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Feasibility of wearable sensor signals and self-reported symptoms to prompt at-home testing for acute respiratory viruses in the USA (DETECT-AHEAD): a decentralised, randomised controlled trial

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Contributors

JVi, KB-M, DT, and SRS made substantial contributions to the study conception and design. EC, JVe, FD, KH, ER, and KB-M made substantial contributions to the acquisition of data. GQ, MG, T-YH, and JTM conducted statistical analysis, and directly accessed and verified the underlying data. GQ, JAP, DT, and SRS made substantial contributions to the interpretation of data. GQ and EC drafted the first version of the manuscript. All authors had access to the data presented in the study, contributed to critical revisions, and approved the final version of the manuscript. All authors take responsibility for the integrity of the work and were responsible for the decision to submit for publication.

For the **DETECT study** see https://detectstudy.org/

For the **MyDataHelps platform** see https://mydatahelps.org/

See **Online** for appendix

For **python** see https://docs.python.org/release/3.8.3/

For **pandas** see https://pypi.org/project/pandas/2.0.3/

For **scipy** see https://pypi.org/project/scipy/1.6.3/

For **statsmodels** see https://pypi.org/project/statsmodels/0.14.1/

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Summary

Background—Early identification of an acute respiratory infection is important for reducing transmission and enabling earlier therapeutic intervention. We aimed to prospectively evaluate the feasibility of home-based diagnostic self-testing of viral pathogens in individuals prompted to do so on the basis of self-reported symptoms or individual changes in physiological parameters detected via a wearable sensor.

Methods—DETECT-AHEAD was a prospective, decentralised, randomised controlled trial carried out in a subpopulation of an existing cohort (DETECT) of individuals enrolled in a digital-only observational study in the USA. Participants aged 18 years or older were randomly assigned (1:1:1) with a block randomisation scheme stratified by under-represented in biomedical research status. All participants were offered a wearable sensor (Fitbit Sense smartwatch). Participants in groups 1 and 2 received an at-home self-test kit (Alveo be.well) for two acute respiratory viral pathogens: SARS-CoV-2 and respiratory syncytial virus. Participants in group 1 could be alerted through the DETECT study app to take the at-home test on the basis of changes in their physiological data (as detected by our algorithm) or due to self-reported symptoms; those in group 2 were prompted via the app to self-test only due to symptoms. Group 3 served as the control group, without alerts or home testing capability. The primary endpoints, assessed on an intention-to-treat basis, were the number of acute respiratory infections presented (self-reported) and diagnosed (electronic health record), and the number of participants using at-home testing in groups 1 and 2. This trial is registered with ClinicalTrials.gov, NCT04336020.

Findings—Between Sept 28 and Dec 30, 2021, 450 participants were recruited and randomly assigned to group 1 (n=149), group 2 (n=151), or group 3 (n=150). 179 (40%) participants were male, 264 (59%) were female, and seven (2%) identified as other. 232 (52%) were from populations historically under-represented in biomedical research. 118 (39%) of the 300 participants in groups 1 and 2 were prompted to self-test, with 61 (52%) successfully completing self-testing. Participants were prompted to home-test more frequently due to symptoms (41 [28%] in group 1 and 51 [34%] in group 2) than due to detected physiological changes (26 [17%] in group 1). Significantly more participants in group 1 received alerts to test than did those in group 2 (67 [45%] *vs* 51 [34%]; p=0·047). Of the 61 individuals who were prompted to test and successfully did so, 19 (31%) tested positive for a viral pathogen—all for SARS-CoV-2. The individuals diagnosed as positive for SARS-CoV-2 in the electronic health record were eight (5%) in group 1, four (3%) in group 2, and two (1%) in group 3, but it was difficult to confirm if they were tied to symptomatic episodes documented in the trial. There were no adverse events.

Interpretation—In this direct-to-participant trial, we showed early feasibility of a decentralised programme to prompt individuals to use a viral pathogen diagnostic test based on symptoms tracked in the study app or physiological changes detected using a wearable sensor. Barriers to adequate participation and performance were also identified, which would need to be addressed before large-scale implementation.

