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ORIGINAL ARTICLE
Digital Health—Other

Personalized digital behaviour interventions increase short-term physical activity: a randomized control crossover trial substudy of the MyHeart Counts Cardiovascular Health Study

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Aims

Physical activity is associated with decreased incidence of the chronic diseases associated with aging. We previously demonstrated that digital interventions delivered through a smartphone app can increase short-term physical activity.

Methods and results

We offered enrolment to community-living iPhone-using adults aged ≥18 years in the USA, UK, and Hong Kong who downloaded the MyHeart Counts app. After completion of a 1-week baseline period, e-consented participants were randomized to four 7-day interventions. Interventions consisted of: (i) daily personalized e-coaching based on the individual's baseline activity patterns, (ii) daily prompts to complete 10 000 steps, (iii) hourly prompts to stand following inactivity, and (iv) daily instructions to read guidelines from the American Heart Association (AHA) website. After completion of one 7-day intervention, participants subsequently randomized to the next intervention of the crossover trial. The trial was completed in a free-living setting, where neither the participants nor investigators were blinded to the intervention. The primary outcome was change in mean daily step count from baseline for each of the four interventions, assessed in a modified intention-to-treat analysis (modified in that participants had to complete 7 days of baseline monitoring and at least 1 day of an intervention to be included in analyses). This trial is registered with ClinicalTrials.gov, NCT03090321.

Conclusion

Between 1 January 2017 and 1 April 2022, 4500 participants consented to enrol in the trial (a subset of the approximately 50 000 participants in the larger MyHeart Counts study), of whom 2458 completed 7 days of baseline monitoring (mean daily steps 4232 ± 73) and at least 1 day of one of the four interventions. Personalized e-coaching prompts, tailored to an individual based on their baseline activity, increased step count significantly (+402 ± 71 steps from baseline, $P = 7.1\times10^{-8}$). Hourly stand prompts (+292 steps from baseline, $P = 0.00029$) and a daily prompt to read AHA guidelines (+215 steps

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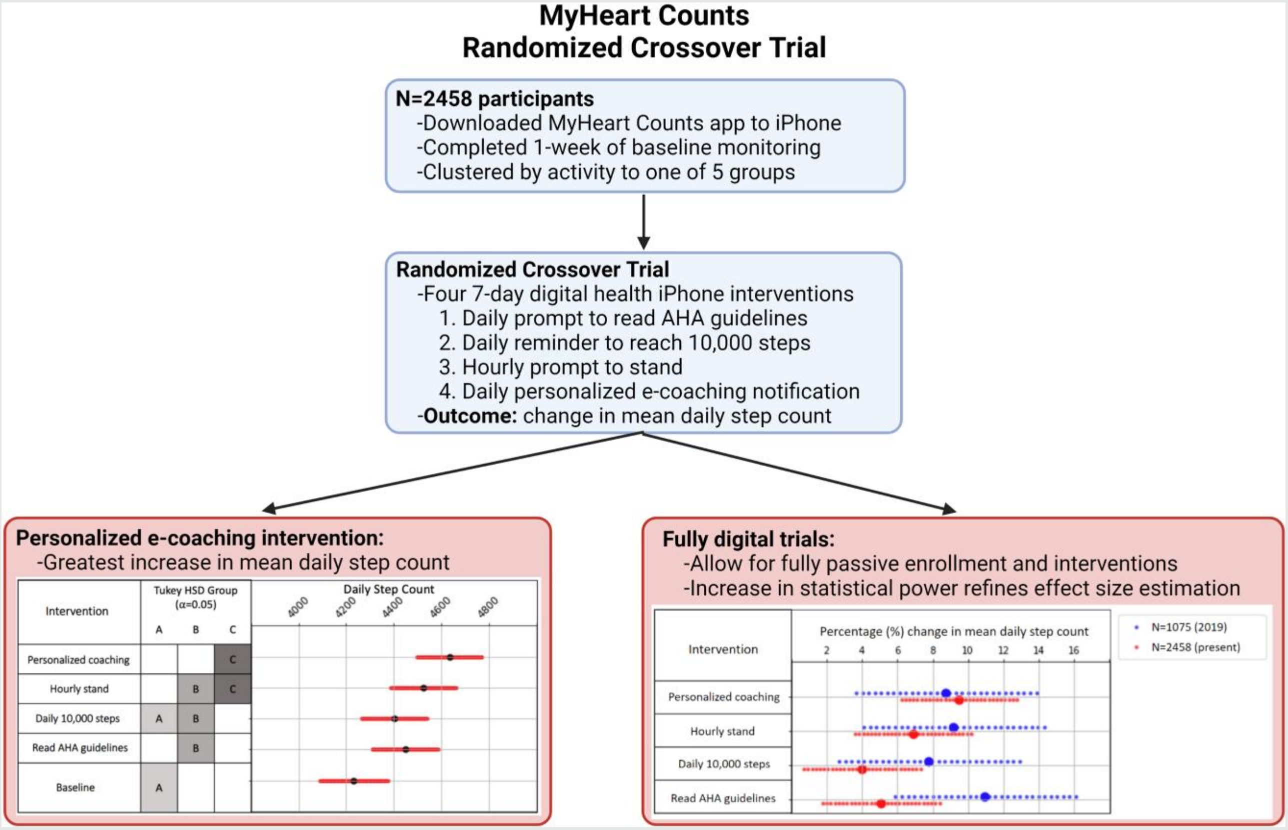
from baseline, $P = 0.021$) were significantly associated with increased mean daily step count, while a daily reminder to complete 10 000 steps was not (+170 steps from baseline, $P = 0.11$). Digital studies have a significant advantage over traditional clinical trials in that they can continuously recruit participants in a cost-effective manner, allowing for new insights provided by increased statistical power and refinement of prior signals. Here, we present a novel finding that digital interventions tailored to an individual are effective in increasing short-term physical activity in a free-living cohort. These data suggest that participants are more likely to react positively and increase their physical activity when prompts are personalized. Further studies are needed to determine the effects of digital interventions on long-term outcomes.

