Digital remote monitoring in adult congenital heart disease patients
Lessons learned and recommendations

Koole, M.A.C.

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DIGITAL REMOTE MONITORING IN ADULT CONGENITAL HEART DISEASE PATIENTS: LESSONS LEARNED AND RECOMMENDATIONS

Maarten Koole

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Thesis, University of Amsterdam

Digital remote monitoring in
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ACADEMISCH PROEFSCHRIFT

ter verkrijging van de graad van doctor
aan de Universiteit van Amsterdam
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in het openbaar te verdedigen in de Agnietenkapel
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door Maarten Antonius Cornelis Koole
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PROMOTIECOMMISSIE

Promotor:	prof. dr. B.J.M. Mulder	AMC-UvA
Copromotores:	dr. B.J. Bouma	AMC-UvA
	dr. M.J. Schuuring	AMC-UvA
Overige leden:	prof. dr. N.A. Blom	AMC-UvA
	prof. dr. J.R. de Groot	AMC-UvA
	prof. dr. M.G.W. Dijkgraaf	AMC-UvA
	dr. L. Hofstra	Cardiologie Centra Nederland
	prof. dr. N.H. Chavannes	Universiteit Leiden
	prof. dr. P. van der Harst	Universiteit Utrecht

Faculteit der Geneeskunde

"Medicine is a science of uncertainty and an art of probability"

Sir William Osler (1849–1919), Canadian Physician

Voor mijn ouders, Lilian, Djuna, Tijn, Lieve en Vos

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Chapter 1

General introduction and thesis outline

INTRODUCTION

The mobile internet revolution

In the traditional health setting patients had to visit clinicians for diagnosis and treatment of their diseases. Nowadays, we see a shift from outpatient visits to online health care, accelerated by the recent COVID-19 pandemic [1]. This is made possible by tremendous development of technological innovations becoming available last decades. Internet has become an easily accessible source of knowledge and communication for almost everyone. Apps on mobile smartphones connected to home monitoring devices for measuring health parameters made it possible to monitor the health status of the owner continuously [2]. The internet and wide-spread availability of these mobile apps can facilitate self-empowerment of patients by education, and thereby supporting shared decision making with their clinicians about their health issues [3,4]. Hereby improving therapy compliance leading to better outcomes [5]. Not only these innovations has an effect on our health status but also have the potential to reduce health care costs by minimizing the frequency of clinic visits and reducing the travel costs for patient and their accompanying relatives. The potential of digital health care in an era of increasing health care costs resulted in stimulating clinicians by the stakeholders to implement these innovative new digital technologies as soon as possible in their work process [6,7].

Remote patient monitoring in cardiology

Before the mobile internet revolution clinicians get an insight into blood pressure and heart rhythm of a selected patient over a longer period of time in their daily live by equipping this patient with an ambulant 24 hour blood pressure or Holter monitoring device. The patients has to visit the clinic to pick up the measuring device and return the device the other day. After the returning of the device the obtained data could be analyzed and a new appointment with the patient was made to discuss the results. Nowadays, it is also possible to connect patient's wearables and biosensors for measuring vital parameters as weight, blood pressure, physical activity and heart rhythm online with their digital electronical health record. Sharing of these data enables health care providers to online optimizing health care management of these patients [8].

In 2013 Margolis et al concluded, as a result of their randomized clinical trial, that home blood pressure remote patient monitoring (RPM) and pharmacist case management achieved better blood pressure control compared with usual care during 12 months of intervention that persisted during 6 months of post intervention follow-up [9].

The REHEARSE-AF Study was published in 2017 which showed that screening with twice-weekly single-lead iECG with remote interpretation in ambulatory patients ≥65 years of age at increased risk of stroke is significantly more likely to identify incident atrial fibrillation than routine care over a 12-month period. This approach is also highly acceptable to this group of patients and supporting further evaluation in an appropriately powered, event-driven clinical trial [10].

Results on RPM in treatment of acquired heart failure (HF) patients are becoming less conflicting. A large study, published in 2010, in the NEJM showed failure of a RPM strategy to improve outcomes over usual care in patients recently hospitalized for HF [11]. The TIM-HF2 trial suggested in 2018 that a structured RPM intervention, when used in a well-defined HF population, could reduce the percentage of days lost due to unplanned cardiovascular hospital admissions and all-cause mortality [12]. In 2023, a meta-analysis for RPM for HF showed that the use of RPM compared to standard care reduced all-cause mortality by 16%, first HF hospitalizations by 19%, and total HF hospitalizations by 15% [13]. The methods of RPM are diverse in this meta-analysis which limits the ability of clinicians to make general conclusions.

Although RPM offers an innovative approach to improve HF care that expands beyond traditional management strategies, the use of RPM in HF is infrequent. This is because of several obstacles: mixed evidence, logistical challenges to broad-scale implementation because of an inadequate understanding of how to translate RPM into practice efficiently, and difficulties in funding of the appropriate infrastructure out of existing resources, so, often a new different payment structure is needed [7,14,15].

In 2014 a Dutch steering committee consisting of hospital directors; cardiologists, nurses specialized in heart failure, heart failure patients, home care organizations, health insurance companies, an independent research agency and renowned supplier of health care technology concluded in a report that if RPM was fully integrated in health care in the Netherlands this will reduce hospital admissions for acute heart failure. Moreover, if half of the Dutch heart failure patients are participating in RPM it could save the community annual 82 million euro [16].

Clinicians could be reluctant to use telemonitoring because of fear of data overload and liability issues. Possibility of data leakages and privacy issues are to be addressed. Devices have to be certified. Last but not least, if the data generated by these new devices will lead to better outcome for patients in terms of mortality, morbidity and quality of life at acceptable health care costs has to be validated [4,7,15].

HartWacht

In 2016 Cardiologie Centra Nederland introduced the HartWacht program: an innovative RPM program for detecting arrhythmia, monitoring blood pressure at home for optimizing hypertension treatment and as part of care for patients with acquired heart failure. The program is innovative in organizational and technical aspects because of integration with the electronic patient record, secure data connections protecting privacy data, and involvement of physicians from the beginning of the project. Incoming data are, after selection by computer algorithms, evaluated by specialized nurses at a dedicated data center. HartWacht has reimbursement by almost all Dutch insurance companies. Moreover, from a user perspective there is a user-friendly interface on smartphone which is available for multiple operating systems [17,18].

Adult Congenital Heart Disease patients

Congenital heart disease (CHD) is one of the most common birth defects [19-21]. During the past decades, the life expectancy of children born with a CHD has increased dramatically. At present, 95% of children with CHD reach adulthood [19]. However, many of the adults with congenital heart disease patients (ACHD) are chronically affected by residual sequelae leading to unpredictable arrhythmias, heart failure and a reduced quality of life [22-26]. In general, ACHD patients have a high utilization of emergency resources; with emergency care utilization increasing as age progresses [22]. As the population of ACHD patients is increasing in number and age, total emergency care utilization of this population is expected to increase [27].

Patients with ACHD are particularly attractive for RPM because of their relatively young age, affinity with mobile devices, chronic condition necessitating lifelong surveillance, and the high burden of disease [28]. ACHD patients commonly experience fears and insecurities [29] and RPM might reduce emergency visits for reassurance or hospital admissions.

THESIS OUTLINE

Implementing RPM in routine care for ACHD patients as a specific new technology needs proof of concept to become part of evidence-based medicine. The aim of the studies in this thesis is to contribute to this proof of concept.

However, funding for a new research project could be a challenge. In **Chapter 2** we performed a study to investigate if crowdfunding by using social media can contribute to the funding of a clinical research project.

To understand which ACHD patients have high emergency care utilization and are willing to use remote monitoring we retrospectively approached ACHD patients who visited the emergency care three or more times in 5 year with a questionnaire. Results can be found in **Chapter 3**. After we identified these patients we enrolled them in the HartWacht program to evaluate RPM. Our first experiences are described in **Chapter 4**. Results of their participation are shared in **Chapter 5**, and illustrated by a case report in **Chapter 6**.

In **Chapter 7** we compared Implantable Loop Recorder (ILR) and smartphone based single-lead electrocardiogram for heart rhythm monitoring in ACHD patients. **Chapter 8** reviews the value of extended arrhythmia monitoring in ACHD patients as found in recent scientific literature.

Finally, RPM as a part of management of ACHD patients and future directions are discussed in **chapter 9.** The thesis is summarized in **chapter 10**.

REFERENCES

1. Mann DM, Chen J, Chunara R, Testa PA, Nov O. COVID-19 transforms health care through telemedicine: Evidence from the field. *Journal of the American Medical Informatics Association*. 2020;27:1132–1135.

2. Kauw D, Koole MAC, Winter MM, Dohmen DAJ, Tulevski II, Blok S, Somsen GA, Schijven MP, Vriend JWJ, Robbers-Visser D, Mulder BJM, Bouma BJ, Schuuring MJ. Advantages of mobile health in the management of adult patients with congenital heart disease. *International Journal of Medical Informatics*. 2019;132:104011.

3. The digital revolution and patient self-empowerment. *Patient Education and Counseling*. 1993;20:1–3.

4. Massoomi MR, Handberg EM. Increasing and Evolving Role of Smart Devices in Modern Medicine. *Eur Cardiol. Review* 2019;14:181–186.

5. Johnston N, Bodegard J, Jerström S, Åkesson J, Brorsson H, Alfredsson J, Albertsson PA, Karlsson J-E, Varenhorst C. Effects of interactive patient smartphone support app on drug adherence and lifestyle changes in myocardial infarction patients: A randomized study. *American Heart Journal*. 2016;178:85–94.

6. Gerrits O. The future of healthcare has arrived: who dares take up the challenge? *Neth Heart J*. 2019;27:3–4.

7. Fraiche AM, Eapen ZJ, McClellan MB. Moving Beyond the Walls of the Clinic. *JACC: Heart Failure*. 2017;5:297–304.

8. Vegesna A, Tran M, Angelaccio M, Arcona S. Remote Patient Monitoring via Non-Invasive Digital Technologies: A Systematic Review. *Telemedicine and e-Health*. 2017;23:3–17.

9. Margolis KL, Asche SE, Bergdall AR, Dehmer SP, Groen SE, Kadrmas HM, Kerby TJ, Klotzle KJ, Maciosek MV, Michels RD, O'Connor PJ, Pritchard RA, Sekenski JL, Sperl-Hillen JM, Trower NK. Effect of Home Blood Pressure Telemonitoring and Pharmacist Management on Blood Pressure Control: A Cluster Randomized Clinical Trial. *JAMA*. 2013;310:46.

10. Halcox JPJ, Wareham K, Cardew A, Gilmore M, Barry JP, Phillips C, Gravenor MB. Assessment of Remote Heart Rhythm Sampling Using the AliveCor Heart Monitor to Screen for Atrial Fibrillation: The REHEARSE-AF Study. *Circulation*. 2017;136:1784–1794.

11. Chaudhry SI, Mattera JA, Curtis JP, Spertus JA, Herrin J, Lin Z, Phillips CO, Hodshon BV, Cooper LS, Krumholz HM. Telemonitoring in Patients with Heart Failure. *N Engl J Med*. 2010;363:2301–2309.

12. Koehler F, Koehler K, Deckwart O, Prescher S, Wegscheider K, Kirwan B-A, Winkler S, Vettorazzi E, Bruch L, Oeff M, Zugck C, Doerr G, Naegele H, Störk S, Butter C, Sechtem U, Angermann C, Gola G, Prondzinsky R, Edelmann F, Spethmann S, Schellong SM, Schulze PC, Bauersachs J, Wellge B, Schoebel C, Tajsic M, Dreger H, Anker SD, Stangl K. Efficacy of telemedical interventional management in patients with heart failure (TIM-HF2): a randomised, controlled, parallel-group, unmasked trial. *The Lancet*. 2018;392:1047–1057.

13. Scholte NTB, Gürgöze MT, Aydin D, Theuns DAMJ, Manintveld OC, Ronner E, Boersma E, De Boer RA, Van Der Boon RMA, Brugts JJ. Telemonitoring for heart failure: a meta-analysis. *European Heart Journal*. 2023;44:2911–2926.

14. Farnia T, Jaulent M-C, Steichen O. Evaluation Criteria of Noninvasive Telemonitoring for Patients With Heart Failure: Systematic Review. *J Med Internet Res*. 2018;20:e16.

15. Tuckson RV, Edmunds M, Hodgkins ML. Telehealth. *N Engl J Med*. 2017;377:1585–1592.

16. Het pad naar duurzame hartfalenzorg: Een praktijkonderzoek naar optimalisatie van het zorgpad chronisch hartfalen met de inzet van telemonitoring. *Effective cardio*. 2014.

17. Selder JL, Breukel L, Blok S, van Rossum AC, Tulevski II, Allaart CP. A mobile one-lead ECG device incorporated in a symptom-driven remote arrhythmia monitoring program. The first 5,982 Hartwacht ECGs. *Neth Heart J*. 2019;27:38–45.

18. Wierda E, Blok S, Somsen GA, Van Der Velde ET, Tulevski II, Stavrov B, De Wildt MCC, Van Den Born BJH, Breukel L, De Mol BAJM, Ploem MC, Winter MM. Protecting patient privacy in digital health technology: the Dutch m-Health infrastructure of Hartwacht as a learning case. *BMJ Innov*. 2020;6:170–176.

19. Tennant PW, Pearce MS, Bythell M, Rankin J. 20-year survival of children born with congenital anomalies: a population-based study. *The Lancet*. 2010;375:649–656.

20. Canfield MA, Honein MA, Yuskiv N, Xing J, Mai CT, Collins JS, Devine O, Petrini J, Ramadhani TA, Hobbs CA, Kirby RS. National estimates and race/ethnic-specific variation of selected birth defects in the United States, 1999–2001. *Birth Defects Research*. 2006;76:747–756.

21. Bird TM, Hobbs CA, Cleves MA, Tilford JM, Robbins JM. National rates of birth defects among hospitalized newborns. *Birth Defects Research*. 2006;76:762–769.

22. Baumgartner H, Bonhoeffer P, De Groot NMS, de Haan F, Deanfield JE, Galie N, Gatzoulis MA, Gohlke-Baerwolf C, Kaemmerer H, Kilner P, Meijboom F, Mulder BJM, Oechslin E, Oliver JM, Serraf A, Szatmari A, Thaulow E, Vouhe PR, Walma E, Task Force on the Management of Grown-up Congenital Heart Disease of the European Society of Cardiology (ESC), Association for European Paediatric Cardiology (AEPC), ESC Committee for Practice Guidelines (CPG). ESC Guidelines for the management of grown-up congenital heart disease (new version 2010). *Eur Heart J*. 2010;31:2915–2957.

23. Koyak Z, Kroon B, de Groot JR, Wagenaar LJ, van Dijk AP, Mulder BA, Van Gelder IC, Post MC, Mulder BJM, Bouma BJ. Efficacy of antiarrhythmic drugs in adults with congenital heart disease and supraventricular tachycardias. *Am J Cardiol*. 2013;112:1461–1467.

24. Schuuring M, van Gulik C, Koolbergen D, Hazekamp M, Lagrand W, Backx A, Mulder B, Bouma B. Determinants of clinical right ventricular failure after congenital cardiac surgery in adults. *Journal of Cardiothoracic and Vascular Anesthesia*. 2013.

25. Zomer AC, Vaartjes I, van der Velde ET, de Jong HMY, Konings TC, Wagenaar LJ, Heesen WF, Eerens F, Baur LHB, Grobbee DE, Mulder BJM. Heart failure admissions in adults with congenital heart disease; risk factors and prognosis. *International Journal of Cardiology*. 2013;168:2487–2493.

26. Schuuring MJ, van Riel ACMJ, Vis JC, Duffels MG, van Dijk APJ, de Bruin-Bon RHACM, Zwinderman AH, Mulder BJM, Bouma BJ. New predictors of mortality in adults with congenital heart disease and pulmonary hypertension: Midterm outcome of a prospective study. *International Journal of Cardiology*. 2015;181:270–276.

27. Tutarel O, Kempny A, Alonso-Gonzalez R, Jabbour R, Li W, Uebing A, Dimopoulos K, Swan L, Gatzoulis MA, Diller G-P. Congenital heart disease beyond the age of 60: emergence of a new population with high resource utilization, high morbidity, and high mortality. *European Heart Journal*. 2014;35:725–732.

1

28. Schuuring MJ, Backx AP, Zwart R, Veelenturf AH, Robbers-Visser D, Groenink M, Abu-Hanna A, Bruining N, Schijven MP, Mulder BJ, Bouma BJ. Mobile health in adults with congenital heart disease: current use and future needs. *Neth Heart J*. 2016;24:647–652.

29. Schoormans D, Sprangers MA, van Melle JP, Pieper PG, van Dijk AP, Sieswerda GT, Hulsbergen-Zwarts MS, Plokker TH, Brunninkhuis LG, Vliegen HW, Mulder BJ. Clinical and psychological characteristics predict future healthcare use in adults with congenital heart disease. *European Journal of Cardiovascular Nursing*. 2016;15:72–81.

Chapter 2

A successful crowdfunding project for eHealth research on grown-up congenital heart disease patients

M.A.C. Koole, D. Kauw, M.M. Winter, M.J. Schuuring

ABSTRACT

Background

Scarce data on crowdfunding report a maximal funding of €10.000,-, and state that research is needed to attract attention of larger granting organizations. The aims of this project were 1) to fund an eHealth study in grown-up congenital heart disease (GUCH) patients 2) to contemplate on critical success factors.

Methods

After peer review of the Dutch Heart Foundation a project was published at a donation platform, which was open for donations during a predetermined period of two months. Copywriters were hired to create an easy-to-understand message to donors. A video teaser was created with a motivated patient, and rewards were available. The crowdfunding targeted €25.000 and the Dutch Heart Foundation doubled the donations to €50.000, and return of donations were guaranteed in case this was not met.

Results

Initially, donations came from the investigators' private inner circle. In total, 44 potential donors were contacted, but refused to donate originally. Multiple (social) media campaigns were published to promote the project, and an offline mailing was sent to contributors to the Dutch Heart Foundation. During the project support emerged, resulting in extra donations and public awareness. In the lasts three weeks, after sufficient private donations, five major donors decided to support the project. The project became a big success: the predetermined target was exceeded and a total of €74.450,- was raised.

Conclusion

Innovative crowdfunding gave the opportunity to start eHealth research in GUCH patients. Critical success factors include support of a professional organization, support of stakeholders, and easy-to-understand messages.

1 INTRODUCTION

Many grown up congenital heart disease (GUCH) patient are lifelong affected by cardiac events, particularly arrhythmias and heart failure [1-5]. Despite lifelong surveillance these patients often deteriorate, which we often notice too late, leading to emergency care presentations, hospitalizations and death. Research is therefore urgently needed in order to investigate new strategies in an attempt to improve clinical outcome.

The last decade novel techniques as eHealth were introduced to obtain patients data. Particularly mobile health (mHealth) seems an appealing eHealth technique to monitor patients. mHealth is the provision of care facilitated by mobile devices, such as smartphones. mHealth gave patients the opportunity to monitor their vital signs on demand and share their data instantly with their health care providers in order to timely respond so this could improve their outcome. Particularly GUCH patients seemed to be a model group to use mHealth because of their relatively young age, affinity with mobile devices, chronic condition necessitating lifelong surveillance, and the need to reduce the burden of disease. A questionnaire study was performed amongst GUCH patients in order to determine whether these patients were using mHealth, and whether they were interested in starting to use mHealth. Interestingly, only a small minority of GUCH patients used mHealth, and the large majority was willing to start using it [1]. Because of this urgent need to improve clinical outcome, the appealing technique of mHealth, and proven motivation of patients a research study on application of mHealth in GUCH patients was warranted.

Several attempts to fund our eHealth study failed, including academic-corporate partnerships, funding by national health institutes and by grants of insurance companies. Unfortunately, all these attempts failed. Difficulty to obtain funding for research is a global problem, with research councils reported to reject up to 70% of the grant applications [6]. Over the last years an increase in competition for public research grants has been observed [7]. Particularly it is reported that junior researchers without a track record have difficulties in fundraising for research projects. Projects of rare and neglected diseases are also suffering from difficulties of funding [8]. So we were not an exception in finding it hard finance our study and therefore we took the challenge to fund our study by performing a crowdfunding project.

Crowdfunding, a funding method of pooling together donations to support a specific initiative by using social media has been demonstrated to have significant success outside the medical

field [9,10]. Its use in the medical field is relatively new [11], and data on its potential success are scarce [7,12]. Existing data suggested that more than half of the crowdfunding campaigns for cardiovascular research are unsuccessful [7]. Crowdfunding gives, however, the opportunity of engagement of the public by social media, and to meet needs of donors [13]. Needs of donors include direct contact with cardiovascular investigators, opportunity to support a project they prefer, and personal benefit as expressed by rewards. We also contemplate on critical success factors of crowdfunding. Literature reports an average amount of raised of funding between €5000 and €10.000 [7]. Literature also state that research is needed first to attract attention of larger granting organizations [7].

2 MATERIALS AND METHODS

2.1 Project design

A project proposal was send to the Dutch Heart Foundation, and was selected after peer review. The commission social impact of the Dutch Heart Foundation also reviewed the proposal. Thereafter, the project was published at an online donation platform, see Figure 1 for a screenshot. The campaign ended. The project is accessible for review purpose only at https://steunmijnonderzoek.hartstichting.nl/project/schuuring. The Dutch Heart Foundation hired professional copywriters to convert crucial elements of the research proposal to an easy-to-understand message to potential donors. Figure 1 demonstrates the easy-to-understand message. This message was only written in Dutch, because of Dutch audience. The Dutch Heart Foundation facilitated this service, and the investigators are unaware of the costs. The project was open for donations during a predetermined period of two months. A video teaser was created, with aid of a very motivated patient. The Dutch Heart Foundation also facilitated this service, without additional cost for the investigators. Collaboration with this motivated patient represented an important value of valorization of the project. The urgency to donate was evident because of her help, because the patient, and not the doctor, emphasized the importance of the project. The patient reported a personal story to demonstrate limitations in current health care, and outlined the need to change this. The crowdfunding targeted €25.000 and the Dutch Heart Foundation doubled the donations to €50.000,- and return of all donations to the donors were guaranteed in case this target was not met.
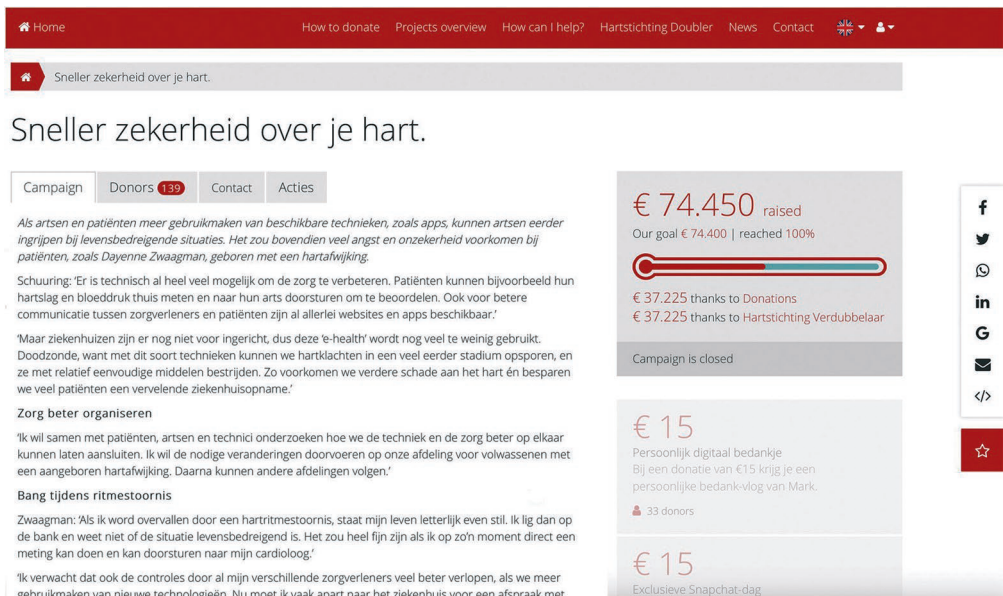
Figure 1 A screenshot of the online donation platform.

2.2 Rewards

Several rewards were available for private donors including a personal message, cycling opportunity with a team member, resuscitation training, tickets to a Shakespeare play, a bottle of the principal investigator's favorite wine, and cruising the Amsterdam canals by boat. Virtually all rewards for the private donors were organized and executed by volunteers, without expenses made (except a time investment). The tickets to a Shakespeare play were a gift, and the principal investigator paid the bottles of the principal investigator's favorite wine. Major donors could be rewarded by a logo on the online platform, a workshop or promise to be mentioned at the kick-off symposium.

2.3 Campaigns and social media posts

Multiple (social) media campaigns and posts were used to promote the project. Three popular network sites were used, namely LinkedIn, Facebook and Twitter. These media campaigns and posts were initiated by all team members and people who supported the project, and were shared online by people who supported the project. The content of the social media messages was diverse, some containing only a link to the donation platform, some containing the video

teaser, and others reporting a status update or a word of thanks. In total 21 posts were done in two months at these three network sites. No fees were paid for posts.

3 RESULTS

3.1 Donations

The investigators started with a significant investment of time and effort. Before submission to the peer review process, the principal investigator investigated 30 h to design the study and to write the proposal. After peer review, the principal investigator investigated 10 h to improve the proposal. Before the campaign started, the investigator visited the Dutch Heart Foundation twice, and worked on the video teaser with the patient for 5 h. All letters to potential donors were written by the principal investigator, which took 10 additional hours. The first month only family and friends of the principal investigator donated. In total, 44 potential donors were contacted. These donors were pharmaceutical companies, technology companies, care institutions, and charity clubs. All these donors refused to donate initially, without disclosing an explanation. Multiple online and social media campaigns were published to promote the project, and a large offline mailing was sent to previous contributors to the Dutch Heart Foundation in week 6. The Dutch Heart Foundation facilitated the large offline mailing, without additional cost for the investigators. During the project support of physicians and public people emerged, resulting in extra donations and public awareness. In the lasts three weeks, after sufficient private donations, five major donors became convinced by the prosperity of the research project and decided to support, see Table 1. Major donors were donors who gave more than €1000,-. These major donors were companies only. Finally, the success of the project was so big that the predetermined target of €50.000,- was exceeded and a total of €74.450,- was raised, see Table 1. A total of 138 private donors and five major donors supported the project. Finally, 73 rewards were given, namely 33 personal messages, 4 cycling opportunities with a team member, 1 resuscitation training with 9 volunteers, 2 tickets to a Shakespeare play, 24 bottles of the principal investigator's favorite wine, and 1 Amsterdam canal cruise. Despite several offers, the 4 donors who chose the cycling opportunities decided not to use this reward.

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3.2 Presumed critical success factors

Because this report is based on observations we can only contemplate on presumed critical success factors of this project. However, the authors experienced that the following factors most significantly influenced the project outcome. Support of a professional organization like the Dutch Heart Foundation resulted in peer review of the research proposal, creation of the online donation platform, production of a teaser video, involvement of professional copywriters creating an easy to understand message for the public, doubling of each donation and send a large offline mailing to previous contributors. Other factors the authors experienced as critical success factors include appealing (social) media campaigns, aid of one or more very motivated patients, and rewards which were interesting for donors.

Table 1 Donations per week.

Week	Number of donors	Amount
1	23	€1.018,00
2	23	€789,00
3	16	€752,00
4	8	€998,00
5	10	€289,00
6	34	€15.624,00
7	5	€97,00
8	19	€17.658,00
Total	138	€37.225,00
Total after doubling		€74.450,00

4 DISCUSSION

In this present era of difficulty to obtain funding for cardiovascular research, we report a new possibility to finance research by crowdfunding and contemplate on presumed critical success factors for future usage. Our result of €74.450,- is a high as compared to literature reports of an average amount of raised of funding between €5000 and €10.000. Interestingly, not only minor donations were received, but also substantial donations from major donors were obtained. A substantial

number of rewards was given to private donors and major donors. To our knowledge, it is also the first time that funding of research on GUCH patients is published.

Research to improve clinical outcome of GUCH patients is urgently needed. The majority faces lifelong problems including arrhythmias, heart failure, hypertension, vascular complications and one or more re-operations [14]. eHealth is a promising technique, particularly mHealth, and clinical research study are needed to evaluate efficacy. After several unsuccessful attempts to obtain funding, crowdfunding was an interesting opportunity to obtain funding for our project.

The authors postulate that the following factors have lead to a success of this crowdfunding project. Support of a professional organization, selection after peer review, support of motivated patient, involvements of motivated physicians, interesting rewards, a funding goal, and strong (social) media campaigns have contributed to a success. Furthermore, the crowdfunding campaign could have met the needs of donors, leading to enforcing of the public engagement. This gave young researchers like our team the opportunity to fund research, and increases funding opportunities in advantage of treatment of rare and neglected diseases.

In the scarce literature available a main determinant of failure of crowdfunding is absence of an easy-to-understand message to potential donors [15]. Unsuccessful campaigns are characterized by project descriptions were difficult to understand because of too many technical terms or no graphical/video presentations. In our project the Dutch Heart Foundation hired professional copywriters to convert crucial elements of the research proposal to an easy-to-understand message to potential donors. The literature reports an average amount of raised of funding between €5000 and €10.000 [7]. Our result was substantially higher, likely because of cooperation with the Dutch Heart Foundation who doubled the profit and well connections of the principal investigator with major donors. Importantly, significant investment of time and effort is required which has been reported in the literature and has been experience by our team [16]. There was a small fiscal incentive for private donors. In the Netherlands, the threshold amount for donations is 1% of a donors threshold income with a minimum of €60,-. These donors may deduct what they have paid more than this threshold amount. However, donations of private donors never exceeded €1000,-.

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Concerns of crowdfunding are, however, also raised in the literature, particularly for project related to patient care instead of research [8,11,17]. Potential abuse from crowdfunding includes fraudulently creation of fake campaigns and those raising money for unproven interventions. Another concern includes ethical issues. Crowdfunding for instance could have an impact on patient privacy, Moreover, investigators with large social networks and sympathetic stories to tell are most likely to be successful. Regarding our project, the Dutch Heart Foundation was involved as a large organization, and our supporting patient involved exposed her medical condition in editorials long before our project.

5 LIMITATIONS

This article is a description of one successful project only. However, because this is the first project with such a result the authors decided to share their experience. Furthermore, the project was only open for donation during a limited time of two months. Whether prolonged acquisition could have led to increased donations is unclear and is a subject of debate. Unfortunately, the investigators have no information about the total number of hits of posts, number of sharings, and number of likes. Because posts were done by multiple social media accounts summaries are unavailable.

6 CONCLUSION

Crowdfunding is a novel opportunity to fund cardiovascular research, and finally gave us the opportunity to start our eHealth project. Critical success factors include support of a professional organization, support of patients and physicians, and interesting rewards. Our project can serve as a model for other researchers to start similar programs.

Conflicts of interest

Funding

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REFERENCES

1. M.J. Schuuring, A.P. Backx, R. Zwart, A.H. Veelenturf, D. Robbers-Visser, M. Groenink, A. Abu-Hanna, N. Bruining, M.P. Schijven, B.J. Mulder, B.J. Bouma, Mobile health in adults with congenital heart disease: current use and future needs. *Neth. Heart J. Mon. J. Neth. Soc. Cardiol. Neth. Heart Found.* 24(2016):647–652, https://doi.org/ 10.1007/s12471-016-0901-z.

2. M.J. Schuuring, J.C. Vis, A.P.J. van Dijk, J.P. van Melle, H.W. Vliegen, P.G. Pieper, G.T. Sieswerda, R.H.A.C.M. de Bruin-Bon, B.J.M. Mulder, B.J. Bouma, Impact of bosentan on exercise capacity in adults after the Fontan procedure: a randomized controlled trial. *Eur. J. Heart Fail.* 15(2013):690–698, https://doi.org/10.1093/eurjhf/hft017.

3. M.M. Winter, B.J. Bouma, M. Hardziyenka, R.H.A.C.M. de Bruin-Bon, H.L. Tan, T.C. Konings, A.P.J. van Dijk, B.J.M. Mulder, Echocardiographic determinants of the clinical condition in patients with a systemic right ventricle. *Echocardiogr. Mt. Kisco N.* (n.d.), https://doi.org/10.1111/j.1540-8175.2010.01233.x.

4. A.C. Zomer, I. Vaartjes, E.T. van der Velde, H.M.Y. de Jong, T.C. Konings, L.J. Wagenaar, W.F. Heesen, F. Eerens, L.H.B. Baur, D.E. Grobbee, B.J.M. Mulder, Heart failure admissions in adults with congenital heart disease; risk factors and prognosis. *Int. J. Cardiol.* 168(2013):2487–2493, https://doi.org/10.1016/j.ijcard.2013.03.003.

5. A.C. Zomer, I. Vaartjes, C.S.P.M. Uiterwaal, E.T. van der Velde, L.F.M. van den Merkhof, L.H.B. Baur, T.J.M. Ansink, L. Cozijnsen, P.G. Pieper, F.J. Meijboom, D.E. Grobbee, B.J.M. Mulder, Circumstances of death in adult congenital heart disease. *Int. J. Cardiol.* 154(2012):168–172.

6. D.-M. Walker, Crowdfunding: an innovative way to fund your project. *Nurse Res.* 25(2017):24–29, https://doi.org/10.7748/nr.2017.e1425.

7. C. Krittanawong, H.J. Zhang, M. Aydar, Z. Wang, T. Sun, Crowdfunding for cardiovascular research. *Int. J. Cardiol.* 250(2018):268–269, https://doi.org/10.1016/j.ijcard.2017.10.029.

8. L. Del Savio, The place of crowdfunding in the discovery of scientific and social value of medical research. *Bioethics* 31(2017):384–392, https://doi.org/10.1111/bioe.12339.

9. O. Sorenson, V. Assenova, G.-C. Li, J. Boada, L. Fleming, Expand innovation finance via crowdfunding. *Science* 354(2016):1526–1528, https://doi.org/10.1126/science. aaf6989.

10. Discover most funded – Kickstarter, (n.d.), https://www.kickstarter.com/discover/ most-funded (accessed January 10, 2018).

11. J. Snyder, P. Chow-White, V.A. Crooks, A. Mathers, Widening the gap: additional concerns with crowdfunding in health care. *Lancet Oncol.* 18(2017):e240, https://doi.org/10.1016/S1470-2045(17)30259-0.

12. W.M. Durand, J.R. Johnson, A.E.M. Eltorai, A.H. Daniels, Medical crowdfunding for patients undergoing orthopedic surgery. *Orthopedics* (2017):1–6, https://doi.org/ 10.3928/01477447-20171114-04.

