

DEVELOPMENT OF A SMARTPHONE APPLICATION TO ENABLE REMOTE MONITORING IN THE OUTPATIENT MANAGEMENT OF CIRRHOTIC ASCITES

Phil Ha MBBS^{1,2}, Sherryne Warner BNsg^{1,2}, Paul O'Neil BNsg^{1,2}, Patricia Anderson BNsg^{1,2}, William Sievert MD^{1,2}

¹ Department of Gastroenterology and Hepatology, Monash Health, Melbourne, Victoria, Australia

² Faculty of Medicine, Nursing and Health Sciences, Monash University, Melbourne, Victoria, Australia

Abstract

Patients who develop hepatic decompensation with ascites have a poor prognosis and often experience other complications including spontaneous bacterial peritonitis, hepatic encephalopathy and variceal bleeding. We hypothesised that smartphone (SP)-enabled remote monitoring of patients with ascites may enable early detection of infection and acute decompensation, facilitate timely intervention and improve patient outcomes. Aim: We aimed to design, develop and implement a remote monitoring system (RMS) for outpatients with cirrhotic ascites. Method: We undertook surveys with patients and hepatologists to quantify the demand for a RMS and identify issues regarding implementation. A smartphone and a web-based application were developed as a RMS. Patients used the RMS in a 6-week prospective non-randomised trial. Results: We surveyed 27 patients (mean age 56 years, 18 (67%) were male, 16 (59%) had Childs Pugh B cirrhosis, and 20 (74%) had a history of alcoholic liver disease) and 5 hepatologists. There were 19 patients (70%) who reported that they would use a RMS. The RMS was used by 10 patients for a mean 53.8days (11-70), who entered 20.6 (0-71) updates. A total of 18 automated alerts occurred. 22% of automated alerts resulted in clinically significant changes to management, such as inpatient admission n=1 (6%), early outpatient appointment n=1 (6%) and reinforced adherence n=2 (11%). Conclusion: We have successfully designed an internet-enabled RMS for outpatients with cirrhotic ascites that could be used as an adjunct to existing outpatient services. Future studies will optimise the alert thresholds, assess long-term patient adoption and quantify clinical impact.

Keywords: telemedicine; cirrhosis; ascites; remote monitoring

Introduction

Portal hypertension is a late complication of cirrhosis that is associated with poor outcomes. Variceal haemorrhage, hepatic encephalopathy and ascites ensue as portal hypertension progresses, and these define the onset of decompensated liver disease. Ascites is the most common decompensation event and the surrounding clinical picture is complex. Multidisciplinary management is required to address the subsequent complications of spontaneous bacterial peritonitis (SBP), hepatorenal syndrome and hepatic hydrothorax. Current guidelines include the long-term implementation of a no-added salt diet and diuretic therapies; primary and secondary antibiotic prophylaxis is employed to prevent SBP. Paracentesis provides immediate symptomatic relief while transjugular intrahepatic portosystemic shunts and liver transplantation may be appropriate in a select few.^{1,2}

Despite these measures, readmission rates in patients with decompensated cirrhosis are high. We performed a retrospective review of 302 patients with cirrhotic ascites in a tertiary Australian hospital and found that 71% of patients required readmission for paracentesis within 90 days of first presentation for ascites.³ Typical characteristics of patients with decompensated cirrhosis included older age, male gender, and alcoholic liver disease (69%). We proposed that more effective measures at reducing the rate of preventable readmissions should be implemented.

Given that the mortality of those with cirrhotic ascites is high, a greater focus on outpatient management may lead to earlier intervention, decrease the frequency of hospital admissions and improve patient outcomes.^{4,5} We hypothesised that an Internet-based remote monitoring system would be feasible in the setting of outpatient cirrhotic ascites management and would allow access to real-time patient information that would improve patient outcomes by enabling the early identification of decompensation events.

The aim of this pilot study was to design, develop and implement a remote monitoring system (RMS) for outpatients with cirrhotic ascites.

Methods

We undertook a prospective study of patients with cirrhotic ascites and hepatologists at a large tertiary hospital.

Inpatients and outpatients presenting with cirrhotic ascites for admission or clinic review were identified by the principal investigator. These patients were invited to participate in a structured paper-based survey evaluating the demand and feasibility of a RMS and assessed baseline characteristics. The presence of cirrhosis was confirmed by clinical, laboratory and/or imaging data. Patients were excluded if the ascites was related to a cause other than cirrhosis.