Graphical Abstract



Keywords Digital health • Digital interventions • Physical activity • eBhavioural interventions • Personalized medicine • Apple Watch

Introduction

Physical activity has a strong epidemiologic association with decreased incidence of the chronic diseases of aging.[1,2] Despite the known benefits of physical activity, many individuals in high socio-economic countries remain sedentary. A recent report from the World Health Organization estimates that between 2020 and 2030, 500 million individuals will develop obesity, diabetes, and/or heart disease because of a physically inactive lifestyle.[3] Recent large-scale data demonstrated that the average American achieved a mean of 4700 daily steps and that the majority do not meet the modest recommendation of 150 min of exercise per week.[4,5]

Step count, as measured by a pedometer or more recently a smart device (phone and/or watch), has been studied as a proxy for physical activity.[6] Daily steps, as measured by a smart device, have been shown in numerous studies and meta-analyses to have decreased risk of incident heart disease.[7] Interventions that successfully increase step count are associated with reduced incidence of hypertension, reduced body mass index (BMI), and improved cardiometabolic biomarkers,[8] highlighting the importance of step count as a metric of overall cardiovascular health.

The MyHeart Counts Cardiovascular Health Study was launched to leverage the rapid improvement in handheld technologies,[9] to better elucidate health patterns of participants and test digital interventions on short-term physical activity. Through the MyHeart Counts smartphone and watch app,[10] researchers are able to continuously enrol participants using automated protocols, benefit from advances in technological platforms, and reveal previously obscure patterns. Since its launch, the MyHeart Counts Cardiovascular Health Study has become an international, multi-arm, federated study with numerous sub-studies in the Netherlands, Canada, and the United Kingdom, with specific sub-study focuses on SARS-CoV2 infection, public health, and cardiovascular health. We first published on the feasibility of a fully digital study examining these varied outcomes using smartphones and smartwatches.[11] Later, we released the data of 50 000 participants who agreed to broad data sharing with the larger scientific community.[10]

We recently reported findings from our first analysis of the randomized crossover trial subset of the MyHeart Counts Cardiovascular Health Study.[12] In this work, we determined that all smartphone-delivered digital interventions increased the mean daily step count.[12] However, this first analysis did not have sufficient statistical power to demonstrate differences between interventions and could not answer the question as to whether personalized or more frequent interventions were superior to more general prompts.

Given the unique design of our fully digital trial, we continued to have passive enrolment into the randomized crossover trial. This coupled with increased adoption of wearable devices allowed for the statistical power to detect differences between different types of digital interventions. Leveraging these unique advantages to digital trials, we present the latest results of an entirely digital randomized crossover trial, using a subset of data from the MyHeart Counts Cardiovascular Health Study, and examine the effects of app-driven digital interventions on step counts.

Methods

Study design and participants

Ethical approval for the study was obtained from Stanford University's Research Compliance Office.

The participants for this randomized controlled crossover trial were a sub-study of the larger MyHeart Counts Cardiovascular Health Study.[10–12] All iPhone (Apple, Cupertino, CA, USA; version 5S or newer; iOS mobile operating system version 9 or newer) users in the USA, the UK, and Hong Kong, aged 18 years or older, who were able to read and understand English, and who had downloaded the latest version of the MyHeart Counts app (version ≥2.0) were eligible to participate in this crossover trial. A full description of the MyHeart Counts app has previously been reported, including a complete set of app screenshots.[12]

After downloading the MyHeart Counts app from the Apple App Store, users were guided through an e-consent process[13] (screenshots of this consent process previously published[12] and available in Appendix pages 15–45). Participants had the option to either share their data narrowly (with Stanford University researchers only) or broadly (with qualified researchers worldwide). All participants had to make an active choice to complete the consent process, as no default choice was selected.[13]