13. D.P. Wiebe, J.M. FitzGerald, Crowdfunding for respiratory research: a new frontier for patient and public engagement? *Eur. Respir. J.* 50(2017), https://doi.org/10. 1183/13993003.01333-2017.

2

14. J.C. Vis, E.T. van der Velde, M.J. Schuuring, L.C.J.M. Engelfriet-Rijk, I.M. Harms, S. Mantels, B.J. Bouma, B.J.M. Mulder, Wanted! 8000 heart patients: identification of adult patients with a congenital heart defect lost to follow-up, *Int. J. Cardiol.* 149(2011):246–247, https://doi.org/10.1016/j.ijcard.2011.02.019.

15. K. Dahlhausen, B.L. Krebs, J.V. Watters, H.H. Ganz, Crowdfunding campaigns help researchers launch projects and generate outreach. *J. Microbiol. Biol. Educ.* 17(2016): 32–37, https://doi.org/10.1128/jmbe.v17i1.1051.

16. J. Vachelard, T. Gambarra-Soares, G. Augustini, P. Riul, V. Maracaja-Coutinho, A guide to scientific crowdfunding. *PLoS Biol.* 14(2016):e1002373, https://doi.org/10.1371/ journal.pbio.1002373.

17. M.J. Young, E. Scheinberg, The rise of crowdfunding for medical care: promises and perils. *JAMA* 317(2017): 1623–1624, https://doi.org/10.1001/jama.2017.3078.

Chapter 3

Adults with congenital heart disease: ready for mobile health?

R.W. Treskes, M.A.C. Koole, M.M. Winter, M. Monteiro, D.A.J. Dohmen, A. Abu-Hanna, M.P. Schijven, B.J.M. Mulder, B.J. Bouma, M.J. Schuuring

ABSTRACT

Purpose

Mobile health (mHealth) could improve outcome and reduce emergency care utilization of grown-up patients with congenital heart disease (GUCH). Inappropriate use of mHealth, however, can lead to data overload for professionals and unnecessary measurements for patients, increasing burden for both. We aimed to determine the clinical characteristics of patients with high emergency care utilization and to test whether these patients were willing to start using mHealth.

Methods

Clinical characteristics and emergency care utilization of consecutive GUCH patients who visited one of the two participating cardiologists at the outpatient clinic of the Academic Medical Center in Amsterdam were studied retrospectively. All patients were approached to fill in an mHealth questionnaire. A frequency of three or more emergency visits in 5 years was defined as high emergency care utilization.

Results

In total, 202 consecutive GUCH patients who visited one of the two participating cardiologists were studied. Median age was 41 years, 47% were male, and 51% were symptomatic. In the past five years, 134 emergency visits were identified. Of all patients, 8% had high emergency care utilization. High emergency care utilization was associated with patients being symptomatic, using anti-arrhythmic drug therapy or diuretics. In total, 75% of all patients with high emergency care utilization were willing to start using mHealth.

Conclusion

GUCH patients who are symptomatic, those on anti-arrhythmic drug therapy and those on diuretics are suitable candidates to enroll in future mHealth initiatives because of both high care utilization and high motivation to start using mHealth.

INTRODUCTION

Congenital heart disease (CHD) is one of the most common birth defects [1-3]. During the past decades, the life expectancy of children born with a CHD has increased dramatically. At present, 95% of children with CHD reach adulthood [1]. However, many of the grown-ups with congenital heart disease (GUCH) are chronically affected by residual sequelae leading to unpredictable arrhythmias, heart failure and a reduced quality of life [4-8]. In general, GUCH patients have a high utilisation of emergency resources, with emergency care utilisation increasing as age progresses [4]. As the population of GUCH patients is increasing in number and age, total emergency care utilisation of this population is expected to increase [9].

Mobile health (mHealth) is the provision of medical care by mobile technologies capable of delivering health information, monitoring clinical signs and enabling direct care and patient education [10]. Using mobile technology, vital signs can be collected and sent immediately to a treating cardiologist. E-visits enable immediate and remote contact between doctor and patient [11]. Therefore, potential benefits of mHealth include: rapid delivery of round-the-clock care; enhanced daily monitoring and hence timely response and more convenience for patients; and improved access for patients [12]. In order to improve outcome and reduce emergency care utilisation, careful selection of patients that are most likely to benefit from an mHealth intervention is warranted. If used in an inappropriate patient population, mHealth can lead to data overload for healthcare professionals and unnecessary data collection for patients, increasing the burden for both [13]. Patients with a high emergency care utilisation and high motivation to start using mHealth are suitable candidates to include in new mHealth initiatives. It is therefore the primary objective of this study to determine the clinical characteristics of GUCH patients with high emergency care utilisation. It is the secondary objective to combine these findings with the results of an mHealth questionnaire, to test whether GUCH patients with high emergency care utilisation are willing to start using mHealth.

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METHODS

Population and data collection

For this study, two cardiologists specialised in GUCH (B.B. and B.M.) approached consecutive patients who had an appointment at the outpatient clinic with them to fill in an mHealth questionnaire. These patients visited the outpatient clinic at the Academic Medical Centre in Amsterdam between April 2016 and September 2016. Clinical characteristics and emergency care utilisation of these GUCH patients were studied retrospectively. Clinical characteristics noted were: severity of the CHD (in accordance with the Bethesda conference) [14], history of cardiac surgery, history of pacemaker or implantable cardioverter defibrillator (ICD) implantation and the use of diuretics or any antiarrhythmic drug therapy. In patients receiving antiarrhythmic drug therapy, the indication was noted as well. Beta-blockers were considered an antiarrhythmic drug therapy if the drug was initiated or the dose was altered for symptoms of palpitations or treatment for arrhythmia control. Cardiac-related symptoms were rated in accordance with the New York Heart Association (NYHA) Functional Classification. GUCH patients with a NYHA class II or higher were considered symptomatic. Emergency care utilization was defined as visits to the emergency room, cardiac care unit or unplanned outpatient clinic visits. Outpatient clinic visits were counted if they included a visit to a cardiologist, cardiologist in training, heart failure nurse or dedicated CHD nurse at the Department of Cardiology of the Academic Medical Centre. An outpatient clinic visit was considered 'unplanned' if the electronic medical record explicitly stated that the patient was seen without a scheduled appointment in case of symptoms. Interventions noted following an emergency care visit were any type of open-heart surgery, aneurysm surgery, pacemaker or ICD implantation or replacement, diagnostic catheterisations, electrical cardioversions (ECV), catheter-based interventions and bronchoscopy in case of haemoptysis. High care utilisation was defined as a score of three or more emergency visits between 1 June 2011 and 31 December 2016.

All patients were approached to fill in an mHealth questionnaire on paper. Details of the questionnaire have been described previously [15]. Exclusion criteria were being mentally impaired (at physician's discretion), having no knowledge of the Dutch language or being younger than 18 years of age.

Data management and statistics

SPSS 22 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. IBM Corp., Armonk, NY, USA) was used for statistical analysis. To identify GUCH patients who would most likely benefit from mHealth, determinants were set off against an emergency care utilisation of three or more emergency visits and/or interventions in the previous 5 years. Variables were compared with a chi-squared test. A p-value ≤0.05 was considered statistically significant.

RESULTS

Population characteristics

In total, 202 consecutive patients who visited the outpatient clinic and had an appointment with one of the two participating cardiologists (B.B. and B.M.) at the Academic Medical Centre in Amsterdam between April 2016 and September 2016 were studied. Median age was 41 years (interquartile range 32–50, range 18–78 years), 47% were male and 51% were symptomatic. Of all patients, 19% had mild CHD, 61% moderate CHD and 20% severe CHD. A total of 83% had a history of cardiac surgery and 8% had had a pacemaker or ICD implanted. Thirty-one per cent received antiarrhythmic drug therapy and 9% used diuretics (Table 1). Only 5% were in NYHA class IV. All patients filled in the mHealth questionnaire.

Emergency visits

In the previous 5 years, 202 patients accounted for 134 emergency visits, 59 (29%) of whom had one or more emergency visit. Sixteen (8%) of the 202 patients had high care utilisation and 186 (92%) low care utilisation. No significant differences in gender, history of cardiac surgery or severity of CHD were found between patients with high and low care utilisation. Significant differences were found in NYHA class (87% vs 49%, $p<0.001$), use of diuretics (44% vs 7%, $p<0.001$) and antiarrhythmic drug therapy (69% vs 27%, $p=0.001$) (Table 1).

Table 2 and Figure 1 show all of the symptoms with which patients presented, the subsequent diagnoses made, and the treatment administered. Most patients presented with either palpitations (41%) or chest pain (24%). In 46% of all cases, no diagnosis of a cardiac nature was made. In 37%, a patient was diagnosed with an arrhythmia (Figure 1).

Emergency visits resulted in a variety of different actions. In 44% of all cases the therapeutic regimen was not changed. Drug therapy was changed in 52 (39%) cases. In 8 (15%) out of 55 cases of palpitations, the therapeutic regimen was not changed. Therapeutic regimen changes included 16 (29%) cases of ECV, 13 (24%) cases of adjusting antiarrhythmic drug therapy after ECV, 7 (13%) cases of adjusting antiarrhythmic drug therapy only, 10 (18%) cases of initiating antiarrhythmic drug therapy and 1 (2%) case of radiofrequency ablation. In 29 (91%) of the 32 cases of chest pain no action was taken. Therapeutic regimen changes included 3 (9%) cases of initiating antibiotic treatment for the suspicion of endocarditis.

Table 1 Comparison of high and low care utilisation. *PM* Pacemaker, *ICD* implantable cardio-verter-defibrillator.

	All patients (*n*=202)	Low care utilization (*n*=186 (92%))	High care utilization (*n*=16 (8%))	*p*
Median Age, years	41 (18–78)	40 (18–78)	42 (23–77)	
Male, (%)	94 (47)	87 (46)	7 (43)	0.816
Congenital heart disease				
Mild, (%)	39 (19)	35 (19)	4 (25)	0.548
Moderate, (%)	123 (61)	115 (62)	8 (50)	0.352
Severe, (%)	40 (20)	36 (19)	4 (25)	0.548
New York Heart Association Class				
Class I, (%)	97 (48)	95 (51)	2 (13)	<0.001
Class ≥II, (%)	105 (52)	91 (49)	14 (87)	<0.001
Event history				
Cardiac surgery, (%)	168 (83)	156 (83)	12 (75)	0.363
PM/ICD implantation, (%)	17 (8)	14 (8)	3 (19)	0.121
Medication				
Diuretics, (%)	19 (9)	12 (6)	7 (44)	<0.001
Anti-arrhythmic, (%)	62 (31)	51 (27)	11 (69)	0.001
mHealth				
Smartphone utilization (%)	186 (92)	172 (92)	14 (87)	0.369
Willing to use mHealth (%)	143 (71)	131 (70)	12 (75)	0.70

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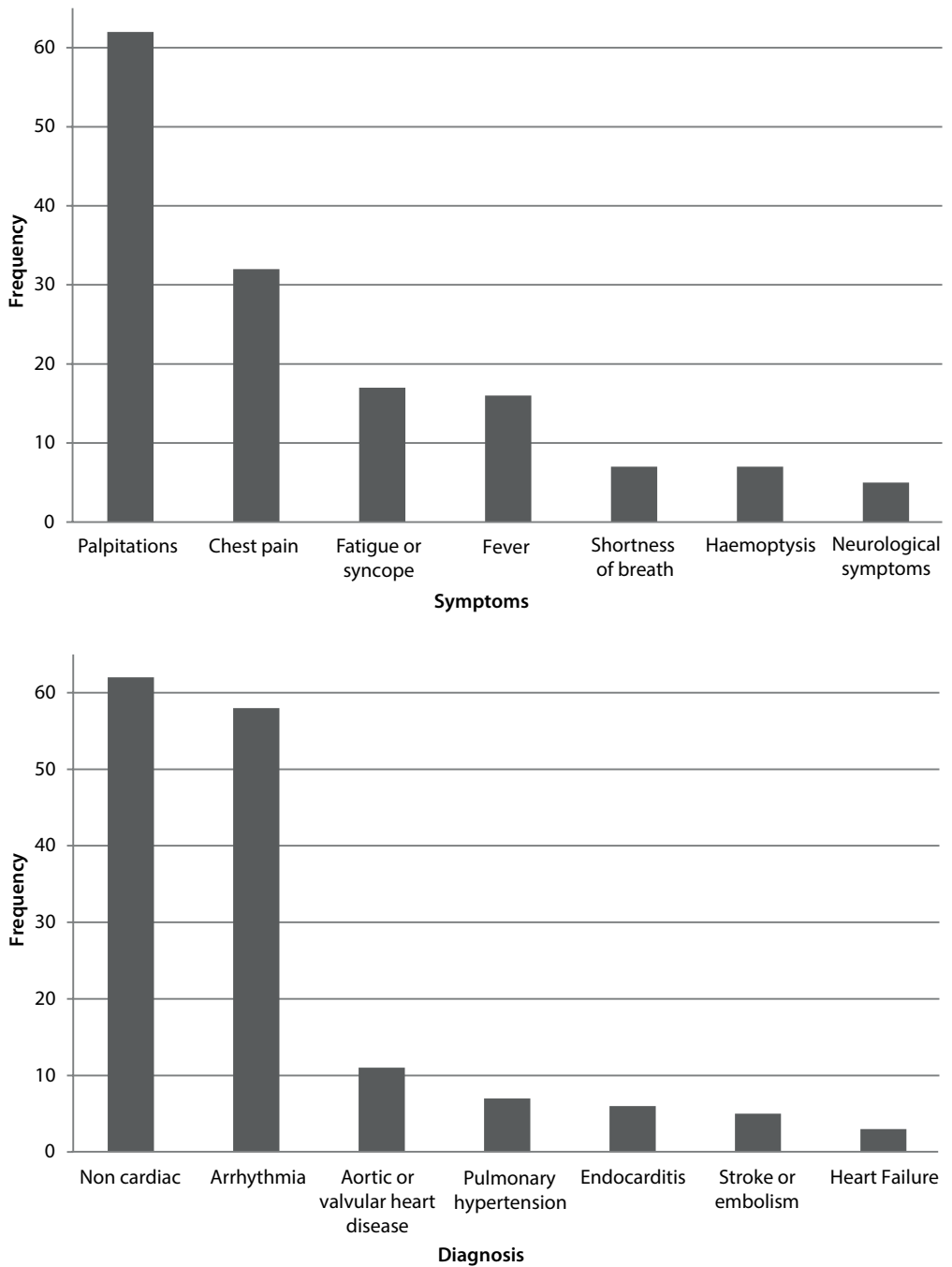
Figure 1 Frequency of emergency care visits, reasons and subsequent diagnoses.

Table 2 Information on emergency visits.

Symptoms	*n* (%)
Palpitations	55 (41%)
Chest pain	32 (24%)
Fever	16 (12%)
Fatigue	13 (10%)
Shortness of breath	7 (5%)
Haemoptysis	6 (4%)
Neurological symptoms	5 (4%)
Diagnoses	
No diagnosis of cardiac nature	62 (46%)
Arrhythmia	50 (37%)
Endocarditis	6 (5%)
Pulmonary hypertension	6 (5%)
Stroke	5 (4%)
Valvular heart disease	3 (2%)
Heart failure	2 (1%)
Therapeutic regimen consequences	
No changes in therapeutic regimen	59 (44%)
Medication changes	52 (39%)
Electrocardioversion	29 (21%)
Interventions	4 (3%)
Planned interventions	3 (2%)

Patient motivation to start using mHealth amongst patients with high emergency care utilization

In total, 16 GUCH patients had high care utilisation. Median age was 46 years, 56% were female and 87% were symptomatic. Of all 202 GUCH patients, 25% had a mild CHD, 50% a moderate and 25% a severe CHD. Antiarrhythmic drugs were used by 69% of patients and diuretics by 44%.

Of all patients with high care utilisation, 87% were in possession of a smartphone and 18% claimed to use mHealth already. Of all patients, 44% wanted information about their disease, while 44% wanted lifestyle advice via mobile technology. A total of 56% were willing to fill in

vital signs on their smartphone, 56% were willing to fill in symptoms on their smartphone, 62% wanted advice in case of aberrant vital signs, 62% wanted advice regarding symptoms of possible cardiac origin and 75% were willing to start using mHealth.

In contrast, in the low care utilisation group, 131 (70%) patients were willing to start using mHealth (Figure 2).

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┌─────────────────────────────────────────────────────────────┐
│  Consecutive GUCH patients who visited outpatient clinic      │
│                         n=202                                  │
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│  Retrospective data collection on emergency care utilisation  │
│                         n=202                                  │
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│  Prospective questionnaire on willingness to start using mHealth │
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                              │
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                    │   Participated    │
                    │      n=202        │
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Low emergency care utilisation and not willing to start using mHealth n=55	Low emergency care utilisation and willing to start using mHealth n=131	High emergency care utilisation and not willing to start using mHealth n=4	High emergency care utilisation and willing to start using mHealth n=12

Optimal candidates

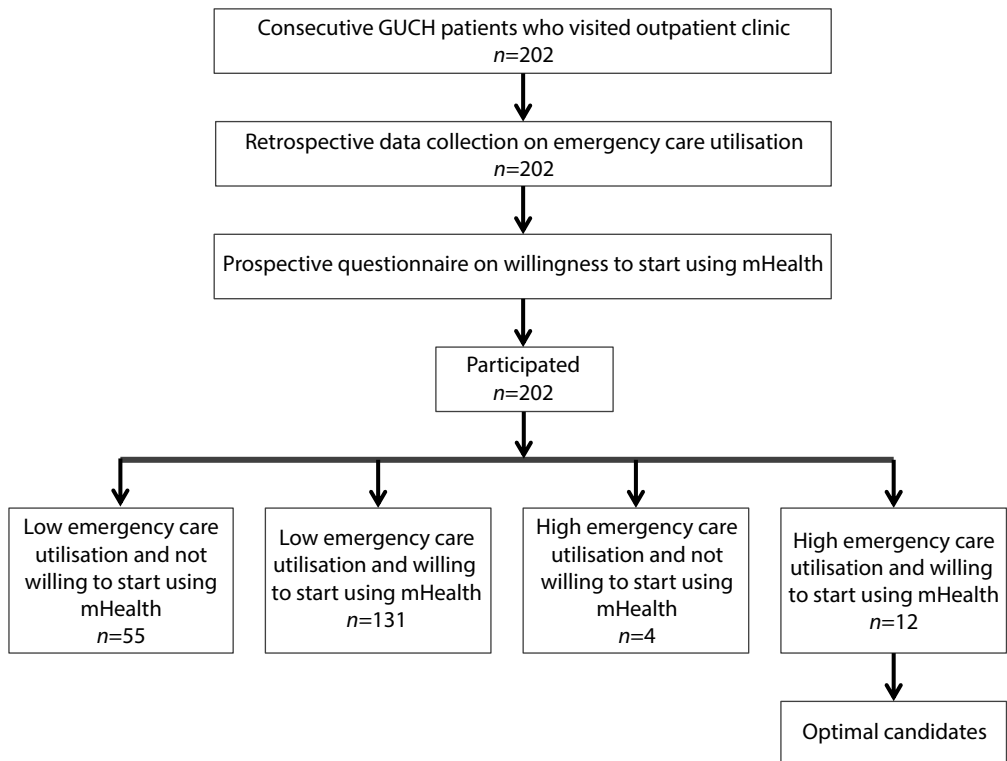**Figure 2** Flow chart of patient selection. *GUCH* grown-up patients with congenital heart disease.

DISCUSSION

To our knowledge this is the first study to determine the suitability of candidates for enrolment in new mHealth initiatives in GUCH patients. In our study, we found that symptomatic patients who are on diuretics or antiarrhythmic drug therapy are more likely to visit the emergency room. These patients might benefit from mHealth, as emergency visits could be prevented via mHealth. In patients with few emergency visits, mHealth is less likely to be beneficial as it is a priori less likely to prevent an emergency visit. Therefore, our study could help to avoid initiation of mHealth with the goal of decreasing emergency care utilisation in an inappropriate patient population and could prevent unnecessary data collection for patients. Furthermore, the therapeutic regimen was not changed at 44% of all emergency visits. The number of such visits might also be reducible via mHealth.

Emergency care utilization

In this study, 29% of all participating GUCH patients had had an emergency visit in the previous 5 years. This percentage was lower than in the study of Mackie et al. [16] and that of Verheugt et al. [17], who reported that 68% and 50% of their study population had had an emergency visit, respectively. Definitions of emergency care utilisation between Mackie et al., Verheugt et al. and our study were comparable. It is therefore hypothesised that this difference is due to the fact that for our study, only emergency visits at the Academic Medical Centre were analysed. The Academic Medical Centre is a tertiary hospital, treating patients from a large geographic region. In emergency cases, these patients are more likely to visit a local hospital close to their homes. These emergency visits are not counted in this study. Therefore, the frequency of emergency visits could be higher in our study population. In our study most patients presented with palpitations and chest pain. Arrhythmias were the most common final diagnosis. Heart failure was diagnosed in only 1% of patients, which was lower than in the studies of Cedars et al. [18] and Negishi et al. [19]. There are several explanations for this difference. First, patients might have been admitted to other hospitals. Second, in our study, diagnoses were classified according to primary diagnosis. Some patients with arrhythmias presented with heart failure symptoms but were diagnosed in the 'arrhythmia category'. Third, two nurse practitioners specialised in heart failure had optimised treatment at the outpatient clinic, which could potentially have led to a reduction of deteriorations in heart function. Finally, in our study population, 31% had been hospitalised in the previous 5 years. This was in line with the study of Mackie et al. [16] and that of Moons et al. [20].

Selecting GUCH patients for mobile health

Our study showed that the majority of patients were willing to use mHealth applications. Several validated technologies that allow for remote electrocardiogram (ECG) monitoring and automatic transmission are already available [21] and easy to use. For the selection of the best candidates for possible future mHealth initiatives inclusion criteria should be: GUCH patients, experiencing frequent palpitations and/or chest pain, able to operate a smartphone and having high care utilisation. Furthermore, having severe CHD, using diuretics and/or antiarrhythmic drugs, having an implant or experiencing symptoms can be taken into account in selecting GUCH patients. Gender and age should not be a discriminant factor. Issues regarding privacy will need to be addressed, since this new technology will be sensitive as regards breach of privacy. Lastly, mHealth literacy is an important predictor of success in mHealth intervention [22]. Therefore, acceptability should be taken into account when initiating mHealth initiatives in this group.

Currently, several devices that allow a user to record an ECG are already available. These devices can be used by patients themselves and do not necessitate the assistance of trained healthcare staff. As the majority of patients presented with palpitations or chest pain, mobile ECGs might contribute to improving care in these patient populations. In this study, the majority of patients with palpitations had a change in medical therapy. Innovations in the delivery of medication, for example the pill-in-the-pocket, might facilitate initial treatment at home. As such, the use of e-Health for remote diagnosis is worth investigating.

Limitations

This study was limited by the fact that data collection was done in a single tertiary medical centre, which could potentially affect generalisability. No data from other hospitals were incorporated in this study. Therefore, data on healthcare utilisation presented in this study might be an underestimation, as GUCH patients that participated could have been admitted to other hospitals. Lastly, 16 patients in our study had a high emergency care utilisation. This sample size is relatively small and the percentages derived from this sample should therefore be interpreted with caution.

Planned healthcare utilization

This study was primarily concerned with the role of mHealth to decrease emergency care utilisation. It might, however, be possible that frequent collection of vital signs and remote doctor-patient contact will decrease the need for planned in-office visits as well. Moreover,

mHealth could also contribute to the improvement of patient satisfaction and patient health engagement [23]. This should be measured in future mHealth initiatives as well.

CONCLUSION

GUCH patients who are symptomatic, those on antiarrhythmic drug therapy and those on diuretics are optimal candidates for enrolment in new mHealth initiatives because of both a high care utilisation and high motivation. Our study contributes to appropriate patient selection for mHealth initiatives that aim to prevent emergency care utilisation, thereby contributing to an efficient use of mHealth.

WHAT'S NEW

- Telemonitoring with mobile phones is promising, but research remains to be done.
- Grown-up patients with congenital heart disease have a proven interest in mobile health.
- This study identifies the characteristics of patients with high healthcare use.
- The vast majority of these patients is in possession of a smartphone and willing to start using mobile health.

Acknowledgements

Conflict of interest

R.W. Treskes, M.A.C. Koole, D. Kauw, M.M. Winter, M. Monteiro, D.A.J. Dohmen, A. Abu-Hanna, M.P. Schijven, B.J.M. Mulder, B.J. Bouma and M.J. Schuuring declare that they have no competing interests.

Ethical approval

For the collection of medical data from all the participating GUCH patients, permission was granted by the Ethics Committee (reference number W16_057). For the questionnaire survey no approval from the Institutions' Ethics Committee was required under Dutch law, since it was not burdensome for the patients.

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REFERENCES

1. Tennant PW, Pearce MS, Bythell M, Rankin J. 20-year survival of children born with congenital anomalies: a population-based study. *Lancet.* 2010;375(9715):649–56.

2. Canfield MA, Honein MA, Yuskiv N, et al. National estimates and race/ethnic-specific variation of selected birth defects in the United States, 1999–2001. *Birth Defects Res A Clin Mol Teratol.* 2006;76(11):747–56.

3. Bird TM, Hobbs CA, Cleves MA, Tilford JM, Robbins JM. National rates of birth defects among hospitalized newborns. B*irth Defects Res A Clin Mol Teratol.* 2006;76(11):762–9.

4. Baumgartner H, Bonhoeffer P, De Groot NM, et al. ESC Guidelines for the management of grown-up congenital heart disease (new version 2010). *Eur Heart J.* 2010;31(23):2915–57.

5. Koyak Z, Kroon B, de Groot JR, et al. Efficacy of antiarrhythmic drugs in adults with congenital heart disease and supraventricular tachycardias. *Am J Cardiol.* 2013;112(9):1461–7.

6. Schuuring MJ, van Gulik EC, Koolbergen DR, et al. Determinants of clinical right ventricular failure after congenital heart surgery in adults. *J Cardiothorac Vasc Anesth.* 2013;27(4):723–7.

7. Zomer AC, Vaartjes I, van der Velde ET, et al. Heart failure admissions in adults with congenital heart disease; risk factors and prognosis. *Int J Cardiol.* 2013;168(3):2487–93.

8. Schuuring MJ, van Riel AC, Vis JC, et al. New predictors of mortality in adults with congenital heart disease and pulmonary hypertension: Midterm outcome of a prospective study. *Int J Cardiol.* 2015;181:270–6.

9. Tutarel O, Kempny A, Alonso-Gonzalez R, et al. Congenital heart disease beyond the age of 60: emergence of a new population with high resource utilization, high morbidity, and high mortality. *Eur Heart J.* 2014;35(11):725–32.

10. Cowie MR, Bax J, Bruining N, et al. e-Health: a position statement of the European Society of Cardiology. *Eur Heart J.* 2016;37(1):63–6.

11. Treskes RW, van der Velde ET, Barendse R, Bruining N. Mobile health in cardiology: a review of currently available medical apps and equipment for remote monitoring. *Expert Rev Med Devices.* 2016;13(9):823–30.

12. Dorsey ER, Topol EJ. State of Telehealth. *N Engl J Med.* 2016;375(2):154–61.

13. Clark PA, Capuzzi K, Harrison J. Telemedicine: medical, legal and ethical perspectives. *Med Sci Monit.* 2010;16(12):RA261–RA72.

14. Warnes CA, Liberthson R, Danielson GK, et al. Task force 1: the changing profile of congenital heart disease in adult life. *J Am Coll Cardiol.* 2001;37(5):1170–5.

15. Schuuring MJ, Backx AP, Zwart R, et al. Mobile health in adults with congenital heart disease: current use and future needs. *Neth Heart J.* 2016.

16. Mackie AS, Pilote L, Ionescu-Ittu R, Rahme E, Marelli AJ. Health care resource utilization in adults with congenital heart disease. *Am J Cardiol.* 2007;99(6):839–43.

17. Verheugt CL, Uiterwaal CS, van der Velde ET, et al. The emerging burden of hospital admissions of adults with congenital heart disease. *Heart.* 2010;96(11):872–8.

18. Cedars AM, Burns S, Novak EL, Amin AP. Predictors of Rehospitalization Among Adults With Congenital Heart Disease Are Lesion Specific. *Circ Cardiovasc Qual Outcomes.* 2016.

19. Negishi J, Ohuchi H, Yasuda K, Miyazaki A, Norifumi N, Yamada O. Unscheduled hospitalization in adults with congenital heart disease. *Korean Circ J.* 2015;45(1):59–66.

20. Moons P, Siebens K, De Geest S, Abraham I, Budts W, Gewillig M. A pilot study of expenditures on, and utilization of resources in, health care in adults with congenital heart disease. *Cardiol Young.* 2001;11(3):301–13.

21. Al-Zaiti SS, Shusterman V, Carey MG. Novel technical solutions for wireless ECG transmission & analysis in the age of the internet cloud. *J Electrocardiol.* 2013;46(6):540–5.

22. Gordon NP, Hornbrook MC. Differences in Access to and Preferences for Using Patient Portals and Other eHealth Technologies Based on Race, Ethnicity, and Age: A Database and Survey Study of Seniors in a Large Health Plan. *J Med Internet Res.* 2016;18(3):e50.

23. De Rosis S, Barsanti S. Patient satisfaction, e-health and the evolution of the patient-general practitioner relationship: Evidence from an Italian survey. *Health Policy.* 2016;120(11):1279–92.

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Chapter 4

First real-world experience with mobile health telemonitoring in adult patients with congenital heart disease

M.A.C. Koole, D. Kauw, M.M. Winter, D.A.J. Dohmen, I.I. Tulevski, R. de Haan, G.A. Somsen, M.P. Schijven, D. Robbers-Visser, B.J.M. Mulder, B.J. Bouma, M.J. Schuuring

ABSTRACT

Background

Arrhythmias and heart failure are common and invalidating sequelae in adult patients with congenital heart disease (CHD). Mobile health (mHealth) enables daily monitoring and a timely response that might prevent deterioration. We present an observational prospective registry to evaluate feasibility of an m-Health telemonitoring program for managing arrhythmia, heart failure and blood pressure in symptomatic adults with CHD.

Methods

Symptomatic adult patients with CHD are enrolled in an m-Health telemonitoring program, which evaluates single-lead ECG, blood pressure and weight measurements. In case of symptoms extra measurements could be performed. Data are collected by mobile apps, matched with individualized thresholds. Patients are contacted if thresholds were exceeded or if arrhythmias were found, for treatment adjustments or reassurance. Data on emergency care utilisation, hospitalisation and patient-reported outcome measures are used to assess quality of life and self-management.

Results

129 symptomatic CHD patients were invited to participate, 55 participated. Reasons for refusing consent included too time consuming to participate in research (30) and to monitor vital signs (14). At baseline 22 patients were in New York Heart Association class ≥II heart failure, 43 patients had palpitations or documented arrhythmias, and 8 had hypertension. Mean follow-up was 3.0 months, one patient dropped out, and adherence was 97%.

Conclusion

The first results indicate that this program is feasible with high adherence.

INTRODUCTION

Telemonitoring is now available and could be a powerful tool for diagnosing and treating arrhythmia and heart failure. It can also be useful for adjusting antihypertensive medication in order to reach optimal blood pressure in real-life circumstances. This may be especially true for adult patients with congenital heart disease (CHD). They are a growing patient population [1,2]. Most of these patients need lifelong follow-up because of residual sequelae predominantly causing heart failure and arrhythmias. Contemporary care is organised by several outpatient visits per year. These visits are needed to optimise dosing of medication and detect complications or disease progression [3-7]. The current organisation of care is hampered by frequent emergency hospitalisations, possibly due to a slow response to clinical signs of deterioration.

Telemonitoring may facilitate a faster response to the first warning signs of deterioration [8]. If directly followed by properly adjusting therapy or surveillance this may result in a reduction in emergency care utilisation. Also patients may be reassured in case of benign but terrifying symptoms resulting in better patient reported outcome measurements (PROMs), quality of life and self-management [9].

Results of studies on telemonitoring in patients with heart failure are conflicting [10–13]. Several meta-analyses suggest clinical and economic benefits, but numerous prospectively initiated clinical trials have not confirmed these findings [12,14]. Moreover, professionals are often hesitant to start using telemonitoring because they fear an overload of data with a subsequent increase in workload [15-17].

However, adult patients with CHD seem particularly suitable for telemonitoring. These patients commonly experience health-related fears and insecurities [18]. They are of a young age, they have affinity with mobile devices and a chronic condition necessitating lifelong surveillance [15,19,20]. In our recent study, only a small minority (14%) of adult patients with CHD were already using telemonitoring, whereas a large majority responded that they would be willing to start using it (75%) [15,16].

An observational prospective registry was initiated to evaluate feasibility of a new mobile health (mHealth) program for telemonitoring in symptomatic adults with CHD.

4

METHODS

This prospective study is being conducted in a tertiary referral centre in the Netherlands. The institutional ethics committee approved the study. Informed consent is obtained in all patients. Consecutive symptomatic adult patients with CHD patients are included. Symptomatic is defined as palpitations or documented arrhythmias in the last 3 years or New York Heart Association (NYHA) heart failure class ≥II. Patients are screened at the outpatient clinic or clinical ward and if eligible they are invited for a detailed explanation of the study. Inclusion and exclusion criteria are listed in Table 1. We distinguish three subgroups: patients with arrhythmias, heart failure, and hypotension or hypertension.

The m-Health program (HartWacht) consisted of hardware for single-lead ECG measurements, equipment to measure blood pressure, and a scale for body weight measurement, in combination with mobile applications to receive and transfer data. Patients were instructed on how to use the devices and mobile applications. Palpitations and arrhythmias were evaluated with single-lead ECG measurements (not only QRS complexes, but also *P* waves could be detected and visualised), which were recorded using a wireless ECG device and transferred to a remote telemonitoring centre using a smartphone application (Kardia [21]). ECGs were assessed daily by trained nurses, under supervision of a cardiologist. If an ECG was uninterpretable (artefacts) patients were asked to send a new recording. Blood pressure and weight parameters were evaluated with a blood pressure monitor (Omron) and a weight scale (i-Health) wireless connected to the patient's smartphone. These data were transferred to the telemonitoring centre through a different smartphone application (cVitals). Data were processed using personalised thresholds and trend deviation settings, and were assessed daily. Routine measurements were done twice a week at predefined times. Patients could perform extra measurements in case of symptoms. If necessary, patients were contacted by their treating cardiologist in order to adjust therapy, for surveillance or in order to provide reassurance. Patients received an app reminder when a measurement was not performed at the required moments. Study measures (i.e. extensive history-taking and PROM questionnaires) were obtained in all participants at baseline. PROM questionnaires were repeated every 3 months. Results were automatically added to the electronic medical record (EMR) of the patient.

