, customization, interactivity, and target group. Based on the ratings, the authors predicted the engagement rate, if the app were developed, to be 71%. This led them to proceed with developing the "My Liver" android app.

Reid *et al*.[15] evaluated engagement by measuring the number of times patients opened the mobile app, which prompted them daily, and also by tracking whether participants responded to questions about hospitalization at 30-day intervals. The overall engagement rate in this study was 59%.

Clinical effects of intervention. Among the included studies, Kazankov *et al*.[12] was the only one that reported feasibility rates and the impact of digital interventions on readmission rates. Feasibility rates were determined through a questionnaire that assessed whether patients found the CirrhoCareApp user friendly and easy to navigate, and by tracking their overall activity time on the app portal. The study reported a high feasibility rate of 88%.

Table 2 Main characteristics of the screened studies

Date of publication	Authors	Country	Study title	Study design	Study population	Control arm	Age
2016	Bajaj *et al.*	USA	Diagnosis of Minimal Hepatic Encephalopathy Using Stroop EncephalApp: A Multicenter US-Based, Norm-Based Study	Cross-sectional study	437	Yes	48.7 ± 11.9
2020	Bloom *et al.*	USA	A Smartphone App to Manage Cirrhotic Ascites Among Outpatients: Feasibility Study	Cohort study	25	No	57.6 ± 13
2017	Ganapathy *et al.*	USA	The PatientBuddy App Can Potentially Prevent Hepatic Encephalopathy-Related Readmissions	Cohort study	40	No	58 ± 10
2020	Lou *et al.*	China	EncephalApp Stroop App Predicts Poor Sleep Quality in Patients with MHE due to HBV-Induced Liver Cirrhosis	Cross-sectional study	180	Yes	56
2013	Bajaj *et al.*	USA	The Stroop Smartpphone App Is a Short and Valid Method to Sreen for MHE	Cohort study	126	Yes	56
2019	Valizadeh *et al.*	Iran	Development and Evaluation of a Self-Care Smartphone Application for Cirrhotic Patients	Methodological	74	No	48.8
2017	Acharya *et al.*	USA	Overt Hepatic Encephalopathy Impairs Learning on the Encephalapp Stroop Which Is Reversible after Liver Transplant	Cross-sectional study	230	Yes	61
2015	Bajaj *et al.*	USA	Validation of EncephalApp, the Smartphone-Based Stroop Test, for the Diagnosis of Covert Hepatic Encephalopathy	Cohort study	167	Yes	55
2022	Kazankov *et al.*	UK	Evaluation of CirrhoCare—A Digital-Health Solution for Home Management of Patients with Cirrhosis	Prospective cohort	20	Yes	59 ± 10
2020	Reid *et al.*	USA	How Engaging Should a Smartphone App be for Patients with Decomp Cirrhosis?	Cohort study	30	No	56

Source of recruitment	Targeted complication	Technology used	Etiology of cirrhosis	Mean MELD	Engagement rates	Clinical effects of the intervesion
Outpatient	HE (minimal MHE)	iPod	HCV (43%), ETOH (15%)	11	Not reported	44% had MHE by App
Inpatient and outpatient	Ascites	Smartphone app, bluetooth scales	ETOH (44%), NASH (36%)	15.8	>50% Patients and Providers	17 readmissions, 4% with ascites
Inpatients	HE	Smartphone app	NASH (13%), HCV (7%), Alcohol (7%)	19.5	Not reported	17 readmissions
Inpatients	HE	iPad	HBV (100%)	9.46	Not reported	85.2% sensitivity, 77.3% specificity for MHE
Outpatient	HE	Smartphone app	HCV (68), ETOH (11),both (10), NASH (22)	12.5	Not reported	App times correlated with MELD, and were worse with prior HE
Outpatient	Any decompensation				71.36%	Not reported
Outpatient	HE	Smartphone app	HCV (110), NASH (49), ETOH (37)	11	Not reported	Cognitive flexibility does not improve in prior OHE
Outpatient	HE	Smartphone app	HCV (35%), ETOH (17%) Both (25%) NASH (14%)	12	Not reported	Cirrhotic patients performed worse
Inpatient	Decompensation	Smartphone app	ETOH (80%), NASH (10%), HBV (5%), NASH/HCV (5%)	16.1	Not reported	38% less readmissions
	HE	Smartphone app			59%	Not reported

Additionally, Kazankov *et al.* found that readmission rates were reduced by 38% in the intervention group compared to the control group.