Activity group clustering after baseline monitoring

After completing the active consent process, users underwent a 1-week period of baseline interaction with the MyHeart Counts app. After this 1-week period, participants were assigned to one of five clusters based on their level of physical activity during the weekdays and the weekend.[11] In brief, *K*-means clustering[14] was used based on 10 activity parameters: time spent stationary, driving, walking, running, or cycling, stratified by weekday vs. weekend. Based on these time parameters, five clusters of physical activity were identified: (i) individuals active (whether walking, running, or cycling) throughout the baseline week (busy bees cluster), (ii) individuals active on weekends but sedentary on weekdays (weekend warriors cluster), (iii) individuals active on weekdays but sedentary on weekends (worker bee cluster), (iv) individuals who were largely stationary throughout the week (sedentary cluster), and (v) individuals who spent at least 15% of their awake time driving (driver cluster). In depth methodology for the *K*-means clustering has been previously reported by our group.[10–12] Differing personalized e-coaching interventions were delivered to participants based on their cluster group in the subsequent randomized crossover trial.

Randomization and masking

When opening the MyHeart Counts app for the first time after completion of the baseline week of monitoring, a pop-up notification with a second consent that required an active choice was presented with the option to participate in a 4-week randomized crossover study of fully digital coaching (see Supplementary material online, *Appendix pages* 46–67). After enrolment, participants were randomly assigned to receive one of four interventions in a random order of 24 total permutations (4 combinations of 4 one-week digital interventions).[12] The interventions consisted of: (i) daily instructions to read guidelines from the American Heart Association (AHA) website, (ii) daily prompts to complete 10 000 steps, (ii) hourly prompts to stand for 1-minute after 1-hour of inactivity/sitting, and (iv) daily e-coaching personalized to the individual's personal activity patterns derived from the baseline week of data collection (see above). Thus, all participants were presented with all interventions, albeit at different times and in a different order.

Due to the nature of the study and interventions, it was not possible to blind participants to intervention assignment.

Procedures

The HealthKit toolkit collected information on daily step count, distance walked, time spent in bed, and time spent asleep during the 1-week baseline interaction period of the MyHeart Counts app.[15] Motion sensors (either from an Apple smartphone or smartwatch) were used to record time spent walking, running, cycling, resting, and driving each day (these sensors have been previously externally validated).[16] After completion of the 1-week baseline monitoring period and consenting to the e-coaching study (see above), participants were randomly assigned to each intervention for 7 days.

The four interventions were delivered serially to users as daily (or hourly, in the case of the stand reminders) prompts to their smartphones. Examples of the specific prompts have previously been published.[12] For the intervention to read the AHA website, a daily prompt was sent with a link to the website. For the daily 10 000 step prompt intervention, if users had not completed 5000 steps by 1500 h local time, they received a prompt indicating the number of steps remaining to reach the goal. If the user had completed more than 5000 steps by 1500 h local time, no prompt was triggered. For the hourly stand intervention, if the user had been seated for the past 1 h, they received a prompt advising them to stand for 60 s. If the user had been active in the past hour, they received no prompt. Finally, for the personalized e-coaching intervention, a daily message was sent to the participant, tailored to the activity cluster that they had been assigned to (see Supplementary material online, *Table S1*).

Amazon Web Services (Amazon, Seattle, WA, USA) was used to store information on user interactions with the four intervention prompts. Through confirmation with mobile analytics, it was ascertained whether or not the participants received intervention prompt messages on their smartphones daily (or at least one hourly stand reminder a day). While this analysis did not guarantee that a participant opened their notification, it did confirm whether or not a notification was displayed on the smart device, and not missed because of other reasons (e.g. cell phone switch off, privacy settings, connectivity, etc.).

Outcomes

Mean daily step count, as recorded by participants' smartphones via HealthKit, was used as the primary outcome. *Post-hoc* sensitivity analyses were performed to determine if there were differences in intervention effects in a subset of individuals who (i) confirmed that they had received intervention prompt messages on their smartphones for the given intervention, (ii) who had both smartphone and Apple Watch data, and (iii) completed all 7 days of at least one intervention.

Statistical analyses

Analyses were performed in a modified intention-to-treat population,[17] which included all participants that completed the 1-week period of baseline monitoring and at least 1 day of one of the four interventions. Prior exploratory analyses demonstrated no differences between using data from participants with 1, 4, and 7 days of at least 200 steps,[12] and this finding is recapitulated in our present data (see Supplementary material online, *Table S4*). Hence, we continued to use the least stringent inclusion criteria for our analyses. Daily step count for each participant was calculated by summing values for the HKQuantityTypeIdentifierStepCount field that flowed from HealthKit into the MyHeart Counts app. Days during which the participant did not reach 200 steps as measured by HealthKit on their smartphone were excluded from analyses. Of note, no participant was excluded from modified intention-to-treat analysis due to achieving less than 200 steps per day during the entirety of the weeklong intervention. Four hundred and seventy participants had specific days that were excluded from analyses due to inactivity; however, they reached the minimum threshold of 200 steps per day on another day during their randomized intervention. Users were considered to have been provided the intervention on days in which they were active and exceeded step count (for the daily step count intervention) or inactivity (for the hourly stand intervention) to avoid triggering reminder prompts.