Hepatologists and hepatology nurses who were a part of the Monash Liver Unit were invited to participate in a semi-structured questionnaire assessing the issues surrounding practical implementation of a RMS. This was administered on an individual basis by the principal investigator.

App development and deployment

Following analysis of survey responses, a smartphone application for Android smartphones and a web-app for all other Internet devices were developed using Eclipse IDE for Java and Google Forms, respectively.^{6,7} The application enabled transmission of the patient's current weight and symptoms via the internet to a nurse-led liver team. Our native Android application was developed using the Parse cloud backend platform, whereas the Google Forms used Google Drive functionalities and scripts to run. Both were integrated with Twilio, a cloud service that allowed for our automatic cellular text messages to be sent.^{8,9} Participants were assigned unique study identification numbers, and these were used in alerts sent to the liver team.

Patients who participated in the initial surveys were invited to use the RMS in a six week non-randomised prospective trial. We held a one-on-one education session with all patients at the start of the trial.

Patients were asked to submit an update every second day. An update consisted of entering the patient's current weight, and answering yes/no to questions regarding abdominal pain, fever, abdominal distension, peripheral oedema and jaundice. Patients

were also asked if they felt unwell and need to be contacted the liver team. (Figure 1)

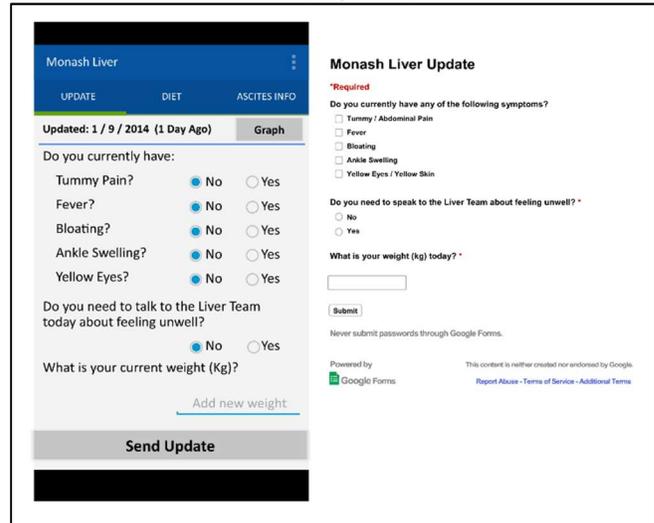


Figure 1. Screenshots of Android smartphone application (left) and Google Forms web application (right) used to remotely monitor patients with cirrhosis.

Automated text message reminders were sent if patients missed their scheduled update time by more than 24 hours. Automatic alerts were triggered when abnormal weight thresholds or the presence of symptoms were transmitted (Figure 2).

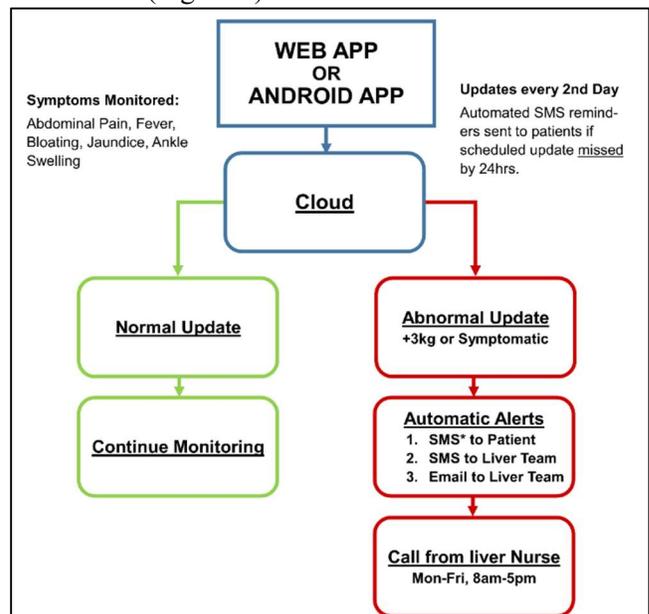


Figure 2. Schematic of remote monitoring system.