The following data are collected during follow-up: 1) emergency care utilisation and 2) PROMs; 3) number of visits to the outpatient clinic; 4) number of telephone contact moments; and 5) medication changes induced by results of the telemonitoring program. Additionally, we were interested in the percentage of consenting patients. Emergency care utilisation was defined as any unplanned visit to the hospital due to cardiac-related symptoms. Outpatient clinic visits were defined as a visit to a cardiologist, cardiologist in training, heart failure nurse or dedicated adult CHD nurse. An outpatient clinical visit was defined as unplanned if the electronic medical record (EMR) explicitly stated that the patient was seen pre-emptively in case of symptoms. Contact moments were defined as a contact initiated by a cardiologist, cardiologist in training or specialised nurse by telephone or email. Interventions were defined as alteration of medication, catheterisations, pacemaker or ICD implantation, electrical cardioversions, catheter-based interventions and any type of open-heart surgery. All the data were extracted from the EMR, so only events registered in the EMR were used. Historical data of care utilisation from the last year before inclusion were obtained to have an indication of disease burden of these patients.

4

Careful evaluation of the patient experienced health status, quality of life and self-management was performed using the PROM questionnaires. Three PROM questionnaires were used (EQ-5D-5L, PAM-13 and CaReQoL Chronic Heart Failure (CHF))[22-24]. EQ-5D-5L and CaReQoL CHF evaluate quality of life, EQ-5D-5L scores general quality of life and health status and CaReQoL CHF uses three subcategories to specify the quality of life: experienced safety, social and emotional problems and physical restrictions. PAM-13 gives an indication of the level of self-management of a patient.

For statistical analyses, SPSS 25.0 (SPSS Inc., Chicago, Illinois) for Windows was used. A two-tailed probability value of <0.05 was considered statistically significant. Descriptive data are presented as numbers with percentage, as mean with standard deviation or as median with range.

Table 1 Inclusion and exclusion criteria.

Inclusion criteria
Symptomatic adult CHD patients;
Documented arrhythmias
Palpitations within last 3 years
Heart failure NYHA class ≥ II
Age ≥18 years
Possession mobile device (e.g. smartphone, tablet)
Exclusion criteria
Impaired cognition, assessed by treating physician
Tremors
Asymptomatic adult CHD patients

RESULTS

Patient enrolment started in June 2017 (Figure 1). Up to March 2018, 129 symptomatic adult CHD patients were eligible, of whom 55 (43%) consented to participate (median age of 45 years (range 19–70), 34.5% male and CHD severity of mild (n=6), moderate (n= 29) and severe (n=20)). Reasons for refusing consent are shown in Table 2. At baseline 22 patients were in NYHA class ≥II heart failure, 43 patients had palpitations or documented arrhythmias and eight patients were known with hypertension. Baseline characteristics of the study population are summarised in Table 3.

One patient dropped out before the first measurement because of difficulties experienced during installation of the smartphone applications and devices. Mean follow-up was 3.0 months, adherence was 97%.