Discussion

The increasing burden and cost of liver cirrhosis on patients and healthcare systems suggests the need for alternative approaches to delivering health care in this population. Mobile devices, such as smartphones and iPads, have become part of daily living and many people are now familiar with their use. Despite the heterogeneity of the studies included in this review, we found that applications tailored for patients with CLD had an overall positive outcome.

The EncephalApp, the most extensively studied digital intervention, was successful in diagnosing minimal HE in 44% of patients. According to Bajaj *et al.*,[12] the overall length of time patients spent on the EncephalApp correlated with the disease severity. The less time spent meant that the patients had more severe disease and therefore higher MELD scores and higher likelihood of previous bouts of encephalopathy. That led them to conclude that the EncephalApp had good sensitivity in diagnosing minimal HE. Lou et al.[16] assessed the EncephalApp from a different perspective and found that the use of the mobile app could predict poor sleep quality in patients with cirrhosis secondary to hepatitis B, with good sensitivity and specificity for diagnosing minimal HE (85.2% and 77.3%, respectively).

In terms of impacts of digital interventions on hospitalization rates in patients with decompensated cirrhosis, Ganapathy *et al.*[8] found that 8 out of 17 HE-related admissions were avoided by using the Patient Buddy app. The more recently developed CirrhoCare app by the U.K. group,[12] which did not focus solely on HE but looked at all potential episodes of decompensation, found that by remotely managing their participants using this smartphone application they were able to reduce readmissions by 38% relative to a control group. They also found that the duration of hospitalization was shorter in the group using the CirrhoCareApp.

Another key finding emerging from our review was the surprisingly high engagement rates with technology that were shown in two of the studies. Bloom *et al.*[13] found that 94% of the study participants preferred using the smartphone app because of its ease, and more than half (60%) of the participants chose to continue using the app after the study period had ended. Reid *et al.*[15] found engagement rates as high as 59% when they studied the use of different smartphone apps in the cirrhotic population. These results suggest that despite the significant disease burden and disability in decompensated cirrhosis, patients appear willing and able to engage remotely via smartphone apps.

Although the engagement rates with digital interventions, when reported, appear high, limited details were provided by authors addressing the important question of reasons for poor engagement. In the Bloom *et al.* study,[13] a 12% participant withdrawal rate was reported. The main reasons for withdrawal were being too ill to stand on scales and failing to respond to phone calls. Ganapathy *et al.* also provided some insights into the poor engagement of 24 participants. The key concern of these participants was unmanageable data entry, particularly the detailed data entry required for daily sodium intake. We therefore suggest that future studies maximize their engagement rates by carefully selecting patients who have the capacity to perform the required tasks such as weighing on scales and to design apps with only simple data-entry requirements tailored to highly comorbid cirrhotic patients.

Although digital interventions show some promise in cirrhosis, it is important to acknowledge the potential limitations of this technology in patients without the required digital literacy. This is particularly relevant for the cirrhotic population, which is frequently frail, highly comorbid, and with encephalopathy-related cognitive impairment and lower socioeconomic status. Therefore, the importance of comprehensive training to increase patient engagement seems to be a critical component of future success. Unfortunately, only two papers[8,13] provided details of the training provided to participants, and we would encourage future papers on digital intervention in cirrhosis to provide a comprehensive description of the training provided to participants.

Another limitation of the current literature is how apps are being modified for use by patients with significant morbidity, poor performance status, and severe cognitive impairment. In most studies, the apps used relied on mobile prompts/notifications to alert the participants to enter data regardless of the morbidity level. However, the study of Ganapathy *et al.*[8] did provide a more intensive support to patients who were struggling with the intervention. Specifically, a team of non-healthcare workers monitored the app data entry, and if the study participants missed an entry, they were called, followed by a call to the caregiver if the former failed to respond. This approach seems useful and relevant for sicker patients, and we believe this model of more intensive support should be considered by investigators in future studies.

