

Digital Technology and Mobile Health in Behavioral Migraine Therapy: A Narrative Review

Authors:

Stubberud A¹; Linde M, PhD^{1,2}

¹ Department of Neuromedicine and Movement Science, NTNU Norwegian University of Science and Technology, NO-7489 Trondheim, Norway

² Norwegian Advisory Unit on Headache, Department of Neurology and Clinical Neurophysiology, St. Olavs Hospital, NO-7006 Trondheim, Norway

Corresponding author:

Anker Stubberud

Department of Neuromedicine and movement science, NTNU Norwegian University of Science and Technology, Norway

Tel.: 004745229174

Email: ankers@stud.ntnu.no

Abstract

Purpose of review: This article reviews the recent research and development of electronic health (eHealth) and, in particular, mobile health (mHealth) strategies to deliver behavioral treatment for migraine. Prospects for future development and research of mobile health in migraine are suggested.

Recent findings: Advances in digital technology and mobile technology have led to an era where electronic and mobile approaches are applied to several aspects of healthcare. Electronic behavioral interventions for migraine seem to be acceptable and feasible, but efficacy measures are uncertain. Clinical trials on mHealth-based classical behavioral therapies such as relaxation, biofeedback and cognitive behavioral therapy are missing in the literature. Within mHealth, headache diaries are the most researched and scientifically developed. Still, there is a gap between commercially available apps and scientifically validated and developed apps.

Summary: Digital technology and mobile health has not yet lived out its potential in behavioral migraine therapy. Application of proper usability and functionality designs towards the right market, together with appraisal of medical and technological recommendations, may facilitate rapid development of eHealth and mHealth while also establishing scientific evidence.

Keywords: electronic health; mobile health; smartphone; wearable; migraine; behavioral therapy

Main Body

Introduction

Migraine is a heterogeneous group of neurological disorders, of which the dominant feature is severe headache often accompanied by nausea and vomiting, as well as photo- and phonophobia [1]. Migraine is prevalent and according to the 2015 Global Burden of Disease Study, the number one cause of neurologic disability, and the second most common cause of years lived with disability [2]. The fact that over one billion individuals had a headache disorder in 2016 further emphasizes the population burden of the disease [2, 3].

All the while, we live in an emerging era of mobile health and digital technology. Telemedicine and electronic health (eHealth) defines the delivery of health services through telecommunications, while a subcategory of eHealth, labeled mobile health (mHealth), encompasses the use of smartphones, applications (apps) and wearables for medical purposes [4]. eHealth and mHealth represent new means for delivering prophylactic behavioral interventions for migraine. These interventions are established as being effective in reducing the burden of migraine, both in the pediatric and adult population [5, 6]. Common behavioral interventions include relaxation training, biofeedback training and cognitive behavioral therapy (CBT) [7].

At the beginning of this decade several researchers praised the potential of eHealth and mHealth for delivering behavioral treatments [7-10]. Now, more than five years later, it is tempting to ask ourselves: has this prophecy been fulfilled and lived out its potential? The aim of this narrative review is to highlight the available recent research and development of eHealth and, in particular, mHealth for migraine, and suggest prospects for future research and development.

Methods

The first section will describe why eHealth and mHealth interventions for migraine are important. The second section will narrate available electronic and mobile behavioral therapies for migraine. MEDLINE and CINAHL were searched for available records from January 1st 2015 and last updated on the 7th of April 2018. The following nested search was used: (“mHealth” OR “eHealth” OR “telemedicine”) AND “migraine”. In addition reference lists of reviews on the topic were hand

searched. Finally, prospects for future mHealth research will be elaborated based on recent reviews concerning development of mHealth.

Why are eHealth and mHealth interventions for migraine important?