During follow-up two emergency presentations and one hospitalisation was recorded (Figure 2). This figure also contains historical data to give further insight, demonstrating ten emergency presentations and nine hospitalisations.
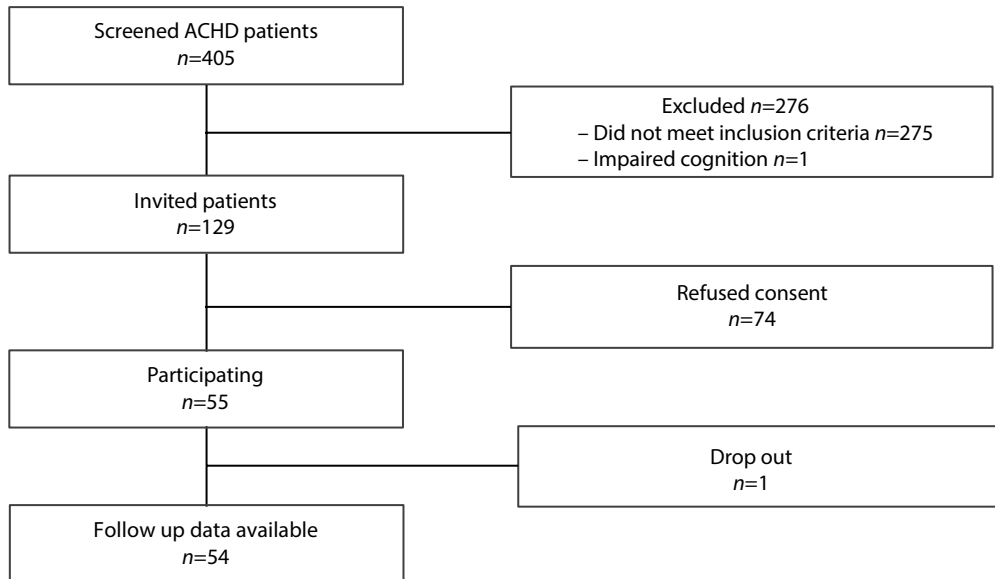
```
┌─────────────────────────┐
│   Screened ACHD patients │
│          n=405           │
└─────────────────────────┘
             │          ┌──────────────────────────────────────────┐
             ├──────────│ Excluded n=276                            │
             │          │ – Did not meet inclusion criteria n=275   │
             │          │ – Impaired cognition n=1                  │
             │          └──────────────────────────────────────────┘
┌─────────────────────────┐
│    Invited patients      │
│         n=129            │
└─────────────────────────┘
             │          ┌──────────────────────────────────────────┐
             ├──────────│ Refused consent                          │
             │          │ n=74                                     │
             │          └──────────────────────────────────────────┘
┌─────────────────────────┐
│     Participating        │
│          n=55            │
└─────────────────────────┘
             │          ┌──────────────────────────────────────────┐
             ├──────────│ Drop out                                 │
             │          │ n=1                                      │
             │          └──────────────────────────────────────────┘
┌─────────────────────────┐
│  Follow up data available│
│          n=54            │
└─────────────────────────┘
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Figure 1 Flowchart of the study, *n*=number.

Serial PROM questionnaires were available for 12 patients at baseline, nine patients after 3 months and six patients after 6 months and showed a nonsignificant change in quality of life during m-Health telemonitoring (Figure 3). Compared with baseline mean scores of PROM questionnaires, quality of life (CaRe-QoL CHF (social, physical and safety) and EQ-5D-5L) improved by 51.7% (p=0.502), 14.3% (p=0.28), 3.3% (p=0.87) and 0.2% (p=0.89) respectively. Interestingly, patient-reported self-management decreased by 7.3% (p=0.153). Also after a first increase in PROMs, this positive effect seems to fade, yet a small positive effect remains.

During follow-up 13 patients visited the outpatient clinic 19 times, medication changes were made in six patients based on telemonitoring measurements. Twelve patients had 21 telephone contacts with their cardiologist (19 were for reassurance, two were referrals to the outpatient clinic for further follow-up). One patient improved in functional class after increasing the dose of diuretics after two consecutive threshold exceeding weight measurements. In two patients antiarrhythmic treatment was adjusted and in three patients antihypertensive treatment was adjusted.

Single-lead ECG measurements were performed frequently, and turned out to predominately be sinus rhythm. In Figure 4 the rhythms of 176 ECGs during symptoms are shown. The majority (74.4%) of the patients could be reassured since sinus rhythm was found while the patient experienced palpitations. In one patient with palpitations, previously undiagnosed atrial fibrillation was found and another ECG also showed asymptomatic sinus node dysfunction. Larger scaled studies are warranted to distinguish which subgroup has most benefits from which type of telemonitoring.

	N= 55	N= 23	N= 20	N= 14	N= 12	N= 7	N= 1
Historical	N= 55	N= 23	N= 20	N= 14	N= 12	N= 7	N= 1
mHealth	N= 55	N= 24	N= 23	N= 17	N= 15	N= 10	N= 1
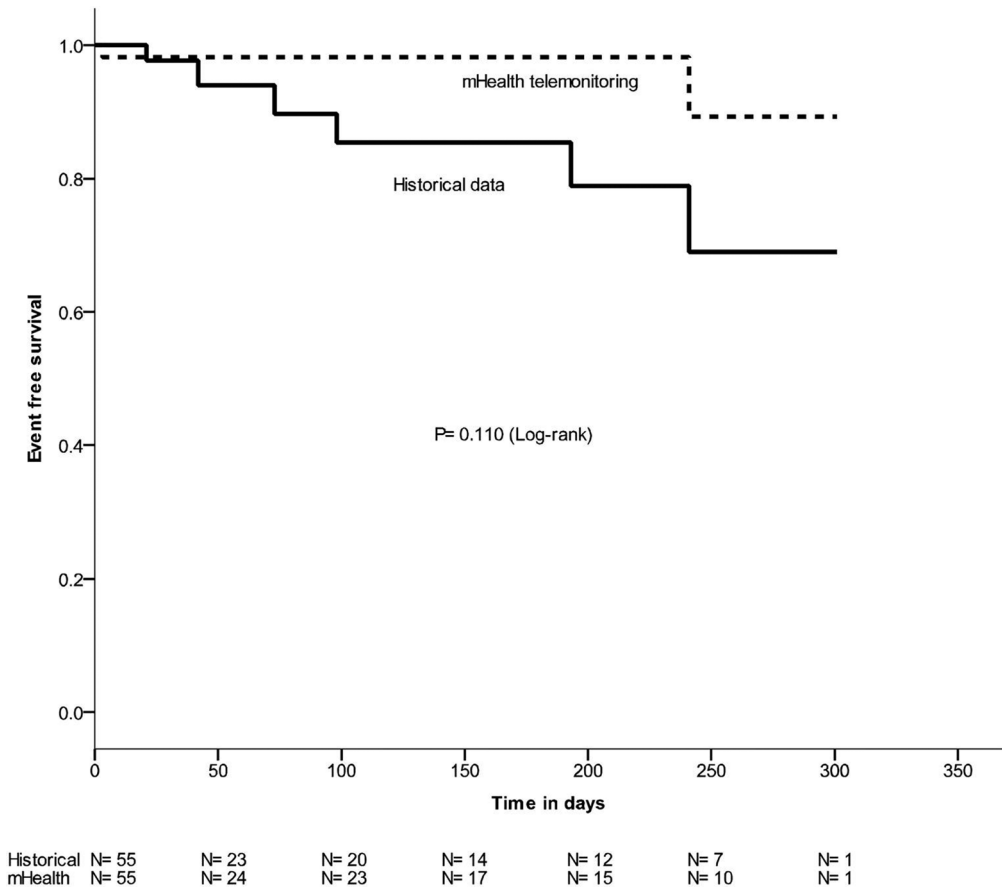
Figure 2 Event-free survival of patients with adult congenital heart disease (*dotted line* events during m-Health telemonitoring, *straight line* events in historical data).

Figure 3 Patient-reported outcome measures (*light blue* baseline, *blue* 3 months, *dark blue* 6 months). Baseline is set as median. (*Selfmanagement* PAM-13, *quality of life, general* EQ-5D-5L, *Safety* CaReQoL safety, *Physical* CaReQoL physical restrictions, *Social and emotional* CaReQoL social and emotional)

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Figure 4 176 rhythms in 17 patients during palpitations in the first 3 months, *n*=number, %.

Table 2 Reasons for refusing consent.

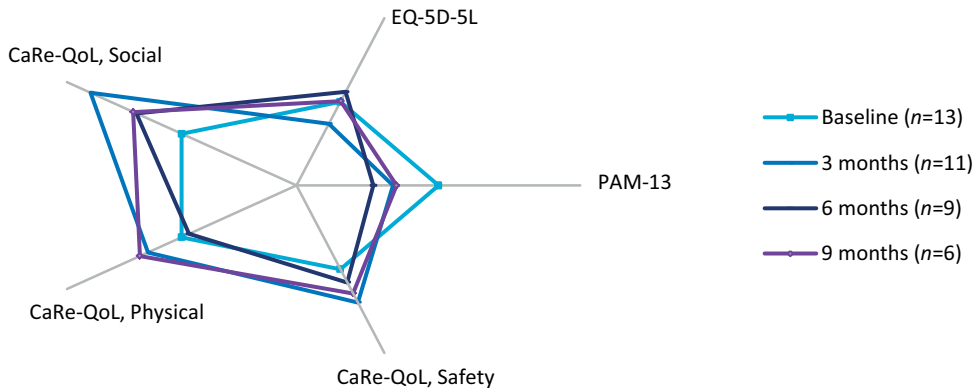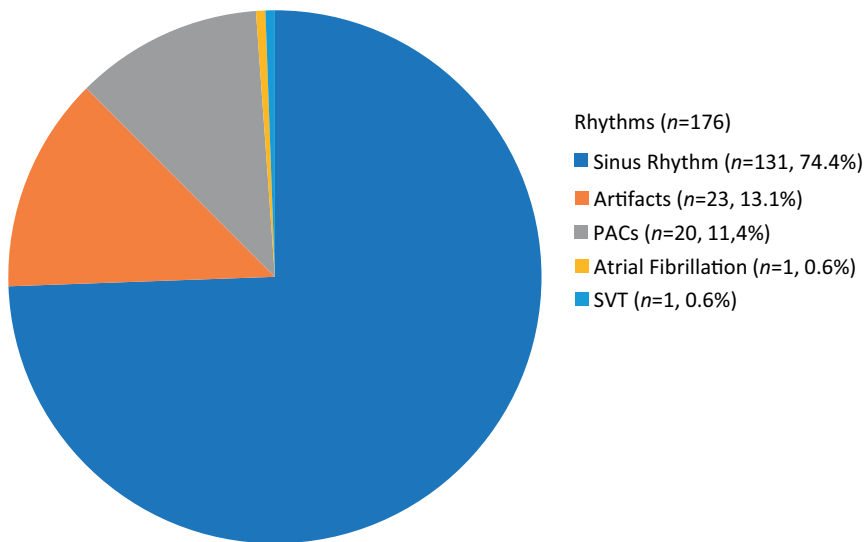| Reasons	Number (%)
Too time consuming to participate in research	30 (40.5)
Too time consuming to monitor vital signs	14 (18.9)
Cost of health insurance deductibles	5 (6.8)
Expected decrease in quality of life	17 (23.0)
No mobile device	0 (0)
Emigration	1 (1.4)
Other	7 (9.5)
Total	74

Table 3 Baseline characteristics.

Characteristics	Total patients (*n*=55)	Heart failure (*n*=22)	palpitations or arrhythmia (*n*= 43)	Hypertension (*n*=8)
Median age (years)	45 (19 to 70)	45.5 (19 to 66)	45 (21 to 70)	60 (32 to 70)
Male (%)	19 (34.5)	9 (40.9)	14 (32.6)	4 (50.0)
Severity of CHD				
Mild (%)	6 (10.9)	0 (0)	6 (14.0)	2 (25.0)
Moderate (%)	29 (52.7)	12 (54.5)	21 (48.8)	4 (50.0)
Severe (%)	20 (36.4)	10 (45.5)	16 (37.2)	2 (25.0)
History of cardiac surgery (%)	52 (94.5)	22 (100)	40 (93.0)	8 (100)
Pacemaker (%)	11 (20.0)	6 (27.3)	10 (23.3)	1 (12.5)
Arrhythmia at baseline (%)	43 (78.2)	10 (45.5)	43 (100)	6 (75.0)
NYHA class				
II (%)	17 (30.9)	17 (77.3)	6 (14.0)	2 (25.0)
III (%)	5 (9.1)	5 (22.7)	4 (9.3)	1 (12.5)
IV (%)	0 (0)	0 (0)	0 (0)	0 (0)
Symptoms				
Palpitations (%)	31 (56.4)	5 (22.7)	31 (72.1)	5 (62.5)
Dyspnoea (%)	8 (14.5)	7 (31.8)	4 (9.3)	0 (0)
Chest pain (%)	4 (7.3)	1 (4.5)	4 (9.3)	0 (0)
Near collapse (%)	2 (3.6)	2 (9.1)	2 (4.7)	0 (0)
Dizziness (%)	7 (12.7)	4 (18.2)	7 (16.3)	1 (12.5)
No symptoms (%)	15 (27.3)	8 (36.4)	7 (16.3)	3 (37.5)

Characteristics	Total patients (*n*=55)	Heart failure (*n*=22)	palpitations or arrhythmia (*n*= 43)	Hypertension (*n*=8)
RV function				
Poor (%)	3 (5.5)	1 (4.5)	3 (7.0)	0 (0)
Moderate (%)	16 (29.1)	8 (36.4)	13 (30.2)	6 (75.0)
Good (%)	36 (65.5)	13 (59.1)	27 (62.8)	2 (25.0)
Medication				
Antiarrhythmics(%)	35 (63.6)	14 (63.6)	31 (72.1)	8 (100)
Diuretics (%)	12 (21.8)	10 (45.5)	9 (20.9)	2 (25.0)
Anticoagulation (%)	28 (50.9)	8 (36.4)	27 (62.8)	5 (62.5)

* Data are number of patients (percentage), median (range) or mean (± standard deviation)

CHD; congenital heart disease, NYHA; New York Heart Association, RV; Right ventricle

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DISCUSSION

The study is the first prospective study that evaluates telemonitoring through a comprehensive m-Health program in adult patients with CHD. The program is well used by symptomatic adults with CHD. The program is feasible with a high adherence.

Data on telemonitoring in patients with heart failure are still conflicting [10-13]. Several meta-analyses suggest clinical and economic benefits, but numerous prospectively initiated clinical trials have not confirmed these findings [12,14]. Reasons for the lack of success could be classified into six dimensions: clinical, economic, user perspective, educational, organisational, and technical [20,25-27]. A meta-analysis of 16 high-quality randomised controlled trials showed that telemonitoring overall yields hardly any significant improvement for the average patient. However, interventions based on personalised coaching and feedback have been associated with successful results [27]. The purpose of the unique infrastructure of our m-Health telemonitoring program (HartWacht) is to overcome limitations mentioned in these earlier studies in order to improve the benefits. This program consists of apps on patients' mobile devices, wireless attached to devices for measuring heart rhythm, body weight and blood pressure, controlled by a dedicated team of cardiac care nurses and cardiologists. Results are directly shown in the patient's EMR. The treating physician could easily find an overview of measurements and therapy in the EMR and this is also true for the PROMs. This makes performing measurements relatively

uncomplicated and accessible for every patient with a mobile device. It enables instant feedback to the patient. If measurements are normal they are reassured by the app and if not, as judged by a dedicated team of well-trained nurses and cardiologists, patients receive quick and reliable feedback when they experience symptoms. The feedback could be adjustment of treatment and/or reassurance. The effect of these interventions may be recognised by the patient while using the app. This could even be true for patients who are already known and being treated for arrhythmias by medication or pacemaker. If these patients suspect a deterioration of the arrhythmia they are able to take immediate action to monitor their heart rhythm and get a direct response.

The program seems to be feasible and the program was well used by our patient cohort. Our recent questionnaire study demonstrated that 75% of all patients responded that they were willing to use telemonitoring. Interestingly, only 43% of all invited patients, however, decided to participate in this program. Predominantly patients refused consent because of the time-consuming nature of participating in research. Another reason was financial, as participation would cost these patients their own health insurance deductibles. A substantial number of patients not willing to participate in this study reported that they expected a decrease of their quality of life by m-Health monitoring. This could be due to the fact that telemonitoring is time-consuming and/or confronts patients with their illness on a more frequent basis.

We postulate that careful patient selection and a program design that not only collects a huge amount of data, but is also integrated within the EMR and supports, if necessary, immediate contact between patient and treating physician might improve healthcare for these patients.

This study has several limitations. The number of patients included so far is small and follow-up duration is still short. This is a single-centre study; more participating centres are needed. The study lacks a control group, however patients are their own controls (based on retrospective historical data). Selection bias by indication could play an important role as documented arrhythmias were one of the inclusion criteria. This could potentially imply that the patient population would be more prone to be admitted for arrhythmias in the last year before inclusion. These patients could have received appropriate antiarrhythmic drug therapy leading to a reduction in visits to the emergency department during follow-up. The adult CHD population is very diverse and the degree of disease burden varies per diagnosis and per patient [28,29]. Therefore, the role of m-Health telemonitoring for specific subgroups of adult CHD

patients cannot yet be determined from the present data. So far we have not compared costs of the HartWacht program with standard care. Equality of clinical results with historical data versus telemonitoring can still be of interest if the costs of the program are lower compared with standard care. Moreover, ECGs taken in patients with symptoms could not always be distinguished from routinely performed ECGs. Furthermore, a larger participation rate was expected. Eligible patients refused to participate for different reasons. Lessons learned from our experience with this study, for instance on measurement intensity, could be used to improve the program and effect of these improvements will be the subject of following studies.

CONCLUSION

A new m-Health telemonitoring program evaluating arrhythmia, heart failure and blood pressure is well used by symptomatic adults with CHD. The relatively young population of adults with CHD demonstrated a high adherence. m-Health telemonitoring might be a powerful tool for diagnosing and managing arrhythmias and heart failure. It can also be useful for adjusting antihypertensive medication in order to reach optimal blood pressure in real-life circumstances. This could result in better quality of healthcare in this patient group. However, randomised control trials are needed to prove this hypothesis.

WHAT'S NEW?

- m-Health seems a very promising new tool for telemonitoring of adult patients with CHD.
- m-Health is well used by adult patients with CHD.
- m-Health is a valuable instrument to give patients immediate feedback and personalized coaching.
- m-Health results shown directly in the electronic medical records overcomes limitations mentioned in first-generation telemonitoring.

Conflict of interest

D.A.J. Dohmen, A.G. Somsen and I.I. Tulevski are shareholders in ventures supplying hardware and software implemented in the methods of this study. M.A.C. Koole, D. Kauw, M.M. Winter, R. de Haan, M.P. Schijven, D. Robbers-Visser, B.J.M. Mulder, B.J. Bouma and M.J. Schuuring declare that they have no competing interests.

REFERENCES

1. Warnes CA, Liberthson R,Danielson GK, et al. Task force 1: the changing profile of congenital heart disease in adult life. *JAmCollCardiol.* 2001;37:1170–5.

2. Moons P, Bovijn L, Budts W, Belmans A, Gewillig M. Temporal trends in survival to adulthood among patients born with congenital heart disease from 1970 to 1992 in Belgium. *Circulation.* 2010;122:2264–72.

3. Baumgartner H, Bonhoeffer P, De Groot NMS, et al. ESC Guidelines for the management of grown-up congenital heart disease (new version 2010). *Eur Heart J.* 2010;31:2915–57.

4. Schuuring MJ, van Gulik EC, Koolbergen DR, et al. Determinants of clinical right ventricular failure after congenital heart surgery in adults. *J Cardiothorac Vasc Anesth.* 2013;27:723–7.

5. Zomer AC, Vaartjes I, van der Velde ET, et al. Heart failure admissions in adults with congenital heart disease; risk factors and prognosis. *Int JCardiol.* 2013;168:2487–93.

6. van der Bom T, Zomer AC, Zwinderman AH, Meijboom FJ, Bouma BJ, Mulder BJM. The changing epidemiology of congenital heart disease. *NatRevCardiol.* 2011;8:50–60.

7. Schuuring MJ, van Riel ACMJ, Vis JC, et al. New predictors of mortality in adults with congenital heart disease and pulmonary hypertension: midterm outcome of a prospective study. *Int JCardiol.* 2015;181:270–6.

8. Dickstein K, Cohen-Solal A, Filippatos G, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2008: the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2008 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association of the ESC (HFA) and endorsed by the European Society of Intensive Care Medicine(ESICM). *EurHeart J.* 2008;29:2388–442.

9. Jayaram NM, Khariton Y, Krumholz HM, et al. Impact of telemonitoring on health status. *CircCardiovascQualOutcomes.* 2017; https://doi.org/10.1161/CIRCOUTCOMES. 117.004148.

10. Anker SD, Koehler F, Abraham WT. Telemedicine and remote management of patients with heart failure. *Lancet.* 2011;378:731–9.

11. Koehler F, Winkler S, Schieber M, et al. Impact of remote telemedical management on mortality and hospitalizations in ambulatory patients with chronic heart failure: the telemedical interventional monitoring in heart failure study. *Circulation.* 2011;123:1873–80.

12. Chaudhry SI, Mattera JA, Curtis JP, et al. Telemonitoring in patients with heart failure. *NEngl JMed.* 2010;363:2301–9.

13. Veenstra W, Op den Buijs J, Pauws S, Westerterp M, Nagelsmit M. Clinical effects of an optimised care program with telehealth in heart failure patients in a community hospital in the Netherlands. *NethHeart J.* 2015;23:334–40.

14. Seto E. Cost comparison between telemonitoring and usual care of heart failure: a systematic review. *TelemedJEHealth.* 2008;14:679–86.

15. Treskes R.W., Koole M, Winter MM, et al. Adults with congenital heart disease: ready for mobile health? *Neth Heart J* (2019) 27:152–160 doi: 10.1007/s12471-019-1237-2

16. Schuuring MJ, Backx AP, Zwart R, et al. Mobile health in adults with congenital heart disease: current use and future needs. *NethHeart J.* 2016;24:647–52.

4

17. Cowie MR, Bax J, Bruining N, et al. e-Health: a position statement of the European Society of Cardiology. *Eur Heart J.* 2016;37:63–6.

18. Schoormans D, Sprangers MA, van Melle JP, et al. Clinical and psychological characteristics predict future health care use in adults with congenital heart disease. *Eur JCardiovasc Nurs.* 2016;15:72–81.

19. Schuuring M, van Gulik C, Koolbergen D, et al. Determinants of clinical right ventricular failure after congenital cardiac surgery in adults. *J CardiothorVasc Anesth.* 2013;27:723–7.

20. Schuuring MJ, Vis JC, van Dijk APJ, et al. Impact of bosentan on exercise capacity in adults after the Fontan procedure: a randomized controlled trial. *Eur JHeart Fail.* 2013;15:690–8.

21. Halcox JPJ, Wareham K, Cardew A, et al. Assessment of remote heart rhythm sampling using the aliveCor heart monitor to screen for atrial fibrillation: the REHEARSE-AF study. *Circulation.* 2017;136:1784–94.

22. Janssen MF, Pickard AS, Golicki D, et al. Measurement properties of the EQ-5D-5L compared to the EQ-5D-3L across eight patient groups: a multi-country study. *QualLifeRes.* 2013;22:1717–27.

23. Hibbard JH, Mahoney ER, Stockard J, Tusler M. Development and testing of a short form of the patient activation measure. *HealthServRes.* 2005;40:1918–30.

24. van Kessel P, de Boer D, Hendriks M, Plass AM. Measuring patient outcomes in chronic heart failure: psychometric properties of the Care-Related Quality of Life survey for Chronic Heart Failure (CaReQoL CHF). *BMC Health ServRes.* 2017;17:536.

25. Swedberg K, Wolf A, Ekman I. Telemonitoring in patients with heart failure. *NEngl JMed.* 2011;364:1078. author reply p:1079–80.

26. Farnia T, Jaulent M-C, Steichen O. Evaluation criteria of noninvasive telemonitoring for patients with heart failure: systematic review. *JMedInternetRes.* 2018;20:e16.

27. Noah B, Keller MS, Mosadeghi S, et al. Impact of remote patient monitoring on clinical outcomes: an updated meta-analysis of randomized controlled trials. *Npj Digit Med.* 2018;1:2.

28. Schoormans D, Mulder BJM, van Melle JP, et al. Illness perceptions of adults with congenital heart disease and their predictive value for quality of life two years later. *Eur J CardiovascNurs.* 2014;13:86–94.

29. Fteropoulli T, Stygall J, Cullen S, Deanfield J, Newman SP. Quality of life of adult congenital heart disease patients: a systematic review of the literature. *Cardiol Young.* 2013;23:473–85.

Chapter 5

Advantages of mobile health in the management of adult patients with congenital heart disease

D. Kauw*, M.A.C. Koole*, M.M. Winter, D.A.J. Dohmen, I.I. Tulevski, S. Blok, G.A. Somsen, M.P. Schijven, J.W.J. Vriend, D. Robbers-Visser, B.J.M. Mulder, B.J. Bouma, M.J. Schuuring

*Both authors contributed equally to this work.

ABSTRACT

Background

Adults with congenital heart disease (ACHD) often suffer from deterioration related to cardiac arrhythmias, hypertension (HT) or heart failure (HF), frequently occurring between planned visits. Mobile health (mHealth) could improve management through remote monitoring by enabling swift therapeutic response and detecting new diagnoses.

Methods

We performed a prospective study employing mHealth in ACHD patients, weekly monitoring heart rhythm, weight and blood pressure. In case of consecutive threshold exceeding measurements or in case of new diagnosis, patients were contacted and if needed the treating physician was consulted. Inclusion criteria were: palpitations within the last three years (with or without arrhythmia diagnosis) or HF NYHA class ≥II. We evaluated the detection of recurrences and new diagnosis of arrhythmias, HT and HF, adherence and patient experience (Net Promotor Score (NPS)).

Results

In total, 109 of the 268 invited ACHD patients were enrolled, 80 with palpitations, 13 with HF, 16 experienced both, mean age 45 (±13) years, 33% male. Median follow-up was 12 (Q1–Q3; 9–14) months, 91 patients initiated all measurements (heart rhythm, weight and blood pressure). In 25% of the patients with diagnosed arrhythmias (14/56) recurrences of arrhythmias were detected; 13% of the patients with undiagnosed palpitations (4/32) were diagnosed with novel arrhythmias. In 38% of the patients with HT at baseline (6/16), treatment adjustment was necessary, 4% of the patients without HT (4/76) received novel HT diagnosis. Diuretics were adjusted in 7% of the patients with HF (2/29). Adherence was >70% in 77% of the patients that started weekly measurements (70/91). Patients that were female, older of age and experienced palpitations at inclusion were more likely to acquire an adherence of >70%. NPS was completed by 68 patients, 57 patients (84%) were promotors or neutral, and 11 patients (16%) were critics.

Conclusions

mHealth offers advantages in the management of selected ACHD patients; it enabled early detection of recurrences and new diagnosis of arrhythmias, hypertension and heart failure, which lead to swift therapeutic response or remote reassurance. Furthermore, mHealth was well accepted with high adherence and positive patient experience.

1 INTRODUCTION

Adult patients with congenital heart disease (ACHD) form a growing patient group, as survival has increased in the last decades [1]. However, these patients remain in lifelong follow-up as they often experience complications at a relatively young age such as arrhythmias, hypertension (HT) and heart failure (HF), often resulting in clinical deterioration [2]. As measurements of vital parameters are usually limited to outpatient clinic and hospital visits, asymptomatic cardiac deterioration can remain unnoticed for a long time and in case of symptoms patients have to plan an additional appointment or have to contact or visit the emergency room (ER) in the hospital. This can delay adequate diagnosis and swift initiation of treatment.

Mobile health telemonitoring (mHealth) is rapidly evolving as wearables, mobile health applications (apps) and smartphone possibilities are improving, and increasing in number [3]. mHealth enables frequent monitoring of vital parameters at home and can provide early intervention or reassurance, possibly preventing ER visits and hospital admissions [4]. Previous studies on telemonitoring of heart rhythm, blood pressure and weight in patients with acquired heart disease showed promising results. In patients with atrial fibrillation mHealth provided rapid recognition of atrial fibrillation and subsequently rapid management of the episode, patients with hypertension were treated more effectively and in selected patients with heart failure mHealth significantly reduced mortality [5-7].

ACHD patients seem particularly eligible to benefit from mHealth, as they often experience complications such as arrhythmias, HT and HF, frequently resulting in deterioration and hospital admissions [2]. Furthermore, previous studies showed that the majority of these patients are willing to start using mHealth and that symptomatic patients are most likely to benefit [8,9]. However, data on mHealth in ACHD patients are scarce [10].

Therefore, we performed a prospective study employing an mHealth program in ACHD patients. The aim of this study was to investigate what advantages mHealth offers in the management of these patients and to evaluate the acceptance of mHealth through adherence and patient experience.

5

2 MATERIAL AND METHODS

2.1 Study design and participants

We performed a prospective study in two medical centers in the Netherlands. The local medical ethical committees of both institutions issued a waiver for this study. ACHD patients were eligible for inclusion if they met the inclusion criteria: Palpitations within the last three years (with or without arrhythmia diagnosis) or HF NYHA class ≥II, and possession of a mobile device. Patients with impaired cognition, as assessed by their treating physician, tremors or patients with an insurance not covering costs of the mHealth program, were excluded. Patients were recruited from the outpatient clinic and clinical wards. After informed consent for the use of their clinical data was acquired, patients were enrolled in the mHealth program.

2.2 mHealth program

The mHealth program required routinely evaluation of heart rhythm, blood pressure and body weight [11]. Measurements were performed at home using a wireless pocket-sized single lead EKG recording device that could record a 30 s single lead EKG (Kardia, AliveCor), wireless digital blood pressure monitor (Omron) and a wireless and digital weight scale (i-Health), connected to their smartphone. Two mobile applications (apps) were used, for heart rhythm recordings (Kardia [12]) and blood pressure and weight (CVitals). Results were integrated in the EMR of the patient and also available for the patients in the apps. At the start of the program, patients received instructions by telephone for the medical devices and corresponding apps and were asked to perform daily measurements for seven days to establish reference values. After the first week, a single lead EKG was recorded once every month and blood pressure and weight were measured twice every week. Patients could perform extra measurements in case of symptoms. However, at the start of the study it was emphasized that the program was not intended for emergency care.

2.3 Protocol mHealth program

Blood pressure and weight measurements were only analyzed in case of consecutive threshold exceeding measurements. All EKGs and measurements exceeding a threshold were analyzed daily on weekdays by trained nurses, Analysis of all measurements for each patient takes approximately a single minute per EKG and similar for weight and blood pressure measurements. Sinus bradycardia was defined as a heart rate of <50 beats per minute and sinus tachycardia was defined as a heart rate of >100 beats per minute; the thresholds for blood pressure were

140 mmHg for systolic blood pressure (SBP) and 90 mmHg for diastolic blood pressure (DBP). The threshold for body weight was personalized for every patient. After the first week the mean weight was calculated and the threshold was set two kilograms above the mean. These thresholds were only modified in consultation with the treating physician. If an arrhythmia was recorded, recurrent or novel, the patient would be contacted for additional information and the frequency of measurements would be intensified and if needed the treating physician would be consulted. The app for weight and blood pressure would generate an alarm if a threshold was exceeded. In case of two consecutive alarms, the patient would also be contacted for additional information. Furthermore, they received life style advice, measurement instructions and were asked to perform daily measurements for seven days. When HF signs and symptoms were present in case of two consecutive weight alarms, the treating physician or specialist nurse would be consulted for treatment adjustments. If hypertension persisted after life style advice and measurement instructions, the treating physician would be consulted for treatment adjustments. Participation in the current mHealth program was reimbursed by the majority of health insurance companies in the Netherlands. Patients without reimbursement did not participate in the study.

2.4 Adherence and patients experience

Adherence was evaluated using the weekly measurements of weight and blood pressure. Adherence rates of >70% were assessed as sufficient for monitoring [7]. Patients experience was evaluated through the Net Promotor Score (NPS), which lets patients rate from 0 to 10 to which extent they would recommend the use of the mHealth program to a friend or colleague [13]. After 6 months of follow-up patients were asked fill in the NPS questionnaire. Patients with a score of 9–10 were promotors, 7–8 were neutrals and 0–6 were critics. The NPS was calculated by subtracting the percentage of critics from the percentage of promotors.

2.5 Outcomes

The primary outcome measures of this study were interventions made based on mHealth data in case of recurrences of arrhythmias, HT or HF and the detection of new diagnoses of arrhythmias and HT. This program was not set-up for establishing new diagnoses of HF. A cardiac arrhythmia was considered a new diagnosis if the arrhythmia had not been previously recorded. Recurrences of arrhythmias were defined as an mHealth recording of previously identified arrhythmias. An episode of HT in our study was defined as three or more consecutive measurements of a SBP of ≥140 mmHg or DBP of ≥90 mmHg. HT was considered a new diagnosis if this had not been previously detected during outpatient clinic visits and no previous treatment was initiated for

HT. Secondary outcome measures were adherence and patients experience measured by the NPS score.

2.6 Data and statistical analysis

All data were extracted from the EMR of each patient and pseudonymized. Data were managed and stored respecting the FAIR (Findable–Accessible–Interoperable–Reusable) principles [14]. Analyses were performed using SPSS version 25 (IBM, Armonk, New York). Chi-square test or independent *t*-test were used to assess differences between patients with an adherence of higher or lower than 70%.

3 RESULTS

3.1 Participants

We screened patients for eligibility from June 2017 until December 2018 and 268 patients with ACHD from two medical centers in the Netherlands were invited to participate in this study. In total, 109 patients were enrolled, of whom 98 started with monthly heart rhythm recordings and 91 with weekly blood pressure and weight measurements (Figure 1). Mean age was 44.8 (±13.1) years and 33% were male (Table 1). The primary diagnoses of the patients are summarized in Supplementary Table 1. Follow-up started in June 2017 and ended in May 2019 with a median follow-up of 12 (Q1–Q3; 9–14) months. Reasons for patients to decline consent (*n*=159) were 1) Lack of time or interest to participate in research (72, 48%) and 2) Fear of experiencing stress due to frequently performing measurements (47, 32%).
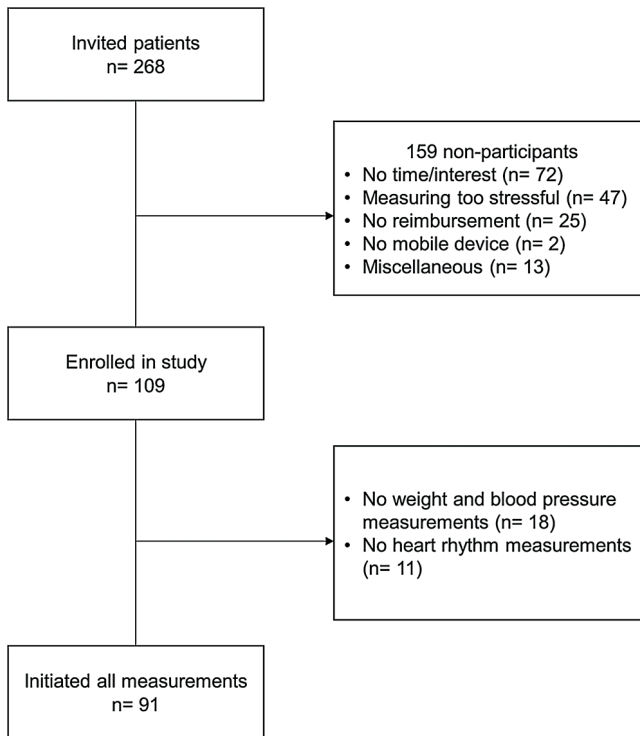
Figure 1 Flowchart for the study population.

3.2 Heart rhythm

A total of 5547 single-lead EKGs were recorded by 98 patients, 56 patients with documented arrhythmias, 31 patients with palpitations without a documented arrhythmia and 11 patients with no previous complaints of palpitations. Of these EKGs, 2925 were recorded by 90 patients during episodes of palpitations with a median of 16 (Q1–Q3; 8–37) recordings per patient. These recordings predominantly showed sinus rhythm (1616/2925, 55%). In 25% of the patients (14/56) with previous arrhythmia diagnosis, recurrences of arrhythmias could be confirmed during palpitations and treatment initiated. In 13% of the patients (4/32) with previous palpitations but without diagnosis that performed EKG measurements, a new arrhythmia was found. In patients without prior palpitations no significant arrhythmias were found. Atrial fibrillation (AF) was the most frequently recorded clinically significant arrhythmia in both groups (Figure 2A and B). Noise was recorded in 3% (174/5547) of all EKGs. All patients that experienced sinus rhythm or benign PACs and PVCs during complaints were remotely reassured. An example of the implications of mHealth on the management of a patient is displayed in Supplementary Figure 1A.

Table 1 Baseline characteristics.

Characteristics	Total patients (*n*=109)*	
Age (years)	44.8	±13.1
Male	36	33%
Severity of CHD		
Mild	25	23%
Moderate	50	46%
Severe	34	31%
History of cardiac surgery	93	85%
Pacemaker	17	16%
Cardiac arrhythmias	61	56%
Palpitations without diagnosis	35	32%
Hypertension at baseline	16	15%
NYHA class		
I	80	73%
II	24	22%
III	5	5%
IV	0	0%
Medication		
Anti-arrhythmics	63	58%
Diuretics	17	16%
Anticoagulation	49	45%
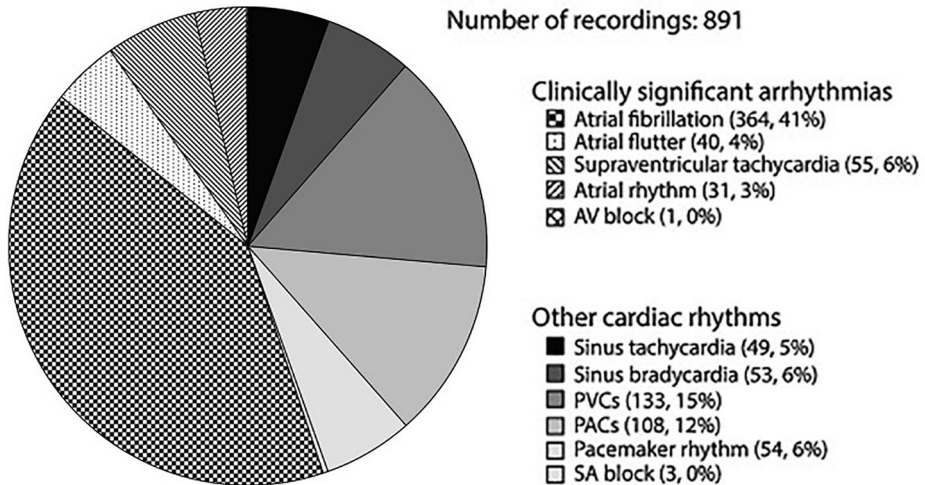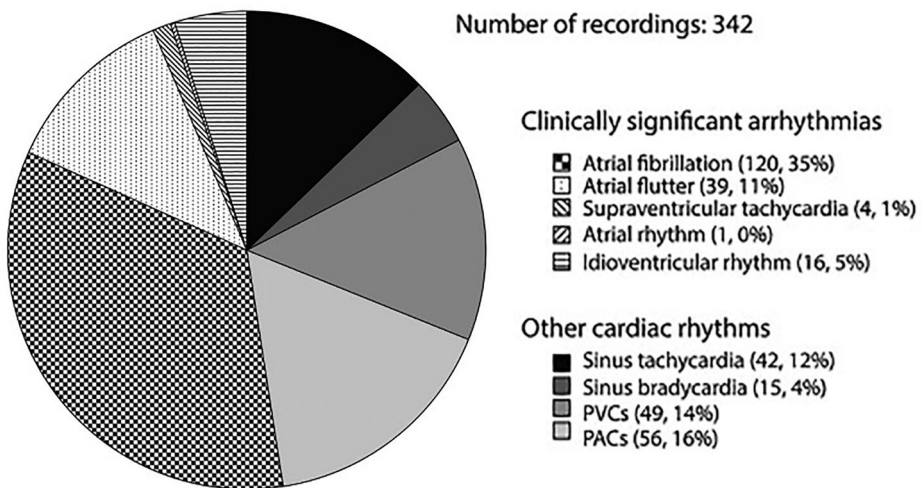
Figure 2 Recordings during palpitations.

A: Recordings of patients with previous arrhythmia diagnosis.
Sinus rhythm *n*=1027, 52%, only noise *n*=41, 2%.
B: Recordings of patients without previous arrhythmia diagnosis.
Sinus rhythm *n*=388, 53%, only noise *n*=11, 1,5%.
Recordings with sinus rhythm and only noise were excluded from these figures.
PVC: Premature ventricular contraction.
PAC: Premature atrial contraction.
AV: Atrioventricular.
SA: Sinoatrial.

3.3 Blood pressure

A total of 8350 blood pressure measurements were performed by 91 patients with a median of 88 (Q1–Q3; 58–119) measurements per patient. Of the 16 patients with HT at baseline, 15 regularly performed measurements, 1 patients experienced difficulties using the devices. Of the 93 patients without HT, 76 regularly performed blood pressure measurements. Eight patients dropped out before starting measurements, 4 never initiated measurements and 5 were just enrolled and were still setting up the devices. In 38% of the patients with HT at baseline (6/16) treatment was adjusted and in 2 patients, blood pressure restored to normal after lifestyle advice. In Supplementary Fig. 1B mHealth interventions are displayed in a patient with HT who had multiple episodes of HT.

3.4 Heart failure

During follow-up, a total of 7984 body weight measurements were performed by 91 patients with a median of 82 (Q1–Q3; 56–117). Seventeen patients did not start weight pressure measurements, 8 patients dropped out before starting measurements, 4 patients never started using the measurement devices and 5 patients were still setting up the measurement devices. In 2 of the 29 patients (7%) with HF NYHA class ≥II at baseline the diuretics were adjusted as a weight gain of ≥2 kg and additional signs and symptoms of HF were detected through mHealth and telephone contact.

3.5 New diagnoses

In 8 patients new diagnoses were established through mHealth; 4 patients received novel arrhythmia diagnosis, 4 patients received novel HT diagnosis (Supplementary Table 2), all patients previously underwent regular diagnostic methods with no resulting diagnosis. Of the 109 enrolled patients, 48 patients did not have prior arrhythmia diagnosis, 35 of whom experienced palpitations in the past three years and 32 regularly performed single lead EKGs. In 13% (4/32) of the patients that experienced palpitations without prior arrhythmia diagnosis and performed EKGs, new diagnoses were established during follow-up through mHealth. In 3 patients AF was registered and in 1 patient sinus node dysfunction was identified. Of the 94 patients without HT, 76 patients regularly performed blood pressure measurements, of whom 4 patients (4%) received new HT diagnosis. No false-positive diagnoses were found during follow-up.

3.6 Adherence and patient experience

Adherence of more than 70% was registered in 77% of the patients (70/91). Patients with an adherence of 70% or higher were more likely to be female, older of age, have palpitations at baseline (with or without a previously identified arrhythmia), have a pacemaker in situ, use anti-arrhythmic drugs and have experienced a clinical event during follow-up (Supplementary Table 3). The NPS questionnaire was completed by 72% (68/95) of the patients that received the NPS questionnaire, 57 patients (84%) were promotors (score 9–10) or neutral (score 7–8), and only 11 patients (16%) were critics (score 0–6), resulting in a total NPS of + 18 for this mHealth program.

4 DISCUSSION

This study is the first to show twelve months follow-up of mobile health in selected ACHD patients. mHealth in these patients offers multiple advantages by providing rapid detection of hypertension, recurrences of arrhythmias and heart failure, and enabling swift intervention. Furthermore, mobile health establishes new diagnoses of arrhythmias and hypertension. This mHealth program was well accepted with a high adherence rate and positive patient experience. ACHD patients often experience cardiac arrhythmias and these arrhythmias are an important cause of unplanned hospital admissions and morbidity [15]. Previous studies showed that regular diagnostic methods in ACHD patients, such as Holter monitoring, often fail to establish diagnoses, as symptoms frequently do not occur during Holter monitoring [16]. In contrast, mHealth provided on demand recordings of heart rhythm during palpitations, enabling swift diagnosis and treatment or remote reassurance, possibly preventing unplanned visits to the hospital.

In our study, in 38% of the patients with HT at baseline (6/16), treatment adjustments were necessary during follow-up as episodes of HT were detected through mHealth. This emphasizes that the management of arterial HT through the outpatient clinic remains cumbersome and over- and undertreatment occurs as blood pressure is only measured during hospital visits. mHealth provides benefits in the treatment of HT by enabling more continuous monitoring of blood pressure at home [17].

In this study the number of patients with HF was limited with 27% of the patients (29/109) experiencing HF NYHA class ≥II at baseline. The majority of these patients were under follow-

up of a specialized HF nurse, organized through frequent contact moments and consultations. Usual care by the nurse included daily weight measurements and the instruction to contact the nurse in case of weight gain or symptoms. The mHealth program only required two weight measurements per week, this might explain the small number of interventions made based on mHealth data in patients with HF in our study. However, in patients with less frequent follow-up and in more remote areas, mHealth could be a valuable tool as telemonitoring has shown to be effective in selected patients with HF [7].