All analyses were performed in R.[18,19] Within-subject analysis was done by fitting a linear mixed effects model using the *nlme* library of R, with daily step count as the outcome variable, intervention group as a fixed linear effect, and participants included as random effects. The intervention variable was categorical, with a base value of baseline and contrasts set to the read AHA literature prompt, 10 000 step daily reminder prompt, hourly stand prompt, and personalized e-coaching prompt. Estimated marginal means and standard error (SE) for daily step count were computed using the *lsmeans* package of R. Tukey's Honestly Significant Difference (HSD) test was used with a significance level of 5% to assess for statistically significant differences in mean daily step count between each pair of interventions and baseline.[20] In addition, a false discovery rate-adjusted *P*-value threshold of 0.05 was used to determine whether differences between two interventions was statistically significant.

Role of the funding source

The funders had no role in study design, data collection, data analysis, data interpretation, or the writing of this manuscript. Apple (Cupertino, CA, USA) provided support for the initial development of the MyHeart Counts app. Google (Mountain View, CA, USA) provided support for ongoing management of the MyHeart Counts app. The corresponding author had full access to the data and the final responsibility to submit for publication.

Results

Between 1 January 2017, and 1 April 2022, 4500 participants consented to participate in the e-coaching study (*Figure 1*). Of these 4500 participants, 2458 completed the 1-week period of baseline monitoring and were included in the modified intention-to-treat analyses (*Table 1*). These participants were majority men (68.6%, $n = 2207$), self-identified white (82.3%, $n = 2017$), with the majority (72%, $n = 1958$) having at least a college degree, with a mean age of 46.1 years (SD 15.5). The distribution of participants BMI ($n = 2209$) categories was 4.9% underweight (BMI < 18.5), 34.4% normal weight (BMI 18.5 to <25), 35.0% overweight (BMI 25 to <30), 15.3% obese (BMI 30 to <35), and 10.4% severely obese (BMI 35 to <40).

During the 1-week baseline monitoring period, the 2458 participants walked an average of 4233 steps daily (*Table 2*). Relative to this baseline monitoring period, all interventions with the exception of the 10 000 step prompt intervention increased mean daily step count (*Table 2*, *Figure 2*). The number of steps recorded by smartphone increased from baseline by 215 (SE 71) for participants in the read AHA website prompt group ($P = 0.021$), by 170 steps (SE 71) for participants in the 10 000 step daily prompt group ($P = 0.11$), by 292 steps (SE 70) for participants in the hourly stand prompt group ($P = 0.00029$), and by 402 steps (SE 70) for participants in the personalized e-coaching prompt group ($P = 7.1 \times 10^{-8}$).

When limiting analyses to a subset of participants for whom mobile analytics confirmed that the device received the intervention prompt ($n = 2452$), similar results were obtained (see Supplementary material online, *Table S2*). As with the primary analyses, the personalized e-coaching group had the greatest increase in mean daily step count at 531 steps (SE 70). As well, the same groups were assigned to interventions when using Tukey HSD analysis (see Supplementary material online, *Table S2*).

A sensitivity analysis was performed to ensure that results were similar in a subset of participants who had both smartphone and smartwatch data ($n = 1823$). The same Tukey HSD groups were obtained for the different digital interventions (see Supplementary material online, *Table S3*). As with the primary analysis, the personalized e-coaching intervention resulted in the greatest increase in mean daily steps from baseline with 411 steps (SE 75) (see Supplementary material online, *Table S3*). When limiting analyses to a smaller subset of participants who completed 7 days of baseline monitoring in addition to 7