If an alert had been triggered, the liver nurse received an automated cellular text message (using the cellular network) and email notification (using the Internet) and

contacted the patient directly by telephone. We designed the alert system to utilise both cellular networks and the internet to alert the liver team to reduce the likelihood of alert transmission failure. In addition, patients were advised via automated text message to seek immediate attention if feeling particularly unwell.

General dietary information (No-Added Salt & High Protein Diet) and information regarding decompensated liver disease and emergencies were also available in the application.

Patients using the RMS were surveyed via telephone at the end of the follow up period for feedback on the service.

Outcomes and follow-up

Our primary outcome was to assess the feasibility of a RMS for models of outpatient care. Contacts with patients, time spent with patients, non-elective admissions and unscheduled outpatient clinic visits were recorded during the prospective RMS trial. Patients were followed from 30 July 2014 until 10 September 2014 or death.

Sample Size

Sample size calculations were not performed for this pilot study. We estimated that 25 patients and 5 hepatologists would provide adequate qualitative data to address key issues raised in implementing a RMS. We estimated that qualitative feedback from 10 patients after using the service would provide valuable information about the short and long-term feasibility of this service.

Statistical Analysis

Tabular and graphical descriptive methods were used to summarise the survey results from patients and liver clinicians. Outcomes from the prospective trial of the RMS were analysed basis with descriptive methods using Microsoft Excel 2011.¹⁰

This study was approved by Monash University Human Research Ethics Committee (MUHREC) (Project Number: CF14/1358 – 2014000633) and the Monash Health Human Research Ethics Committee (Project ID: Ref 14036L).

Results

Surveys with cirrhotic patients

Of 27 patients with cirrhotic ascites, 93% (n=25) were inpatients at the time of interview; of these, 41% were not attending outpatient liver care. 7% (n=2) of patients

were interviewed in outpatient clinics. Baseline characteristics are presented in Table 1.

Table 1. Baseline characteristics of surveyed.

Age (Mean)	56.0 y
Male	18 (67.0%)
Ethnicity	
Caucasian	21 (78.0%)
Asian	5 (19.0%)
African	1 (4.0%)
Employment	
Employed	5 (18.5%)
Highest level of education achieved	
Primary School	7 (25.9%)
Secondary School	15 (55.6%)
Tertiary	5 (18.5%)
Aetiology of Cirrhosis	
Alcohol	20 (74.0%)
HCV	3 (11.1%)
NASH	2 (7.4%)
HBV	2 (7.4%)
Other	4 (14.8%)
Outpatient Care	
Public	9 (33.4%)
Private	7 (25.9%)
Nil	11 (40.7%)
Child's Pugh	
A	2 (7.4%)
B	16 (59.2%)
C	9 (33.3%)
MELD / MELD-Na	14.74 / 18.33
Number of previous paracentesis	
1	9 (33.3%)
≤ 5	10 (37.0%)
> 5	8 (29.6%)

HCV: Hepatitis C, HBV: Hepatitis B, HDV: Hepatitis D, NASH: Non-alcoholic steatohepatitis, MELD: model for end-stage liver disease, Meld-Na: MELD-Sodium ^{11,12}

Perceptions of a Remote Monitoring Service

There were 19 (70%) patients who reported that they wanted a RMS for outpatient care. Of these patients, 89% (n=17) had access to the internet via smartphones and the remainder had access via computer.

Of the participants keen to use a RMS, 8 (47%) patients stated that they would self-report weights, while family members would perform the updates for the remainder. All patients stated that they were willing to send at least 2 updates per week and have our liver team automatically notified if abnormal values were present. There were 24 (89%) patients who requested information regarding diet and/or liver disease to be

included in the service. All patients desired an outpatient appointment reminder service, however only one (5%) patient requested a medication reminder service.

Of the 8 patients who did not want a RMS, 6 (75%) desired a telephone service which could be called when required.

Surveys with gastroenterologists and liver nurses

All five hepatologists (consultants n=3, specialist nurses n=2) believed that a RMS could prove useful. There was consensus that the symptoms of acute decompensation and SBP should be monitored. All deemed a weight gain of 3kg to be an appropriate alert threshold, and that an outpatient nurse service should oversee the RMS.