One study depicts 12 application areas for mHealth, whereof several are useful for migraine therapy [11]. Firstly mHealth has the potential to make the time- and resource demanding behavioral interventions widely and easily available, and at the same time make them easy to learn and self-administer for the patient [10]. This is also safe considering the limited number of adverse events, and the potential for complementing drug therapies [12]. Secondly it allows for point-of-care data collection [13], such as headache diaries and migraine trigger trackers, which may be used to enhance treatment, and accelerate research in the field. Thirdly, it may increase adherence by enabling medication monitoring, support and motivation [14]. And finally, the vast amount of the population that has access to smartphones, both in developed and developing countries; combined with the fact that mobile technology is popular, and almost integrated in the upcoming generations [15], means it will be available to most at need. The WHO surveys of eHealth and mHealth show that the spread of governmental initiatives is massive globally [4, 16]. The number of private and commercial initiatives is probably even larger. Despite these promises, problems remain: the great multitude of available eHealth and mHealth options makes it difficult for consumers to choose the proper, and the most personally relevant tool. The options are furthermore limited by the fact that most mHealth apps are not scientifically developed and validated [17-20].

eHealth and mHealth for migraine

eHealth

In a systematic review from 2016 Minen et. al. [21] investigated the use of electronic behavioral interventions for primary headache with a search updated to December 2015. The review described 23 studies. CBT was the most common therapy format, and Internet was the most common mean of delivery. Table 1 gives an overview of therapies and delivery strategies. Moderate to high rates of acceptability and feasibility were found, but efficacy data were limited. Sixteen of 23 studies had 30 or more participants, and six of these had statistically significant primary outcomes in favor of the electronic behavioral interventions compared to the controls, whereas the

others had no significant difference in primary outcome between intervention and control, or did not have a control group. Thus, it was not possible to conclude whether using electronic systems to deliver behavioral treatment for migraine was as effective as therapist-delivered strategies. Surprisingly, none of the therapies were delivered through mHealth technologies, and the authors concluded that there was a paucity in the literature, that definitely had potential and needed to be explored.

Table 1. Distribution of therapy strategies and delivery tools for electronic behavioral interventions for primary headache after Minen et. al. [21].

Behavioral therapy strategy	n
Cognitive behavioral therapy	11
Relaxation	8
Biofeedback	5
Other	3
Means of delivery	
Internet	14
CD ROMs	2
Personal digital assistants	2
Other	5

mHealth

Already in 2013, a systematic review found 247 mHealth papers and more than 3,673 apps related to the eight most prevalent health conditions as defined by WHO [22]. At the time, apps for migraine were the third most common health apps when searching the large global app stores, following diabetes and depression. On the other hand migraine apps were the least researched of the eight conditions. This implies that development of mHealth for migraine has a commercial and economic, rather than a scientific, incentive. In 2017 over 325,000 mHealth apps were available [23]. As an example, Google play store had a 50% increase in health apps since the previous year, while Apple AppStore had an increase of 20% [23]. Considering that, now in 2018, approximately 50% of the world's 3.4 billion smartphone and tablet users are estimated to have downloaded mHealth applications [24], it is crucial that mHealth actually works as desired.

Even though there is a lack of clinical trials of smartphone-based behavioral interventions in migraine [21], several other aspects of mHealth in headache treatment have been explored. A systematic review by Mosadeghi-Nik et. al. [25], with a search updated to May 2016, investigated available studies on mHealth for headache. At the

time, there were six papers investigating apps for headache treatment, whereof three included migraine sufferers exclusively. All of the six studies included headache diary elements as headache interventions, and none employed classical behavioral interventions, such as biofeedback and CBT. The authors conclude that there were no studies of high quality and robust design, studies were mainly proof of concept and feasibility studies, and that the evidence base on the effectiveness of mobile apps for treating headache is weak. Currently no systematic review specific for migraine exists.