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Introduction

To limit transmission of pathogens that cause acute respiratory infection, such as SARS-CoV-2 and respiratory syncytial virus, the early identification of infected individuals is crucial. During the COVID-19 pandemic, several possible solutions were identified, including the use of self-reported symptoms[1] and wearable sensor data.[2–8] The Digital Engagement and Tracking for Early Control and Treatment (DETECT) digital clinical study, among several others, showed the potential usefulness of wearable sensor data in early diagnosis of acute respiratory infection.[2] In DETECT, by December, 2021, 39 501 participants had enrolled and donated data from their wearable sensors plus their self-reported symptoms. These data were foundational in the development of an algorithm, used in this substudy, to identify individuals more likely to have COVID-19.[8] Several studies[3,4,9] have subsequently reinforced these findings based on wrist-wearable sensors, and a number of additional physiological signals for early detection of acute respiratory infection, including acoustics[10] and fever mapping,[11] continue to be explored. A logical next step for use of these potential early markers of infection is to couple them with early diagnostic testing.

Home-based self-testing for viral pathogens was essentially non-existent before COVID-19. However, as the pandemic evolved, dozens of home tests received regulatory emergency use authorisation,[12] with more than 1 billion being distributed to US households under just one government programme.[13] The performance of these tests has resulted in the rapid acceleration of their acceptance and an expanded demand for home testing capabilities.

Early diagnosis of acute respiratory infection is also a substantial challenge in clinical research. The traditional approach to the conduct of clinical trials for prevention of acute respiratory infections relies on a centralised approach to the identification of clinically relevant events, which is subject to underdiagnosis and missing data. Development and implementation of a digital platform, enabling early viral pathogen diagnosis and monitoring of patients with acute respiratory infections in a real-world environment in the context of a clinical trial, might address these crucial challenges.

We aimed to evaluate the feasibility of combining two novel technologies developed in response to the COVID-19 pandemic—a closed-loop digital program built around novel at-home viral diagnostic testing coupled with an algorithm-based alert system using wearable sensor data and mobile app symptom monitoring—that could enable the early diagnosis of viral respiratory infections in a real-world environment.

Methods

Study design and population

DETECT At-Home Early Alert and Diagnosis (DETECT-AHEAD) was a prospective, decentralised, randomised controlled trial done in a subpopulation of an existing cohort of individuals enrolled in a nationwide, digital-only observational study in the USA.

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The study population was composed of individuals who had previously consented to enrol in the DETECT study.[2] Participants in the parent DETECT study, who were aged 18 years or older and living in the USA, were asked to donate their wearable sensor data and input any self-reported symptoms, viral testing results, and COVID-19 vaccination dates and types via the MyDataHelps app. Additional inclusion criteria for DETECT-AHEAD were signed informed consent for the substudy, connection of the participant's electronic health records to the study app, completion of a baseline survey, and ability to receive and return study devices via mail, to use a smartphone, and to read and write in English. There were no additional exclusion criteria. An additional group of 30 participants with cardiorespiratory disease was enrolled in a separate, exploratory group for acoustic lung sound signal detection, but the findings are not reported here.

DETECT participants were invited by email to open the MyDataHelps app then, in the app, they could verify if they were eligible for the DETECT-AHEAD substudy. The substudy prioritised enrolment of individuals historically under-represented in biomedical research (UBR), which was previously defined across several diversity categories.[14] Specifically, participants were considered to be UBR if they self-identified as at least one of the following: race and ethnicity other than White and non-Hispanic; gender identity other than male or female; age older than 65 years; household income less than US$10 000 or less than $25 000 for a household of four or more; education level lower than a high school diploma; residence in a rural ZIP code. The target recruitment goals for DETECT-AHEAD were for a minimum of 50% of the cohort to be recognised as having UBR status (target n=225). An additional goal was for 30% of the cohort to have indicated UBR status specific to race or ethnicity (target n=135). To achieve this recruitment goal, after confirming eligibility, each participant who was UBR on the basis of race or ethnicity was immediately and automatically invited to participate in DETECT-AHEAD. Participants who were UBR on the basis of other factors were prioritised through a manual selection process, and participants typically represented in biomedical research were selected with lower priority (figure 1). Gender data were self-reported (male, female, or other).

Individuals who consented to enrol in DETECT-AHEAD had previously consented as participants in the larger DETECT study. All those participating in the DETECT-AHEAD substudy provided additional signed informed consent electronically. The protocol for DETECT-AHEAD was reviewed and approved by the Scripps Office for the Protection of Research Subjects (IRB 20–7531). This trial is registered with ClinicalTrials.gov, NCT04336020.

Randomisation and masking

Consented participants were randomly assigned (1:1:1) into three groups (two interventional groups and one observational group) stratified by UBR status. Randomisation was conducted by the study clinical biostatistician using a random number generator with permuted block sizes of 3 and 6.