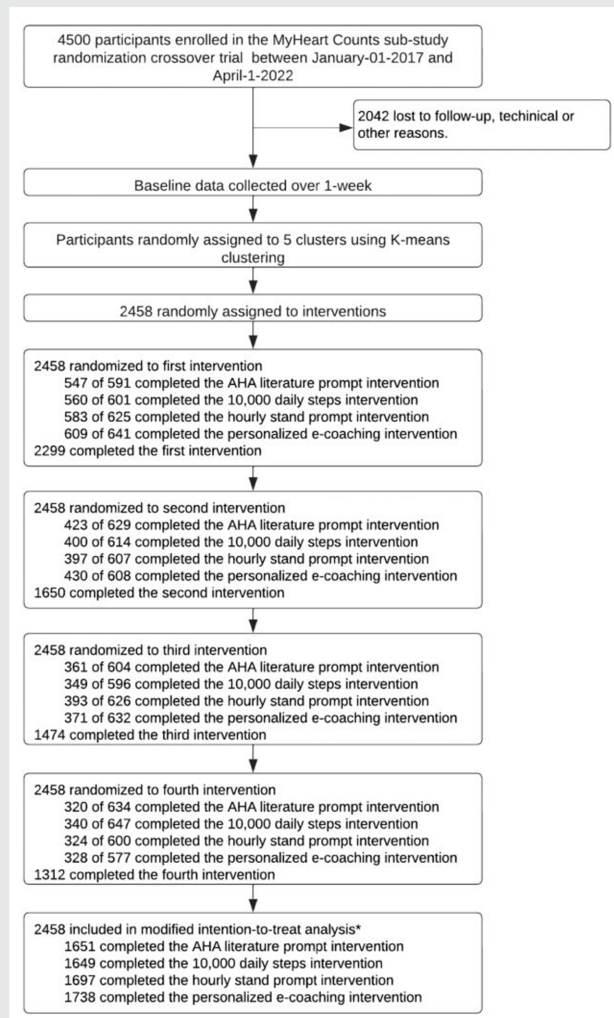


Figure 1 Flow of participants through the study. AHA, American Heart Association. *Participants who completed 7 days of baseline monitoring and at least 1 day of one of the four interventions were included in the modified intention-to-treat analysis set. Participants could participate in as few as one intervention or all four interventions. As a result, the sum of participants who completed the four different interventions exceeds that of the participants included in the modified intention-to-treat analysis.

Table 1 Baseline self-reported characteristics of the studied subset of the MyHeart Counts Cardiovascular Health Study included in the modified intention-to-treat analyses

		Participants who completed baseline and at least one intervention (n = 2458)[a]
Age, years	$n = 2216$	46.1 (15.5)
Self-identified biological sex, *n* (%)		
Male		1544 (68.6%)
Female		707 (31.4%)
Unknown		207
Self-identified race/ethnicity, *n* (%)	$n = 2017$	
White		1660 (82.3%)
East/Southeast Asian		101 (5.0%)
Black		62 (3.1%)
South Asian		44 (2.2%)
Hispanic		18 (0.89%)
American Indian		6 (0.3%)
Multi-Racial		55 (2.7%)
Other		71 (3.5%)
Unknown		441
Self-reported level of education, *n* (%)	$n = 1958$	
Didn't go to school		1 (0.1%)
Grade school		15 (0.8%)
High school or General Education Development		106 (5.4%)
College, vocational school, or associate degree		424 (21.7%)
College graduate or baccalaureate degree		664 (33.9%)
Master's degree		479 (24.4%)
Doctoral degree		269 (13.7%)
Unknown		500
Body mass index (BMI) category, *n* (%)	$n = 2209$	
Underweight (BMI < 18.5)		110 (4.9%)
Normal weight (BMI 18.5 to <25)		760 (34.4%)
Overweight (BMI 25 to <30)		773 (35.0%)
Obese (BMI 30 to <35)		337 (15.3%)
Obese II (BMI 35 to <40)		229 (10.4%)
Unknown		249
Height, inches	$n = 2229$	68.5 (3.9)
Weight, pounds	$n = 2210$	183.9 (45.7)
Device use, *n* (%)	$n = 2410$	
Smartphone + Smartwatch		1823 (75.6%)
Smartphone only		393 (16.4%)
Smartwatch only		194 (8.0%)
Unknown		48

[a]Unknown device use due to interpretation of device naming. For example, 'John's iPhone' would be classified as a smartphone, while 'John's Apple Watch' would be classified as a smartwatch. However, a device named 'John' would be classified as 'unknown'.

days of at least one intervention, the mean baseline daily step count increased to 5332 (SE 120). However, the results remained consistent, with the personalized e-coaching intervention associated with the greatest increase in daily activity with 347 steps (SE 87, Supplementary material online, *Table S4*).

When comparing the present analysis ($n = 2458$) to our previously reported work[12] ($n = 1075$), there is refinement in both effect and error estimation (*Figure 3*). With a smaller sample size, we previously reported that no digital intervention was significantly different than another. However, with the addition of 1383 participants, effect estimation was improved, with more narrow confidence intervals, and the personalized coaching intervention was the only intervention to increase participant mean daily step count estimate compared with the prior analysis.

Discussion

This follow-up analysis of a randomized crossover trial demonstrates the power of digital studies to continually enrol participants through

Table 2 Intervention effects on mean daily step count in the modified intention-to-treat subset of the MyHeart Counts randomized crossover trial ($n = 2458$)

	Baseline	Read AHA guidelines prompt	Daily 10 000 step prompt	Hourly stand prompt	Personalized coaching prompt
Participants, *n*	2458	1651	1649	1697	1738
Mean step count, *n* (SD)	4233 (4456)	4448 (4520)	4402 (4512)	4525 (4612)	4634 (4775)
Effect size (SE)	—	215 (71)	170 (71)	292 (70)	402 (70)
P-value	—	0.021	0.11	0.00029	7.1×10^{-8}
A/B test of 'Personalized coaching' prompt vs. other interventions					
Effect size (SE)	—	187 (62)	232 (61)	110 (61)	—
P-value	—	0.020	0.0016	0.37	—
A/B test of 'Hourly stand' prompt vs. other interventions					
Effect size (SE)	—	77 (62)	121 (61)	—	—
P-value	—	0.72	0.27	—	—
A/B test of 'Daily 10 000 step' prompt vs. other interventions					
Effect size (SE)	—	−45 (62)	—	—	—
P-value	—	0.95	—	—	—
Tukey group based on above A/B tests					
	A	B	A + B	B + C	C

A/B test, a randomized experiment involving two variables: 'A' and 'B'; AHA, American Heart Association; *n*, number of participants; SE, standard error.