The bulk of available mHealth in migraine includes headache diaries [25]. A systematic review from 2014 assessed the commercially available headache diary apps, and even though the report was published some years ago, it illustrates a trend [26]. None of the identified diaries fulfilled all the expert-opinion criteria for headache diaries; only 18% of the apps were created with scientific or clinical headache expertise; and none had gone through feasibility and psychometric testing. Consequently the authors of the review conducted a study to develop a headache diary app for adolescents and young adult migraine sufferers, while applying an iterative and incremental design to optimize the usability and psychometric properties of the diary [27]. The participants perceived the final version of the diary as useful, easy to learn, and efficient; and the authors concluded that such a diary had the potential to improve self-management of headaches.

mHealth diaries have also been used to monitor other means of migraine intervention. A 2016 study assessed adherence to preventive drug treatment and lifestyle recommendations in adolescent migraine sufferers by aid of electronic prospective self-monitoring [28]. This was compared to an objective measurement by electronic registration of number of times the pill bottle was opened. Adherence in the self-reporting app was lower than the objective measurement. The self-reporting of adherence to lifestyle recommendations was lower than desired, but the use of an app was regarded as potentially beneficial in increasing adherence and for providing new and better outcomes for children and adolescents with migraine. On the other hand, a South-Korean study from 2016 [29] evaluated the use of a smartphone headache diary app for detecting migraine trigger factors. The app encouraged the users to record potential triggers occurring on the same day as the migraine attack from a list of 18

triggers defined by the users themselves. The authors concluded that such a tool was effective for assessing potential migraine trigger factors, even though the study was not designed to establish causality [30]. At worst, triggers may be misidentified, which in turn could lead to unnecessary and unhelpful lifestyle changes. Still, mHealth has a potential in advancing the understanding of migraine biology with regards to trigger factors, i.e. by combining diary data with external variables such as weather reports [30], wearable technology documenting internal physiological data, and artificial intelligence [31].

Telemedicine

Regarding telemedicine, in a recent project researchers used a remote internet-based video-conference system to set non-acute headache diagnoses [32]. The telemedicine consultation was found to be acceptable, feasible and cost-saving compared to face-to-face traditional consultations with a neurologist. In a following non-inferiority study with over 400 participants they found the same one-time telemedicine consultation to be non-inferior to the traditional consultations for non-acute primary headaches, and it was estimated that over 20,000 telemedicine consultations is necessary to miss one secondary headache [33]. Using this study, as an example of how appropriate applied telemedicine may be acceptable and efficient, it is tempting to envision effective mass delivery of eHealth and mHealth behavioral therapy to the vast amount of migraine sufferers. However, this eased access to health care service comes with questions. Who is to decide to whom the services should be offered, and how should resources be prioritized?

How should new solutions be developed?

Several researchers propose means for assessing app quality and recommendations for mHealth development [11, 34-38]. From these, five domains may be extracted. New solutions should (1) apply proper usability and functionality designs with involvement of both healthcare professionals and end-users; (2) meet market and society demands; (3) adhere to guidelines, recommendations and regulations; (4) ensure accountability and availability; and (5) consider including concepts from big data and the Internet of Things. The lack of these factors is likely to play a role in the at times limited adherence, uncertain efficacy and low acceptability and credibility of mHealth [17-20].

Firstly, the importance of usability and functionality in development of both eHealth and mHealth should be emphasized. Recently, several studies have been conducted within other fields of health care that may be used as examples and inspiration for usability development of behavioral mHealth therapies in migraine [39-42]. One example is a study from 2016 in which the researchers used iterative usability testing to develop a biofeedback device and app for so called neurocardiac training [40]. This study exemplifies the process of developing both hardware and software while simultaneously identifying, addressing and improving themes related to usability. Several different iterative development designs exist, and if employed in conjunction with rigorous effectiveness assessments they enable a way to cost-efficiently establish the evidence needed to recommend new therapies [43]. In addition, several usability metrics, such as the classic Systems Usability Scale [44] and the newly developed Mobile App Rating Scale (MARS) [45] could provide useful when designing new programs. Implementation of such usability methodologies also helps ensure healthcare professional and end-user involvement and should be applied and emphasized when conducting studies.