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Procedures

All participants were given free access to a Fitbit Sense smartwatch (Fitbit, San Francisco, CA, USA) and the MyDataHelps app with the DETECT-AHEAD substudy. Those assigned to the interventional groups (groups 1 and 2) also received the Alveo be.well home molecular testing kit (Alveo Technologies, Alameda, CA, USA), which was designed to test for SARS-CoV-2 and respiratory syncytial virus. These pathogens were selected by the manufacturer of the kit due to their high incidence and potential severity. All participants could visualise their own biometrics as routinely provided by the smartwatch, which they were asked to wear as much as possible, including while sleeping. All participants were asked to complete respiratory symptom surveys on the downloaded mobile app if they developed any symptom.

Participants assigned to group 1 could be alerted to self-test at most once, either by an algorithm that computed an anomaly score based on physiological sensor data[8] or by symptoms self-reported in the study app, whichever one occurred first. At least two acute respiratory infection symptoms needed to be reported to generate an alert, in order to reduce the number of false-positive alerts. The complete list of acute respiratory infection symptoms considered is provided in the appendix (p 1). Participants assigned to group 2 could be alerted on the basis of self-reported symptoms only. Participants assigned to group 3 received no home molecular testing kit and no alerts for self-testing. All participants were encouraged to follow their routine care practices and to track any symptoms in the DETECT app until they were resolved. Data collection was stopped on May 7, 2022.

The measured values of resting heart rate, sleep duration, and activity (measured as steps) collected by Fitbit Sense were used each day to calculate a risk score for infection. This risk assessment was based on the adaptation of an algorithm for detection of COVID-19, which has been shown previously to provide a positive predictive value of 0·50 and negative predictive value of 0·90 based on deviations from an individual's baseline (with baseline calculated on the basis of at least 27 days of the wearer's 60 days of data before the day of interest, but excluding the 6 days immediately before).[8] Briefly, a risk threshold for resting heart rate was defined as an increase on at least one of the previous 3 days exceeding 1·5 standard deviations with respect to the individual baseline. Similarly, risk thresholds for sleep and activity were defined as an increase (sleep) or decrease (activity) of 2·0 standard deviations with respect to the individual baseline.

To capture positive cases with a minimal delay after infection, the physiological alert was activated when the risk simultaneously exceeded the predefined threshold for resting heart rate and for at least one of sleep or activity. This system, which triggered an alert only when at least two physiological signals exceeded their threshold, was designed to limit the number of false positives, since by design each individual could be alerted only once during the study period.

The Alveo be.well at-home diagnostic test enables molecular testing for SARS-CoV-2 and respiratory syncytial virus at home.[15] The be.well kit comes with nasal swabs, disposable cartridges, a handheld analyser, and directions for use in both the Alveo mobile app and hard copies. Participants in group 1 and 2 downloaded the Alveo app and linked their analyser

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to their mobile devices via Bluetooth at the time of testing. If alerted, the participant was instructed to collect a biosample with the nasal swab, place it in the test cartridge, and insert the cartridge into the analyser (appendix p 5). As the test did not have regulatory approval for diagnostic testing, it was not used for any clinical decisions. Participants were encouraged to follow standard practice patterns and not to take any acute actions based on the test result. To enforce this, participants were informed they would not receive the results of their test until around 2 weeks after testing (figure 2). Furthermore, we could not exclude the presence of false negatives, since one antigen test was requested, whereas two antigen tests separated by 48 h are suggested by the Centers for Disease Control and Prevention to confirm a negative result for SARS-CoV-2.

If and when participants developed symptoms suggestive of a possible acute respiratory infection, they were asked to document the presence of specific symptoms on a daily basis until they resolved. Participants in groups 1 and 2 were alerted to test with the Alveo be.well kit if their symptom score met prespecified criteria (appendix p 1).

A usability survey created for this study was provided after a participant used the be.well kit. This survey asked about ease of use, comfort level of the nasal swab and self-administration, clarity of instructions, and overall experience (appendix p 2).

A behaviour survey, also created for this study, administered to obtain information about participants' behaviour around the time of the alert, was delivered after results of the Alveo test were returned to participants. Behaviour questions included how the alert affected their actions, if any, before and after being prompted to test, including isolation, care seeking, and taking time off work. We also asked the participants to speculate whether or not immediate return of test results would have affected their care seeking or isolation (appendix p 3).