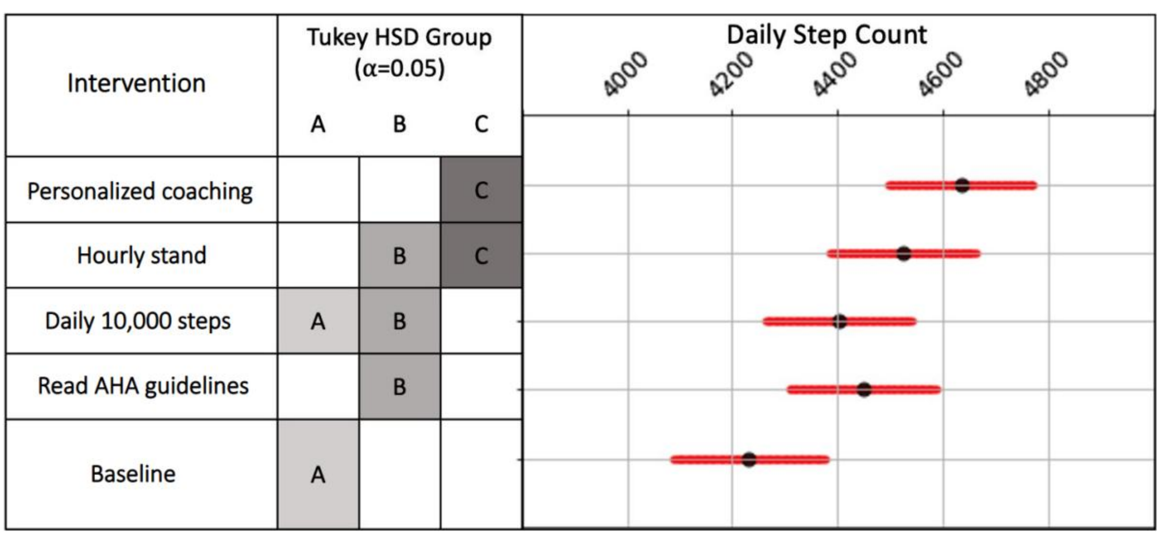


Figure 2 Mean daily step count for the 1-week baseline period and for the four interventions in the modified intention-to-treat subset of the randomized crossover MyHeart Counts Study ($n = 2458$). Mean daily step count was recorded by the MyHeart Counts iPhone app. Error bars show 95% CI. Interventions assigned to different Tukey groups are significantly different from each other.

a smartphone app and complete interventions in a fully automated manner. Leveraging the increased statistical power provided by further passive enrolment, we determined that personalized e-coaching resulted in the greatest increase in mean daily step count (9.5% increase; our prior work was unable to differentiate between the effects of the varied interventions[12]). These data highlight the potential of digital studies to extend the reach of clinical trials in a cost-effective manner.[21] Moreover, our results suggest that tailoring interventions to the individual is superior to a 'one-size-fits-all' approach.[22–24]

Digital trials have the potential to greatly improve future research given that they are cheaper and less labour intensive than traditional clinical trials.[25,26] Moreover, as the only requirement to participate in such trials is a smartphone, digital trials have the potential to increase equity by including people around the world, rather than focusing on those