Implementation of Remote Monitoring Service

Of the original 27 patients interviewed, four died and one was transferred to palliative care before the six-week trial began. We recruited patients for the RMS trial from those who had expressed interest in using the service.

We closed recruitment of patients for the RMS trial once we had had recruited 10 patients. One patient stopped using the RMS because of issues with English proficiency, and one patient was transferred into palliative care a few days into the commencement of trialling the RMS.

Table 2. Baseline characteristics of participants in the remote monitoring service (n=10).

Age (mean)	51.2
Male	8 (80%)
Aetiology	
Alcohol	9 (90%)
HCV	2 (20%)
HBV	1 (10%)
Child Pugh (Mean)	7.9
A	2 (20%)
B	6 (60%)
C	2 (20%)
MELD (Mean)	12.5
MELD-Na (Mean)	15.3
Past History of:	
Spontaneous Bacterial Peritonitis	1 (10%)
Upper Gastrointestinal Bleed	3 (30%)
Hepatic Encephalopathy	1 (10%)
Hepatocellular Carcinoma	0 (0%)
Who was performing the updates	
Patient	6 (60%)
Family	4 (40%)

Patients were followed up for a mean of 53.8 days (range 11-70). Patients using the RMS entered a mean of 20.6 updates (range 0-71) over the follow up period. There were 4 (40%) patients who entered an average of at least two updates per week, 4 (40%) patients who entered less than two updates per week, and 2 (20%) patients entered no updates (these patients stopped the trial early due to issues with language proficiency and being transferred into palliative care).

There were a total of 25 telephone contacts, of which 18 were triggered by automated alerts based on abnormal patient updates and 7 were nursing initiated (due to a lack of recent updates). These telephone contacts lasted a total time of 193 minutes, of which 115 minutes (60%) were spent with two patients.

The automated alerts were most commonly triggered for isolated increases in weight (n=10, 56%), symptoms (n=7, 39%) or both (n=1, 6%). (Table 3) There were 15 (83%) automated alerts triggered within business hours (weekdays between 8am-5pm). Of all the automated alerts, 22% resulted in a change to patient management (n=1 admission, n=1 early outpatient review, n=2 reinforced adherence to therapies).

Table 3. Automatically triggered alerts and their outcomes.

Reason for Automated Alert	n	Outcome	n
Weight Alert	10	Change weight threshold	6
		Reinforced adherence to therapies	2
		Continue monitoring	1
		Not contactable	1
Abdominal Pain	2	Inpatient Admission	1
		Continue Monitoring	1
Bloating + Jaundice	3	Continue Monitoring	2
		Uncontactable	1
Weight Alert & Bloating	1	Early Outpatient Appointment	1
Bloating	1	Continue Monitoring	1
Ankle Swelling	1	Continue Monitoring	1
Fever	0		

All of the patients who continued to use the RMS (n=8) stated that they would use the service in the future and send updates every second day. Of the 5 patients who were sent at least one reminder text, all were satisfied with the implementation of the automatic reminder. One patient would have preferred the service to be available for extended hours, rather than limited to business hours. Four patients reported that they would

like a scheduled call from an outpatient liver nurse. Access to medical advice was a positive feature of the RMS although there was uncertainty among patients about reporting persistent baseline symptoms. Internet accessibility was a barrier at times.

Discussion

In this pilot study we have demonstrated that remote monitoring of outpatients with cirrhotic ascites is feasible. In our original cohort of 27 patients only 21 were alive and not in palliative care at the conclusion follow up, thus avoidance of hospital admissions is particularly important in this group of patients who have particularly poor prognoses. The RMS detected one episode requiring inpatient intervention, and importantly, we were able to potentially avoid three inpatient admissions with early unscheduled outpatient appointments and telephone consultations.

Telemedicine and smartphone integration into healthcare

Demand for smartphones and smartphone applications has grown exponentially in the past decade due to their convenience and connectivity.^{13,14} Health and medical apps are expanding in number, and while the majority track exercise, weight loss, medication and women's health issues, an increasing proportion is dedicated to the management of chronic disease. Unfortunately, many apps are limited in their integration to existing healthcare provider networks, and this may be a contributing factor to the lack of evidence for their clinical usefulness.¹⁵⁻¹⁷ Bridging this gap between patient and healthcare provider and allowing two-way data transmission, remote monitoring and potentially immediate feedback could allow these apps to become more clinically useful.¹⁸

The concept of enhancing models of outpatient care with the integration of smartphones and Internet based services builds upon previous research into telemedicine and remote monitoring which have traditionally relied upon landline and cellular services. While the real-time data provided by telemedicine can be difficult to interpret accurately, countless opportunities exist in this emerging smartphone era.