Conclusion

Patients with liver cirrhosis have poor quality of life,[17] mainly as a consequence of decompensation episodes in the form of HE, ascites, and gastrointestinal bleeding. This review suggests that despite the challenges liver cirrhosis imposes, patients with CLD are willing to engage with healthcare workers via mobile applications. Although based on limited data, the review also suggests that digital interventions may have clinically significant impacts including diagnosis of minimal HE and reductions in hospital admissions. Further high-quality studies of well-designed digital interventions are now needed to advance the potential of this promising early experienc.

References

1 Wood E. Liver disease skyrockets thanks to alcohol, Hep C and obesity. 2019. Available from URL: https://www.thesenior.com.au/story/6011618/australia-faces-liver-disease-epidemic/
2 Welfare AIoHa. Australian Institute of Health and Welfare. 2015. Available from URL: https://www.aihw.gov.au/getmedia/a088f80f-fcdb-4c5d-aa00-ca776bd7f792/phe199-liver.pdf.aspx
3 Powell EE, Skoien R, Rahman T *et al.* Increasing hospitalization rates for cirrhosis: overrepresentation of disadvantaged Australians. *EClinicalMedicine*. 2019; **11**: 44–53.
4 Louissaint J, Lok AS, Fortune BE, Tapper EB. Acceptance and use of a smartphone application in cirrhosis. *Liver Int.* 2020; **40**: 1556–63.

5 Gines P, Quintero E, Arroyo V *et al*. Compensated cirrhosis: natural history and prognostic factors. *Hepatology*. 1987; **7**: 122–8.
6 Arroyo V, Fernandez J. Pathophysiological basis of albumin use in cirrhosis. *Ann. Hepatol.* 2011; **10**: S6–S14.
7 Bajaj JS, Thacker LR, Heuman DM *et al*. The Stroop smartphone application is a short and valid method to screen for minimal hepatic encephalopathy. *Hepatology*. 2013; **58**: 1122–32.
8 Ganapathy D, Acharya C, Lachar J *et al*. The patient buddy app can potentially prevent hepatic encephalopathy-related readmissions. *Liver Int.* 2017; **37**: 1843–51.
9 Bajaj JS, Heuman DM, Sterling RK *et al*. Validation of EncephalApp, smartphone-based stroop test, for the diagnosis of covert hepatic encephalopathy. *Clin. Gastroenterol. Hepatol.* 2015; **13**: 1828–1835 e1.
10 Chanda Ho NS, Alshurafa N, Shahbazi B, Ghasemzadeh H, Terrault N. Beyond Dr. Google: Early results of a personalized weight-tracking smartphone application and alert system for patients with ascites. *J. Hepatol.* 2014: 330A–331A.
11 Kazankov K, Novelli S, Chatterjee DA *et al*. Evaluation of CirrhoCare(R)—a digital health solution for home management of individuals with cirrhosis. *J. Hepatol.* 2023; **78**: 123–32.
12 Allampati S, Duarte-Rojo A, Thacker LR *et al*. Diagnosis of minimal hepatic encephalopathy using stroop EncephalApp: A multicenter US-based, norm-based study. *Am. J. Gastroenterol.* 2016; **111**: 78–86.
13 Bloom P, Wang T, Marx M *et al*. A smartphone App to manage cirrhotic ascites among outpatients: Feasibility study. *JMIR Med. Inform.* 2020; **8**: e17770.
14 Alieh Valizadeh NA. Development and evaluation of a self-care smartphone Application for cirrhotic patients. *Evid. Based Care J.* 2019; **9**: 32–40.
15 Todd G, Reid JS, Schlossberg E, Hashemi N. How Engaging Should a Smartphone App Be for Patients with Decompensated Cirrhosis? *AASLD*. 2019; **156**: 1277–8.
16 Ming Luo X-BY, Sheng-Juan H, Bai F-H. EncephalApp Stroop App predicts poor sleep quality in patients with minimal hepatic encephalopathy due to hepatitis B-induced liver cirrhosis. *Saudi J. Gastroenterol.* 2020; **26**: 120–8.
17 Janani K, Jain M, Vargese J *et al*. Health-related quality of life in liver cirrhosis patients using SF-36 and CLDQ questionnaires. *Clin. Exp. Hepatol.* 2018; **4**: 232–9.