Secondly, in order for any eHealth or mHealth intervention to be successful there has to be a need and a wish from the target population to use it [36, 38]. Methods for recruitment and usage need to be developed towards the intended market and society. The “Cloudy with a Chance of Pain” study from 2017 [46], demonstrated the ability of mHealth apps to rapidly and successfully recruit a large representative, and engaged sample. It provided evidence that smartphones could be a feasible alternative to traditional data collection methods. This study still had a problem of attrition, and only one in seven users were considered frequent users. Another example is a Parkinson disease study [47], which used the Apple ResearchKit [48], an open source framework streamlining the remote consent process to successfully recruit participants. Sample sizes in mHealth studies needs to be scaled up [18, 21, 22], and these new innovative recruitment strategies may enable this. Given the new methods for recruitment and the simple availability of mHealth, the definition of adherence in mHealth should also be revised [49]. It may be fruitful to justify a threshold of usage, set in relation to the desired outcome goal and target population, to define adherence, instead of simply measuring number of downloads or uses [49].

Thirdly, developers should be aware that incorrect designs might in worst-case lead to worsening of the very medical condition the program was intended to improve [50-52]. Therefore, medical evidence must be adhered to when developing new mHealth programs. A systematic review from 2015 found that several medical apps had very limited expert involvement and grounding in medical evidence [52]. The review furthermore discussed several “peer-review” strategies for medical apps that could be applied to overcome these challenges, including web pages [53] and tools such as the Health Apps Library developed by the National Health Service in the United Kingdom [54]. However, such strategies may not undoubtedly secure app quality. In addition to medical evidence, regulatory considerations, such as from the Mobile Medical Applications Guidance for Industry and Food and Drug Administration Staff [51], should be adhered to. Developers should take care to consider the legal framework in the intended area of use [55]. All the while, guidelines and checklists, such as the CONSORT-EHEALTH [37] should be appraised when conducting electronic and mobile health intervention studies.

Fourthly, the aforementioned domains all play part in the accountability and availability of eHealth and mHealth. Proper development designs, healthcare professional involvement and adherence to regulations and recommendations secure accountability; and availability could be improved through medical validation [56], and recruitment and usage within the intended market and society. A review published in 2017 [57] highlighted the importance of having website availability of the mHealth interventions. Only one fifth of apps (57/268, 21%) had functional websites. It is likely that sufficient information and accessibility is a necessity for use of minimal contact therapies, which may help achieve the desired adherence and thereby effectiveness. In addition, strategies such as deploying a set of apps, one for migraine patients and one for the treating neurologists [58], may facilitate communication between the patient and the doctor and thereby increase accountability and availability.

Finally, big data and the Internet of Things (IoT) should be mentioned. The former defines the collection and analysis of large amounts of data to reveal patterns, trends and associations [59]; and the latter encompasses the interconnection of everyday objects by embedded computing devices [60]. The general elements required for

health IoT systems include body area sensor networks, internet-connected smart gateways, and cloud and big data support [61]. In particular the popularity of wearable devices has significantly increased the recent years [62]. Wearables as a means to correlate disease mechanisms and migraine may be very useful [63]. As an example, one research group is working with reduction of computational burden and sensor energy optimization within a wireless body sensor network developed to predict migraine headaches [31]. Such development certainly seems to be a part of future migraine treatment. Another interesting approach to big data is highlighted in a recent Twitter-infodemiology study. In this study 14,028 tweets of real-time sharing of migraine suffering were found during the course of seven days. These studies highlight that big data and IoT have potential for, recruitment, data collection, and intervention for a wide range of diseases, including migraines [64].

So what do migraine sufferers want? Among other things, they want interventions that are easily accessible, freedom of pain and freedom of adverse events [65]. They also want wearables that can be used to detect premonitory symptoms to avoid or reduce the burden of attacks [66]. eHealth and mHealth has the potential to provide this for migraine sufferers.