Remote monitoring of both subjective data on patient symptoms and objective physiological data (e.g. blood glucose levels, oxygen saturation) has been implemented to varying levels of success in a variety of clinical settings, including chronic respiratory disease,

diabetes mellitus, diseases affecting mobility, perioperative care and psychiatric conditions.¹⁹⁻³¹

Telemedicine can be used to supplement a Patient-Centred Care approach to management of cirrhosis. The American Association for the Study of Liver Diseases have recently outlined the importance individualising the care provided to cirrhotic patients, while also empowering patients to become more involved in their management.³² Part of this model includes utilising telemedicine and remote monitoring to optimise outpatient cirrhosis management.³³

Although smartphones have been used to diagnose encephalopathy with Stroop testing, we could find no published literature implementing telemedicine specifically in the setting of cirrhotic ascites. However, remote monitoring has been studied in a pathophysiologically similar condition, congestive cardiac failure (CCF).^{34,35}

Five large RCTs examining the implementation of telemedicine using telephones in CCF have shown no benefit in regard to mortality, hospitalisation or length of stay in hospital.³⁶⁻⁴⁰ Two issues that arose were declining patient adherence and an incomplete understanding of weight fluctuations preceding decompensation, although using dynamic baseline weights may improve the clinical utility of monitoring weights.^{41,42}

Emphasis on symptomatology, qualitative patient assessments and education may also yield better results. Giordano's outpatient heart failure model used scheduled weekly or fortnightly consultations to qualitatively assess patients on wellbeing and health prevention.³⁸ Patients were able to contact the care team at any time for 'teleassistance', and this model showed a 40% reduction in episodes of haemodynamic instability and in cardiovascular mortality at one-year follow-up. From a morbidity perspective, Seto showed that the implementation of remote monitoring resulted in better quality of life for patients.⁴³

Many past RMSs have relied on landlines or direct telephone calls for the reporting of physiological and symptomatic data. We believe that smartphone apps have an advantage over more traditional systems because apps can be more convenient for patients and care-providers, have built-in reminder systems and allow for multiple different alert pathways to be activated simultaneously. Additionally, having patients 'check-in' with normal updates can provide useful information to caregivers who would otherwise have no

means to monitor their patients in real-time.

Remote monitoring of patients with cirrhotic ascites

Our Android specific smartphone app and the generic web-based app based on Google Forms allowed patients with any phone, tablet or computer to participate in this service. Australia has seen rapid uptake of smartphone usage and smart devices in recent years, with the most marked smartphone growth occurring in older generations. Currently the demographic of middle to older aged patients is rapidly transitioning to take up more internet-enabled devices.⁴⁴⁻⁴⁶ We were initially uncertain of how patients would adopt this technology, and although some initial telephone contacts were for technical difficulty, most were for minor issues that were quickly resolved.

Long-term patient adherence is essential if remote monitoring is to be of benefit. The frequency of updates is a balance between patient convenience, being able to obtain useful clinical information and maintaining a routine for patients. Based on survey data, updates every second day seemed reasonable and our automated reminder system was only activated if the second daily update had been missed by 24h (and daily subsequently). We found that choosing the preferred timing of scheduled updates to be important. Given that our small service only operated during business hours, during which we captured 15 (85%) of all automated alerts, asking patients to transmit updates on weekdays allowed changes in management before the weekend.

We were encouraged by the level of family involvement in this trial. Patients with family members who were actively involved in using the RMS had a higher frequency of updates than patients who used the system independently. We believe that another advantage of familial involvement is the indirect education of household contacts about the red flags of decompensation. Ultimately, even with all the measures used in our RMS to reduce the risk of data and alert transmission error education is key in aiding early presentation to medical services.