Outcomes

The primary endpoints were the number of acute respiratory infections presented (self-reported) and diagnosed (electronic health record), and the number of participants using at-home testing. Secondary endpoints reported here were the number of positive, negative, and null tests, and the corresponding percentages over the total number of tests, and the usability of the at-home tests.

Some endpoints initially specified in the protocol could not be measured due to limitations in availability of linked electronic health record data. We were unaware of these limitations until carrying out the study. It was not possible to establish acute respiratory infection presentation for individuals in group 3 who did not have a clinical visit reported in the electronic health record. It was also not possible to collect the difference in days of symptoms from initial detection to contact with a medical provider, nor correlation of sensor data with symptom severity, as it was not possible to consistently assess duration and severity of symptoms. Changes in medications used for chronic conditions were not assessed. Finally, a planned substudy including behavioural testing of study platform communications was not implemented. A study coordinator at Scripps Research was responsible for recording adverse events.

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Statistical analysis

In this descriptive feasibility trial, a convenience sample of 450 participants was determined empirically to provide adequate sample size for real-word usability and feasibility data, based on the investigators' previous experience with direct-to-participants studies using novel digital devices. The number of participants was calculated by setting the dropout or loss to follow-up to 10% (estimated from previous related studies[2,8]) and the number of acute respiratory infection events per patient to 0·7 (estimated on the basis of previous flu seasons).

The objective was to assess the feasibility and usability of the multiple interconnected components of this digital technology-enabled decentralised trial. Therefore, the analysis was conducted on an intention-to-treat basis. We calculated the ratio of individuals alerted to test and who completed the symptom survey among the 450 individuals in the three groups or individuals in a specific group. Comparisons between the two interventional groups were also tested for statistical significance (ie, p value <0·05) with standard two-tailed χ^2 tests. The statistical analysis was performed using publicly available statistical tools (python version 3.8.3, pandas version 2.0.3, scipy version 1.6.3, and statsmodels version 0.14.1).

Role of the funding source

Researchers employed by the funder of the study participated in study design and data collection, but they did not have access to the raw data and had no role in data analysis; they did contribute to data interpretation and writing of the report.

Results

Between Sept 28 and Dec 30, 2021, 450 participants were recruited and randomly assigned to group 1 (n=149), group 2 (n=151), or group 3 (n=150; figure 3). 179 (40%) of 450 participants were male, 264 (59%) were female, and seven (2%) identified as other. 232 (52%) of 450 individuals were considered to be UBR. Among those considered to be UBR, 137 (59%) were UBR on the basis of race or ethnicity (ie, self-identified as other than White or non-Hispanic). No major differences in the demographic compositions of the groups were observed (table 1). The median age range for each of the three groups was 45–54 years (IQR 35–44 to 55–64). The approximate mean age (obtained from the reported age ranges) was 49·5 years (group 1), 48·3 years (group 2), and 50·4 years (group 3). No adverse events were reported to the study coordinator. Of the 450 individuals who completed consent, 372 (83%) completed all post-consent onboarding steps, including connection of the Fitbit device received during the trial (appendix p 4).

Over the study period, 118 (39%) of the 300 participants in groups 1 and 2 were prompted to self-test. More participants in group 1 received alerts to test (67 [45%] of 149) than did those in group 2 (51 [34%] of 151; p=0·047; table 2). 26 (39%) of the 67 test prompts in group 1 were due to physiological alerts. Participants considered to be UBR received slightly fewer alerts than did the rest of the study participants (appendix p 6).

Following prompting, 61 (52%) of 118 individuals successfully completed self-testing. In group 1, 29 (43%) of 67 individuals who were alerted performed the at-home test, with

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a marked difference in testing rates based on what triggered the alert: six (23%) of 26 participants completed self-testing after physiological alerts and 23 (56%) of 41 did so after symptom alerts. 32 (63%) of 51 participants in group 2 completed their home test after being alerted, significantly more than in group 1 (p=0·036). Among the 61 people who tested after receiving an alert, 19 (31%) tested positive for SARS-CoV-2 (eight [28%] in group 1 and 11 [34%] in group 2), none tested positive for respiratory syncytial virus, 24 (39%) tested negative for both (13 [45%] in group 1 and 11 [34%] in group 2), and 18 (30%) obtained an invalid result (eight [28%] in group 1 and ten [31%] in group 2; figure 3). An invalid test result was defined as a test without enough sample to be analysed by the be. well system.