Conclusion

eHealth and mHealth for behavioral treatments of migraine has been a promising field for long. Electronic behavioral interventions for migraine seem to be acceptable and feasible, but efficacy measures are uncertain. Still, clinical trials on mHealth-based classical behavioral therapies such as CBT, biofeedback and relaxation are missing in the literature. Some aspects of mHealth in migraine have been explored, but there is a gap between commercially available apps and scientifically validated and developed apps. Migraine researchers should draw inspiration from other fields when developing new eHealth and mHealth solutions. Application of proper usability and functionality designs towards the right market, together with appraisal of medical and technological recommendations, may facilitate rapid development of eHealth and mHealth while also establishing scientific evidence.

Annotated articles

[21] •• This systematic review thoroughly describes the available evidence of electronic behavioral interventions for migraine.

[33] • This randomized controlled trial describes the efficient use of an acceptable, feasible and cost-saving telemedicine consultation for headache sufferers.

[31] • This engineering oriented paper describes a very exciting research field in which migraine prediction based on sensor technology could be achieved.

References

1. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. *Cephalalgia*. 2018;38(1):1-211. doi:10.1177/0333102417738202.
2. Vos T, Allen C, Arora M, Barber RM, Bhutta ZA, Brown A et al. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *The Lancet*. 2016;388(10053):1545-602.
3. Stovner L, Hagen K, Jensen R, Katsarava Z, Lipton R, Scher A et al. The global burden of headache: a documentation of headache prevalence and disability worldwide. *Cephalalgia*. 2007;27(3):193-210. doi:10.1111/j.1468-2982.2007.01288.x.
4. Kay M, Santos J, Takane M. mHealth: New horizons for health through mobile technologies. *World Health Organization*. 2011;3:66-71.
5. Nestoriuc Y, Martin A. Efficacy of biofeedback for migraine: a meta-analysis. *Pain*. 2007;128(1-2):111-27. doi:10.1016/j.pain.2006.09.007.
6. Stubberud A, Varkey E, McCrory DC, Pedersen SA, Linde M. Biofeedback as Prophylaxis for Pediatric Migraine: A Meta-analysis. *Pediatrics*. 2016;138(2). doi:10.1542/peds.2016-0675.
7. Penzien DB, Irby MB, Smitherman TA, Rains JC, Houle TT. Well-Established and Empirically Supported Behavioral Treatments for Migraine. *Current pain and headache reports*. 2015;19(7):34. doi:10.1007/s11916-015-0500-5.
8. Luxton DD, McCann RA, Bush NE, Mishkind MC, Reger GM. mHealth for mental health: Integrating smartphone technology in behavioral healthcare. *Professional Psychology: Research and Practice*. 2011;42(6):505. doi:10.1037/a0024485.
9. Zhu Q, Liu C, Holroyd KA, editors. From a traditional behavioral management program to an m-health app: Lessons learned in developing m-health apps for existing health care programs. *Software Engineering in Health Care (SEHC), 2012 4th International Workshop on; 2012: IEEE*.
10. Andrasik F. Behavioral treatment of headaches: extending the reach. *Neurol Sci*. 2012;33 Suppl 1:S127-30. doi:10.1007/s10072-012-1073-2.
11. Labrique AB, Vasudevan L, Kochi E, Fabricant R, Mehl G. mHealth innovations as health system strengthening tools: 12 common applications and a visual framework. *Global health: science and practice*. 2013;1(2):160-71.
12. Harris P, Loveman E, Clegg A, Easton S, Berry N. Systematic review of cognitive behavioural therapy for the management of headaches and migraines in adults. *British journal of pain*. 2015;9(4):213-24.
13. Tomlinson M, Solomon W, Singh Y, Doherty T, Chopra M, Ijumba P et al. The use of mobile phones as a data collection tool: a report from a household survey in South Africa. *BMC Med Inform Decis Mak*. 2009;9(1):51.
14. Ebner H, Schreier G. Medication Adherence and Monitoring. *Developing Drug Products in an Aging Society*. Springer; 2016. p. 659-74.
15. Lenhart A, Madden M, Duggan M, Cortesi S, Gasser U. *Teens and Technology 2013*. Pew Internet & American Life Project and Harvard's Berkman. 2013.
16. WHO. *Atlas of eHealth Country Profiles 2015: The use of eHealth in support of universal health coverage*. 2015 http://www.who.int/goe/publications/atlas_2015/en/ Accessed 4 Mar 2017.
17. de la Vega R, Miró J. mHealth: a strategic field without a solid scientific soul. a systematic review of pain-related apps. *PLoS One*. 2014;9(7):e101312.