Alerts triggered by symptomatic patients were more useful than alerts from isolated weight gain. Our intent for the RMS was to detect pending decompensation and facilitate early admission or ideally to prevent inpatient admission completely. To improve the specificity of automated alerts in future models, we would assess changes in symptoms (rather than the presence of symptoms which may be a patient's norm), and also ask patients to grade symptoms such as abdominal distension. Furthermore, while implementation of more

dynamic and complex interpretations of weight thresholds may improve the clinical utility of monitoring weight patterns, this may be confounded by measurement errors, fluctuations in lean muscle mass, fluid retention and normal daily variation.

An issue we encountered in deploying this service was low participation rates by our higher risk patients. One particular patient entered a total of one update for the follow up period despite our attempts to engage him further. This patient had a history of alcoholic cirrhosis, social isolation and detachment from medical services – not an uncommon clinical picture in patients presenting with decompensated liver disease. Successfully implementing an RMS with high participation and long term adherence from this demographic will be quite challenging; avenues to better engage these patients with medical services will be particularly important.

Limitations and future direction

Two limitations of our pilot study were its size and short follow up period, and it is difficult to draw conclusions without more data. Furthermore, there was inherent bias in our study given that the participants who were involved in the initial surveys were the same group who participated in the RMS implementation and commented on its success/failures.

We recognise that the results from the follow up survey suggesting that all patients would be keen to continue using the RMS were not necessarily accurate. Given that not all patients completely adopted the service and regularly sent updates, it is unlikely that all patients would truly continue to use a RMS. We anticipate that long term adherence is predicted to be an issue in this group of patients.

Future Direction

This study provides support for future randomised trials to investigate long term patient adoption, and whether an internet-based adjunct to outpatient care offers clinical or economic benefit over traditional models of outpatient care in cirrhosis. In particular, the sensitivity and specificity of weight thresholds and symptoms for detecting impending decompensation should be investigated. Screening measures for hepatic encephalopathy could also be implemented.

Conclusion

We have successfully designed a prototype internet-enabled remote monitoring system for outpatients with cirrhotic ascites. Ideally this system would be an

adjunct to existing outpatient services. Optimisation of weight and symptom alert thresholds is essential to future implementation. Assessment of long-term patient adoption and the clinical benefits of a remote monitoring system requires more research.

Corresponding author:

Phil Ha
 Department of Gastroenterology and Hepatology
 Monash Medical Centre
 246 Clayton Road
 Clayton, VIC 3168
 Australia
 Email: philha91@gmail.com

Conflict of Interest. The authors declare no conflicts of interest.

Acknowledgements. We would like to acknowledge the patients who participated in this trial. Without their contribution this trial would not have been possible. We would also like to acknowledge Dr Suong Le for her work in the conception of this study.

References

1. European Association for the Study of the Liver. EASL clinical practice guidelines on the management of ascites, spontaneous bacterial peritonitis, and hepatorenal syndrome in cirrhosis. *J Hepatol* 2010;53(3):397–417.
2. Runyon BA, AASLD Practice Guidelines Committee. Management of adult patients with ascites due to cirrhosis: an update. *Hepatology* 2009;49(6):20872–107.
3. Le S, Spelman T, Chong C-P, et al.. Could adherence to quality of care indicators for hospitalized patients with cirrhosis-related ascites improve clinical outcomes? *Am J Gastroenterol.* 2016;111(1):87–92.
4. D’Amico G, Garcia-Tsao G, Pagliaro L. Natural history and prognostic indicators of survival in cirrhosis: A systematic review of 118 studies. *J Hepatol* 2006;44(1):217–231.
5. Morando F, Maresio G, Piano S, et al.. How to improve care in outpatients with cirrhosis and ascites: A new model of care coordination by consultant hepatologists. *J Hepatol* 2013;59(2):257–264.
6. Google. Google Forms. 1600 Amphitheatre Parkway, Mountain View, CA 94043, United States: Google Inc.
7. Foundation E. Eclipse IDE [Internet]. Eclipse Foundation; 2014. Available from: www.eclipse.org accessed 1 March 2014.
8. Twilio, Inc. Twilio [Internet]. Communication APIs for SMS, Voice, Video and Authentication. 2014. Available at: <https://www.twilio.com/> accessed 21 March 2018
9. Parse, Inc. Menlo Park, CA, USA: Parse, inc; 2014. Available from www.parse.com (now <http://parseplatform.org/>) accessed 1 March 2014.
10. Microsoft. Microsoft Excel 2011. Redmond, Washington, USA: Microsoft Corporation.
11. Wiesner R, Edwards E, Freeman R, et al. Model for end-stage liver disease (MELD) and allocation of donor livers. *Gastroenterology* 2003;124(1):91–96.
12. Biggins SW, Kim WR, Terrault NA, et al.. Evidence-based incorporation of serum sodium concentration into MELD. *Gastroenterology* 2006;130(6):1652–1660.
13. Singh S. Smartphone Market Share by Country - Q3 2013: Android Dominates Outside US, Windows Phone Grows in Europe | Tech-Thoughts by Sameer Singh [Internet]. Available at: <http://www.tech-thoughts.net/2013/11/smartphone-market-share-by-country-q3-2013.html> accessed 19 March 2014
14. Lunden I. 6.1B Smartphone Users Globally By 2020, Overtaking Basic Fixed Phone Subscriptions. TechCrunch. (2015). Available at: <http://social.techcrunch.com/2015/06/02/6-1b-smartphone-users-globally-by-2020-overtaking-basic-fixed-phone-subscriptions/> accessed on 9 January 2018.
15. Charani E, Castro-Sánchez E, Moore LSP, Holmes A. Do smartphone applications in healthcare require a governance and legal framework? It depends on the application! *BMC Med* 2014;12(1):29.
16. Savitz E. 5 Ways Mobile Apps Will Transform Healthcare [Internet]. Forbes.(2012) Available at: <https://www.forbes.com/sites/ciocentral/2012/06/04/5-ways-mobile-apps-will-transform-healthcare/> accessed 7 January 2018