Our study demonstrated an adherence rate that was similar to previous studies [18,19]. Interestingly, patients who experienced clinical events during follow-up were more adherent to the program. This emphasizes that adequate patient selection for telemonitoring seems essential as was also demonstrated by Koehler et al. in the TIM-HF2 trial. In patients, hospitalized for HF less than a year before inclusion, telemonitoring demonstrated a reduction of all-cause mortality and days lost due to unplanned cardiovascular hospital admissions [7].

This study is limited by the lack of a control group, this hampered evaluation of the effect of mHealth on clinical outcomes such as emergency hospital visits and admissions. Randomized controlled trials are therefore warranted to further evaluate the effects of mHealth in ACHD patients, other important outcomes including quality of life and costs of the mHealth intervention should be further evaluated. Only patients with a health insurance covering the costs of the mHealth program were included and the number of patients that declined participation was greater than the number of participants due to no interest or time, possibly introducing a systemic bias. Furthermore, this study population of ACHD patients was very heterogeneous as all complexities of CHD were included in this study and severity of disease differed greatly, possibly introducing a great heterogeneity in outcomes.

4.1 Conclusion

In this pilot study, we showed that the use of mHealth offers multiple advantages in selected ACHD patients; it enabled early detection of recurrences and new diagnoses of arrhythmias, hypertension and heart failure and enabled swift therapeutic response. As mHealth was also well accepted by these patients with high adherence and positive patient experience, mHealth could play a significant role in the management of this patient group.

Disclosures

Funding sources

5

SUMMARY TABLE

What was already known?

- Mobile health has shown promising results in patients with acquired disease.
- Only little data is available on mobile health in adult patients with congenital heart disease.

What this study added to our knowledge

- Mobile health provides more continuous care and remote reassurance for adult patients with congenital heart disease, a patient group with high mortality and morbidity.
- Mobile health in adult patients with congenital heart disease provides clinical benefits such as establishing new diagnosis and quick detection of recurrences of arrhythmias enabling rapid treatment.
- Mobile health in patients with hypertension can aid to optimize medical treatment.
- Mobile health is well accepted in adult patients with congenital heart disease, especially in patients that experienced clinical events.
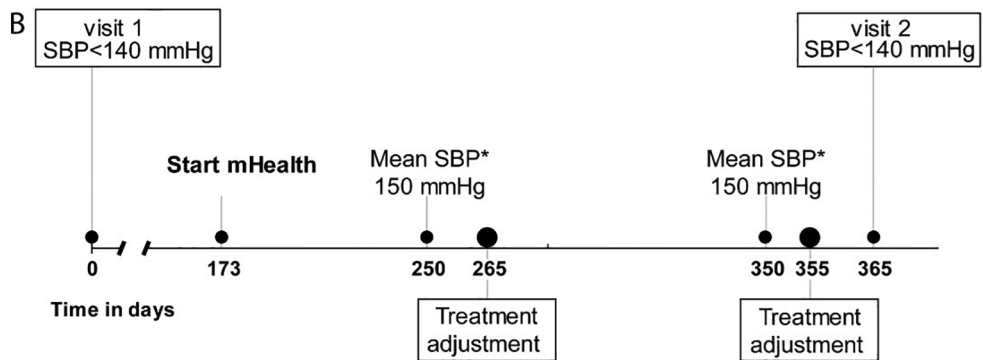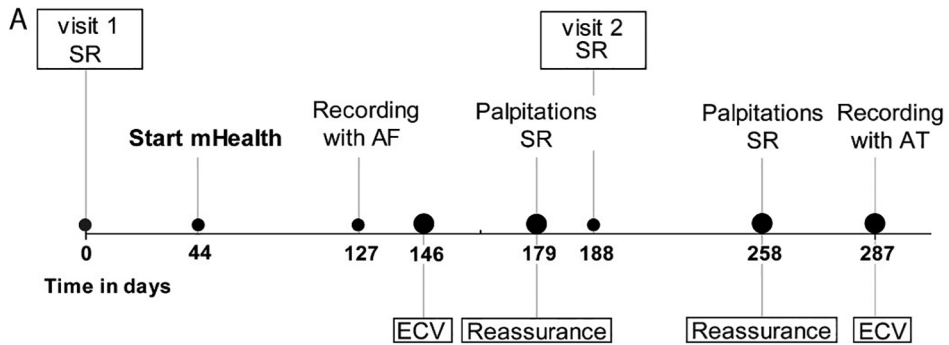
Acknowledgements

REFERENCES

1. T. van der Bom, A.C. Zomer, A.H. Zwinderman, F.J. Meijboom, B.J. Bouma, B.J.M. Mulder, The changing epidemiology of congenital heart disease. *Nat. Rev. Cardiol.* 8(2011):50–60, https://doi.org/10.1038/nrcardio.2010.166.

2. H. Baumgartner, P. Bonhoeffer, N.M.S. De Groot, F. de Haan, J.E. Deanfield, N. Galie, M.A. Gatzoulis, C. Gohlke-Baerwolf, H. Kaemmerer, P. Kilner, F. Meijboom, B.J.M. Mulder, E. Oechslin, J.M. Oliver, A. Serraf, A. Szatmari, E. Thaulow, P.R. Vouhe, E. Walma, Task Force on the Management of Grown-up Congenital Heart Disease of the European Society of Cardiology (ESC), Association for European Paediatric Cardiology (AEPC), ESC Committee for Practice Guidelines (CPG), ESC Guidelines for the management of grown-up congenital heart disease (new version 2010). *Eur. Heart J.* 31(2010): 2915–2957, https://doi.org/10.1093/eurheartj/ehq249.

3. S.R. Steinhubl, E.D. Muse, E.J. Topol, The emerging field of mobile health. *Sci. Transl. Med.* 7(2015) 283rv3, https://doi.org/10.1126/scitranslmed.aaa3487.

4. N. Bruining, E. Caiani, C. Chronaki, P. Guzik, E. van der Velde, Task Force of the e-Cardiology Working, Acquisition and analysis of cardiovascular signals on smartphones: potential, pitfalls and perspectives: by the Task Force of the e-Cardiology Working Group of European Society of Cardiology. *Eur. J. Prev. Cardiol.* 21(2014):4–13, https://doi.org/10.1177/2047487314552604.

5. J. Shacham, E.Y. Birati, N. Malov, Y. Yanay, D.M. Steinberg, M. Tamari, M. Golovner, A. Roth, Telemedicine for diagnosing and managing paroxysmal atrial fibrillation in outpatients, The phone in the pocket. *Int. J. Cardiol.* 157(2012):91–95, https://doi.org/ 10.1016/j.ijcard.2010.12.014.

6. R.J. McManus, J. Mant, M. Franssen, A. Nickless, C. Schwartz, J. Hodgkinson, P. Bradburn, A. Farmer, S. Grant, S.M. Greenfield, C. Heneghan, S. Jowett, U. Martin, S. Milner, M. Monahan, S. Mort, E. Ogburn, R. Perera-Salazar, S.A. Shah, L.-M. Yu, L. Tarassenko, F.D.R. Hobbs, TASMINH4 investigators, Efficacy of self-monitored blood pressure, with or without telemonitoring, for titration of antihypertensive medication (TASMINH4): an unmasked randomised controlled trial, *Lancet Lond. Engl.* 391(2018): 949–959, https://doi.org/10.1016/S0140-6736(18):30309-X.

7. F. Koehler, K. Koehler, O. Deckwart, S. Prescher, K. Wegscheider, B.-A. Kirwan, S. Winkler, E. Vettorazzi, L. Bruch, M. Oeff, C. Zugck, G. Doerr, H. Naegele, S. Störk, C. Butter, U. Sechtem, C. Angermann, G. Gola, R. Prondzinsky, F. Edelmann, S. Spethmann, S.M. Schellong, P.C. Schulze, J. Bauersachs, B. Wellge, C. Schoebel, M. Tajsic, H. Dreger, S.D. Anker, K. Stangl, Efficacy of telemedical interventional management in patients with heart failure (TIM-HF2): a randomised, controlled, parallelgroup, unmasked trial. *Lancet Lond. Engl.* 392(2018):1047–1057, https://doi.org/10.1016/ S0140-6736(18):31880-4.

8. M.J. Schuuring, A.P. Backx, R. Zwart, A.H. Veelenturf, D. Robbers-Visser, M. Groenink, A. Abu-Hanna, N. Bruining, M.P. Schijven, B.J. Mulder, B.J. Bouma, Mobile health in adults with congenital heart disease: current use and future needs. *Neth. Heart J. Mon. J. Neth. Soc. Cardiol. Neth. Heart Found.* 24 (2016):647–652, https://doi.org/10.1007/s12471-016-0901-z.

9. R.W. Treskes, M. Koole, D. Kauw, M.M. Winter, M. Monteiro, D. Dohmen, A. Abu-Hanna, M.P. Schijven, B.J. Mulder, B.J. Bouma, M.J. Schuuring, Adults with congenital heart disease: ready for mobile health? *Neth. Heart J. Mon. J. Neth. Soc. Cardiol. Neth. Heart Found.* 27(2019):152–160, https://doi.org/10.1007/s12471-019-1237-2.

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10. D. Kauw, M. Koole, J.R. van Dorth, I.I. Tulevski, G.A. Somsen, M.P. Schijven, D.A.J. Dohmen, B.J. Bouma, B.J.M. Mulder, M.J. Schuuring, M.M. Winter, eHealth in patients with congenital heart disease: a review. *Expert Rev. Cardiovasc. Ther.* 16(2018):627–634, https://doi.org/10.1080/147790 72.2018.1508343.

11. M. Koole, D. Kauw, M.M. Winter, D. Dohmen, I.I. Tulevski, R. de Haan, G.A. Somsen, M.P. Schijven, D. Robbers-Visser, B.J.M. Mulder, B.J. Bouma, M.J. Schuuring, First realworld experience with mobile health telemonitoring in adult patients with congenital heart disease. *Neth. Heart J. Mon. J. Neth. Soc. Cardiol. Neth. Heart Found.* 27(2019):30–37, https://doi.org/10.1007/s12471-018-1201-6.

12. J.P.J. Halcox, K. Wareham, A. Cardew, M. Gilmore, J.P. Barry, C. Phillips, M.B. Gravenor, Assessment of remote heart rhythm sampling using the AliveCor heart monitor to screen for atrial fibrillation: the REHEARSE-AF study. *Circulation* 136(2017):1784–1794, https://doi.org/10.1161/ CIRCULATIONAHA.117.030583.

13. F.F. Reichheld, The one number you need to grow. *Harv. Bus. Rev.* 81(2003):46–54 124.

14. M.D. Wilkinson, M. Dumontier, Ij.J. Aalbersberg, G. Appleton, M. Axton, A. Baak, N. Blomberg, J.-W. Boiten, L.B. da Silva Santos, P.E. Bourne, J. Bouwman, A.J. Brookes, T. Clark, M. Crosas, I. Dillo, O. Dumon, S. Edmunds, C.T. Evelo, R. Finkers, A. Gonzalez-Beltran, A.J.G. Gray, P. Groth, C. Goble, J.S. Grethe, J. Heringa, P.A.C. 't Hoen, R. Hooft, T. Kuhn, R. Kok, J. Kok, S.J. Lusher, M.E. Martone, A. Mons, A.L. Packer, B. Persson, P. Rocca-Serra, M. Roos, R. van Schaik, S.-A. Sansone, E. Schultes, T. Sengstag, T. Slater, G. Strawn, M.A. Swertz, M. Thompson, J. van der Lei, E. van Mulligen, J. Velterop, A. Waagmeester, P. Wittenburg, K. Wolstencroft, J. Zhao, B. Mons, The FAIR Guiding Principles for scientific data management and stewardship. *Sci. Data* 3(2016), https://doi.org/10.1038/ sdata.2016.18.

15. H. Yang, J.M. Kuijpers, J.R. de Groot, T.C. Konings, A. van Dijk, G.Tj. Sieswerda, M.C. Post, B.J.M. Mulder, B.J. Bouma, Impact of atrial arrhythmias on outcome in adults with congenital heart disease. *Int. J. Cardiol.* 248(2017):152–154, https://doi.org/10.1016/j.ijcard.2017.06.073.

16. R.J. Czosek, J. Anderson, P.R. Khoury, T.K. Knilans, D.S. Spar, B.S. Marino, Utility of ambulatory monitoring in patients with congenital heart disease. *Am. J. Cardiol.* 111(2013):723–730, https:// doi.org/10.1016/j.amjcard.2012.11.021.

17. B. Williams, G. Mancia, W. Spiering, E. Agabiti Rosei, M. Azizi, M. Burnier, D.L. Clement, A. Coca, G. de Simone, A. Dominiczak, T. Kahan, F. Mahfoud, J. Redon, L. Ruilope, A. Zanchetti, M. Kerins, S.E. Kjeldsen, R. Kreutz, S. Laurent, G.Y.H. Lip, R. McManus, K. Narkiewicz, F. Ruschitzka, R.E. Schmieder, E. Shlyakhto, C. Tsioufis, V. Aboyans, I. Desormais, ESC Scientific Document Group, 2018 ESC/ESH Guidelines for the management of arterial hypertension. *Eur. Heart J.* 39(2018):3021–3104, https:// doi.org/10. 1093/eurheartj/ehy339.

18. J. Evans, A. Papadopoulos, C.T. Silvers, N. Charness, W.R. Boot, L. Schlachta-Fairchild, C. Crump, M. Martinez, C.B. Ent, Remote health monitoring for older adults and those with heart failure: adherence and system usability. *Telemed. J. E-Health Off. J. Am. Telemed. Assoc.* 22(2016):480–488, https://doi.org/10.1089/tmj.2015.0140.

19. F. Koehler, S. Winkler, M. Schieber, U. Sechtem, K. Stangl, M. Böhm, H. Boll, G. Baumann, M. Honold, K. Koehler, G. Gelbrich, B.-A. Kirwan, S.D. Anker, Impact of remote telemedical management on mortality and hospitalizations in ambulatory patients with chronic heart failure: the telemedical interventional monitoring in heart failure study. *Circulation* 123(2011):1873–1880, https://doi. org/10.1161/CIRCULATIONAHA.111.018473.

SUPPLEMENTARY MATERIAL

A

visit 1
SR

visit 2
SR

Start mHealth

Recording
with AF

Palpitations
SR

Palpitations
SR

Recording
with AT

0   44   127   146   179   188   258   287

Time in days

ECV   Reassurance   Reassurance   ECV

B

visit 1
SBP<140 mmHg

visit 2
SBP<140 mmHg

5

Start mHealth

Mean SBP*
150 mmHg

Mean SBP*
150 mmHg

0   173   250   265   350 355   365

Time in days

Treatment
adjustment

Treatment
adjustment

Supplementary Figure 1 mHealth interventions.

A: Patients with previous arrhythmia diagnosis
SR=Sinus rhythm
AF=Atrial fibrillation
AT=Atrial tachycardia
ECV=Electrical cardioversion
B: Patient with hypertension at baseline
*Mean SBP=mean systolic blood pressure of two weeks (at least 4 measurements)

Supplementary Table 1 Diagnoses of participants.

Diagnosis	n	%
Tetralogy of Fallot	14	12.8
Atrial septal defect	13	11.9
Transposition of the great arteries	13	11.9
Coarctation aortae	12	11
Marfan syndrome	10	9.2
Ventricular septal defect	10	9.2
Native isolated congenital aortic valve disease	7	6.4
Pulmonary valve stenosis	5	4.6
Ebstein's anomaly	4	3.7
Pulmonary atresia	4	3.7
Atrioventricular septal defect	3	2.8
Anomalous pulmonary venous drainage	2	1.8
Persistent ductus arteriosus	2	1.8
Persistent foramen ovale	2	1.8
Double outlet right ventricle	1	0.9
Left isomerism	1	0.9
native isolated congenital mitral valve disease	1	0.9
Tricuspid atresia	1	0.9
Univentricular heart	1	0.9
Other	3	2.8
Total	109	

Supplementary Table 2 Details of patients with new diagnosis.

Patient number	Age (years)	Used diagnostic methods	Days to diagnosis	mHealth diagnosis	intervention
Newly diagnosed cardiac arrhythmias					
5	52	Holter, X-ECG	56	SND	Wait-and-see
21	29	Holter, X-ECG, ER	149	pAF	Wait-and-see
56	58	Holter, X-ECG	262	pAF	medication
58	32	Holter	123	pAF	ECV, medication
Newly diagnosed hypertension					
24	64	GP	126	HT	medication
30	48	X-ECG, ABPM	290	HT	medication
51	46	X-ECG, ABPM	63	HT	GP
86	51	ABPM	136	HT	medication

X-ECG=Exercise stress test
SND=Sinus node dysfunction
ER=Event recorder
pAF=paroxysmal atrial fibrillation
GP=follow-up by general practitioner
HT=Hypertension
ABPM=24-hours ambulant blood pressure monitor

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Supplementary Table 3 Characteristics of patients with adherence >70%.

Variable	Adherence >70% n=70		Adherence <70% n=21		p-value
Age (years)	47	±11	38	±12	0.002
Male	19	27%	11	52%	0.031
CHD severity					0.269
Mild	18	26%	3	14%	
Moderate	34	49%	9	43%	
Severe	18	26%	9	43%	
Palpitations at baseline	65	93%	15	71%	0.008
NYHA class ≥II	20	29%	6	29%	1
Hypertension at baseline	12	17%	3	14%	0.757
Pacemaker in situ	15	21%	0	0%	0.02
Medication					
Diuretics	14	20%	2	10%	0.269
Anticoagulation	36	51%	7	33%	0.145
Anti-arrhythmic drugs	46	66%	8	38%	0.024
Clinical events	20	29%	1	5%	0.023
Net Promotor Score					0.59
Critics (0–6)	10	18%	1	9%	
Neutrals (7–8)	27	47%	7	64%	
Promotors (9–10)	20	35%	3	27%	

* plus-minus values are means ±SD
CHD=Congenital Heart Disease
NYHA=New York Heart Association

Chapter 6

At last, mobile health leading to a diagnosis in a young patient with congenital heart disease

M.A.C. Koole, G.A. Somsen, I.I. Tulevski, M.M. Winter, B.J. Bouma, M.J. Schuuring

A woman with congenital pulmonary valve stenosis treated by balloon valvulotomy had been visiting the outpatient clinic for many years with complaints of palpitations. Several 24-h electrocardiogram (ECG) recordings and resting ECGs (Figure 1A) showed frequent premature ventricular contractions and two regular wide-complex asymptomatic tachycardias of a maximum of eight beats with a maximal frequency of 120 beats/min. However, these findings could not be related to her complaints.

The patient was included in a novel mHealth telemonitoring program. While the patient was having palpitations, a single-lead ECG was recorded (Figure 1B). On these additional recordings atrial fibrillation could be diagnosed with intermittent bundle branch block.

There is a broad aetiology of palpitations, and these often occur outside the window of 24 h Holter monitoring. This case is one of the first to illustrate that mHealth programs, including on-demand ECG monitoring, can be of great importance in the diagnosis of arrhythmias.
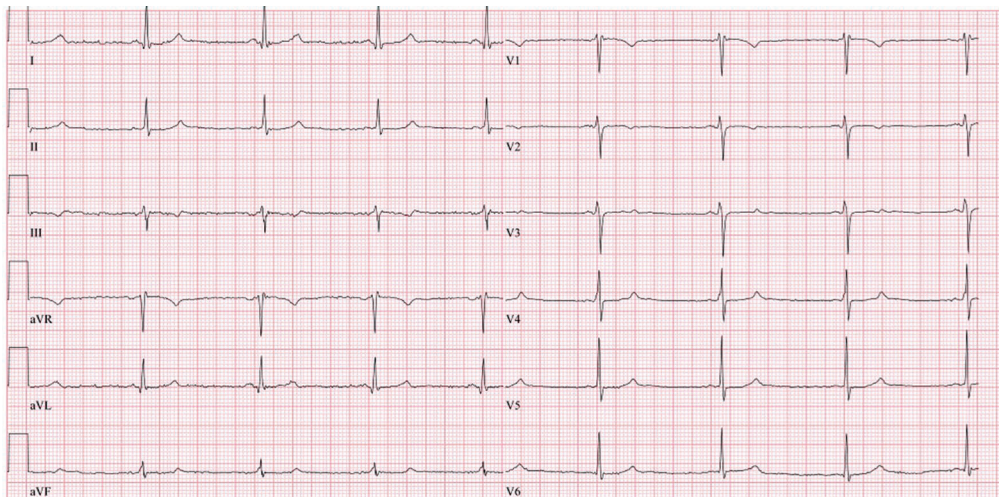
Figure 1A Routine resting electrocardiogram (ECG) of the patient.
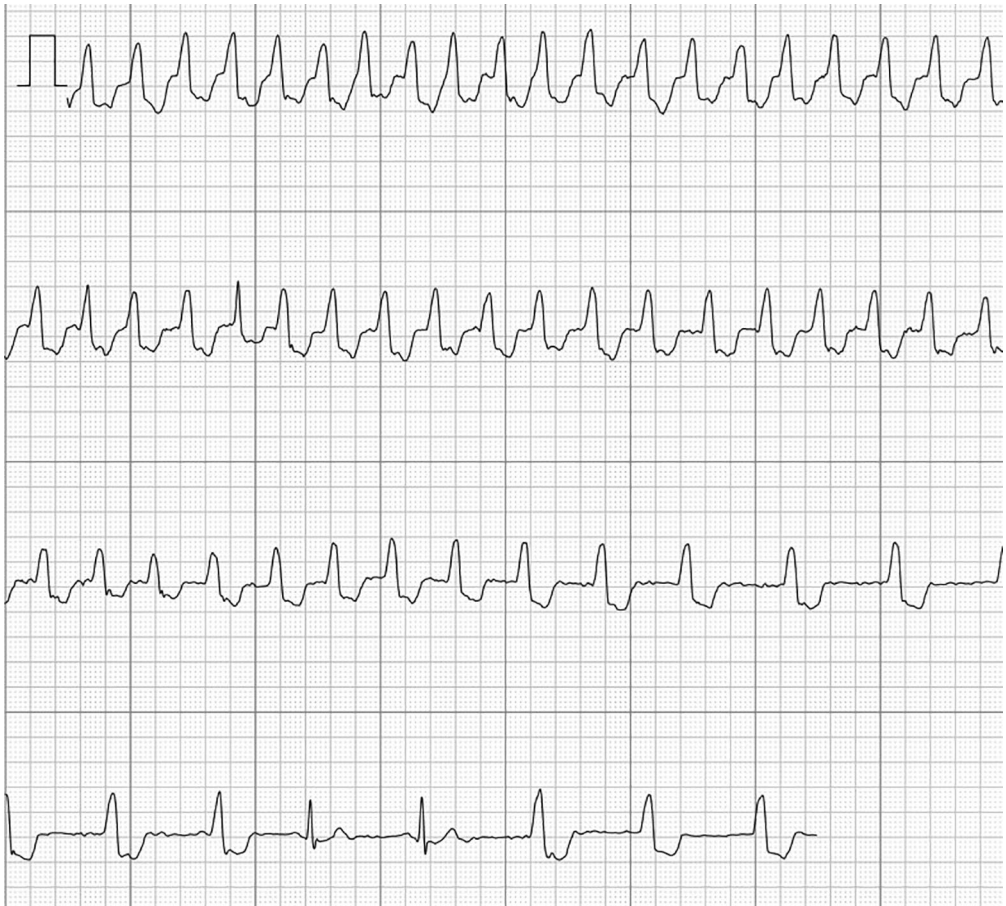
Figure 1B Recording of atrial fibrillation with intermittent bundle branch block by on-demand single-lead ECG in the mHealth program.

Conflict of interest

M.A.C. Koole, G.A. Somsen, I.I. Tulevski, M.M. Winter, B.J. Bouma and M.J. Schuuring declare that they have no competing interests.

Chapter 7

An implantable loop recorder or smartphone based single-lead electrocardiogram to detect arrhythmia in adults with congenital heart disease?

M.A.C. Koole, D. Kauw, K.M. Kooiman, J.R. de Groot, D. Robbers-Visser, I.I. Tulevski, B.J.M. Mulder, B.J. Bouma and M.J. Schuuring

ABSTRACT

Background

The European Society of Cardiology (ESC) guidelines for the management of adult congenital heart disease (ACHD) recommend screening in patients at risk for arrhythmic events. However, the optimal mode of detection is unknown.

Methods

Baseline and follow-up data of symptomatic ACHD patients who received an implantable loop recorder (ILR) or who participated in a smartphone based single-lead electrocardiogram study were collected. The primary endpoint was time to first detected arrhythmia.

Results

In total 116 ACHD patients (mean age 42 years, 44% male) were studied. The ILR group (n=23) differed from the smartphone based single-lead electrocardiogram group (n=93) in having a greater part of males and had more severe CHD and (near) syncope as qualifying diagnosis. In the smartphone based single-lead electrocardiogram group history of arrhythmia and palpitations were more frequent (all p<0.05). Monitoring was performed for 40 and 79 patient-years for the ILR- and smartphone based single-lead electrocardiogram group, respectively. Arrhythmias occurred in 33 patients with an equal median time for both groups to first arrhythmia of 3 months (HR of 0.7, p=0.81). Furthermore, atrial fibrillation occurred most often (n=16) and common therapy changes included medication changes (n=7) and implantation of pacemaker or Implantable Cardioverter Defibrillator (ICD) (N=4). Symptoms or mode of detection were not a determinant of the first event.

Conclusion

Non-invasive smartphone based single-lead electrocardiogram monitoring could be an acceptable alternative for ILR implantation in detecting arrhythmia in symptomatic ACHD patients in respect to diagnostic yield, safety and management decisions, especially in those without syncope.

1 INTRODUCTION

1.1 Adult congenital heart disease

Congenital heart disease has a worldwide prevalence of ~9 per 1000 newborns. Nowadays, the number of adult congenital heart disease (ACHD) patients exceeds the number of children with congenital heart disease and the population of ACHD patients is still increasing by 5% per year [1,2]. These ACHD patients are under lifelong surveillance in specialized centers. Although their prognosis has significantly improved compared to only a few decades ago, these patients are not cured. Data from the Dutch National CONCOR registry showed that the median age of death is 49 years and that two third of adult patients with CHD die from a cardiac cause [3-6]. One of the most common causes of death is sudden cardiac death (19%), which occurs at a median age of 39 years [3,4,7]. It is estimated that 1 out of 6 ACHD patients develops bradycardias or tachyarrhythmia during life, that often precede syncope and/or sudden death [3]. Over one-third of tetralogy of Fallot (ToF) patients develop symptomatic atrial tachyarrhythmia by adulthood, 10% develop high-grade ventricular arrhythmia, and 5% require a pacemaker implantation for surgically acquired atrioventricular block or sinus node dysfunction. After Senning or Mustard repairs for Transposition of the Great Arteries (TGA), loss of sinus rhythm occurs in 60% of patients in the 20-year period after surgery [8].

1.2 Arrhythmia detection

The European Society of Cardiology (ESC) guidelines recommend periodical screening in symptomatic ACHD patients, without arrhythmia documentation at presentation, evaluation for arrhythmia [1]. Subgroups of patients who are at increased risk are identified in the guideline. In patients with pacemakers or implantable cardioverter defibrillators (ICDs), device interrogation is used to screen for arrhythmias [9,10]. In patients without implantable device, short term screening is commonly performed with Holter studies, and prolonged screening with Implantable Loop Recorders (ILR). However, smartphone based single-lead electrocardiogram solutions may provide new alternatives [11,12]. Mobile devices for heart rhythm monitoring, defined as ambulant diagnostics, is rapidly evolving as wearables, mobile health applications (apps) and smartphone possibilities are improving, and increasing in number [13-15]. ACHD patients seem particularly eligible to benefit from these alternative solutions, as these patients have a higher burden of arrhythmia compared to the general population and having their first arrhythmia at younger age. So they are generally well motivated to apply eHealth. However, data on smartphone based single-lead electrocardiogram are scarce. Therefore, the study aimed

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to explore whether smartphone based single-lead electrocardiogram can be a good alternative to ILR in detecting arrhythmia.

2 METHODS

2.1 Study data

Baseline and follow-up data were collected of two cohorts of ACHD patients with symptoms which could be caused by arrhythmia. One cohort were patients who participated in a smartphone based single-lead electrocardiogram study and the other cohort are patients gathered by a retrospective chart review of patients with an ILR. Indications for ILR implantation were symptoms which could be related to arrhythmia. The smartphone based single-lead electrocardiogram group of patients participated in a prospective study in two medical centers in the Netherlands (Haga Teaching Hospital and Amsterdam UMC, location AMC). The study protocol required routine evaluation of heart rhythm using a wireless pocket sized single lead EKG recording device that could record a 30 s single lead EKG (Kardia, AliveCor). After a 1-week run-in period, a single lead EKG was recorded once every week. Patients could perform extra measurements in case of symptoms. Data of events were sent by the application the smartphone to our telemedicine center and within 48 h judged by specialized nurses. Data of the ILR were read as soon as possible after an event at our outpatient clinic. All patients were explained to contact a physician directly in case of emergency. Detailed description of the study has been published elsewhere [15]. A retrospective chart review has been performed to collect ILR data of all symptomatic ACHD patients having an ILR implanted between 2003 and 2019 (Amsterdam UMC, location AMC).

2.2 Study criteria

The smartphone based single-lead electrocardiogram study ACHD patients were eligible for inclusion if they met the following inclusion criteria: palpitations within the last 3 years (with or without arrhythmia diagnosis) or HF NYHA class II, and possession of a smartphone. Patients with impaired cognition, as assessed by their treating physician, tremors or patients with an insurance not covering costs of the smartphone based single-lead electrocardiogram program, were excluded. Patients were recruited from the outpatient clinic and clinical wards. Enrollment in this study followed after informed consent for the use of their clinical data was acquired. The local medical ethics committees of both institutions issued a waiver for this study. This included

a waived consent for the retrospective chart review, because data were processed anonymously by the investigator.

2.3 Study outcome

The primary endpoint was time to first arrhythmia detected (AF, SVT, VT, sinus node defect, or AV block) in both study groups. Device implantation and change in medication were not an outcome but also registered as a result of detecting arrhythmia for both groups. Data were analyzed with Kaplan-Meier survival curves and Cox proportional hazard analysis (SPSS version 28, IBM, Armonk, New York, NY, USA). Chi-square test or independent t-test were used to assess differences between patient-groups.

3 RESULTS

3.1 Baseline characteristics

In total 116 ACHD patients were studied, see Table 1. Mean age was 42 years and 44% were male. There were 25 (22%) patients with mild CHD, 45 (39%) patients with moderate CHD, and 46 (39%) patients with severe CHD. The rate of hypertension (n=16, 14%) or coronary artery disease was low (n=7, 6%). The ILR group consisted of 23 patients and the smartphone based single-lead electrocardiogram consisted of 93 patients.

The ILR group (n=23) differed from the smartphone based single-lead electrocardiogram group (n=93) in having a greater part of males. They had more severe CHD and (near) syncope (65 vs 3%) as qualifying symptom of possible arrhythmia. In the smartphone based single-lead electrocardiogram group history of arrhythmia and suffering from palpitations were more frequent.

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Table 1 Baseline characteristics.

	All *N*=116	ILR *N*=23	Smartphone ECG *N*=93	*p*
Age, years	42	44	42	0.573
Male, *N* (%)	51 (44)	17 (74)	34 (37)	**0.001**
Severity of CHD				
Mild, *N* (%)	25 (22)	3 (23)	22 (24)	
Moderate, *N* (%)	45 (39)	5 (22)	40 (93)	**0.020**
Severe, *N* (%)	46 (39)	15 (65)	31 (33)	
Medical history				
Cardiac surgery, *N* (%)	92 (79)	17 (74)	75 (81)	0.475
Non-cardiac surgery, *N* (%)	54 (47)	5 (22)	49 (53)	**0.007**
Coronary artery disease, *N* (%)	7 (6)	2 (9)	5 (5)	0.559
Arrhythmia, *N* (%)	91 (78)	10 (43)	81 (87)	**<0.01**
Heart failure, *N* (%)	22 (19)	3 (13)	19 (20)	0.418
Hypertension, *N* (%)	16 (14)	1 (4)	15 (16)	0.142
Systemic EF <40%, *N* (%)	6 (5)	0	6 (6)	0.208
Subpulmonic EF <40%, *N* (%)	4 (3)	1 (4)	3 (3)	0.399
NYHA class				
I, *N* (%)	90 (78)	16 (70)	74 (80)	0.303
≥2, *N* (%)	26 (22)	7 (30)	19 (20)	
Arrhythmia symptoms, *N* (%)	95 (82)	19 (83)	76 (82)	0.921
Palpitations, *N* (%)	78 (67)	8 (35)	70 (75)	**< 0.01**
Dyspnea, *N* (%)	12 (10)	2 (9)	10 (11)	0.772
(Near) syncope, *N* (%)	18 (16)	15 (65)	3 (3)	**< 0.01**
Medication				
Antiarrhythmic agents, *N* (%)	52 (45)	7 (30)	45 (48)	0.121
Diuretics, *N* (%)	13 (11)	3 (13)	10 (11)	0.701
Anticoagulation, *N* (%)	45 (39)	7 (30)	38 (41)	0.358

N=Number
EF=Ejection Fraction
ILR=Implantable Loop Recorder
CHD=Congenital Heart Disease
NYHA=New York Heart Association.
Bold values represent the significant values.

3.2 Monitoring details

In total patients were monitored for 119 patient years. Monitoring was performed for 40 and 79 patient years, respectively, in the ILR and smartphone based single-lead electrocardiogram groups. The median time to first arrhythmia was 92 (16–233) days for the complete study cohort, for the ILR group 40 (15–681) days and for the smartphone based single-lead electrocardiogram group 102 (21–232) days (p=0.80, HR of 0.7) (Figure 1 and Table 2). Arrhythmias occurred in 33 patients, of which 11 (48%) were documented in the ILR group and 22 (24%) in the smartphone based single-lead electrocardiogram group (p=0.021). In both groups atrial fibrillation was the most frequently documented arrhythmia and no patient died.
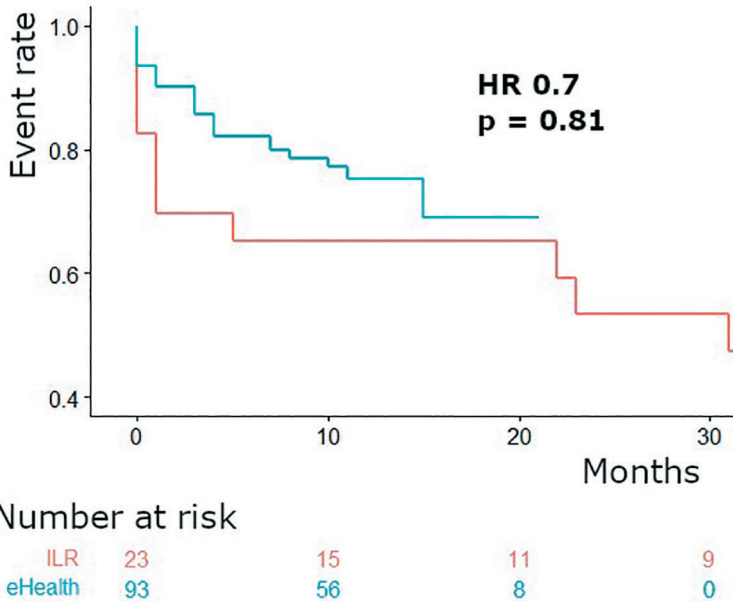
Figure 1 Time to first arrhythmia.

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Table 2 Details on monitoring.

A

	All N=116	ILR N=23	Smartphone ECG N=93	p
Median time to first arrhythmia, days (IQR)	92 (16–233)	40 (15–681)	102 (21–232)	0.801
Median monitoring time per patient, days (IQR)	322 (148–428)	567 (40–1217)	317 (188–399)	**0.045**

B

Details on first arrhythmia	All N=116	ILR N=23	Smartphone N=93	p
Arrhythmia occured, N (%)	33 (28)	11 (48)	22 (24)	0.021
Atrial fibrillation, N (%)	16 (14)	2 (9)	14 (15)	0.428
Supraventricular tachycardia, N (%)	14 (12)	6 (26)	8 (9)	0.021
Ventricular tachycardia, N (%)	1 (1)	1 (4)	0	0.043
Sinus node defect, N (%)	2 (2)	2 (9)	0	0.004
Atrioventricular block, N (%)	0	0	0	1.000

N=Number
IQR=Interquartile Ranges
ILR=Implantable Loop Recorder
Bold values represent the significant values.

3.3 Changes in patient management

Arrhythmia detection led to the important care changes, displayed in Figure 2. In the ILR group device implantation to treat arrhythmia was performed in four patients (three pacemaker and one ICD) and medication changes were performed in two patients (start of beta-blocker). Furthermore, in the ILR group a wait and see strategy was chosen in five patients. In the smartphone based single-lead electrocardiogram group ablation was performed in one patient and electrical cardioversion was performed in three patients. In five patients monitored with smartphone based single-lead electrocardiogram medication changes were performed, including start of a direct oral anticoagulant, start of amiodarone, and both start and increase of beta blocker. In one patient it was decided to perform additional Holter monitoring and in 12 patients no change in management was initiated.

Figure 2 Care changes (**A**) ILR and (**B**) smartphone ECG.

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3.4 Determinants of the first arrhythmia event
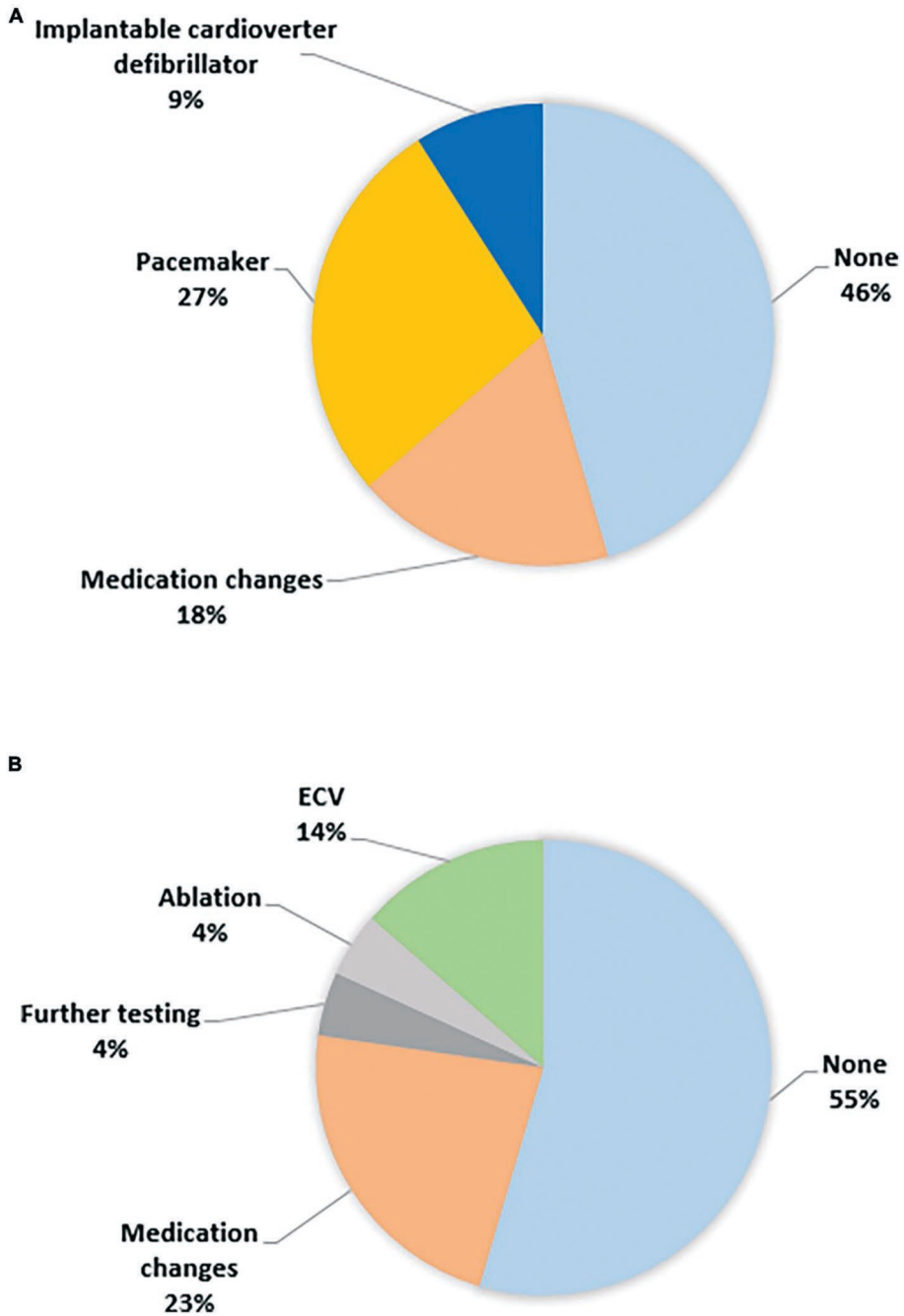
The mode of detection (HR 0,688 95% CI 0.3–1.6, 0,371) appeared not to be associated with the first detection of arrhythmia in the study period (HR 3.2, 95% CI 1.5–6.8, *p*=0.002). The use of anti-arrhythmic drugs was associated with an arrhythmia event because patients with anti-arrhythmic drugs are at high risk of arrhythmia.

4 DISCUSSION

4.1 Principal findings

Rhythm monitoring is important in ACHD patients as they are at high risk for arrhythmic and brady-arrhythmic events, but with the currently expanded possibilities of diagnostics no optimal diagnostic strategy has been defined yet. To our knowledge this is the first study that performed a comparison of ILR and smartphone based single-lead electrocardiogram for heart rhythm monitoring in ACHD patients. Smartphone based single-lead electrocardiogram seems to be a reasonable noninvasive alternative diagnostic tool for symptomatic patients instead of an invasive ILR for detecting arrhythmia.

4.2 Diagnostic yield of ambulatory rhythm monitoring in ACHD patients

Our findings of a high burden of arrhythmia in selected ACHD patients is comparable to the literature. Dodeja et al. evaluated traditional ILR monitoring in ACHD patients and showed a useful adjunct with clinically relevant events in 41% of patients [9]. Schultz et al. performed a retrospective cohort study on remote ambulatory monitoring in 307 ACHD patients with symptoms, a history of arrhythmia or screening due to an increased risk. Their 14-day screening detected arrhythmia in 153 (50%) ACHD patients. Management changes, including medication changes (30%), further testing or imaging (10%), and procedures (6%), were made based on results of these prolonged monitoring strategy [16]. Huntgeburth et al. performed a single center, retrospective observational study in which all CHD-patients with an ILR who were under care of the German Heart Center Munich between February 2015 and January 2019 were identified [17]. The authors found a considerable complementary diagnostic value of ILR for the detection and differentiation of benign and malignant arrhythmias. Huntgeburth et al. concluded that ILR implantation should be considered in patients with CHD of any complexity who need medium or long-term arrhythmia monitoring, especially if short-term Holter monitoring cannot provide sufficient diagnostic certainty.

4.3 Smartphone based single-lead electrocardiogram for heart rhythm monitoring in ACHD patients

Smartphone based single-lead electrocardiogram is a promising tool to improve care and detect arrhythmia in ACHD patients [18-21]. Smartphone based single-lead electrocardiogram has been shown to enable early detection of recurrences and new diagnosis of arrhythmia, which led to swift therapeutic response or remote reassurance. Furthermore, smartphone based single-lead electrocardiogram was well accepted in ACHD patients with high adherence and positive patient experience [15,22]. The risk of ILR implantation such as need for re-implantation, wound dehiscence or device erosion of 1–9% can be avoided [17,23,24]. Smartphone based single-lead electrocardiogram as a non-invasive diagnostic tool has no such risk of surgical complications. In our analysis smartphone based single-lead electrocardiogram proofed to be an effective tool in detecting arrhythmia. In our study there was a lower rate of arrhythmia detection in the smartphone based single-lead electrocardiogram group, potentially due to the fact that this group had less patients with severe ACHD. Although ILR is better at detecting arrhythmias in patients because the window of measurement is continuous, it has the before mentioned disadvantage of being an invasive tool. So, we suggest in symptomatic patients, if symptoms occur on daily basis, 24 Holter monitoring for diagnosing arrhythmia is a good option. If symptoms occur less frequently smartphone based single-lead electrocardiogram could be an alternative option and save the ILR for patients where no diagnosis could be found with these modalities and for whom detecting arrhythmia is important to their prognosis. Furthermore, new wearables with smart algorithms can monitor patients continuous and alert patient and physician if arrhythmia is detected [25,26].

4.4 Prolonged rhythm monitoring in acquired heart disease patients

Diagnostic yield of prolonged monitoring is also well established in AF screening in cryptogenic stroke patients [27]. Longer durations of monitoring were associated with the highest diagnostic yield in these patients [28,29]. However, the optimal monitoring method and duration of monitoring is unclear [30-32]. Solbiati et al. performed a systematic Cochrane review on ILR performance and concluded that available data are non-conclusive. The authors therefore recommended further research on ILR with clinically relevant outcomes [33]. Our study suggests our smartphone based single-lead electrocardiogram protocol compared to ILR can be a good alternative in detecting arrhythmia in patients with symptoms other than syncope. Especially if these complaints are less frequent than once a day for which 24–48 h Holter monitoring is still a good alternative option.

4.5 Future directions

Beside clinical effectiveness other aspects of implementation include amongst others: cost evaluation, governance, patient, and technological factors. Studies on costs of smartphone based single-lead electrocardiogram are scarce. In the first study that compared eHealth with the standard outpatient clinic setting it was suggested that eHealth was likely cost-effective [34]. That study was performed in patients who suffered from acute myocardial infarction. Hypothetically, smartphone based single-lead electrocardiogram is more cost-effective than ILR because it saves on the costs of implantation and explantation, but if wearables for heart rhythm monitoring use a service center with medical personnel, the costs for this solution could also become significant. Furthermore, health system governance, health provider, patient and technological factors may complicate implementation. However, tools to identify barriers to implementing digital health and recommendations for overcoming them are increasingly available [35-37].

4.6 Limitations

Our study was limited by a combination of two datasets, without randomization of patients between the two monitoring strategies. Moreover, short arrhythmia and asymptomatic arrhythmia or bradycardias may remain unnoticed in both groups. Despite we screened all ACHD patients visiting our outpatient clinic between 2003 and 2019 for having an ILR, the number of patients we found having an ILR was much smaller compared to the smartphone based single-lead electrocardiogram group. We postulate that the threshold for using an invasive diagnostic tool to find arrhythmia in symptomatic patients is higher compared to non-invasive Holter monitoring. The decision to implant an ILR to detect arrhythmia was most often reserved for ACHD patients with unexplained syncope or cerebral vascular accident after unsuccessful period of Holter monitoring. However, in the emerging field of non-invasive wearable heart rhythm monitoring solutions we are the first to report a comparison in this high-risk patient population. Matching was not performed in the study. The smartphone based single-lead electrocardiogram has a significantly higher number of patients with a history of previous arrhythmia. Previous arrhythmia could make arrhythmia recurrence more likely than no previous arrhythmia. However, arrhythmia could also make arrhythmia recurrence less likely because of the treatment with antiarrhythmic drugs. Potentially this could have introduced bias the process of arrhythmia detection.

5 CONCLUSION

Non-invasive smartphone based single-lead electrocardiogram monitoring could be an acceptable alternative in detecting arrhythmia in symptomatic ACHD patients instead of an ILR in respect to diagnostic yield, safety and management decisions, especially in those patients without syncope.

Data availability statement

The data underlying this article will be shared on reasonable request to the corresponding author.

Ethics statement

The studies involving human participants were reviewed and approved by the Amsterdam UMC. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements. Written informed consent was not obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

MK, BB, and MS drafted the manuscript, which was critically revised and edited by BM, DR-V, DK, IT, JG, and KK. All authors agree to be accountable for all aspects of the work.

Conflict of interest

IT was shareholder in ventures supplying hardware and software implemented in the methods of this study. The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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REFERENCES

1. Baumgartner H, De Backer J, Babu-Narayan SV, Budts W, Chessa M, Diller GP, et al. 2020 ESC Guidelines for the management of adult congenital heart disease. *Eur Heart J.* (2021)42:563–645. doi: 10.1093/eurheartj/ehaa554

2. Stout KK, Daniels CJ, Aboulhosn JA, Bozkurt B, Broberg CS, Colman JM, et al. 2018 AHA/ACC guideline for the management of adults with congenital heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol.* (2019)73:e81–192. doi: 10.1016/j.jacc.2018.08.1029

3. Koyak Z, Harris L, de Groot JR, Silversides CK, Oechslin EN, Bouma BJ, et al. Sudden cardiac death in adult congenital heart disease. *Circulation.* (2012)126:1944–54. doi: 10.1161/CIRCULATIONAHA.112.104786