18. Lalloo C, Jibb LA, Rivera J, Agarwal A, Stinson JN. "There's a pain app for that": Review of patient-targeted smartphone applications for pain management. *The Clinical journal of pain*. 2015;31(6):557-63.
19. Huckvale K, Morrison C, Ouyang J, Ghaghda A, Car J. The evolution of mobile apps for asthma: an updated systematic assessment of content and tools. *BMC Med*. 2015;13(1):58.
20. Neubeck L, Lowres N, Benjamin EJ, Freedman SB, Coorey G, Redfern J. The mobile revolution—using smartphone apps to prevent cardiovascular disease. *Nature Reviews Cardiology*. 2015;12(6):350.
21. Minen MT, Torous J, Raynowska J, Piazza A, Grudzen C, Powers S et al. Electronic behavioral interventions for headache: a systematic review. *J Headache Pain*. 2016;17:51. doi:10.1186/s10194-016-0608-y.
22. Martinez-Perez B, de la Torre-Diez I, Lopez-Coronado M. Mobile health applications for the most prevalent conditions by the World Health Organization: review and analysis. *J Med Internet Res*. 2013;15(6):e120. doi:10.2196/jmir.2600.
23. Research2Guidance. 325,000 mobile health apps available in 2017 – Android now the leading mHealth platform. 2017. <https://research2guidance.com/325000-mobile-health-apps-available-in-2017/>. Accessed Feb 27 2018.
24. Administration USFaD. Mobile Medical Applications. 2018. <https://www.fda.gov/MedicalDevices/DigitalHealth/MobileMedicalApplications/default.htm>. Accessed 22 Feb 2018.
25. Mosadeghi-Nik M, Askari MS, Fatehi F. Mobile health (mHealth) for headache disorders: A review of the evidence base. *J Telemed Telecare*. 2016;22(8):472-7.
26. Hundert AS, Huguet A, McGrath PJ, Stinson JN, Wheaton M. Commercially available mobile phone headache diary apps: a systematic review. *JMIR mHealth and uHealth*. 2014;2(3):e36. doi:10.2196/mhealth.3452.
27. Huguet A, McGrath PJ, Wheaton M, Mackinnon SP, Rozario S, Tougas ME et al. Testing the Feasibility and Psychometric Properties of a Mobile Diary (myWHI) in Adolescents and Young Adults With Headaches. *JMIR mHealth and uHealth*. 2015;3(2):e39. doi:10.2196/mhealth.3879.
28. Kroon Van Diest AM, Ramsey R, Aylward B, Kroner JW, Sullivan SM, Nause K et al. Adherence to Biobehavioral Recommendations in Pediatric Migraine as Measured by Electronic Monitoring: The Adherence in Migraine (AIM) Study. *Headache*. 2016;56(7):1137-46. doi:10.1111/head.12836.
29. Park J-W, Chu MK, Kim J-M, Park S-G, Cho S-J. Analysis of trigger factors in episodic migraineurs using a smartphone headache diary applications. *PLoS One*. 2016;11(2):e0149577.
30. Lipton RB, Pavlovic JM, Haut SR, Grosberg BM, Buse DC. Methodological issues in studying trigger factors and premonitory features of migraine. *Headache: The Journal of Head and Face Pain*. 2014;54(10):1661-9.
31. Pagán J, Zapater M, Ayala JL. Power transmission and workload balancing policies in eHealth mobile cloud computing scenarios. *Future Generation Computer Systems*. 2018;78:587-601.
32. Müller KI, Alstadhaug KB, Bekkelund SI. Acceptability, feasibility, and cost of telemedicine for nonacute headaches: a randomized study comparing video and traditional consultations. *J Med Internet Res*. 2016;18(5).
33. Müller KI, Alstadhaug KB, Bekkelund SI. A randomized trial of telemedicine efficacy and safety for nonacute headaches. *Neurology*. 2017;89(2):153-62.
34. BinDhim NF, Hawkey A, Trevena L. A systematic review of quality assessment methods for smartphone health apps. *Telemedicine and e-Health*. 2015;21(2):97-104.