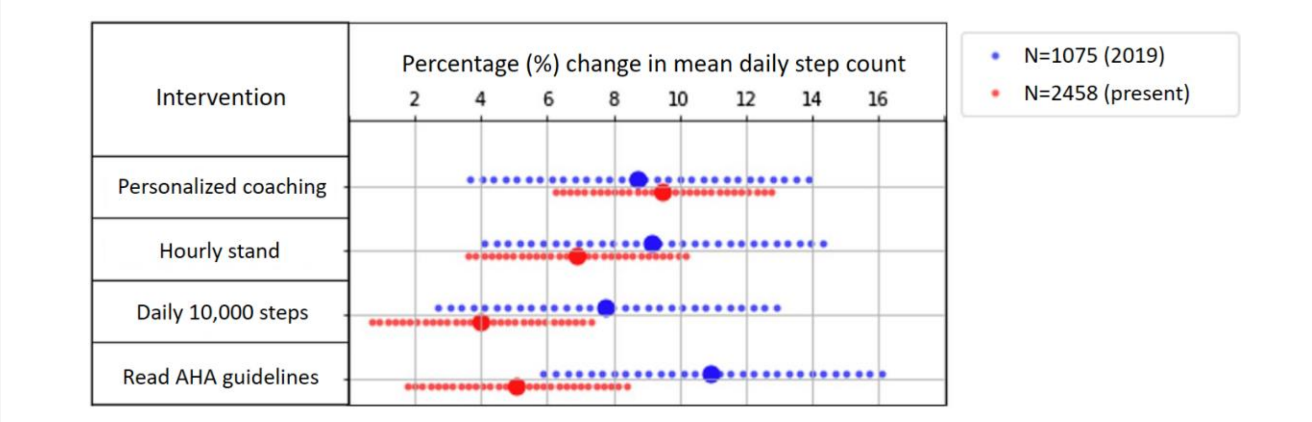


Figure 3 Comparison of intervention effects in present data (*n* = 2458) as compared to previously published, partially overlapping data (*n* = 1075) in the modified intention-to-treat subset of the MyHeart Counts randomized crossover trial. Error bars show 95% CI.

only in first-world countries. Particularly during the SARS-CoV2 pandemic, digital trials had a significant advantage over traditional trials, due to continued cost-effective enrolment without requiring face-to-face interactions on the investigators' end.[27] Specific to MyHeart Counts, our present work was made possible only through the unique and fully digital design of our randomized crossover trial.[10–12] By then leveraging this continued passive enrolment into the MyHeart Counts coaching trial and the resultant increased statistical power, we were able to further refine prior signals and identify that personalized e-coaching interventions were superior in increasing short-term physical activity (*Figure 3*). Our results can be extrapolated to other ongoing digital trials, and demonstrate another significant advantage of fully mobile/automated studies as compared to traditional trials.

Our present data suggests that personalized e-coaching prompts, specific to an individual's baseline activity level, is the most effective intervention in increasing their short-term physical activity. Although 'precision medicine' has become synonymous with tailoring therapies to an individual's genetic background,[22–24] the broader principle reflects integrating all available data to make the most informed clinical decision for each individual patient.[23] Within this context, our findings highlight the importance of tailoring interventions (whether genetic, medication, or digital) to each individual to achieve maximum efficacy.

Interestingly, we found that daily prompts to complete 10 000 steps did not significantly increase the mean daily step count from baseline, in contrast to our prior report from 1075 participants.[12] This may be due to the timing of this prompt, which triggered at 1500 h local time if the participant had not yet reached 5000 steps, leading to a prompt that was too late to elicit significant behavioural change for the day. Moreover, recent evidence has shown protective effects of physical activity beginning at 6000 steps/day (rather than 10 000 steps/day as studied in our current work).[28] Future work will be needed to elucidate the effect of more-refined and possibly, more realistic step goals as digital interventions.

In contrast to the findings with the daily step count intervention, hourly reminders to stand after inactivity were nearly as effective as personalized e-coaching in our study, possibly due to increased prompting (hourly vs. daily). These data suggest that, in addition to personalizing interventions to the individual, more frequent interventions and those earlier in the day are more effective in increasing short-term physical activity.

Several other studies have reported the effects of digital health interventions delivered via smartphone app on physical activity in diverse populations. In a meta-analysis of 3555 participants across 18 studies (our prior work[12] was not included in this study), there was a significant association between app-based digital interventions and participants' physical activity.[29] As well, a significant decrease in digital intervention effect size was noted with larger studies and with pragmatic trials.[29] In comparison to this meta-analysis, several recent studies in unique populations merit discussion: first, digital 'nudging' in the form of text messages or Facebook prompts did not significantly increase physical activity in congenital heart disease[30] or cancer-survivor[31] patient populations. Similarly, in a trial of patients with heart disease, the MyHeartMate app was used to gamify cardiac rehabilitation and exercise by illustrating a self-avatar that improved in appearance with physical activity. However, retention at 1 month was only approximately 27%, and there were no differences in 6-month outcomes, including metabolic equivalents of task, reflecting a lack of improvement in general cardiometabolic health.[32] However, in a trial of young medical interns, gamified intervention via mobile phone app was significantly associated with increased short-term physical activity, however, with waning casual effects over time.[33] These results suggest that while there is a significant increase in physical activity with app-based digital interventions,[29] the effect wanes over time with decreased app engagement[33] and may not be present in populations with significant medical comorbidities.[30–32] Further work is needed in high-risk groups that would benefit from exercise (e.g. those with heart failure or with coronary artery disease) to establish effect of digital interventions in these populations and demonstrate possible associations with health outcomes.