4. van der Velde ET, Vander VET, Vriend JWJ, Mannens MMAM, Uiterwaal CSPM, Brand R, et al. CONCOR, an initiative towards a national registry and DNA bank of patients with congenital heart disease in the Netherlands: rationale, design, and first results. *Eur J Epidemiol.* (2005)20:549–57. doi: 10.1007/s10654-005-4264-9

5. Zomer AC, Vaartjes I, Uiterwaal CSPM, van der Velde ET, van den Merkhof LFM, Baur LHB, et al. Circumstances of death in adult congenital heart disease. *Int J Cardiol.* (2012)154:168–72.

6. van der Bom T, Zomer AC, Zwinderman AH, Meijboom FJ, Bouma BJ, Mulder BJM. The changing epidemiology of congenital heart disease. *Nat Rev Cardiol.* (2011)8:50–60.

7. Vehmeijer JT, Koyak Z, Leerink JM, Zwinderman AH, Harris L, Peinado R, et al. Identification of patients at risk of sudden cardiac death in congenital heart disease: the PRospEctiVE study on implaNTable cardIOverter defibrillator therapy and suddeN cardiac death in Adults with Congenital Heart Disease (PREVENTION-ACHD). *Heart Rhythm.* (2021)18:785–92. doi: 10.1016/j.hrthm.2021.01.009

8. Bouma BJ, Mulder BJM. Changing landscape of congenital heart disease. *CircRes.* (2017)120:908–22. doi: 10.1161/CIRCRESAHA.116.309302

9. Dodeja AK, Thomas C, Daniels CJ, Kertesz N, Kamp A. Detection of arrhythmias in adult congenital heart disease patients with LINQTM implantable loop recorder. *Congenit Heart Dis.* (2019)14:745–51. doi: 10.1111/chd.12815

10. Dussault C, Toeg H, Nathan M, Wang ZJ, Roux J-F, Secemsky E.Electrocardiographic monitoring for detecting atrial fibrillation after ischemic stroke or transient ischemic attack: systematic review and meta-analysis. *Circ Arrhythm Electrophysiol.* (2015)8:263–9. doi: 10.1161/CIRCEP.114.002521

11. Jensen MT, Treskes RW, Caiani EG, Casado-Arroyo R, Cowie MR, Dilaveris P, et al. ESC working group on e-cardiology position paper: use of commercially available wearable technology for heart rate and activity tracking in primary and secondary cardiovascular prevention – in collaboration with the European Heart Rhythm Association, European Association of Preventive Cardiology, Association of Cardiovascular Nursing and Allied Professionals, Patient Forum, and the Digital Health Committee. *Eur Heart J Digit Health.* (2021)2:49–59. doi: 10.1093/ehjdh/ztab011

12. Schuuring MJ, Kauw D. How to initiate eHealth in congenital heart disease patients? *Eur Heart J Digit Health.* (2020)1:83–6. doi: 10.1093/ehjdh/ztaa012

13. Svennberg E, Tjong F, Goette A, Akoum N, Di Biase L, Bordachar P, et al. How to use digital devices to detect and manage arrhythmias: an EHRA practical guide. *Europace.* (2022)24:979–1005. doi: 10.1093/europace/euac038

14. Cowie MR, Bax J, Bruining N, Cleland JGF, Koehler F, Malik M, et al. e-Health: a position statement of the European Society of Cardiology. *Eur Heart J.* (2015)37:63–6. doi: 10.1093/eurheartj/ehv416

15. Kauw D, Koole MAC, Winter MM, Dohmen DAJ, Tulevski II, Blok S, et al. Advantages of mobile health in the management of adult patients with congenital heart disease. *Int J Med Inform.* (2019) 132:104011. doi: 10.1016/j.ijmedinf.2019.104011

16. Schultz KE, Lui GK, McElhinney DB, Long J, Balasubramanian V, Sakarovitch C, et al. Extended cardiac ambulatory rhythm monitoring in adults with congenital heart disease: arrhythmia detection and impact of extended monitoring. *Congenit Heart Dis.* (2019)14:410–8. doi: 10.1111/chd.12736

17. Huntgeburth M, Hohmann C, Ewert P, Freilinger S, Nagdyman N, Neidenbach R, et al. Implantable loop recorder for monitoring patients with congenital heart disease. *Cardiovasc Diagn Ther.* (2021) 11:1334–43. doi: 10.21037/cdt-20-677

18. Schuuring MJ, Mischie AN, Caiani EG. Editorial: digital solutions in cardiology. Front Cardiovasc Med. (2022) 9:873991. doi: 10.3389/fcvm.2022.873991 19. Duncker D, Svennberg E. Editorial: wearable devices for cardiac rhythm monitoring. *Front Cardiovasc Med.* (2022)9:951769. doi: 10.3389/fcvm.2022.951769

19. Duncker D, Svennberg E. Editorial: wearable devices for cardiac rhythm monitoring. *Front Cardiovasc Med.* (2022)9:951769. doi: 10.3389/fcvm.2022. 951769

20. Abu-Alrub S, Strik M, Ramirez FD, Moussaoui N, Racine HP, Marchand H, et al. Smartwatch electrocardiograms for automated and manual diagnosis of atrial fibrillation: a comparative analysis of three models. *Front Cardiovasc Med.* (2022)9:836375. doi: 10.3389/fcvm.2022.836375

21. Pengel LKD, Robbers-Visser D, Groenink M, Winter MM, Schuuring MJ, Bouma BJ, et al. A comparison of ECG-based home monitoring devices in adults with CHD. *Cardiol Young.* (2022) [Online ahead of print]. doi: 10.1017/S1047951122002244

22. Koole MAC, Kauw D, Winter MM, Dohmen DAJ, Tulevski II, de Haan R, et al. First real-world experience with mobile health telemonitoring in adult patients with congenital heart disease. *Neth Heart J.* (2019)27:30–7. doi: 10.1007/s12471-018-1201-6

23. Lim WY, Papageorgiou N, Sukumar SM, Alexiou S, Srinivasan NT, Monkhouse C, et al. A nurse-led implantable loop recorder service is safe and cost effective. *J Cardiovasc Electrophysiol.* (2019) 30:2900–6. doi: 10.1111/jce.14206

24. Bezzerides VJ, Walsh A, Martuscello M, Escudero CA, Gauvreau K, Lam G, et al. The real-world utility of the LINQ implantable loop recorder in pediatric and adult congenital heart patients. *JACC Clin Electrophysiol.* (2019)5:245–51. doi: 10.1016/j.jacep.2018.09.016

25. Avram R, Ramsis M, Cristal AD, Nathan V, Zhu L, Kim J, et al. Validation of an algorithm for continuous monitoring of atrial fibrillation using a consumer smartwatch. *Heart Rhythm.* (2021)18:1482–90. doi: 10.1016/j.hrthm.2021.03.044

26. Garikapati K, Turnbull S, Bennett RG, Campbell TG, Kanawati J, Wong MS, et al. The role of contemporary wearable and handheld devices in the diagnosis and management of cardiac arrhythmias. *Heart Lung Circ.* (2022)31:1432–49.doi: 10.1016/j.hlc.2022.08.001

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27. Dilaveris PE, Antoniou CK, Caiani EG, Casado-Arroyo R, Climent AM, Cluitmans M, et al. ESC Working Group on e-Cardiology Position Paper: accuracy and reliability of electrocardiogram monitoring in the detection of atrial fibrillation in cryptogenic stroke patients: in collaboration with the Council on Stroke, the European Heart Rhythm Association, and the Digital Health Committee. *Eur Heart J Digit Health.* (2022)3:341–58. doi: 10.1093/ehjdh/ztac026

28. Wachter R, Gröschel K, Gelbrich G, Hamann GF, Kermer P, Liman J, et al. Holter-electrocardiogram-monitoring in patients with acute ischaemic stroke (Find-AFRANDOMISED): an open-label randomised controlled trial. *Lancet Neurol.* (2017)16:282–90. doi: 10.1016/S1474-4422(17)3 002-9

29. Healey JS, Connolly SJ, Gold MR, Israel CW, Van Gelder IC, Capucci A, et al. Subclinical atrial fibrillation and the risk of stroke. *N Engl J Med.* (2012)366:120–9. doi: 10.1056/NEJMoa1105575

30. Kishore A, Vail A, Majid A, Dawson J, Lees KR, Tyrrell PJ, et al. Detection of atrial fibrillation after ischemic stroke or transient ischemic attack: a systematic review and meta-analysis. *Stroke.* (2014) 45:520–6. doi: 10.1161/STROKEAHA.113. 003433

31. Albers GW, Bernstein RA, Brachmann J, Camm J, Easton JD, Fromm P, et al. Heart rhythm monitoring strategies for cryptogenic stroke: 2015 diagnostics and monitoring stroke focus group report. *J Am Heart Assoc.* (2016)5:e002944. doi: 10.1161/JAHA.115.002944

32. Steinberg JS, Varma N, Cygankiewicz I, Aziz P, Balsam P, Baranchuk A, et al. 2017 ISHNE-HRS expert consensus statement on ambulatory ECG and external cardiac monitoring/telemetry. *Heart Rhythm.* (2017)14:e55–96. doi: 10.1016/j.hrthm.2017.03.038

33. Solbiati M, Costantino G, Casazza G, Dipaola F, Galli A, Furlan R, et al. Implantable loop recorder versus conventional diagnostic workup for unexplained recurrent syncope. *Cochrane Database Syst Rev.* (2016)4:CD011637. doi: 10.1002/14651858.CD011637.pub2

34. Treskes RW, van den Akker-vanMarle ME, vanWinden L, van Keulen N, van der Velde ET, Beeres S, et al. The box-eHealth in the outpatient clinic follow-up of patients with acute myocardial infarction: cost-utility analysis. *J Med Internet Res.* (2022)24:e30236. doi: 10.2196/30236

35. Tromp J, Jindal D, Redfern J, Bhatt A, Séverin T, Banerjee A, et al. World heart federation roadmap for digital health in cardiology. *Glob Heart.* (2022)17:61. doi: 10.5334/gh.1141

36. Kauw D, Huisma PR, Medlock SK, Koole MAC, Wierda E, Abu-Hanna A, et al. Mobile health in cardiac patients: an overview on experiences and challenges of stakeholders involved in daily use and development. *BMJ Innovat. (*2020)6:1–8. doi: 10.1136/bmjinnov-2019-000418

37. Treskes RW, Wildbergh TX, Schalij MJ, Scherptong RWC. Expectations and perceived barriers to widespread implementation of e-Health in cardiology practice: results from a national survey in the Netherlands. *Neth Heart J.* (2019)27:18–23. doi: 10.1007/s12471-018-1199-9

Chapter 8

Value of extended arrhythmia screening in adult congenital heart disease patients

M.A.C. Koole, S. de Jong, B.J.M. Mulder, B.J. Bouma, M.J. Schuuring

ABSTRACT

The European Society of Cardiology guidelines for the management of Adult Congenital Heart Disease (ACHD) patients recommend screening for arrhythmias and bradycardias in symptomatic patients, often being done by means of an ambulatory 24–48 hour Holter or Implantable Loop Recorder (ILR). However, nowadays non-invasive instruments such as patches, smartwatches and smartphone based on single-lead electrocardiograms which perform extended monitoring, are also available. The aim of this narrative review is to assess whether these instruments, when they detect arrhythmias and bradycardias in patients with ACHD, will lead to meaningful changes in clinical care. Clinical meaningful changes include adjustment of medication, cardioversion, electrophysiology study (EPS), ablation or implantation of a cardiovascular implantable electronic device. The following monitoring instruments are discussed: 1) cumulative Holter, 2) two-week continuous monitor, 3) smartwatch and smartphone based single-lead electrocardiogram and 4) ILR. The diagnostic yield of extended rhythm monitoring is high and varies between 18% (smartphone-based single lead ECG) and 41% with ILR. In conclusion, contemporary arrhythmia screening includes new various non-invasive technologies that are promising new tools as an alternative for Holter monitoring or ILR. However, the optimal mode of detection is still unclear due to the lack of head-to-head comparisons.

CLINICAL PERSPECTIVE

Extended arrhythmia monitoring in ACHD patients has a high diagnostic yield. Nowadays a variety of non-invasive tools are available for ambulant continuous heart rhythm monitoring. We need more studies for choosing the best available option for extended heart rhythm monitoring in ACHD patients.

1 INTRODUCTION

Over the past decades, life expectancy of children born with congenital heart disease (CHD) has improved considerably [1,2]. Hence, the population of adult congenital heart disease (ACHD) patients is growing.3 Many of the ACHD patients are affected lifelong by cardiac symptoms, reduced quality of life, and cardiac events [2].

Clinical arrhythmias are important regarding morbidity and mortality in patients with ACHD [4-6]. Clinical arrhythmias and subclinical arrhythmias are crucial signs in the management of ACHD patients due to their potential impact on their overall cardiovascular health. Clinical arrhythmias, with noticeable symptoms, can significantly affect quality of life and may necessitate prompt intervention to prevent complications. Subclinical arrhythmias, although asymptomatic, may be an early sign of deterioration and can still contribute to increased morbidity and mortality. Therefore, regular monitoring and timely intervention is essential in the comprehensive care of ACHD patients [1]. It is estimated that 1 out of 6 ACHD patients develop bradycardia or tachyarrhythmia during life, that often precede syncope and/or sudden death [5]. For example, over one-third of tetralogy of Fallot (TOF) patients develop symptomatic atrial tachyarrhythmia at adult age, and 10% develop high-grade ventricular arrhythmia. Moreover, of these TOF patients 5% requires a pacemaker implantation for surgically acquired atrioventricular block or sinus node dysfunction [3]. To prevent sudden cardiac death, adequate risk assessment is needed to identify patients at high risk for sudden cardiac death. In TOF patients mortality and ventricular arrhythmia are associated, among other clinical parameters as: older age at repair, prior palliative shunt, longer QRS duration, at least moderate right ventricular function, lower left ventricular ejection fraction, previous ventriculotomy and higher right ventricular end-diastolic volume. The more these factors are present in a patient, the more repeated monitoring for detecting arrhythmias becomes important [7]. In patients with Senning or Mustard repair for Transposition of the Great Arteries, a group declining in size, loss of sinus rhythm is demonstrated in 60% of the patients. The risk of atrial and ventricular arrhythmias increases with age [8]. At every arrhythmic event, symptomatic or asymptomatic, a change in patient management should be considered, e.g. initiation of anticoagulation, change in anti-arrhythmic drugs, catheter ablation or implantation of a pacemaker or ICD. Also, evaluation of possible underlying structural abnormalities, which may be causal and correctable, is an essential part of clinical management in patients with arrhythmias.

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Care for ACHD patients is mainly organized in outpatient clinics, where brief evaluations of clinical status, patient education and treatment strategies during consultation are made [9]. These outpatient evaluations are only momentary snapshots, ranging from a few times a year to once every five years. The most recent European Society of Cardiology guidelines for the management of ACHD patients advice screening for arrhythmia if patients are symptomatic or for selected patients if bradycardia and/or tachyarrhythmias are suspected [2]. In ACHD patients with pacemakers or implantable cardioverter defibrillators arrhythmias can be detected by device interrogation [10,11]. Holter monitors are used to perform screening for arrhythmias or assess arrhythmia burden for a short term. Instruments to perform extended ambulatory heart rhythm monitoring are increasingly available. The aim of this review was to assess the added value of these instruments in respect to detecting arrhythmias in patients with ACHD leading to meaningful changes in clinical care.

2 METHODS AND DEFINITIONS

A PubMed database search was performed. Relevant search terms regarding CHD were combined with search terms regarding screening instruments and adults. The search domain was restricted to January 2007 to October 2022. This restriction on publication dates before 2007 was used because of the fast development of electrophysiology reading techniques over the past decades. Additionally, the search was restricted to publications in English language. Four categories were created; 1) cumulative Holter findings, 2) two-week continuous monitor, 3) smartwatch and smartphone based single-lead electrocardiogram and 4) Implantable Loop Recorder (ILR).

Cumulative Holter findings were defined as the ≥1 Holter studies from each individual patient for the detection of clinically significant arrhythmia by individual case history [8]. Clinically significant arrhythmias and bradycardias were defined as any of the following: atrial fibrillation or flutter (AF) >30 seconds, ventricular tachycardia (VT), non-sustained VT (NSVT), supraventricular tachycardia (SVT), sinus pauses of more than three seconds, second-degree type II (Mobitz II) atrioventricular block (AVB) and third-degree AVB. The diagnostic yield was the primary outcome measure if reported, defined as the incidence of clinically relevant arrhythmia detected resulting in a change in patient management. These changes consisted of initiation or adjustment of medication, cardioversion, electrophysiology study (EPS), ablation or implantation of a

Table 1 Study characteristics

First authors	Year	Design	N	Age	Female %	CHD	Follow-up	Intervention	Control	Endpoint
Repetitive Holter										
Czosek	2013	Retrospective cohort	189	27 (19–35)	45	TOF (134), d-TGA (44), Fontan (67)	NR	Repetitive Holter	Single Holter	Primary: Positive and negative predictive value of individual Holter monitoring Secondary: a) Sensitivity, specificity, and negative predictive value of the detection of clinically significant arrhythmias from consecutive Holters. b) Cost analysis of ambulatory monitoring
Two-week continuous monitor (patch)										
Schultz	2019	Retrospective cohort	314	31 (IQR 25–41)	61	TOF (61), d-TGA (32), ASD and/or PAPVR (42), single ventricle (38), PHT (25), VSD (23), L-TGA (15), Ebsteins (11), other RVOT disease (25), AV canal (6), left heart obstruction (34)	9.5±4.1 days	Two-week Holter	Standard care	Primary: % clinically significant arrhythmias after 48 hours Secondary: Whether this leads to a change in management
Smartwatch and smartphone based handheld device										
Striepe	2022	Prospective cohort, cross sectional	106	34 (18–75)	48	TOF (24), d-TGA (5), L-TGA (4), TAC (2), single ventricle (10), AS (18), VSD (13), structural normal heart (22)	NR	Einthoven I/II/III-like iECG (30 sec)	Own 12-lead ECG	The correlation of the three iECG leads with those of the gold standard ECG

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Smartwatch and smartphone based handheld device *(Continued)*

First authors	Year	Design	N	Age	Female %	CHD	Follow-up	Intervention	Control	Endpoint
Pengel	2022	Prospective, cross- sectional	176	40 (23–57)	66	TOF (19), Fontan (4), Fallot (20), CoA (15), Marfan (19), ASD (25), VSD (14), BAV (14), other (46)	–	Withings Scanwatch, Eko DUO ECG, Kardia 6L	Own 12- lead ECG	Primary: Accuracy of the devices compared to the 12-lead ECG. Secondary: a) Quality of the ECGs from the devices on a 5-point Likert Scale b) Willingness of patient to use devices in daily life
Koole	2018	Prospective cohort	55	45 (19–70)	66	Mild CHD (6), moderate CHD (29), severe CHD (20)	3 (max. 9) months	mHealth program	No	Primary: % patients with exceeded thresholds which lead to a change in management. Secondary: quality of life and self-management
Kauw	2019	Prospective cohort	109	45 (IQR 32–58)	67	Mild CHD (25), Moderate CHD (50), severe CHD (34)	12 months (Q1–Q3; 9–14)	mHealth program	No	Primary: % changes in management based on mHealth data. Secondary: Adherence and patients experience(NPS score)
Implantable Loop Recorder										
Dodeja	2019	Retrospective cohort	22	25	50	TOF (7), Fontan (7), LGTA (1),Ebsteins (1), BAV (1), IAA (1), CoA (1), Congenital AS (1)	23±13 months	LINQ ILR	No	% ILR findings resulting in change in management
Huntgeburth	2021	Retrospective cohort	33	43 (+-20 SD)	42,2	PFO (6), PA-VSD (3), TOF (3), Brugada (3), AVSD (2), Ebsteins (2), VSD (2), PAPVR (1), CoA (1), ASD, BAV (1), D-ORV (1), PVS (1), SVA (1), TGA (1), TA (1), Fabry (1), Marfan, TAC (1)	97±433 day	LINQ ILR	No	Primary: % clinically significant arrhythmias. Secondary: Whether this leads to a change in management

Abbreviations: AS=Aortic Stenosis; ASD=Atrial Septum Defect; AV=Atrioventricular; AVSD=Atrioventricular Septal Defect; BAV=Bicuspid Aortic Valve; CoA=Coarctatio of Aorta; CHD=Congenital Heart Disease; D-ORV=Double-Outlet Right Ventricle; d-TGA=d-Transposition of the Great Arteries after an atrial switch operation; Ebsteins=Ebsteins Anomaly; Fontan=Patients with single ventricle after Fontan palliation; IAA=Interrupted Aortic Arch; ILR=Impantable Loop Recorder; L-TGA=L-Tranpostion of the Great Arteries; LINQ, Reveal LINQ Medtronis Inc; N=Number; NR=Not Reported; PAPVR=Partial Anomalous Pulmonary Venous Return; PA-VSD=Pulmonary Atresia with Ventricular Septum Defect; PFO=Patent Foramen Ovale; PHT=Pulmonary Hypertension; PVS=Pulmonary Valve Stenose; RVOT=Right Ventricular Outflow Tract; SVA=Sinus Valsalva Aneurysm; TA=Tricuspid Atresia; TAC=Truncus Arteriosus Communis; TGA=Transposition of Great Arteries after switch; TOF=Tetralogy of Fallot; VSD=Ventricle Septum Defect; XT=Reveal XT Medtonic Inc

Table 2 Study results

Author	Study arm	Symptoms	PAC couplet/triplet	tachy	AF/flutter	PVC couplet/triplet	nsVT	VT	second degree AV block	Sinus node disease	clinical Arrhythmias	total	EP	PM	ICD	Medication	testing	CV	Ablation	Quality
			Atrial arrhytmias			**Ventricular arrhythmias**						**Management changes**								
Repetive Holter																				
Czosek	findings/holter	20%	7%	20%	8%	9%	22%	3%	0%	2%	14%	4%								
Two-week continous monitoring (patch)																				
Schultz	N/A	39%	N/A	N/A	35% (34% had care changes)	N/A	11% (66% had care)	N/A	N/A	1%	50% (46% within 48h)	16% (57% within 48h)	N/A	N/A	3%	14%	5%	N/A	N/A	Over-reading 10% by study principal investigators, no
Smartwatch and smartphone based handheld device																				
Striepe	N/A	N/A	N/A	N/A	1,89%	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	12-lead and iECG rhythm similar in 77,4%

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Smartwatch and smartphone based handheld device (Contiued)

Author	Study arm	Symptoms	Atrial arrhytmias				Ventricular arrhythmias			second degree AV block	Sinus node disease	clinical Arrhythmias	Management changes								Quality
			PAC	couplet /triplet	tachy	AF/ flutter	PVC couplet/ triplet	nsVT	VT				total	EP	PM	ICD	Medica- tion	test- ing	CV	Abla- tion	
Pengel	Withings	N/A	N/A	N/A	N/A	Sens: 100%	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	5% inconclusive (p<0.001)
		N/A	N/A	N/A	N/A	Spec: 100%	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	51% ECG good/ excellent
		N/A	N/A	N/A	N/A	3%	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	Kardia 6L	N/A	N/A	N/A	N/A	Sens: 100%	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
		N/A	N/A	N/A	N/A	Spec: 97%	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	74% good/ excellent
		N/A	N/A	N/A	N/A	3%	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	Eko DUO	N/A	N/A	N/A	N/A	3%	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	70% good/ excellent
Kauw	registration Kardia with palpitations	100%	6%	N/A	2%	21%	7%	N/A	N/A	N/A	N/A	18%	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2% noise
Koole	registration Kardia with palpitations	100%	11%	N/A	1%	1,00%	N/A	N/A	N/A	N/A	N/A	N/A	4%	N/A	N/A	N/A	4%	N/A	N/A	N/A	13% noise

Author	Study arm	Symptoms	Diagnosis								clinical Arrhyth-mias	Management changes								Quality
			Atrial arrhytmias			Ventricular arrhythmias			second degree AV block	Sinus node disease		total								
			PAC	couplet /triplet	tachy	AF/ flutter	PVC couplet/ triplet	nsVT	VT					EP	PM	ICD	Medica-tion	test-ing	CV	Abla-tion	
Implantable Loop Recorder																				
Dodeja		82%	N/A	N/A	36%	14%	N/A	5%	5%	N/A	9%	41%	41%	5%	5%	5%	18%	N/A	5%	N/A	14% false positives
Huntgeburth		79%	21%	N/A	15%	15%	21%	6%	6%	N/A	6%	N/A	27%	N/A	N/A	3%	12%	N/A	N/A	15%	N/A

Abbreviations: N/A=Not Applicable, AF=Atrial Fibrillation; AV=Atrioventricular; nsVT=non sustained Ventricular Tachycardia; PAC=Premature Atrial Complex; PVC=Premature Ventricular Complex; VT=Ventricular Tachycardia

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cardiovascular implantable electronic device [10]. The secondary outcome measure was the patient experience (Net Promotor Score (NPS)) and quality of life evaluated by using the patient reported outcome measurement (PROM) questionnaires and other techniques [12,13]. The quality and accuracy of the Electrocardiogram (ECG) were also evaluated if reported. The study characteristics are summarized in Table 1, the study results are summarized in Table 2.

3 CUMULATIVE HOLTER

Czosek et al. evaluated 589 cumulative Holter screenings in 189 ACHD patients (TOF after surgical repair, d-TGA with previous atrial switch operation, including Mustard or Senning palliation and single ventricle physiology after Fontan palliation). The clinical utility and cost effectiveness of consecutive Holter monitoring were evaluated. There were 22 (4%) Holter screenings that changed clinical management. However, 10 occurred after an earlier Holter with normal findings. A change of clinical management was defined as: ≥1 of the following clinical events: initiation of an electrophysiologic study, pacemaker or ICD implantation or replacement, initiation or change in antiarrhythmic drug therapy, or findings that directly led to additional diagnostics. The opportunity of finding an arrhythmia causing a change in management increased with age. Patients aged 18–25 years undergoing a Holter received a change in management in 4% of Holter studies while patients older than 25 years received a change in management in 6% of Holter studies. Furthermore, the underlying disease had an influence on the percentage of changes in management. After the Fontan procedure the changes in management were 6%. d-TGA resulted in changes in management in 5%. The accuracy of a single Holter can be projected by the positive and negative predicting value (PPV&NVP). The individual Holter studies were analyzed as separate events to determine the PPV and NPV of Holter monitoring in patients with and without clinical symptoms. The PPV of patient symptoms predicting a clinically significant finding on Holter study was low: 0.08 and the NPV was 0.97 [8].

4 TWO-WEEK CONTINUOUS MONITOR

Schultz et al. evaluated the diagnostic yield of two-week continuous rhythm monitoring with an adhesive patch extended cardiac ambulatory monitoring (Zio monitor, iRhythm, San Francisco, California) in a retrospective cohort study of ACHD patients. The indications for

extended monitoring included history of arrhythmia (20%), symptoms (39%), screening of arrhythmias due to history of CHD (28%), both symptoms and history of arrhythmia (10%), and abnormal testing (4%). The number and type of arrhythmias detected within and beyond the first 48 hours of monitoring were compared using Kaplan-Meier curves and Cox proportional hazard [14]. In 50% of studies the authors found clinically significant arrhythmia, of which 54% occurred after the first 48 hours. These findings led to a change in management including pacemaker or ICD implantation, medication changes or electrophysiology testing in 16% of the total amount of two-week continuous monitor studies. In 42% this resulted from a finding that presented after 48 hours. So, 7% of the total amount of two-week continuous monitor studies contained an arrhythmia after 48 hours that resulted in a change in management. Whereas 34% of the supraventricular tachycardia (SVT)'s resulted in a change in management, 66% of the non-sustained ventricular tachycardia (NSVT)'s resulted in a change. Atrial and ventricular arrhythmia have been shown to occur in up to 43% of patients with TOF and 100% of patients with Fontan physiology in long term follow-up. Accuracy of the two-week continuous monitor was evaluated by over-reading 10% of the two-week continuous monitor recordings by a study principal investigator. The authors concluded that no changes were indicated because of the good quality, and therefore no further over-reading was deemed necessary [14].

5 SMARTWATCH AND SMARTPHONE BASED SINGLE-LEAD ELECTROCARDIOGRAM

Striepe et al. evaluated the accuracy of 30 second Intelligent ECG's (iECG) of ACHD patients in three leads: Einthoven I/II/III-like leads [15]. The aim of their study was to evaluate if the Apple Watch iECG is interpretable in patients with CHD because a high-quality iECG would enable adult patients with CHD to use such a smartwatch as an event recorder. The iECGs were recorded by an Apple Watch Series 4. Included were 106 CHD patients. The ECG parameters seemed to be independent of the patient's characteristics, especially anatomy, electrical axis, or situs. They were compared to a 12-channel ECG. 77,4% of the iECG's diagnosed the same rhythm as by analysis of a cardiologist of the corresponding 12 lead ECG [15]. However the Apple Watch cannot recognize an escape rhythm, pacemaker rhythm or VT due to lack of algorithms: the smartwatch can only display sinus rhythm, atrial fibrillation or inconclusive. Therefore, seven pacemaker rhythms were automatically diagnosed as sinus rhythms, nine sinus rhythms were recognized as unclassifiable, and one sinus rhythm was defined as atrial fibrillation.

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Pengel et al. compared in a single-center, prospective cross-sectionals study Withings Scanwatch, EKO DUO (precordial lead) and Kardia 6L (6 leads) to the standard 12-lead ECG. They evaluated 30s ECGs of ACHD patients acquired by the Withings Scanwatch in I lead [16]. Of the ECGs acquired by the Scanwatch 51% were either of good or excellent quality. 70% of the EKO DUO device registrations and 74% of Kardia 6L registrations were of good or excellent quality. The Whitings Scanwatch algorithm was accurate for AF screening with a sensitivity of 100% and a specificity of 100%. Of these three devices 54% of the patients preferred the Withings Scanwatch, 23% preferred the Kardia 6L and 11% preferred EKO DUO. A majority of 80% was willing to use these devices.

Koole et al. studied 54 ACHD patients in a smartphone single lead ECG program consisting of routine single-lead ECGs once a month and on demand in case of symptoms [12]. In short, data were collected by mobile apps and matched with individualized thresholds. A management change by changing antiarrhythmic medication due arrhythmias found by smartphone single lead ECG was seen in 4% of patients. Of the recordings, 13% consisted of artifacts. They observed an overall positive effect on the quality of life of the ACHD patients who participated in a mHealth program. An extension of the same smartphone single lead ECG to 98 patients was evaluated by Kauw et al. [13]. The authors reported that clinically significant arrhythmia were found in 18% of patients. The majority of which were atrial fibrillation or flutter. They found in this group 4 new diagnosis (1 patient with sinus node dysfunction and 3 patients with paroxysmal atrial fibrillation) which led to intervention (electrical cardioversion) in 2 of these 4 cases.

6 IMPLANTABLE LOOP RECORDERS (ILR)

ILRs, instruments for long time rhythm monitoring, are used in a selected group of ACHD patients to detect arrhythmia especially in cases of unexplained syncope, infrequent symptomatic palpitations and cryptogenic ischemic stroke. Dodeja et al. evaluated in a single center retrospective review medical records of 22 ACHD patients who underwent an ILR implantation (Reveal LINQ, Medtronic) from 2014–2017 [10]. The ILR findings were compared to the prior Holter/event monitors. Also, the changes in management because of the ILR findings were specified. In 41% of their patients (Fontan 32%, TOF 32%, Other 36%) with ILR-implantations the authors found clinically significant arrhythmia that led to a change in patient management [10]. This percentage was higher in the patient group with Fontan (57%) and lower in the patient

group with TOF (14%). These changes in management consisted of medication changes (50%), ICD/pacemaker implantation (25%), cardioversion (12,5%) and electrophysiology studies (12,5%). Moreover, 14% of the ILR-registered arrhythmia was false positive. Huntgeburth et al. performed a single center, retrospective observational study in the German Heart Center Munich [17]. The ILR was implanted in 33 ACHD-patients (mean age, 43±20 years; 42.4% female). During a mean observation period of 697±433 days, clinically relevant arrhythmias, correlating with the patients' complaints and symptoms, were detected in 19 patients (59.4%) of whom in 9 patients (28.1%) the detected arrhythmia was considered an event requiring treatment. No acute complications are reported. Huntgeburth reported that 3 out of 33 patients needed explanation of the device because of pain or wound dehiscence.

The authors concluded that in symptomatic ACHD patients at risk for life-threatening cardiac events, ILR has a considerable complementary diagnostic value for the detection of malignant arrhythmias and in the differentiation with benign arrhythmias.

7 DISCUSSION

7.1 Diagnostic yield

The studies, although limited in number, were reviewed on extended rhythm monitoring in ACHD patients. The diagnostic yield of extended rhythm monitoring was high and determined between 18% (using smartphone single lead ECG program) and 41% using ILR. So more relevant new diagnosis of arrhythmia can be found by extending continuous monitoring over a longer period [12-14]. This finding is comparable to extended monitoring for atrial fibrillation in patients with cryptogenic stroke patients [18]. Also in these patients longer durations of monitoring were associated with the highest diagnostic yield [19,20]. Moreover, the optimal monitoring method and duration of monitoring are also in this population unclear [21-23]. Solbiati et al. performed a systematic Cochrane review on ILR performance and concluded that available data are non-conclusive. The authors therefore recommended further research on ILR with clinically relevant outcomes [24]. This could also be true for patients with ACHD.

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7.2 Change in clinical care management

The finding of an arrhythmia, important conduction disorder or severe bradycardia can cause change in clinical care management e.g.: correction of underlying structural abnormalities, initiation or adjustment of medication, cardioversion, electrophysiology study (EPS), ablation, or implantation of a cardiovascular implantable electronic device. Schultz et al showed detection of first arrhythmia that resulted in a change in management in 7% of ACHD patients only after 48 hours of rhythm monitoring (average time of monitoring 9.5±3.1 days) [14]. Dodeja et al. demonstrated ILR findings resulted in change in management was as high as 41%. Although these outcomes could not be compared directly due to differences in patient characteristics and indications for rhythm monitoring it still emphasizes the potency of extended rhythm screening beyond 48 hours, since it could have a considerable effect on patient care. Clinically significant arrhythmia could be missed by a short period of rhythm monitoring. Solbiati et al. came to the conclusion in a Cochrane Review that there is no evidence that an ILR-based diagnostic strategy reduces long-term mortality as compared to a standard diagnostic assessment (very low-quality evidence). No data were available for short-term all-cause mortality. Moderate quality evidence shows that an ILR-based diagnostic strategy increased the rate of aetiologic diagnosis as compared to a standard diagnostic pathway [24]. So it is still debated if a change in clinical management has the ability to change clinically relevant outcomes, not only on mortality but also on quality of life, syncope relapse and costs.

7.3 Device accuracy

Our results demonstrate a high device accuracy of smartwatches and other ambulant ECG monitors like Zio patch, EKO DUO or Kardia 6L in ACHD patients [16]. Striepe et al. demonstrated that the Apple Watch can record reliable iECGs in patients with congenital heart disease of any type [15].

Although false positive event recordings do occur and can lead to unnecessary stress for the patients and a higher workload for the healthcare workers, they probably outweigh the importance for the health of the ACHD patients in not missing clinically significant arrhythmia.

7.4 Limitations

This review was conducted to make an overview of the current arrhythmia screening instruments for ACHD patients as new innovative devices for this purpose are nowadays largely available. However, studies of ambulant extended screening of these patients for arrhythmia

with new devices as an alternative for Holter monitoring or ILR are scarce. The outcomes and the manner of measuring the outcomes differed between the articles. The most prominent division was between articles who evaluated the changes in patient management resulting from their findings and the articles who evaluated the accuracy of their device. Therefore, it was difficult to compare the articles we reviewed. Most of the articles discussed in this review have a single-centered study design (6/8). This is a limitation because it possibly degrades the transferability of the results. Also, two of the studies included are cross-sectional. Cross-sectional studies are less valuable since it is not possible to evaluate changes over time. The sample size in all the studies was relatively small, because ACHD is not a common disease. In addition, most of the studies did not use a control group or used the patients as their own control group. Another limitation is the selection bias by indication, which could play an important role as documented arrhythmia were one of the inclusion criteria in most of the articles. This could potentially imply that the patient population would be more prone to be admitted for arrhythmia in the last year before inclusion. On the other hand, these patients could have received appropriate antiarrhythmic drug therapy leading to a reduction in subsequent changes in management during the study period [2]. There is also a risk of bias because of risk profile. ILR is implanted in highly selected ACHD patients with a high-risk profile, accounting potentially for a higher diagnostic yield. Furthermore, for this review only one database was used, namely PubMed, and a restriction was put on language. Which possibly resulted in the overlooking of relevant articles from other databases or languages. Besides, a restriction was put on publication date; older relevant articles may have been missed.