17. Cui M, Wu X, Mao J, Wang X, Nie M. T2DM Self-Management via Smartphone Applications: A Systematic Review and Meta-Analysis. *PLoS One* 2016;11(11):e0166718.
18. Haze KA, Lynaugh J. Building patient relationships: a smartphone application supporting communication between teenagers with asthma and the RN care coordinator. *Comput Inform Nurs* 2013;31(6):266-271; quiz 272-273.
19. Licskai C, Sands TW, Ferrone M. Development and pilot testing of a mobile health solution for asthma self-management: asthma action plan smartphone application pilot study. *Can Respir J* 2013 20(4):301–306.
20. Johnston NW, Lambert K, Hussack P, et al. Detection of COPD Exacerbations and compliance with patient-reported daily symptom diaries using a smart phone-based information system [corrected]. *Chest* 2013;144(2):507–514.
21. Işık AH, Güler I. Pulse oximeter based mobile biotelemetry application. *Stud Health Technol Inform* 2012;181:197–201.
22. Kirwan M, Vandelanotte C, Fenning A, Duncan MJ. Diabetes self-management smartphone application for adults with type 1 diabetes: randomized controlled trial. *J Med Internet Res* 2013;15(11):e235.
23. Hewson DJ, Jaber R, Chkeir A, et al.. Development of a monitoring system for physical frailty in independent elderly. *Conf Proc Annu Int Conf IEEE Eng Med Biol Soc IEEE Eng Med Biol Soc Annu Conf.* 2013;2013:6215–6218.
24. Nishiguchi S, Ito H, Yamada MY et al. Self-assessment tool of disease activity of rheumatoid arthritis by using a smartphone application. *Telemed J E-Health* 2014r;20(3):235–340.
25. Shinohara A, Ito T, Ura T, et al.. Development of lifelog sharing system for rheumatoid arthritis patients using smartphone. *Conf Proc Annu Int Conf IEEE Eng Med Biol Soc IEEE Eng Med Biol Soc Annu Conf.* 2013;2013:7266–9.
26. Wagner R, Ganz A. PAGAS: Portable and accurate gait analysis system. *Conf Proc Annu Int Conf IEEE Eng Med Biol Soc IEEE Eng Med Biol Soc Annu Conf.* 2012;2012:280–283.
27. Yamada M, Aoyama T, Mori S, et al. Objective assessment of abnormal gait in patients with rheumatoid arthritis using a smartphone. *Rheumatol Int* 2012;32(12):3869–3874.
28. Faurholt-Jepsen M, Vinberg M, Christensen EM, et al.. Daily electronic self-monitoring of subjective and objective symptoms in bipolar disorder—the MONARCA trial protocol (MONitoring, treAtment and pRediCtion of bipolar disorder episodes): a randomised controlled single-blind trial. *BMJ Open* 2013;3(7):e003353. doi:10.1136/bmjopen-2013-003353.
29. Lu K, Marino NE, Russell D, Singareddy A, et al.. Use of Short message service and smartphone applications in the management of surgical patients: a systematic review. *Telemed J E-Health* 2017 Nov 7;
30. Soto-Perez-De-Celis E, Kim H, Rojo-Castillo MP, et al. A pilot study of an accelerometer-equipped smartphone to monitor older adults with cancer receiving chemotherapy in Mexico. *J Geriatr Oncol* 2018; 9(2):145-151
31. Cai RA, Beste D, Chaplin H, et al.. Developing and evaluating jiapp: acceptability and usability of a smartphone app system to improve self-management in young people with juvenile idiopathic arthritis. *JMIR MHealth UHealth* 2017;5(8):e121.
32. Verma M, Navarro V. Patient-centered care: A new paradigm for chronic liver disease. *Hepatology* 2015 Oct;62(4):988–990.
33. Mellinger JL, Volk ML. Multidisciplinary Management of Patients With Cirrhosis: A Need for Care Coordination. *Clin Gastroenterol Hepatol* 2013;11(3):217–223.
34. 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(10):1828–1835.e1.
35. Bajaj JS, Thacker LR, Heuman DM, et al.. The Stroop Smartphone app is a short and valid method to screen for minimal hepatic encephalopathy. *Hepatology* 2013;58(3):1122–1132.
36. Chaudhry SI, Mattera JA, Curtis JP, et al.. Telemonitoring in patients with heart failure. *N Engl J Med* 2010;363(24):2301–2309.
37. Cleland JGF, Louis AA, Rigby AS, Janssens U, Balk AHMM, TEN-HMS Investigators. Noninvasive home telemonitoring for patients with heart failure at high risk of recurrent admission and death: the Trans-European