35. McKay FH, Cheng C, Wright A, Shill J, Stephens H, Uccellini M. Evaluating mobile phone applications for health behaviour change: A systematic review. *J Telemed Telecare*. 2016;1357633X16673538.
36. Grundy QH, Wang Z, Bero LA. Challenges in assessing mobile health app quality: a systematic review of prevalent and innovative methods. *Am J Prev Med*. 2016;51(6):1051-9.
37. Eysenbach G, Group C-E. CONSORT-EHEALTH: improving and standardizing evaluation reports of Web-based and mobile health interventions. *J Med Internet Res*. 2011;13(4).
38. Chatzipavlou IA, Christoforidou SA, Vlachopoulou M. A recommended guideline for the development of mHealth Apps. *mHealth*. 2016;2(5).
39. Jibb LA, Cafazzo JA, Nathan PC, Seto E, Stevens BJ, Nguyen C et al. Development of a mHealth Real-Time Pain Self-Management App for Adolescents With Cancer: An Iterative Usability Testing Study. *J Pediatr Oncol Nurs*. 2017;1043454217697022.
40. Uddin AA, Morita PP, Tallevi K, Armour K, Li J, Nolan RP et al. Development of a Wearable Cardiac Monitoring System for Behavioral Neurocardiac Training: A Usability Study. *JMIR mHealth and uHealth*. 2016;4(2):e45. doi:10.2196/mhealth.5288.
41. Stinson JN, Lalloo C, Harris L, Isaac L, Campbell F, Brown S et al. iCanCope with Pain™: user-centred design of a web-and mobile-based self-management program for youth with chronic pain based on identified health care needs. *Pain Research and Management*. 2014;19(5):257-65.
42. Cafazzo JA, Casselman M, Hamming N, Katzman DK, Palmert MR. Design of an mHealth app for the self-management of adolescent type 1 diabetes: a pilot study. *J Med Internet Res*. 2012;14(3):e70.
43. Jacobs MA, Graham AL. Iterative development and evaluation methods of mHealth behavior change interventions. *Current Opinion in Psychology*. 2016;9:33-7.
44. Zapata BC, Fernández-Alemán JL, Idri A, Toval A. Empirical Studies on Usability of mHealth Apps: A Systematic Literature Review. *J Med Syst*. 2015;39(2):1. doi:10.1007/s10916-014-0182-2.
45. Stoyanov SR, Hides L, Kavanagh DJ, Zelenko O, Tjondronegoro D, Mani M. Mobile app rating scale: a new tool for assessing the quality of health mobile apps. *JMIR mHealth and uHealth*. 2015;3(1):e27.
46. Druce KL, McBeth J, van der Veer SN, Selby DA, Vidgen B, Georgatzis K et al. Recruitment and Ongoing Engagement in a UK Smartphone Study Examining the Association Between Weather and Pain: Cohort Study. *JMIR mHealth and uHealth*. 2017;5(11).
47. Bot BM, Suver C, Neto EC, Kellen M, Klein A, Bare C et al. The mPower study, Parkinson disease mobile data collected using ResearchKit. *Scientific data*. 2016;3:160011.
48. Apple. ResearchKit. 2018. <http://researchkit.org>. Accessed 5 Mar 2018.
49. Sieverink F, Kelders SM, van Gemert-Pijnen JE. Clarifying the Concept of Adherence to eHealth Technology: Systematic Review on When Usage Becomes Adherence. *J Med Internet Res*. 2017;19(12):e402. doi:10.2196/jmir.8578.
50. Misra S, Lewis TL, Aungst TD. Medical application use and the need for further research and assessment for clinical practice: creation and integration of standards for best practice to alleviate poor application design. *JAMA dermatology*. 2013;149(6):661-2.