7.5 Future directions

mHealth, defined as ambulant diagnostics, as wearables, mobile health applications (apps), patches with sensors and smartphone possibilities are rapidly evolving, and increasing in number [25,26,13]. mHealth can be an alternative for Holter monitoring and ILR monitoring. It has the advantage of the possibility of, almost continuously, monitoring heart rhythm for lifetime where Holter monitoring is limited to approximately 48 hours and ILR monitoring is limited by lifespan of the implanted battery.

However, to implement mHealth in routine care of ACHD patients is a challenge. First patients and physicians should be convinced of the added value using mHealth. Second these solutions should include a critical assessment of the associated costs [27]. The financial implications of mHealth include initial setup and maintenance expenses, and the potential long-term economic

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benefits. Insight in these costs is pivotal for stakeholders to make robust decisions and ensure the sustainable and equitable deployment of mHealth technologies. To be affordable, data-handling should be optimized and automized. Furthermore cost are dependent of the number of participants of a specific mHealth program because upfront investment costs might be considerable, fixed and variable costs change very little per additional patient compared to usual care [28]. Costs might be different between healthcare systems and countries. More research is needed to analyze cost-effectiveness of mHealth solutions regarding to these aspects.

Although health system governance, reimbursement and technological factors may complicate implementation; tools to identify barriers to implementing digital health and recommendations for overcoming them are increasingly available [29-32].

The optimal mode and duration of screening for arrhythmia can be different for asymptomatic patients compared with patients with palpitations or with patients who have experienced sudden syncope [33]. So new research initiatives for extended screening for arrhythmias in ACHD patients are needed to reveal whether a reduction in morbidity and mortality can be achieved in a specific patient population with early event recognition and intervention.

8 CONCLUSION

A limited number of studies on rhythm monitoring in ACHD patients demonstrated a higher rate of arrhythmia and bradycardia detection leading to clinical care changes by extending the time of rhythm monitoring to more than 24 hours. These clinical care changes include medication optimization, cardioversion, electrophysiology study, ablation, or implantation of a cardiovascular implantable electronic device. So extended monitoring seems to be important for patient care. Cumulative Holter monitoring, monitoring by wearable patches, smartwatches and smartphone single-lead ECG's are, in symptomatic patients, a good alternative for ILRs. However, the optimal mode of detection is still unclear due to the lack of head-to-head comparisons. These findings emphasize that randomized studies are needed to determine efficacy and indications for the various available instruments in ACHD patients.

To our knowledge, this is the first review on all available rhythm detection devices in ACHD patients to perform extended screening for arrhythmia. Our findings provide a broad insight in the device accuracy, diagnostic yield, and clinical outcome.

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REFERENCES

1. Stout KK, Daniels CJ, Aboulhosn JA, Bozkurt B, Broberg CS, Colman JM, Crumb SR, Dearani JA, Fuller S, Gurvitz M, Khairy P, Landzberg MJ, Saidi A, Valente AM, Van Hare GF. 2018 AHA/ACC Guideline for the Management of Adults With Congenital Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2019;73:e81–e192.

2. Baumgartner H, De Backer J, Babu-Narayan SV, Budts W, Chessa M, Diller G-P, Lung B, Kluin J, Lang IM, Meijboom F, Moons P, Mulder BJM, Oechslin E, Roos-Hesselink JW, Schwerzmann M, Sondergaard L, Zeppenfeld K, ESC Scientific Document Group. 2020 ESC Guidelines for the management of adult congenital heart disease. *Eur Heart J*. 2021;42:563–645.

3. Bouma BJ, Mulder BJM. Changing Landscape of Congenital Heart Disease. *Circ Res*. 2017;120:908–922.

4. van der Velde ET, Vander VET, Vriend JWJ, Mannens MMAM, Uiterwaal CSPM, Brand R, Mulder BJM. CONCOR, an initiative towards a national registry and DNA-bank of patients with congenital heart disease in the Netherlands: rationale, design, and first results. *Eur J Epidemiol*. 2005;20:549–557.

5. Koyak Z, Harris L, de Groot JR, Silversides CK, Oechslin EN, Bouma BJ, Budts W, Zwinderman AH, Van Gelder IC, Mulder BJM. Sudden cardiac death in adult congenital heart disease. *Circulation*. 2012;126:1944–1954.

6. Vehmeijer JT, Koyak Z, Leerink JM, Zwinderman AH, Harris L, Peinado R, Oechslin EN, Robbers-Visser D, Groenink M, Boekholdt SM, de Winter RJ, Oliver JM, Bouma BJ, Budts W, Van Gelder IC, Mulder BJM, de Groot JR. Identification of patients at risk of sudden cardiac death in congenital heart disease: The PRospEctiVE study on implaNTable cardIOverter defibrillator therapy and suddeN cardiac death in Adults with Congenital Heart Disease (PREVENTION-ACHD). *Heart Rhythm*. 2021.

7. Cohen MI, Khairy P, Zeppenfeld K, Van Hare GF, Lakkireddy DR, Triedman JK. Preventing Arrhythmic Death in Patients With Tetralogy of Fallot. *Journal of the American College of Cardiology* [Internet]. 2021 [cited 2023 Nov 24];77:761–771. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0735109720381079

8. Czosek RJ, Anderson J, Khoury PR, Knilans TK, Spar DS, Marino BS. Utility of ambulatory monitoring in patients with congenital heart disease. *Am J Cardiol*. 2013;111:723–730.

9. Schuuring MJ, Backx AP, Zwart R, Veelenturf AH, Robbers-Visser D, Groenink M, Abu-Hanna A, Bruining N, Schijven MP, Mulder BJ, Bouma BJ. Mobile health in adults with congenital heart disease: current use and future needs. *Neth Heart J*. 2016;24:647–652.

10. Dodeja AK, Thomas C, Daniels CJ, Kertesz N, Kamp A. Detection of arrhythmias in adult congenital heart disease patients with LINQTM implantable loop recorder. *Congenit Heart Dis*. 2019;14:745–751.

11. Dussault C, Toeg H, Nathan M, Wang ZJ, Roux J-F, Secemsky E. Electrocardiographic monitoring for detecting atrial fibrillation after ischemic stroke or transient ischemic attack: systematic review and meta-analysis. *Circ Arrhythm Electrophysiol*. 2015;8:263–269.

12. Koole M a. C, Kauw D, Winter MM, Dohmen D a. J, Tulevski II, de Haan R, Somsen GA, Schijven MP, Robbers-Visser D, Mulder BJM, Bouma BJ, Schuuring MJ. First real-world experience with mobile health telemonitoring in adult patients with congenital heart disease. *Neth Heart J*. 2019;27:30–37.

13. Kauw D, Koole MAC, Winter MM, Dohmen DAJ, Tulevski II, Blok S, Somsen GA, Schijven MP, Vriend JWJ, Robbers-Visser D, Mulder BJM, Bouma BJ, Schuuring MJ. Advantages of mobile health in the management of adult patients with congenital heart disease. *Int J Med Inform*. 2019;132:104011.

14. Schultz KE, Lui GK, McElhinney DB, Long J, Balasubramanian V, Sakarovitch C, Fernandes SM, Dubin AM, Rogers IS, Romfh AW, Motonaga KS, Viswanathan MN, Ceresnak SR. Extended cardiac ambulatory rhythm monitoring in adults with congenital heart disease: Arrhythmia detection and impact of extended monitoring. *Congenit Heart Dis*. 2019;14:410–418.

15. Striepe S, Michaelis A, Markel F, Kalden P, Löffelbein F, Bollmann A, Sepehri Shamloo A, Dähnert I, Gebauer RA, Paech C. Use of the Apple Watch iECG in adult congenital heart disease patients. *Indian Pacing Electrophysiol J*. 2022;22:131–136.

16. Pengel LKD, Robbers-Visser D, Groenink M, Winter MM, Schuuring MJ, Bouma BJ, Bokma JP. A comparison of ECG-based home monitoring devices in adults with CHD. *Cardiol Young*. 2022;1–7.

17. Huntgeburth M, Hohmann C, Ewert P, Freilinger S, Nagdyman N, Neidenbach R, Pieper L, Pieringer F, Lennerz C, Kaemmerer H, Kolb C. Implantable loop recorder for monitoring patients with congenital heart disease. *Cardiovasc Diagn Ther*. 2021;11:1334–1343.

18. Dilaveris PE, Antoniou CK, Caiani EG, Casado-Arroyo R, Climent AM, Cluitmans M, Cowie MR, Doehner W, Guerra F, Jensen MT, Kalarus Z, Locati ET, Platonov P, Simova I, Schnabel RB, Schuuring M, Tsivgoulis G, Lumens J. ESC Working Group on e-Cardiology Position Paper: accuracy and reliability of electrocardiogram monitoring in the detection of atrial fibrillation in cryptogenic stroke patients : In collaboration with the Council on Stroke, the European Heart Rhythm Association, and the Digital Health Committee. *European Heart Journal - Digital Health*. 2022;3:341–358.

19. Wachter R, Gröschel K, Gelbrich G, Hamann GF, Kermer P, Liman J, Seegers J, Wasser K, Schulte A, Jürries F, Messerschmid A, Behnke N, Gröschel S, Uphaus T, Grings A, Ibis T, Klimpe S, Wagner-Heck M, Arnold M, Protsenko E, Heuschmann PU, Conen D, Weber-Krüger M, Find-AF(randomised) Investigators and Coordinators. Holter-electrocardiogram-monitoring in patients with acute ischaemic stroke (Find-AFRANDOMISED): an open-label randomised controlled trial. *Lancet Neurol*. 2017;16:282–290.

20. Healey JS, Connolly SJ, Gold MR, Israel CW, Van Gelder IC, Capucci A, Lau CP, Fain E, Yang S, Bailleul C, Morillo CA, Carlson M, Themeles E, Kaufman ES, Hohnloser SH, ASSERT Investigators. Subclinical atrial fibrillation and the risk of stroke. *N Engl J Med*. 2012;366:120–129.

21. Kishore A, Vail A, Majid A, Dawson J, Lees KR, Tyrrell PJ, Smith CJ. Detection of atrial fibrillation after ischemic stroke or transient ischemic attack: a systematic review and meta-analysis. *Stroke*. 2014;45:520–526.

22. Albers GW, Bernstein RA, Brachmann J, Camm J, Easton JD, Fromm P, Goto S, Granger CB, Hohnloser SH, Hylek E, Jaffer AK, Krieger DW, Passman R, Pines JM, Reed SD, Rothwell PM, Kowey PR. Heart Rhythm Monitoring Strategies for Cryptogenic Stroke: 2015 Diagnostics and Monitoring Stroke Focus Group Report. *J Am Heart Assoc*. 2016;5:e002944.

23. Steinberg JS, Varma N, Cygankiewicz I, Aziz P, Balsam P, Baranchuk A, Cantillon DJ, Dilaveris P, Dubner SJ, El-Sherif N, Krol J, Kurpesa M, La Rovere MT, Lobodzinski SS, Locati ET, Mittal S, Olshansky B, Piotrowicz E, Saxon L, Stone PH, Tereshchenko L, Turitto G, Wimmer NJ, Verrier RL, Zareba W, Piotrowicz R. 2017 ISHNE-HRS expert consensus statement on ambulatory ECG and external cardiac monitoring/telemetry. *Heart Rhythm*. 2017;14:e55–e96.

8

24. Solbiati M, Costantino G, Casazza G, Dipaola F, Galli A, Furlan R, Montano N, Sheldon R. Implantable loop recorder versus conventional diagnostic workup for unexplained recurrent syncope. *Cochrane Database Syst Rev*. 2016;4:CD011637.

25. Svennberg E, Tjong F, Goette A, Akoum N, Di Biase L, Bordachar P, Boriani G, Burri H, Conte G, Deharo JC, Deneke T, Drossart I, Duncker D, Han JK, Heidbuchel H, Jais P, de Oliviera Figueiredo MJ, Linz D, Lip GYH, Malaczynska-Rajpold K, Márquez M, Ploem C, Soejima K, Stiles MK, Wierda E, Vernooy K, Leclercq C, Meyer C, Pisani C, Pak HN, Gupta D, Pürerfellner H, Crijns HJGM, Chavez EA, Willems S, Waldmann V, Dekker L, Wan E, Kavoor P, Turagam MK, Sinner M. How to use digital devices to detect and manage arrhythmias: an EHRA practical guide. *Europace*. 2022;24:979–1005.

26. Cowie MR, Bax J, Bruining N, Cleland JGF, Koehler F, Malik M, Pinto F, van der Velde E, Vardas P. e-Health: a position statement of the European Society of Cardiology. *Eur Heart J*. 2015.

27. Gentili A, Failla G, Melnyk A, Puleo V, Tanna GLD, Ricciardi W, Cascini F. The cost-effectiveness of digital health interventions: A systematic review of the literature. *Front Public Health* [Internet]. 2022 [cited 2023 Dec 12];10:787135. Available from: https://www.frontiersin.org/articles/10.3389/fpubh.2022.787135/full

28. Blok S, Van Der Linden EL, Somsen GA, Tulevski II, Winter MM, Van Den Born B-JH. Success factors in high-effect, low-cost eHealth programs for patients with hypertension: a systematic review and meta-analysis. *European Journal of Preventive Cardiology* [Internet]. 2021 [cited 2023 Oct 17];28:1579–1587. Available from: https://academic.oup.com/eurjpc/article/28/14/1579/6470904

29. Tromp J, Jindal D, Redfern J, Bhatt A, Séverin T, Banerjee A, Ge J, Itchhaporia D, Jaarsma T, Lanas F, Lopez-Jimenez F, Mohamed A, Perel P, Perez GE, Pinto F, Vedanthan R, Verstrael A, Yeo KK, Zulfiya K, Prabhakaran D, Lam CSP, Cowie MR. World Heart Federation Roadmap for Digital Health in Cardiology. *Glob Heart*. 2022;17:61.

30. Kauw D, Huisma PR, Medlock SK, Koole MAC, Wierda E, Abu-Hanna A, Schijven MP, Mulder BJM, Bouma BJ, Winter MM, Schuuring MJ. Mobile health in cardiac patients: an overview on experiences and challenges of stakeholders involved in daily use and development. *BMJ Innovations*. 2020;bmjinnov-2019-000418.

31. Treskes RW, Wildbergh TX, Schalij MJ, Scherptong RWC. Expectations and perceived barriers to widespread implementation of e-Health in cardiology practice: Results from a national survey in the Netherlands. *Neth Heart J*. 2019;27:18–23.

32. Schuuring MJ, Man JP, Chamuleau SAJ. Inclusive Health Tracking: Unlock the True Potential of Digital Health Solutions∗. *JACC: Advances*. 2023;2:100545.

33. Koole MA, Kauw D, Kooiman KM, de Groot JR, Robbers-Visser D, Tulevski II, Mulder BJ, Bouma BJ, Schuuring MJ. An implantable loop recorder or smartphone based single-lead electrocardiogram to detect arrhythmia in adults with congenital heart disease? *Front Cardiovasc Med* [Internet]. 2023 [cited 2023 Feb 7];9:1099014. Available from: https://www.frontiersin.org/articles/10.3389/fcvm.2022.1099014/full

Chapter 9

**General discussion,
future directions**

1 OVERVIEW DEVELOPMENT TELEMEDICINE AND DIGITAL REMOTE PATIENT MONITORING OVER THE LAST 25 YEARS

At the beginning of this century the technology of telemedicine became a realistic option for delivering healthcare. Telemedicine enables physicians to monitor and manage patients in nontraditional healthcare settings. Telemedicine uses technologies to collect health data from individuals in one location, such as a patient's home, and electronically transmit the information to healthcare providers in a different location for assessment and recommendations [1]. This information can support and optimize their care.

Rapid development of technical innovations (biosenors, mobile devices, apps) makes digital remote patient monitoring (DRPM) nowadays possible for the general population. Health parameters such as symptoms, pictures of skin, weight, heart rate, EKG, blood pressure, temperature, oxygen saturation and physical activity can be collected frequently at home, stored in an electronic health record and used to guide patients, to adjust therapy or to seek further advice.

Telemedicine including DRPM promises maintaining or even improving quality of care, facilitating rapid access to care when needed, reducing patient travel costs, minimizing the frequency of clinic visits and empowering patients by educational options of the apps connected to the monitoring devices. Furthermore it promises to be cost-effective compared to traditional healthcare [2]. So expectations of telemedicine are high by all stakeholders: patients, physicians, government, health insurance companies and industry. Many research projects have been done since to find out if these promises can be made true. However, in the beginning introduction of telemedicine in routine healthcare went slow, because of several reasons of which lack of knowledge of how to implement telemedicine in routine healthcare and lack of evidence for doing so were very important. This gap between awareness of the potential of eHealth and reality was recognized by the European Union resulting in an eHealth action plan for 2012–2020 which identified several barriers to widespread adoption of eHealth and by the European Society of Cardiology who published in 2015 a position statement on eHealth with an action plan to overcome these barriers [3]. In 2017 Tuckson et al. presented a special report in the New Journal of England which described five key trends that will influence the growth of telehealth care delivery and gave recommendations on 10 topics for designing and conducting telehealth

research projects. This topics are: physician leadership, reimbursement, licensure, liability, human factors, device interoperability and data integration, privacy and security, performance measurement, patient engagement and the evolving patient-physician relationship, research design and methods [4]. These great amount of topics reflects how huge the challenge is to develop a successful research program in this field. Many stakeholders are involved and the program can only be successful if they are successful in linking these topics. Moreover the weakest link can be determinative for the success of the program [5].

The outbreak of the COVID-19 pandemic in the beginning or 2020, resulted in healthcare givers to consider remote care for their chronic patients because face-to-face contacts during outpatient visits became limited to save hospital resources and limit disease transmission [6]. May 2023 marks the end of the pandemic and at that time we can conclude that the pandemia indeed had accelerated our knowledge by research results of applying telemedicine in specific patient populations [7,8].

In conclusion research in the field of telemedicine is challenging but necessary to obtain evidence and general agreement concerning the usefulness and effectivity of telemedicine. If this evidence and general agreement is obtained it deserves to be a part of routine health care delivery and become part of the guidelines of managing diseases. In chapter 2 we describe crowdfunding as a possibility for funding these research projects [9].

2 DIGITAL REMOTE PATIENT MONITORING IN CARDIOLOGY

In diagnosing and treatment of heart failure and arrhythmia, physiological parameters as for example heart rhythm, blood pressure, filling pressures, weight and physical activity, can nowadays be easily obtained by DRPM. However, how to interpret these data and the value of these data for managing heart failure and arrhythmias, obtained by DRPM, is still part of scientific debate.

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2.1 Heart failure

Early telemonitoring of weight and symptoms did not decrease heart failure hospitalizations but helped identify steps toward effective monitoring programs [10]. This resulted in monitoring programs that are nowadays more and more successful.

In a recent telemonitoring for heart failure meta-analysis the use of (non-)invasive telemonitoring systems compared to standard care reduced all-cause mortality by 16%, first hospitalizations by 19%, and total heart failure hospitalizations by 15% [11]. However, the results of the primary endpoint of the 73 included telemedicine randomized clinical trials shows exceedingly heterogeneity. This can be explained by several factors; such as:

- *Communication pathways*: intervention effects are strongly influenced by communication processes and interactions between caregiver and patient in digital care;
- *Patient selection*: of all heart failure patients only certain subpopulations may benefit from telemonitoring;
- *Technology:* the telemedical sensor technologies used differ significantly with respect to the type of signal obtained remotely and the usefulness of the signal to guide therapy;
- *Time to intervention*: critical factor for effectiveness is the speed at which transmitted diagnostic information is translated into medical action by the caregiver [12].

According to the current European Society of Cardiology guidelines home telemonitoring may be now considered as part of treatment of heart failure [13]. These guidelines also advise to realize optimal medical therapy with rapid sequencing and to avoid delays [13]. Digital consults to improve efficiency on guideline-directed therapy optimization for patients with heart failure is now being evaluated in the ADMINISTER trial [14].

2.2 Arrhythmia

Mobile devices for heart rhythm monitoring, defined as ambulant diagnostics, is rapidly evolving as wearables, mobile health applications (apps) and smartphone possibilities are improving, and increasing in number [2,12,13]. Remote monitoring of heart rhythm with implantable or wearable devices is becoming increasingly popular among health care practitioners and patients for long-term continuous monitoring and diagnosis of cardiac diseases [15,16]. As a consequence of continuous ambulant monitoring low burden arrhythmias are now easily detected. However the therapeutic consequences of a low burden arrythmia can be different comparing to high burden arrhythmia as, for example, is demonstrated by the NOAH-AFNET 6 trial [17].

3 DIGITAL REMOTE MONITORING IN ADULT CONGENITAL HEART DISEASE PATIENTS

Many ACHD patients are lifelong affected by cardiac events [18,19]. This is a growing patient group, as survival has increased in the last decades [20]. Clinical and subclinical heart failure and arrhythmias play a critical role in the morbidity and mortality of ACHD patients [21]. Regular monitoring and timely intervention are essential for comprehensive care. Timely intervention may prevent hospitalization for acute heart failure. The potential association between arrhythmias and sudden cardiac death underscores the need for effective screening strategies [22]. Due to the heterogeneity of the pathophysiology of cardiorespiratory dysfunction in the ACHD population extrapolation of current heart failure treatment guidelines to ACHD patients is not always appropriate. Furthermore, the few available data on heart failure treatments are often inconclusive and are derived from small patients cohorts. As a consequence, ACHD specific recommendations are mostly based on clinical position statements [13,23].

So although DRPM is nowadays widely available this has still not a significant position in the guidelines for management of ACHD patients.

Our research project aimed to get more insights into the value of DRPM in this specific, but heterogeneous, population [24-27]. Traditional methods such as Holter monitors have been the standard for arrhythmia screening, as recommended by the European Society of Cardiology guidelines for the management of ACHD [28]. Our narrative review highlights the emergence of novel, non-invasive monitoring technologies (chapter 8). These include smartwatch/ smartphone-based single-lead electrocardiograms (ECGs), presenting promising alternatives to traditional approaches [27]. Extended rhythm monitoring resulted in meaningful changes in clinical care for ACHD patients. Changes included adjustments in medication, cardioversion, electrophysiology studies, ablation, and the implantation of cardiovascular implantable electronic devices. Our review suggests that extended monitoring beyond the conventional 24–48 hours may lead to more precise and timely interventions, also in ACHD patients, potentially improving patient outcomes. The accuracy of the devices used for extended monitoring, such as smartwatches and patch-based monitors, was generally high. However, false-positive recordings were acknowledged, indicating the need for ongoing refinement in algorithms to minimize unnecessary stress for patients and healthcare providers. Limitations in the reviewed studies, including small sample sizes, selection bias, and variations in outcome measurement, must be considered when interpreting the results.

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4 FUTURE DIRECTIONS

Future directions for DRPM are related to continuous technological advancements, mHealth apps for patient engagement, data security and privacy issues and evolving remote consultations and telemedicine. Key points for future research are given.

4.1.1 Continuous technological advancements

Given the rapidly evolving landscape of DRPM technologies, continuous monitoring of technological advancements is essential. Advancements in wearable technology, such as smart-watches and patches, will play a pivotal role in continuous monitoring. Future devices may offer extended battery life, improved data accuracy, and enhanced connectivity.

Long-term remote monitoring generates substantial amounts of data. Artificial intelligence (AI) can analyze complex data patterns, detect subtle changes in cardiac parameters, and provide early warnings for potential issues. Leveraging of AI for longitudinal data analysis and predictive analytics can assist in identifying trends, predicting disease progression, and individualizing treatment plans. Machine learning algorithms can learn from patient-specific data, leading to personalized risk assessments and tailored interventions. Integration of AI in wearables can enable real-time data analysis, allowing for the immediate identification of abnormal heart rhythms or other concerning trends.

4.1.2 mHealth apps for patient engagement

Future mobile health (mHealth) applications should focus on promoting active patient engagement. User-friendly apps that encourage self-monitoring, medication adherence, and lifestyle management can significantly contribute to overall cardiovascular health. AI-powered apps can provide personalized health recommendations based on individual patient data, fostering a proactive approach to managing ACHD.

4.1.3 Data security and privacy

Ensuring compliance with healthcare data protection regulations is essential to build trust among patients and healthcare providers. AI algorithms should be developed with a focus on privacy-preserving techniques, allowing for effective analysis while safeguarding sensitive patient information.

4.1.4 Remote consultations and telemedicine

Telemedicine platforms should continue to evolve, providing not only remote consultations but also comprehensive cardiac assessments. Integration of advanced imaging technologies and AI in telemedicine can enhance the accuracy of remote diagnostics. Implementing secure and efficient communication channels will be crucial for remote consultations between patients, caregivers, and healthcare providers. Future solutions should facilitate seamless collaboration between patients and healthcare professionals. Integration of AI in electronic health records can streamline data interpretation, enabling more efficient decision-making during clinical consultations. AI-assisted decision support systems can offer evidence-based recommendations to healthcare providers, aiding in the management of complex ACHD cases.

4.2 Key points for future research

4.2.1 Comparative effectiveness studies

Given the lack of head-to-head comparisons among different monitoring instruments, future studies should focus on comparative effectiveness. Randomized controlled trials can help identify the optimal mode of detection for various devices, considering factors such as accuracy, patient preference, and costs-effectiveness.

4.2.2 Long-term outcomes

While changes in clinical care management were observed in response to extended monitoring, there is a need for research assessing long-term outcomes. Studies should investigate whether these changes translate into improvements in morbidity, mortality, quality of life, and healthcare costs for ACHD patients.

4.2.3 Patient and Physician Perspectives

Exploring the perspectives of both patients and physicians is vital for successful implementation. Studies should investigate factors influencing acceptance, usability, and satisfaction with extended arrhythmia monitoring technologies among ACHD patients and healthcare providers.

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4.2.4 Tailoring Monitoring Strategies

Research initiatives should explore the optimal monitoring strategy based on patient characteristics, including asymptomatic patients, those with palpitations, and individuals with a history of syncope. Tailoring monitoring approaches to specific patient populations can enhance the precision of arrhythmia detection.

4.2.5 Barriers to implementation

Identifying and addressing barriers to the implementation of digital health solutions is crucial [5,29]. Research should focus on governance, reimbursement policies, and technological factors that may impact the widespread adoption of extended arrhythmia monitoring in routine care.

4.2.6 Cost-effectiveness and health economics

Future research should evaluate the cost-effectiveness of implementing mHealth, eHealth, and telemonitoring solutions for ACHD patients. Understanding the economic impact and demonstrating the value of these technologies will be crucial for widespread adoption. Cost-effectiveness analyses should be conducted to evaluate the financial impact of these technologies on healthcare systems, considering factors such as initial setup costs, maintenance expenses, and long-term economic benefits.

With respect to the costs Blok et al. concluded in 2020 in a systematic review and meta-analysis that effective DRPM with limited additional costs should focus on high intensity interventions, involve a large number of participants and use DRPM as a partial replacement for usual care [30]. Furthermore future research should strive to standardize modes of effective DRPM [11].

5 CONCLUSION

DRPM using innovative technologies shows great promise in improving the care of ACHD patients. The high diagnostic yield and potential for meaningful changes in clinical care underscore the need for further research, including randomized studies to determine the efficacy and indications of different monitoring instruments. As mHealth technologies continue to evolve, they can play a crucial role in enhancing the management of health care in the growing population of ACHD patients.

The future of remote monitoring for ACHD patients lies in the integration of AI, continuous advancements in wearable technology, a focus on patient engagement, and a commitment to data security and privacy. These innovations have the potential to revolutionize the management of congenital heart disease, leading to improved outcomes and enhanced quality of life for patients.

An expert team consisting of IT specialists, lawyers, managers, dedicated physicians and patients could be crucial for successful implementation and maintaining DRPM.

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REFERENCES

1.   Vegesna A, Tran M, Angelaccio M, Arcona S. Remote Patient Monitoring via Non-Invasive Digital Technologies: A Systematic Review. *Telemedicine and e-Health*. 2017;23:3–17.

2.   Gentili A, Failla G, Melnyk A, Puleo V, Tanna GLD, Ricciardi W, Cascini F. The cost-effectiveness of digital health interventions: A systematic review of the literature. *Front Public Health*. 2022;10:787135.

3.   Cowie MR, Bax J, Bruining N, Cleland JGF, Koehler F, Malik M, Pinto F, van der Velde E, Vardas P. e-Health: a position statement of the European Society of Cardiology. *Eur Heart J*. 2016;37:63–66.

4.   Tuckson RV, Edmunds M, Hodgkins ML. Telehealth. *N Engl J Med*. 2017;377:1585–1592.

5.   Kauw D, Huisma PR, Medlock SK, Koole MAC, Wierda E, Abu-Hanna A, Schijven MP, Mulder BJM, Bouma BJ, Winter MM, Schuuring MJ. Mobile health in cardiac patients: an overview on experiences and challenges of stakeholders involved in daily use and development. *BMJ Innov*. 2020;bmjinnov-2019-000418.

6.   Schuuring MJ, Kauw D, Bouma BJ. COVID-19 pandemic: practical considerations on rapid initiation of remote care in chronic cardiac patients. *European Heart Journal – Digital Health*. 2020;1:8–9.

7.   Mann DM, Chen J, Chunara R, Testa PA, Nov O. COVID-19 transforms health care through telemedicine: Evidence from the field. *Journal of the American Medical Informatics Association*. 2020;27:1132–1135.

8.   Garfan S, Alamoodi AH, Zaidan BB, Al-Zobbi M, Hamid RA, Alwan JK, Ahmaro IYY, Khalid ET, Jumaah FM, Albahri OS, Zaidan AA, Albahri AS, Al-qaysi ZT, Ahmed MA, Shuwandy ML, Salih MM, Zughoul O, Mohammed KI, Momani F. Telehealth utilization during the Covid-19 pandemic: A systematic review. *Computers in Biology and Medicine*. 2021;138:104878.

9.   Koole MAC, Kauw D, Winter MM, Schuuring MJ. A successful crowdfunding project for eHealth research on grown-up congenital heart disease patients. *International Journal of Cardiology*. 2018;273:96–99.

10.   Stevenson LW, Ross HJ, Rathman LD, Boehmer JP. Remote Monitoring for Heart Failure Management at Home. *Journal of the American College of Cardiology*. 2023;81:2272–2291.

11.   Scholte NTB, Gürgöze MT, Aydin D, Theuns DAMJ, Manintveld OC, Ronner E, Boersma E, De Boer RA, Van Der Boon RMA, Brugts JJ. Telemonitoring for heart failure: a meta-analysis. *European Heart Journal*. 2023;44:2911–2926.

12.   Koehler F, Hindricks G. Is telemonitoring for heart failure ready after a journey longer than two decades? *European Heart Journal*. 2023;44:2927–2929.

13.   McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, Burri H, Butler J, Čelutkienė J, Chioncel O, Cleland JGF, Coats AJS, Crespo-Leiro MG, Farmakis D, Gilard M, Heymans S, Hoes AW, Jaarsma T, Jankowska EA, Lainscak M, Lam CSP, Lyon AR, McMurray JJV, Mebazaa A, Mindham R, Muneretto C, Francesco Piepoli M, Price S, Rosano GMC, Ruschitzka F, Kathrine Skibelund A, ESC Scientific Document Group. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC. *European Heart Journal*. 2021;42:3599–3726.

14. Man JP, Dijkgraaf MGW, Handoko ML, De Lange FJ, Winter MM, Schijven MP, Stienen S, Meregalli P, Kok WEM, Kuipers DI, Van Der Harst P, Koole MAC, Chamuleau SAJ, Schuuring MJ. Digital consults to optimize guideline-directed therapy: design of a pragmatic multicenter randomized controlled trial. *ESC Heart Failure*. 2023;ehf2.14634.

15. Patel S, Park H, Bonato P, Chan L, Rodgers M. A review of wearable sensors and systems with application in rehabilitation. *J Neuroeng Rehabil*. 2012;9:21.

16. Sana F, Isselbacher EM, Singh JP, Heist EK, Pathik B, Armoundas AA. Wearable Devices for Ambulatory Cardiac Monitoring. *Journal of the American College of Cardiology*. 2020;75:1582–1592.

17. Kirchhof P, Toennis T, Goette A, Camm AJ, Diener HC, Becher N, Bertaglia E, Blomstrom Lundqvist C, Borlich M, Brandes A, Cabanelas N, Calvert M, Chlouverakis G, Dan G-A, De Groot JR, Dichtl W, Kravchuk B, Lubiński A, Marijon E, Merkely B, Mont L, Ozga A-K, Rajappan K, Sarkozy A, Scherr D, Sznajder R, Velchev V, Wichterle D, Sehner S, Simantirakis E, Lip GYH, Vardas P, Schotten U, Zapf A. Anticoagulation with Edoxaban in Patients with Atrial High-Rate Episodes. *N Engl J Med*. 2023;389:1167–1179.

18. Zomer AC, Vaartjes I, van der Velde ET, de Jong HMY, Konings TC, Wagenaar LJ, Heesen WF, Eerens F, Baur LHB, Grobbee DE, Mulder BJM. Heart failure admissions in adults with congenital heart disease; risk factors and prognosis. *Int J Cardiol*. 2013;168:2487–2493.

19. Zomer AC, Vaartjes I, Uiterwaal CSPM, van der Velde ET, van den Merkhof LFM, Baur LHB, Ansink TJM, Cozijnsen L, Pieper PG, Meijboom FJ, Grobbee DE, Mulder BJM. Circumstances of death in adult congenital heart disease. *International Journal of Cardiology*. 2012;154:168–172.

20. van der Bom T, Zomer AC, Zwinderman AH, Meijboom FJ, Bouma BJ, Mulder BJM. The changing epidemiology of congenital heart disease. *Nat Rev Cardiol*. 2011;8:50–60.

21. Diller G-P, Kempny A, Alonso-Gonzalez R, Swan L, Uebing A, Li W, Babu-Narayan S, Wort SJ, Dimopoulos K, Gatzoulis MA. Survival Prospects and Circumstances of Death in Contemporary Adult Congenital Heart Disease Patients Under Follow-Up at a Large Tertiary Centre. *Circulation*. 2015;132:2118–2125.

22. Koyak Z, Harris L, de Groot JR, Silversides CK, Oechslin EN, Bouma BJ, Budts W, Zwinderman AH, Van Gelder IC, Mulder BJM. Sudden cardiac death in adult congenital heart disease. *Circulation*. 2012;126:1944–1954.

23. Budts W, Roos-Hesselink J, Rädle-Hurst T, Eicken A, McDonagh TA, Lambrinou E, Crespo-Leiro MG, Walker F, Frogoudaki AA. Treatment of heart failure in adult congenital heart disease: a position paper of the Working Group of Grown-Up Congenital Heart Disease and the Heart Failure Association of the European Society of Cardiology. *Eur Heart J*. 2016;37:1419–1427.

24. Roderick W Treskes, Maarten Koole, Dirkjan Kauw, Michiel M Winter, Moreno Monteiro, Daan Dohmen, Ameen Abu-Hanna, Marlies P Schijven, Barbara J Mulder, Berto J Bouma, Mark J Schuuring. Adults with congenital heart disease: ready for mobile health? *NEHJ*. 2019;27:152–160.

25. Koole MAC, Kauw D, Winter MM, Dohmen DAJ, Tulevski II, de Haan R, Somsen GA, Schijven MP, Robbers-Visser D, Mulder BJM, Bouma BJ, Schuuring MJ. First real-world experience with mobile health telemonitoring in adult patients with congenital heart disease. *Neth Heart J*. 2019;27:30–37.

26. Kauw D, Koole MAC, Winter MM, Dohmen DAJ, Tulevski II, Blok S, Somsen GA, Schijven MP, Vriend JWJ, Robbers-Visser D, Mulder BJM, Bouma BJ, Schuuring MJ. Advantages of mobile health in the management of adult patients with congenital heart disease. *International Journal of Medical Informatics*. 2019;132:104011.

9