Almost as many participants (n=60; 28 [19%] from group 1 and 32 [21%] from group 2) self-tested spontaneously (unrelated to being alerted) as those who were alerted (figure 3). Of those individuals, 11 (18%) tested positive (ten for SARS-CoV-2 and one for respiratory syncytial virus), 33 (55%) tested negative, and 16 (27%) had an invalid result.

Of 26 participants who received an alert to test based on physiological changes, 17 (65%) never reported any symptoms. Eight (31%) participants with a physiological alert reported symptoms in the 7 days (median 3·00 days [IQR 0·75–5·00]) after the alert (table 2).

All participants agreed to share their electronic health record data. At least one electronic health record entry was available for 444 (99%) of 450 individuals. 238 (53%) had at least one encounter within the health-care system entered in their electronic health record since enrolment in DETECT-AHEAD (table 3). Of these individuals, 57 (24%) were documented as having received a SARS-CoV-2 test as part of an encounter after DETECT-AHEAD enrolment, 14 (25%) of whom had at least one positive test and 43 (75%) only negative tests. In groups 1 and 2, testing within the health-care system occurred in 42 (14%) participants. Among the participants who got tested, at least one test occurred within 2 weeks after a study alert in eight (19%) individuals (two positive and six negative); a test occurred only outside this timeframe in 11 (26%) individuals (five positive and six negative). Among the five individuals who tested positive outside the 2 weeks after the alert, two tested positive in the week before the alert. Among the six individuals who tested negative outside the 2-week post-alert timeframe, one tested negative within 1 week before the alert. In groups 1 and 2, 23 (55%) individuals were not alerted but had a test recorded in their electronic health record (three positive and 20 negative). In group 3, testing occurred in 15 (10%) participants, two with at least one positive result and 13 with only negative results.

For all three participants who received an alert and tested at home, and had an electronic health record encounter within 2 weeks after that event, the home test was concordant with the electronic health record result (both positive for two participants, both negative for one participant). No acute respiratory infection-related hospitalisations were reported in the electronic health records.

Of the 450 participants who were offered a smartwatch at no cost, 399 (89%) ordered the device and 372 (83%) connected its data to the study platform. Of these 372 participants, 300 (81%) used the device consistently throughout the trial, defined as wearing it for at least 6 h per day on at least 95% of the study days. 292 (78%) participants wore the device for

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at least 10 h per day for 95% of the study days. The wearing time was determined by the presence of heart rate signal. Among the 372 participants who connected the wearable data, 162 (44%) were considered to be UBR, of whom 131 (81%) used the device consistently for at least 6 h per day.

The usability survey was provided to the 121 individuals who used the at-home test kit and was completed by 89 (74%) participants. 73 (82%) participants confirmed the ease of use of the test and 78 (88%) confirmed a high comfort level of the nasal swab. Among the individuals who answered the survey, 65 (73%) would recommend this test (appendix p 2).

The behaviour survey was also delivered to the 121 participants who completed an at-home test, and was completed by 51 (42%) individuals. When asked how the alert impacted their actions when prompted to test, 27 (53%) answered that they isolated themselves at the time of receiving the alert to test. When asked if immediate return of test results would have impacted their care seeking, 31 (61%) answered that they would not have done anything differently, whereas 13 (25%) would have been more likely to isolate themselves (appendix p 3).

Discussion

Our results show the feasibility of a decentralised acute respiratory infection monitoring platform and some of the potential barriers that should be overcome to improve participant engagement and participant-generated data quality. The platform was designed for patients at risk of acute respiratory infections, with early alerts for possible infection through self-reported symptoms and wearable technology. Home diagnostic testing became mainstream during the COVID-19 pandemic,[16–19] reinforcing the future role of home testing for a wide range of viral and bacterial infections. Additionally, some studies have shown the ability of wearable technology to identify infection-related physiological changes even before symptoms appear.[20–23] To show the potential value of the simultaneous implementation of wearable technology and at-home testing, in clinical research and potentially clinical care, we studied an alert system to inform participants to home test when they developed either physiological changes or symptoms suggestive of an acute respiratory infection.