51. Yetisen AK, Martinez-Hurtado J, da Cruz Vasconcellos F, Simsekler ME, Akram MS, Lowe CR. The regulation of mobile medical applications. *Lab on a Chip*. 2014;14(5):833-40.
52. Subhi Y, Bube SH, Rolskov Bojsen S, Skou Thomsen AS, Konge L. Expert Involvement and Adherence to Medical Evidence in Medical Mobile Phone Apps: A Systematic Review. *JMIR mHealth and uHealth*. 2015;3(3):e79. doi:10.2196/mhealth.4169.
53. Husain I, Misra S. *iMedicalApps*. 2018. <https://www.imedicalapps.com>. Accessed 1 Apr 2018.
54. Service NH. *The Health Apps Library*. London, UK. 2018. <https://www.nhs.uk/pages/home.aspx>. Accessed 22 Mar 2018.
55. Charani E, Castro-Sánchez E, Moore LS, Holmes A. Do smartphone applications in healthcare require a governance and legal framework? It depends on the application! *BMC Med*. 2014;12(1):29.
56. Stubberud A, Omland PM, Tronvik E, Olsen A, Sand T, Linde M. Wireless Surface Electromyography and Skin Temperature Sensors for Biofeedback Treatment of Headache: Validation Study with Stationary Control Equipment. *JMIR Biomedical Engineering*. 2018;3(1):e1.
57. Rogers MA, Lemmen K, Kramer R, Mann J, Chopra V. Internet-delivered health interventions that work: systematic review of meta-analyses and evaluation of website availability. *J Med Internet Res*. 2017;19(3).
58. Guerrero Peral A, Ruiz Pinero M, Miralles J, editors. " MyMigraines" community: improving communication between migraine patient and neurologist. *EUROPEAN JOURNAL OF NEUROLOGY*; 2015: WILEY-BLACKWELL 111 RIVER ST, HOBOKEN 07030-5774, NJ USA.
59. Bates DW, Saria S, Ohno-Machado L, Shah A, Escobar G. Big data in health care: using analytics to identify and manage high-risk and high-cost patients. *Health Aff (Millwood)*. 2014;33(7):1123-31.
60. Islam SR, Kwak D, Kabir MH, Hossain M, Kwak K-S. The internet of things for health care: a comprehensive survey. *IEEE Access*. 2015;3:678-708.
61. Farahani B, Firouzi F, Chang V, Badaroglu M, Constant N, Mankodiya K. Towards fog-driven IoT eHealth: Promises and challenges of IoT in medicine and healthcare. *Future Generation Computer Systems*. 2018;78:659-76.
62. Firouzi F, Rahmani AM, Mankodiya K, Badaroglu M, Merrett G, Wong P et al. Internet-of-Things and big data for smarter healthcare: From device to architecture, applications and analytics. Elsevier; 2018.
63. Buse DC, Lipton RB. Primary headache: What's stress got to do with it? *Cephalalgia*. 2015;35(10):844-9. doi:10.1177/0333102414567382.
64. Nascimento TD, DosSantos MF, Danciu T, DeBoer M, van Holsbeeck H, Lucas SR et al. Real-time sharing and expression of migraine headache suffering on Twitter: a cross-sectional infodemiology study. *J Med Internet Res*. 2014;16(4).
65. Lantéri-Minet M. What do patients want from their acute migraine therapy? *Eur Neurol*. 2005;53(Suppl. 1):3-9.
66. Huttunen H-L, Halonen R, Koskimäki H. *Wishes For Wearables From Patients With Migraine*. 2017.