27. Koole MA, Kauw D, Kooiman KM, de Groot JR, Robbers-Visser D, Tulevski II, Mulder BJ, Bouma BJ, Schuuring MJ. An implantable loop recorder or smartphone based single-lead electrocardiogram to detect arrhythmia in adults with congenital heart disease? *Front Cardiovasc Med*. 2023;9:1099014.

28. Baumgartner H, De Backer J, Babu-Narayan SV, Budts W, Chessa M, Diller G-P, Lung B, Kluin J, Lang IM, Meijboom F, Moons P, Mulder BJM, Oechslin E, Roos-Hesselink JW, Schwerzmann M, Sondergaard L, Zeppenfeld K, ESC Scientific Document Group. 2020 ESC Guidelines for the management of adult congenital heart disease. *Eur Heart J*. 2021;42:563–645.

29. Voogt MP, Opmeer BC, Kastelein AW, Jaspers MWM, Peute LW. Obstacles to Successful Implementation of eHealth Applications into Clinical Practice. *Stud Health Technol Inform*. 2018;247:521–525.

30. Blok S, Van Der Linden EL, Somsen GA, Tulevski II, Winter MM, Van Den Born B-JH. Success factors in high-effect, low-cost eHealth programs for patients with hypertension: a systematic review and meta-analysis. *European Journal of Preventive Cardiology*. 2021;28:1579–1587.

Chapter 10

Summary

CHAPTER 1

A general introduction and outline of this thesis is given in chapter 1. It describes the shift of monitoring patients from outpatient setting to remote monitoring at home made possible by the digital revolution. This thesis focuses on the question whether introducing digital remote patient monitoring (DRPM) by a dedicated eHealth program in the routine care management of adult congenital heart disease (ACHD) patients improves care for these patients.

CHAPTER 2

We describe in chapter 2 the successfully funding of our mHealth project with crowdfunding. We postulate the following critical success factors have contributed to success of the crowdfunding project: support of a professional organisation, selection after peer review, support of motivated patient, involvements of motivated physicians, interesting rewards, a funding goal, and strong (social) media. Furthermore, the crowdfunding campaign could have met the needs of donors, leading to enforcing of the public engagement.

CHAPTER 3

We identify in chapter 3 the clinical characteristics of ACHD patients with high emergency care utilisation and test whether these patients were willing to start using mHealth. Patients who are symptomatic, those on antiarrhythmic drug therapy and those on diuretics are not only optimal candidates but also motivated for enrolment in using mHealth. Our study contributes to appropriate patient selection for mHealth initiatives that aims to prevent emergency care utilisation, thereby contributing to an efficient use of mHealth.

CHAPTER 4

In chapter 4 we present the first results of an observational prospective registry to evaluate feasibility of a mHealth telemonitoring program for managing arrhythmia, heart failure and blood pressure in symptomatic ACHD patients. The relatively young population of ACHD patients demonstrated a high adherence. mHealth telemonitoring might be a powerful tool for remote diagnosing and managing arrhythmias, heart failure and blood pressure This can result in better quality of healthcare in this patient group.

CHAPTER 5

In chapter 5 we disclose the results of the study, described in chapter 4, after a follow-up of 12 months. We found that with this telemonitoring program early detection of recurrences and new diagnosis of arrhythmias, hypertension and heart failure are found which lead to swift therapeutic response or remote reassurance.

CHAPTER 6

Chapter 6 the authors illustrates the potential of participation in a mHealth program by a patient case. After many years of complaints and several 24h electrocardiogram recordings at last diagnosis was found in this patient soon after inclusion in a mHealth telemonitoring program.

CHAPTER 7

Chapter 7 describes a study in which baseline and follow-up data of symptomatic ACHD patients who received an implantable loop recorder (ILR) were compared to data of patients who participated in a smartphone based single-lead electrocardiogram study. The primary endpoint was time to first detected arrhythmia. The authors concluded that non-invasive smartphone based single-lead electrocardiogram monitoring can be an acceptable alternative for ILR implantation in detecting arrhythmia in symptomatic ACHD patients in respect to diagnostic yield, safety and management decisions, especially in those without syncope.

CHAPTER 8

A narrative review is presented in chapter 8 of scientific publications published between January 2007 and October 2022 regarding extended arrhythmia screening in ACHD patients. The number of studies found was limited. The studies demonstrated a higher rate of arrhythmia and bradycardia detection leading to clinical care changes by extending the time of rhythm monitoring to more than 24 hours. Cumulative Holter monitoring, monitoring by wearable patches, smartwatches and smartphone single-lead ECG's are, in symptomatic patients, a good alternative for ILRs. However, the optimal mode of detection is still unclear due to the lack of head-to-head comparisons.

CHAPTER 9

This chapter presents an overview of the development of telemedicine and digital remote patient monitoring over the last 25 years. In cardiology telemedicine is introduced, among other things, for care for patients with heart failure and (possible) arrhythmia. This chapter explains why this can be of special interest for adult patients with congenital heart disease. Future directions for DRPM and key points for future DRPM research are given.

Chapter 11

Samenvatting (summary in Dutch)

HOOFDSTUK 1

Hoofdstuk 1 is een algemene inleiding bij dit proefschrift met daarbij ook een inleiding op de hoofdlijnen en de studies die in dit proefschrift worden gepresenteerd. In dit proefschrift staat de vraag centraal of het introduceren van een programma voor thuismonitoring de zorg voor volwassen patiënten met een aangeboren hartafwijkingen (ACHD) kan verbeteren.

HOOFDSTUK 2

In hoofdstuk 2 beschrijven wij de succesvolle financiering van ons onderzoek naar thuis-monitoring programma door middel van crowdfunding. We veronderstellen dat een aantal belangrijke factoren hebben bijgedragen aan het succes. Deze factoren zijn: ondersteuning door een professionele organisatie, selectie van het onderzoek door middel van peer review, promotie door gemotiveerde patiënten, betrokkenheid van toegewijde artsen, interessante beloningen voor donateurs, een duidelijke financieel doel en optimale benutting van (social) media. Bovendien kan de crowdfunding campagne voldoen aan de behoeften van donateurs, wat kan leiden tot grotere publieke betrokkenheid.

HOOFDSTUK 3

In hoofdstuk 3 identificeren wij de klinische kenmerken van ACHD-patiënten die wegens klachten de Eerste Hulp afdeling van het ziekenhuis hadden bezocht. Vervolgens onderzochten wij of patiënten met deze kenmerken bereid zijn deel te nemen aan een mHealth programma. Symptomatische patiënten en patiënten die medicatie voor hartritmestoornissen en/of diuretica gebruiken, blijken niet alleen optimale kandidaten te zijn, maar zijn ook gemotiveerd om deel te nemen aan een mHealth programma. Onze studie draagt bij aan een geschikte selectie van patiënten voor deelname aan mHealth initiatieven met als doel de vraag naar spoedeisende zorg te voorkomen en daardoor een efficiëntere zorgverlening te bewerkstelligen.

HOOFDSTUK 4

In hoofdstuk 4 presenteren we de eerste resultaten van ons onderzoek naar de haalbaarheid van een mHealth programma dat door middel monitoring op afstand bijdraagt aan de behandeling van aritmie, hartfalen en hypertensie bij symptomatische ACHD-patiënten. Deze relatief jonge patiënten waren enthousiast over hun deelname aan dit programma. Thuismonitoring van bepaalde gezondheidsparameters kan een krachtig hulpmiddel zijn voor het op afstand diagnosticeren en behandelen van hartritmestoornissen, hartfalen en hypertensie. Dit kan leiden tot een betere kwaliteit van zorg in deze patiëntengroep.

HOOFDSTUK 5

In hoofdstuk 5 worden de resultaten van ons onderzoek (zoals beschreven in hoofdstuk 4) na een follow-up termijn van 12 maanden gepresenteerd. We zagen dat met ons thuismonitoring programma recidieven en nieuwe diagnoses van aritmie, hartfalen en hypertensie in een vroeg stadium werden gevonden. Dit heeft geleid tot een snelle therapeutische respons of gerust-stelling op afstand.

HOOFDSTUK 6

In hoofdstuk 6 illustreren de auteurs aan de hand van een casus de meerwaarde van thuismonitoring. Bij een patiënt kon, na vele jaren van klachten en meerdere 24-uurs Holter onderzoeken, uiteindelijk door deelname aan ons thuismonitoring programma de diagnose worden gesteld.

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HOOFDSTUK 7

Hoofdstuk 7 beschrijft een studie waarin baseline- en follow-up gegevens van symptomatische ACHD-patiënten die een implanteerbare loop recorder (ILR) kregen, werden vergeleken met gegevens van patiënten die thuis ritmestroken registreerden met behulp van hun mobiele telefoon. Het primaire eindpunt was de tijd nodig om de eerste aritmie te detecteren. De auteurs komen tot de conclusie het vastleggen van het hartritme met behulp van 1 afleiding ritmestroken door de mobiele telefoon voor het detecteren van aritmie bij deze patiënten een acceptabel alternatief kunnen zijn voor een ILR. Dit geldt zowel voor de diagnostische opbrengst, als voor de veiligheid en het kiezen van de juiste behandeling.

HOOFDSTUK 8

In hoofdstuk 8 wordt een narratief overzicht gepresenteerd van wetenschappelijke studies (gepubliceerd tussen januari 2007 en oktober 2022) met als onderwerp het screenen van ACHD patiënten op aritmie gedurende langere tijd dan de gebruikelijke 24–48 uur. Het aantal studies dat werd gevonden was beperkt. Bij ritme monitoring gedurende langere periode dan 24 uur werden regelmatig niet eerder ontdekte ritme- of geleidingstoornissen gevonden. Deze gaven vaak aanleiding de behandeling aan te passen. Cumulatieve Holter-monitoring, monitoring door draagbare patches, smartwatches en smartphone-ECG's met één afleiding kunnen bij symptomatische patiënten een goed alternatief zijn voor ILR's. De optimale detectiemethode is echter nog onduidelijk vanwege het gebrek aan onderling vergelijkende studies.

HOOFDSTUK 9

Dit hoofdstuk geeft een overzicht van de ontwikkeling van telemonitoring in de afgelopen 25 jaar. In de cardiologie wordt telemonitoring onder meer geïntroduceerd bij de zorg voor patiënten met hartfalen en (mogelijke) hartritmestoornissen. In dit hoofdstuk wordt uitgelegd waarom dit ook de zorg voor ACHD patiënten ten goede kan komen. Er wordt stil gestaan bij de toekomstige ontwikkelingen in telemonitoring en de belangrijkste aandachtspunten voor toekomstig telemonitoring onderzoek worden genoemd.

Appendices

List of publications

Contributing authors

PhD Portfolio

Dankwoord

About the author (curriculum vitae)

List of publications

Included in this thesis:

M.A.C. Koole, D. Kauw, M.M. Winter, M.J. Schuuring. A successful crowdfunding project for eHealth research on grown-up congenital heart disease patients. *International Journal of Cardiology.* 2018;273:96–99.

M.A.C. Koole, D. Kauw, M.M. Winter, D.A.J. Dohmen, I.I. Tulevski, R. de Haan, G.A. Somsen, M.P. Schijven, D. Robbers-Visser, B.J.M. Mulder, B.J. Bouma, M.J. Schuuring. First real-world experience with mobile health telemonitoring in adult patients with congenital heart disease. *Netherlands Heart Journal.* 2019;27:152–160.

D. Kauw*, M.A.C. Koole*, M.M. Winter, D.A.J. Dohmen, I.I. Tulevski, S. Blok, G.A. Somsen, M.P. Schijven, J.W.J. Vriend, D. Robbers-Visser, B.J.M. Mulder, B.J. Bouma, M.J. Schuuring. Advantages of mobile health in the management of adult patients with congenital heart disease. *International Journal of Medical Informatics.* 2019;132:104011. *Both authors contributed equally to this work*

M.A.C. Koole, G.A. Somsen, I.I. Tulevski, M.M. Winter, B.J. Bouma, M.J. Schuuring. At last, mobile health leading to a diagnosis in a young patient with congenital heart disease. *Netherlands Heart Journal* 2019;27:162–163.

M.A.C. Koole, D. Kauw, K.M. Kooiman, J.R. de Groot, D. Robbers-Visser, I.I. Tulevski, B.J.M. Mulder, B.J. Bouma, M.J. Schuuring. An implantable loop recorder or smartphone based single-lead electrocardiogram to detect arrhythmia in adults with congenital heart disease? *Frontiers Cardiovascular Medicine.* 9:1099014.

M.A.C. Koole, S. de Jong, B.J.M. Mulder, B.J. Bouma, M.J. Schuuring. Value of extended arrhythmia screening in adult congenital heart disease patients. *Arrhythmia & Electrophysiology Review 2024;13:e07*

Not included in this thesis:

G. Van Camp, R.R. Franken, D. Schoors, Y. Hagers, M.A.C. Koole, D. Demoor, P. Melis, P. Block. Impact of Second Harmonic Imaging on the Determination of the Global and Regional Left Ventricular Function by 2D Echocardiography: a Comparison with MIBI Gated SPECT. *Eur J Echocardiography* (2000);1:122–129.

Y. Hagers**,** M.A.C. Koole, D. Schoors, G. Van Camp. Tricuspid Stenosis: A Rare Complication of Pacemaker-Related Endocarditis. *J.Am.Soc.Echocardiogr* 2000;13:66–8

M.A.C. Koole, A. Aerts, J. Praet, R.R. Franken, P. Dendale. P. Block. Venous pooling during nitrate-stimulated tilt testing in patients with vasovagal syncope. *Europace* (2000) 2, 343–345

V. Rizzello, J.R.T.C. Roelandt, A.F.L. Schinkel, M.A.C. Koole, D. Poldermans. Polymorphic ventricular tachycardia during dobutamine stress echocardiography in a patient with severe aortic stenosis. *Thoraxcentre Journal vol 15,* (2), 34–36.

N. de Jonge, J.H. Kirkels, C. Klöpping, J.R. Laphor, K. Caliskan, A.P.W.M. Maat, J. Brügemann, M.E. Erasmus, R.J.M. Klautz, H.F.Verwey, A. Oomen, C.H.Peels, A.E.J. Golüke, D. Nicastia, M.A.C. Koole, A.H.M.M. Balk. Guidelines for heart transplantation. *Netherlands Heart Journal,* 16, 79–87.

D. Kauw, M.A.C. Koole, J.R. van Dorth, I I. Tulevski, G A. Somsen, M.P. Schijven, D.A.J. Dohmen, B.J. Bouma, B.J.M. Mulder, M.J. Schuuring, M.M. Winter. eHealth in patients with congenital heart disease: a review. *Expert Review of Cardiovascular Therapy vol 16,* 2018,617–625.

M.A.C. Koole, J.A. Winkelman, A. Kaya, M.A. Beijk. Little devil takes your breath away. *Neth Heart J* (2019)27:636.

D. Kauw, P.R. Huisma, S.K. Medlock, M A.C. Koole, E. Wierda, A. Abu-Hanna, M.P. Schijven, B.J.M. Mulder, B.J Bouma, M.M Winter, M.J Schuuring. Mobile health in cardiac patients: an overview on experiences and challenges of stakeholders involved in daily use and development. *BMJ Innovations* 2020;6:184–191.

The CAPACITY-COVID Collaborative Consortium and LEOSS Study Group. Clinical presentation, disease course, and outcome of COVID-19 in hospitalized patients with and without pre-existing cardiac disease: a cohort study across 18 countries. *European Heart Journal* (2022)43:1104–1120.

J.P. Man, M.G.W. Dijkgraaf, M.L. Handoko, F.J. de Lange, M.M. Winter, M.P. Schijven, S. Stienen, P. Meregalli, W.E M. Kok, D.I. Kuipers, P. van der Harst, M.A.C. Koole, S.A.J. Chamuleau, M.J. Schuuring. Digital consults to optimize guideline-directed therapy: design of a pragmatic multicenter randomized controlled trial. *ESC Heart Failure* (2023) DOI: 10.1002/ehf2.14634

Contributing authors

A. Abu-Hanna, Department of Medical Informatics, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands

S. Blok, Cardiologie Centra Nederland, Amsterdam, the Netherlands

B.J. Bouma, Department of Cardiology, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands

D.A.J. Dohmen, Luscii, Amsterdam, the Netherlands

J.R. de Groot, Department of Cardiology, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands

R. de Haan, Cardiologie Centra Nederland, Amsterdam, the Netherlands

S. de Jong, Department of Cardiology, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands

D. Kauw, Department of Cardiology, HagaZiekenhuis, The Hague, the Netherlands

K.M. Kooiman, Department of Cardiology, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands

M. Monteiro, Department of Cardiology, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands

B.J.M. Mulder, Department of Cardiology, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands

D. Robbers-Visser, Department of Cardiology, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands

M.P. Schijven, Department of Surgery, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands

M.J. Schuuring, Department of Cardiology, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands

G.A. Somsen, Cardiologie Centra Nederland, Amsterdam, the Netherlands

R.W. Treskes, Department of Cardiology, Leiden UMC, University of Leiden, Leiden, the Netherlands

I.I. Tulevski, Cardiologie Centra Nederland, Amsterdam, the Netherlands

J.W.J. Vriend, Department of Cardiology, HagaZiekenhuis, The Hague, the Netherlands

M.M. Winter, Department of Cardiology, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands

Portfolio

PhD student: Maarten A.C. Koole

PhD period   2017–2024

PhD supervisor and co-supervisors: prof. dr. B.J.M. Mulder, dr. B.J. Bouma, dr. M.J. Schuuring

Oral presentations

- 4th Congress eCardio & eHealth Berlin, Germany. "*Ehealth monitoring of adults with GUCH using a mobile eHealth program evaluated by a Registry : preliminary results*" M.A.C. Koole, R. de Haan; M.M. Winter, D.A.J. Dohmen; I.I. Tulevski; M.P. Schijven, B.J.M. Mulder, B.J. Bouma, M.J. Schuuring

- NVVC-NVT najaarscongres 1 november 2018: "*Will telemonitoring by mHealth program be cost-effective in adults with congenital heart disease?*" M.A.C. Koole, I.I. Tulevski, G.A. Somsen, D. Kauw, M.M. Winter, D.A.J. Dohmen, B.J.M. Mulder, B.J. Bouma, M.J. Schuuring

- NVVC voorjaarscongres 21 april 2022: "*An implantable loop recorder or eHealth to detect arrhythmia in adults with congenital heart disease?*" M.A.C. Koole, D. Kauw, K.M. Kooiman, J.R. de Groot, I.I. Tulevski, B.J.M. Mulder, B.J. Bouma, M.J. Schuuring

General course

2017

- The Leadless Intracardiac Transcatheter Pacing System
- Voorjaarscongres NVVC in combinatie met Connect Symposium
- Tour d'horizon
- ESC Congress Barcelona
- Fourth European Congress on eCardiology and eHealth Berlin

2018

- Advanced Lipid Management Cape Town
- ESC Congress Munich
- Noord-Hollands Hartfalen Symposium
- NVVC/NVT Najaarscongres
- AHA Scientific Sessions Chicago

2019

- TEE screening bij patiënten met een MR
- 10ᵉ cursus praktische echocardiografie Lenzerheide
- Tour d'horizon
- ESC Congress Paris
- Afscheidssymposium prof. dr. B.J.M. Mulder

2020

- Webinar COVID-19
- CVOI webinar: Smartwatch ECG

2021

- De medisch specialist: samen werken aan een heldere koers
- Summerschool: lunchsessies Medische Statistiek
- Live webinar zorg op afstand
- ESC Congress 2021 – The Digital Experience
- ESC Digital Summit

2022

- ESC Heart Failure Madrid
- CVOI webinar: Pericarditis
- Noord-Hollands Hartfalen Symposium
- AHA Webcast
- Symposium Patent Foramen Ovale in Young Patients with Stroke

2023

- Doctor on board? Luchtvaartgeneeskunde en infectieziekten
- Jaarcongres College van Clubartsen en Consulenten
- Successfully completed online training program on ICH GCP E6(R2) (facilitated by Brookwood Global)
- Symposium Hartfalenzorg in de volle breedte
- Live webcast Heart Failure Highlights
- ESC congress Amsterdam
- 9ᵗʰ EAPC Sports Cardiology Course Amsterdam

Sub-investigator of clinical trials 2017–2024:

ADMINISTER: multicenter randomized controlled trial to evaluate efficacy and safety of digital consult in patients on heart failure treatment.

CAPACITY-COVID registry: cohort study across 18 countries to evaluate clinical presentation, disease course, and outcome of COVID-19 in hospitalized patients with and without pre-existing cardiac disease.

CAROLINA: randomized clinical trial to evaluate the effect of Linagliptin vs Glimepiride on major adverse cardiovascular outcomes in patients with type 2 diabetes.

CLEAR: double-blind, randomized, placebo-controlled trial to evaluate cardiovascular outcomes of Bempedoic acid in statin-intolerant patients,

DECISION: national, multicenter, randomized, double-blind placebo-controlled, clinical trial to evaluate Digoxin in chronic heart failure in outpatients in the Netherlands.

EMPEROR-Preserved: randomized double-blind trial to evaluate cardiovascular and renal outcomes with Empagliflozin in heart failure with preserved ejection fraction.

EMPEROR-Reduced: randomized double-blind trial to evaluate cardiovascular and renal outcomes with Empagliflozin in heart failure with ejection fraction.

ETNA-AF: prospective, multicenter, post-authorization, observational study to evaluate Edoxaban treatment in routine clinical practice for patients with non-valvular atrial fibrillation.

FOURIER: randomized, double-blind, placebo-controlled clinical trial comparing Evolocumab, with placebo in patients with cardiovascular disease and high cholesterol levels despite being treated with statins.

Fourier Legacy: 5 year questionnaire follow up of patients who completed the FOURIER outcomes study.

LoDoCo: randomized, controlled, double blind trial to evaluate the effect of Colchicine in patients with chronic coronary disease.

NOAH-AFNET 6: event-driven, double-blind, double-dummy, randomized trial to evaluate if anticoagulation with Edoxaban is justified in patients with atrial high-rate episodes.

OCEANIC-AF: multicenter, international, randomized, active comparator-controlled, double-blind, double-dummy study to compare the efficacy and safety of the oral FXIa inhibitor Asundexian with Apixaban for the prevention of stroke or systemic embolism in male and female participants aged 18 years and older with atrial fibrillation at risk for stroke.

PARADISE-MI: multicenter, international, randomized, double-blind, active comparator trial to assess the efficacy and safety of Sacubitril/Valsartan compared with Ramipril in a contemporary acute myocardial infarction (AMI) population.

PREVAIL: double-blind, randomized, phase 2 trial to evaluate the safety and lipid-altering efficacy of Obicetrapib plus Ezetimibe combination therapy as an adjunct to high-intensity statin therapy.

RAPID NODE-301: multi-center, randomized, double-blind, placebo-controlled, efficacy, and safety study of Etripamil nasal spray for the termination of spontaneous episodes of paroxysmal supraventricular tachycardia.

STEP-HFpEF: international, randomized, double-blind, placebo-controlled trial comparing Semaglutide with placebo, plus lifestyle changes, in obese adults without diabetes.

STEP HFpEF-DM: international, randomized, double-blind, placebo-controlled trial comparing Semaglutide with placebo, plus lifestyle changes, in obese adults with type 2 diabetes.

THEMIS: randomized, double-blind, placebo-controlled trial to evaluate Ticagrelor/Aspirin compared with placebo/Aspirin among patients with stable coronary artery disease and type 2 diabetes.

VESALIUS-CV: double-blind, randomized, placebo-controlled, multicenter study to evaluate the impact of Evolocumab on major cardiovascular events in patients at high cardiovascular risk without prior myocardial infarction or stroke.

VICTORIAN-1 Prevent: randomized, double-blind, placebo-controlled multicenter study to evaluate the effect of Inclisiran on preventing major adverse cardiovascular events in high-risk primary prevention patients.

Teaching and supervision

Nurses, physician-assistants and residents in the "Rode Kruis Ziekenhuis Beverwijk".

Dankwoord
(acknowledgements in Dutch)

Alleen ben je niets. Het zijn mijn familie, vrienden, collega's, de mensen om mij heen die mijn leven betekenis geven door, onder andere, mij te inspireren en te steunen in de dingen die ik doe. Dit heeft gemaakt tot wie ik ben. Het maakt mij gelukkig en ik ben al deze mensen hier zeer dankbaar voor.

Dit proefschrift is het resultaat van teamwerk. Alleen mijn naam staat op de kaft; dit doet helaas geen recht aan allen die hebben bijgedragen aan het onderzoek zoals beschreven in dit proefschrift. Gelukkig kan ik dit grotendeels rechtzetten in mijn dankwoord.

Na mijn studie geneeskunde kwam met enige regelmaat de mogelijkheid voorbij om een promotie traject te beginnen. Meerdere mensen om mij heen lieten niet na mij er op te wijzen dat het aangaan van deze uitdaging mij goed zou passen. Lang wist ik deze boot af te houden. Het idee heeft mij echter nooit losgelaten. Een goede vriend, Igor Tulevski, stuurde mij begin 2017 een mail met de volgende korte tekst: "Iets voor jou? Als promotie onderzoek?" In de bijlagen van deze mail zat een mailwisseling tussen Mark Schuuring, Daan Dohmen, Berto Bouma en Barbara Mulder. Het betrof het voornemen het Hartwacht programma aan te bieden aan patiënten met een aangeboren hartafwijking en de effecten hiervan op een wetenschappelijke wijze vast te leggen. Hier kwam mijn enthousiasme voor het Hartwacht programma samen met de mogelijkheid zelf een bijdrage te leveren aan de vraag wat dit programma kan bijdragen aan de zorg voor mensen met hartaandoeningen. Als ik ooit nog de uitdaging voor promotie wilde aangaan, was het nu of nooit. Het werd nu.

Mijn Promotor
Prof. dr. B.J.M. Mulder
Beste Barbara, nadat ik positief had gereageerd op de mail van Igor zat ik al snel op jouw kamer in het Amsterdam UMC locatie AMC. Berto en Mark waren daar ook. Schoorvoetend legde ik mijn ambitie bij jou op tafel om als promovendus mee te doen aan het onderzoek naar de toegevoegde waarde van het Hartwacht programma bij patiënten met aangeboren hartaandoeningen. Het voelde als een sprong in het diepe. Zou het mogelijk zijn dit avontuur tot een goed einde te brengen naast mijn dagelijks werk en mijn gezinsleven met vier jonge

kinderen? Je gunde mij het voordeel van de twijfel en het was aan mij je niet teleur te stellen. Ik heb genoten van de discussies op de dinsdagen over de onderzoek opzet en uitvoering op jouw kamer en in de Rode Luifel. De kritische, maar altijd terechte opmerkingen op de door mij aangeleverde concepten voor publicaties hebben steeds tot nog betere versies geleid. De etentjes met jouw onderzoeksgroep in Amsterdam of tijdens een ESC congres elders waren de kers op de pudding. Heel veel dank!

Mijn copromotores
Dr. B.J. Bouma en dr. M.J. Schuuring
Beste Berto, ik kende al je voortreffelijke klinische kwaliteiten als cardioloog: menig casus heb ik met je kunnen overleggen en naar je kunnen doorverwijzen, nu ken ik ook je wetenschappelijke kwaliteiten en heb daar dankbaar gebruik van mogen maken. Ik hoop nog lang met je te kunnen samenwerken!

Beste Mark, al vroeg, nog tijdens je opleiding tot cardioloog, had jij door dat de ontwikkeling van digitale toepassingen voor thuismonitoring tot een revolutie kan leiden in het cardiologische zorglandschap. Je bent gaan staan in de wetenschappelijk frontlinie van deze ontwikkelingen en je stond aan de wieg van het onderzoek zoals in dit proefschrift beschreven. Toen duidelijk werd dat meer mankracht nodig was om de voortgang van het onderzoek te garanderen, had je snel een oplossing gevonden: er kwam nog een promovendus, Dirkjan. Hij kon zich voltijds inzetten voor ons onderzoek en met zijn hulp werd dit project succesvol afgerond, waarna hij midden in de COVID pandemie kon promoveren op de behaalde resultaten. Het had hierbij kunnen blijven. Echter jij wist steeds bij mij de juiste snaar te raken waardoor uiteindelijk ook mijn promotietraject succesvol kon worden afgerond. Ik ben blij dat onze samenwerking hier niet is gestopt en jij mij weer hebt betrokken bij een nieuwe veelbelovende studie. Dank voor dit alles!

Overige leden van de promotiecommissie
Prof. dr. N.A. Blom, prof. dr. J.R. de Groot, prof. dr. M.G.W. Dijkgraaf, dr. L. Hofstra, prof. dr. N.H. Chavannes, prof. dr. P. van der Harst
Zeer veel dank voor het kritisch doorlezen van het manuscript en voor het zitting nemen in de promotiecommissie!

Mensen met aangeboren hartziekten; Dayenne Zwaagman, dokters van het Amsterdam UMC

Zoals gezegd betreft ons onderzoek een klinische studie. Dit kon alleen met de welwillendheid van mensen met aangeboren hartziekten om mee te doen aan ons onderzoek. Dit vroeg een tijdinvestering en commitment waarbij vooraf de uitkomst niet zeker was. Jullie deden mee en dankzij jullie feedback konden wij ons onderzoek goed uitvoeren en lessen leren voor de toekomst. Veel dank hiervoor!

Beste Dayenne, speciaal op deze plek wil ik jou bedanken. Jij hebt een aangeboren hartaandoening en kwam daardoor al heel jong in aanraking met de gezondheidzorg. Je wist, als ervaringsdeskundige, met onder andere je uitstekende communicatieve vaardigheden, de afstand te verkleinen tussen enerzijds de mensen met een aangeboren hartaandoening en anderzijds de mensen werkzaam in de gezondheidszorg. In het bijzonder gaf je ons onderzoek de nodige support waardoor onder andere ons crowdfunding project zo succesvol kon zijn.

Dank aan alle dokters van het Amsterdam UMC die hun patiënten hebben gevraagd en gemotiveerd hebben om mee te doen aan ons onderzoek.

Coauteurs

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Dr. D. Kauw

Beste Dirkjan, de planning was om samen te promoveren schrijf je in het dankwoord van je proefschrift, om dan te vervolgen: dat helaas de planning niet helemaal zo is verlopen. Immers, jij bent een paar jaar geleden al gepromoveerd op ons project. Vervolgens schrijf je dat zonder mijn tomeloze inzet voor de projecten het niet zover gekomen was. Nu mag ik schrijven dat voor jou het zelfde geldt: zonder jouw inzet waren we ook niet hier gekomen. Ik heb met bewondering gezien hoe snel jij je je verdiept had in de materie en je je weg vond. Het was een plezier met je samen te werken en veel succes met je opleiding tot cardioloog!

Prof. dr. M.P. Schijven

Beste Marlies, jij hebt al vroeg de potentie van mobiele applicaties in de gezondheidszorg herkend en brengt de "stakeholders" bij elkaar die nodig zijn om deze applicaties ook daadwerkelijk in te zetten in de gezondheidszorg. Dat is je ook gelukt bij ons project, dank daarvoor!

Prof. dr. ir. D. Dohmen

Beste Daan, in jouw persoon komen samen: het out of the box denken om met creatieve innovatieve oplossingen zorg te verplaatsen van de kliniek naar de mensen thuis, het onder-nemerschap om deze oplossingen mogelijk te maken en de wetenschappelijke drive om aan te tonen dat je oplossingen ook echt werken. Dank voor je uiterst waardevolle inspirerende bijdrage!

Amsterdam UMC, Cardiologie Centra Nederland, Castor EDC, FocusCura, NFU eHealth Citrienfonds, RKZ Beverwijk

Voor dit onderzoek werden de deelnemers uitgerust met een bloeddrukmeter, single lead ECG device en weegschaal. Lijkt simpel, maar de logistiek om apparatuur bij de deelnemers te krijgen, na afloop weer in te nemen, de data van de duizenden thuismetingen te verwerken in EPD en geanonimiseerde bestanden voor onderzoeksdoeleinden en gepaste actie te ondernemen bij afwijkende metingen. Ook de financiële afwikkeling was een enorme uitdaging en hierbij waren velen betrokken. Veel dank!

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Sponsoren

Inmiddels valt thuismonitoring onder verzekerde zorg, bij aanvang van ons onderzoek was dat nog niet zo. Met hulp van Het Crowdfunding Team van de Hartstichting konden wij via de steunmijnonderzoek website van de Hartstichting geld ophalen om een start te maken met ons onderzoek. Dank aan alle gulle donateurs!

Sylvia Mantels

Beste Sylvia, als het onderzoek is gedaan en de inkt van de publicaties is opgedroogd, komt de afronding in de vorm van een promotie ceremonie. Dank voor al je hulp bij de organisatie hiervan!

Paranimfen

Igor Tulevski, Fons Windhausen

Beste Igor, we leerden elkaar kennen aan het begin van deze eeuw, waarschijnlijk in het Amsterdamse uitgangsleven na afloop van een nascholing. Ik, net cardioloog, al snel werkzaam in Beverwijk en jij nog in opleiding in het AMC. Ik, gefrustreerd door de wachttijden en de vaak tenenkrommende omgang van de gevestigde orde met deze problematiek, jij had de oplossing. Samen met Aernout wist je, nog voordat jezelf cardioloog was, een uiterst succesvolle kliniek neer te zetten met korte wachttijden en snelle doorlooptijden. We zijn veel meer dan goed bevriende collega's geworden, onze band voelt als een familieband en ik ben dan ook blij dat jij mijn paranimf bent!

Beste Fons, samen hebben we een geweldig bedrijf neergezet in de regio IJmond, waarmee we de cardiologische zorg in deze regio vormgeven. Maar meer dan dat: dagelijks delen we tussen de bedrijven door ons lief en leed en is een hechte vriendschap ontstaan. Ook voor jou geldt dat onze band voelt als een familieband: wat we ook doen, we blijven met elkaar verbonden. Dank hiervoor!

Familie

Het succesvol afronden van dit proefschrift is een klein, maar niet onbelangrijk, onderdeel van mijn rijke leven. Dit leven heb ik te danken aan mijn ouders.

Lieve papa en mama, bijna is het zover en mag ik dit proefschrift verdedigen. Jullie geduld werd op de proef gesteld. Ik weet hoe trots jullie op mij zijn en hoe graag jullie het bereiken van deze mijlpaal met mij willen vieren. Het ziet er naar uit dat dat gaat lukken. Terecht straalt dit succes ook op jullie af. Ik leerde van jullie om het beste uit mij zelf te halen, jullie geloof in mijn kunnen is de onmisbare steun die ik nodig had om hier te komen. Jullie zijn nog altijd een voorbeeld voor mij en ik leer nog dagelijks van jullie. Ik noem de overlevingsdrang van mijn moeder met de "waar een wil is, is een weg" mentaliteit. Niet alleen vroeger in je werk, maar ook nu, met al je fysieke beperkingen. En ik noem de bevlogenheid van mijn vader om, tot de dag van vandaag,

je bijdrage te leveren aan deze maatschappij. Hiervoor werd je heel terecht, niet lang geleden, koninklijk onderscheiden door de burgemeester van Den Haag.

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Lieve Djuna, Tijn, Lieve en Vos. Dit proefschrift is ook aan jullie opgedragen. Ik hoop dat jullie lang en gelukkig leven. Kijk om je heen, durf te vallen en sta weer op. Maak je eigen keuzes, rekening houdend met de ander, succes en geluk volgen dan vanzelf. Ik ben trots op jullie en hou zielsveel van jullie, wat er ook gebeurt.

De aanhouder wint en met die gedachte heb ik niet alleen dit proefschrift volbracht, maar ook eerder het hart van Lilian veroverd. Jij bent mijn grootste liefde en hebt mij vier prachtige kinderen gegeven. Je bewaakt liefdevol mijn balans tussen gezin, werk en sport en daarmee ons geluk. Ik zou en zal nooit anders willen. Dank je wel!

The journey is the destination

About the author

Maarten Koole was born on the third of July 1964 in The Hague, the Netherlands. He graduated from high school (Gymnasium Haganum) in 1982 and started medicine at the University of Amsterdam in the same year. In 1989 he travelled for some of his internships to Paramaribo, Surinam. After he obtained his degree as a medical doctor in 1990 he fulfilled his mandatory military service as military physician. Thereafter he worked as a resident cardiology and pulmonary medicine at West-Fries Gasthuis, Hoorn and decided to become a cardiologist. In 1993 he started as a junior physician at the Thoraxcenter, University Hospital Rotterdam-Dijkzigt. However, at that moment there was no vacancy for a traineeship in cardiology, and, with a recommendation of prof. dr. M.L. Simoons, he could start in 1994 his training in cardiology in Belgium. First spending 2 years as an internal medicine resident in Ostend. He continued his training in cardiology under supervision of prof. dr. P. Block at the University Hospital Brussels, associated with the Vrije Universiteit Brussel. His career as a cardiologist started in the first month of the new millennium as a staff member of the department cardiology of the OLVG, Amsterdam. In 2001 he moved back to the Thoraxcenter in Rotterdam to work at the Coronary Care Unit under supervision of prof. dr. M.L. Simoons and Heart transplantation department under supervision of dr. A.H.M.M. Balk. They gave him the opportunity to start a fellowship Intensive Care at the OLVG under supervision of prof. dr. D.F. Zandstra. In 2004 he became one of the first Dutch cardiologist-intensivists. However instead of returning to Rotterdam to start an academic career he decided to accept a job as general cardiologist in the Rode Kruis Ziekenhuis, Beverwijk. Here, he became head of the department cardiology, was member of the board of the medical staff and started, in collaboration with Cardiologie Centra Nederland (CCN), an outpatient clinic in Ijmuiden.

In 2017 he started, along his daily work, a PhD program, under supervision of prof. dr. B.J. M. Mulder at the Academisch Medisch Centrum, Amsterdam, associated with the University of Amsterdam.

He lives in Amsterdam with his wife Lilian Koole-Hanekamp and their children Djuna, Tijn, Lieve and Vos.

Wearables might be a powerful tool for remote diagnosing and managing cardiac disease. This thesis focuses on the question whether introducing digital remote patient monitoring by a dedicated program in the routine care management of adult congenital heart disease patients improves care for these patients.

This research project was funded by a successful crowdfunding campaign. The crowdfunding campaign has met the needs of donors, leading to enforcing of the public engagement.

Appropriate patient selection for participation in telemonitoring contributes to an efficient use of these wearables.

A higher rate of arrhythmia and bradycardia detection by wearables, leading to clinical impactful management changes, has been demonstrated.

Future directions and key points for digital remote patient monitoring are given.