- Network-Home-Care Management System (TEN-HMS) study. *J Am Coll Cardiol* 2005;45(10):1654–1664.
38. Giordano A, Scalvini S, Zanelli E, et al.. Multicenter randomised trial on home-based telemanagement to prevent hospital readmission of patients with chronic heart failure. *Int J Cardiol* 2009;131(2):192–199.
 39. Koehler F, Winkler S, Schieber M, et al.. Telemedicine in heart failure: pre-specified and exploratory subgroup analyses from the TIM-HF trial. *Int J Cardiol* 2012;161(3):143–150.
 40. Lyngå P, Persson H, Hägg-Martinell A, Hägglund E, et al.. Weight monitoring in patients with severe heart failure (WISH). A randomized controlled trial. *Eur J Heart Fail* 2012;14(4):438–444.
 41. Ledwidge MT, O’Hanlon R, Lalor L, et al.. Can individualized weight monitoring using the HeartPhone algorithm improve sensitivity for clinical deterioration of heart failure? *Eur J Heart Fail* 2013;15(4):447–455.
 42. Zhang J, Goode KM, Cuddihy PE, Cleland JGF, TEN-HMS Investigators. Predicting hospitalization due to worsening heart failure using daily weight measurement: analysis of the Trans-European Network-Home-Care Management System (TEN-HMS) study. *Eur J Heart Fail* 2009;11(4):420–427.
 43. Seto E, Leonard KJ, Cafazzo JA, et al.. Mobile phone-based telemonitoring for heart failure management: a randomized controlled trial. *J Med Internet Res* 2012;14(1):e31.
 44. Commonwealth of Australia: Australian Bureau of Statistics. Personal internet use. Australian Bureau of Statistics. 2014. Available at: <http://www.abs.gov.au/ausstats/abs@.nsf/0/D11394A54F8B9ED1CA25796600152C62?opendocument> accessed 8 October 2015
 45. Commonwealth of Australia: Australian Bureau of Statistics. Personal Internet Use [Internet]. Australian Bureau of Statistics. 2014. Available from: <http://www.abs.gov.au/ausstats/abs@.nsf/Lookup/8146.0Chapter32012-13> accessed 8 October 2015
 46. Drumm J, White N, Swiegers M, Davie M. Mobile Consumer Survey 2017 : The Australian Cut. Deloitte Touche Tohmatsu Limited; 2017.