We note that a significantly higher proportion of participants had smartwatch data in our current analyses as compared to our prior work (82.1% vs. 24.7%). In our present data and in prior analyses,[12] we found that those with smartwatches had higher mean daily step count as compared to smartphone-only users, likely due to smartwatches being worn for all daily activities. As smartwatches are more accurate than phones in tracking step count,[34] this allows for greater sensitivity to detect changes with each intervention. However, as not all of our trial participants used smartwatches, there are possible biases introduced by combined use of iPhone vs. iPhone/Apple Watch combination users, as those who used iPhone alone could have a lower step count due to decreased sensor sensitivity and accuracy.[35]

Strengths of our study include its internal validity demonstrated by our sensitivity analyses. In separate *post-hoc* analyses of those who confirmed received notifications and those with smartwatches, consistent results with personalized e-coaching yielding the greatest increase in mean daily step count were obtained. We previously demonstrated that there were no significant differences in attrition of participants across the four interventions and separately, that there were no demographic differences in participants who dropped out as compared to those who were included in the modified intention-to-treat analyses.[12]

Several limitations of our study should be considered. As with other digital trials,[36,37] our study had significantly decreased user retention as compared with traditional trials. Other studies have demonstrated that gamification, such as badges earned for completing activities, improves retention[38] and this was previously implemented into the MyHeart Counts study.[12] A separate meta-analysis suggested that useful feedback and financial compensation were effective in increasing retention rates in digital health trials.[39] These possibilities will be explored in further extensions of the MyHeart Counts Cardiovascular Health Study.

In addition to the above limitations, our cohort demographics and the unblinded nature of our trial limit generalizability of our findings. The average subject in the randomization control trial subset of MyHeart Counts was a middle-aged white male, while physical activity is affected by age, gender, and race/ethnicity.[3,40] As well, the trial subset was performed only in the USA, UK, and Hong Kong, and it is possible that results cannot be generalized to populations with greater baseline physical activity. Furthermore, our trial only included iPhone users due to app design, and iPhone users generally are of higher socio-economic status and are more likely to have a graduate degree.[41] Moreover, while we did not observe differences in demographics between those who dropped out vs. those included in the modified intention-to-treat analyses,[12] it is possible that there was an element of selection bias, in that those who downloaded the MyHeart Counts app (or purchased an Apple Watch or other fitness tracker device) and completed interventions in our trial were self-motivated to increase their physical activity and improve their cardiovascular health.[42] Interestingly, this selection bias was seen within our trial, where those who completed 7 days of baseline monitoring and 7 days of monitoring in at least one intervention had drastically higher mean daily step counts as compared with the larger cohort (see Supplementary material online, *Table S4*). Moreover, once enrolled in the trial, it is possible that the knowledge that their activity was being logged led to more active behaviour (the so-called Hawthorne effect).[43] As well, it is unlikely that participants with significant medical comorbidities completed our trial due to the aforementioned demographic skew. Finally, while we demonstrated a 402 steps/day increase during the week of personalized e-coaching prompts as compared to baseline, the clinical significance of these short-term effects on chronic diseases remain unknown. Studies are ongoing to determine the effects of digital prompts on physical activity with long-term follow-up,[25] particularly with e-coaching interventions.[44]

Conclusions

Our extended randomized crossover trial demonstrates the strength and cost-effectiveness of fully digital and automated trials in continuing enrolment after primary analyses have concluded. Through this increased statistical power, we were able to identify that personalized e-coaching interventions were most effective in increasing short-term physical activity, with results that were consistent across sensitivity analyses. These data highlight the promise of digital trials and emphasize the importance of tailoring interventions to the individual, rather than applying a single therapy to all patients.

Author contributions

M.V.M., A.C.K., and E.A.A. conceptualized and designed the study. S.G.H. managed app development. A.C.K. and E.A.A. designed the interventions. A.J. and D.S.K. did statistical analysis. A.J., D.S.K., A.J., A.T., J.W.O., M.T.W., and E.A.A. contributed to acquisition, analysis, or interpretation of the data. D.S.K. and E.A.A. drafted the manuscript. A.J., S.G.H., A.S., J.W.O., M.V.M., L.L., A.C.K., J.W.C., M.O., C.M.M., R.A.A., M.T.W., and E.A.A. critically revised the manuscript for important intellectual content. M.T.W. and E.A.A. supervised the study.

Supplementary material

Supplementary material is available at *European Heart Journal – Digital Health*.

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Conflict of interest: M.T.W. reports grants and personal fees from Verily, Myokardia, and ArrayBio, and consultancy fees from BioTelemetry, outside the submitted work. E.A.A. reports advisory board fees from Apple and Foresite Labs. E.A.A. has ownership interest in Nuevocor, DeepCell, and Personalis, outside the submitted work. E.A.A. is a board member of AstraZeneca. E.A.A. and C.M.M. have ownership interest in SVEXA, outside of the submitted work. M.V.M. is an employee at identifeye HEALTH, a previous employee at Google/Fitbit (until 2022), a member of the medical advisory board of 4Catalyzer Corp., and on the board of directors of the National Fitness Foundation. S.G.H. is an employee of Biofourmis. D.S.K. is supported by the Wu-Tsai Human Performance Alliance. The remainder of authors report no potential conflicts of interest.

Data availability

The data that support the findings of this study are available on request from the corresponding authors, DSK and EAA. The data are not publicly available due to the Health Insurance Portability and Accountability Act of 1996.

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