Although we showed that such a decentralised monitoring platform is feasible, we also uncovered many barriers that need to be overcome before a similar approach can be deployed on a larger scale. First, just half of participants self-tested after receiving an alert to do so, despite the study enrolling from what would be regarded as an engaged population, as participants were already members of the DETECT study and actively responded to outreach. Second, among participants in groups 1 and 2 who tested after receiving an alert, around 30% had invalid test results, a level that is higher than expected and was not anticipated in an at-home test setting. Third, almost as many people self-tested without receiving an alert as did after receiving an alert. This suggests that digitally shared instructions were inadequate to assure that all study participants understood the study purpose and methodology. It is also possible that some participants did not report the presence of symptoms. Further studies are needed to investigate whether providing information in a different format could drive greater comprehension. In addition, we hoped

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to connect home testing with real-world health-care procedures through connection to each participant's electronic health records. Although 238 (53%) participants did have a documented encounter within the health-care system of their connected electronic health record since enrolment in the study, it was difficult to passively confirm an association between symptomatic episodes documented in the trial and whether they were tied to a specific electronic health record encounter.

Symptoms were reported in slightly less than a third of participants who received an alert due to physiological changes detected via their wearable device. Considering the early stages of development of the proposed symptom reporting system, which requires the reporting of two symptoms to minimise false-positive alerts, and the potential for recall bias in reporting of symptoms, this finding is still encouraging. However, less than a quarter of people in group 1 who received a physiological alert, performed the at-home test when prompted. One potential explanation for this is that the physiological alert could occur at any time, triggering a notification at a time that might make it easy to disregard. Conversely, about 60% of participants in groups 1 and 2 who received a symptom alert self-tested, which might be because symptom-based alerts occurred only while the participant was on the app reporting symptoms, and receipt of a notification while using the app prompted testing.

An encouraging finding was that the use of the provided wearable devices in our trial was higher than expected, with 81% of participants using the device consistently throughout the trial. The prospect of using wearable sensor data to enable earlier, potentially presymptomatic alerting has been studied,[24] but to our knowledge this is the first prospective trial that includes both alerting and testing. Another limitation that should be highlighted is that factors others than acute respiratory infection can affect resting heart rate, and there is more to learn about rare participant exposures that might affect their physiology. For example, it is known that medications, alcohol consumption, or stress can alter the wearable sensor data and, if infrequent, might fall out of the range of that individual's expected baseline variability. Furthermore, it is not possible to analyse separately the effects of the physiological sensor and the self-reported symptoms, as both were used by the alert system for group 1.

The DETECT-AHEAD trial builds on DETECT's digital platform to collect data and provide information to participants about COVID-19 and other infectious diseases. The DETECT study, like most bring-your-own-device studies, could lead to enrolment of non-representative populations and risk contributing to health disparities.[25] Given existing health disparities,[26] reinforced by the COVID-19 pandemic,[27] we designed this substudy to recruit a highly diverse population with more than 50% of enrolled individuals being considered UBR. Traditional studies rely on recruitment from a few health-care institutions, thus excluding a large part of the population not living near to these institutions. In our study, it was possible to recruit a more diverse population thanks to the large pool of engaged participants in DETECT and the decentralised nature of this substudy,[28] which allowed us to use online media to reach a much larger number of interested individuals in the USA.

The DETECT-AHEAD trial tested the feasibility of a decentralised monitoring platform for patients with acute respiratory infections that could potentially benefit both clinical research

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and the public health response against future pandemics. Despite the use of multiple digital health innovations to diagnose acute respiratory infections early, these devices and their potential to serve as supplemental public health tools currently lack the infrastructure needed to support them.[29] Because digital health tools can recognise COVID-19 and other acute respiratory infections earlier than symptoms in some individuals, they could prompt people to test and confirm infection, thereby minimising exposure to others and optimising both testing and public health resources.[30]

In the DETECT-AHEAD trial, we showed the feasibility of a decentralised monitoring platform for the detection of people who might develop an acute respiratory infection by showing the successful, entirely digital recruitment of 450 participants, with a majority being from UBR populations. Of these participants, 39% were alerted by our algorithm, and 99% had at least one electronic health record entry assessed. We believe that the decentralised format of this trial lays the groundwork for future at-home testing studies, including participant-provided wearable data and self-reported symptoms, and for closing the loop by returning information back to the participant. The use of a novel, low-touch, and decentralised format is pragmatic and allows both a representative study population and electronic health record data linkage. Nonetheless, a good deal of refinement is needed before the conduct of large, pragmatic clinical trials using these relatively inexpensive remote monitoring technologies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Declaration of interests

JVi, KH, JVe, MA, LK, JWC, and DT are employed by Janssen Pharmaceuticals. JMR was supported by The Rockefeller Foundation and is now employed by Moderna. ER is employed by CareEvolution. KB-M is a consultant for CareEvolution and was on the Heartline Study Executive Committee. SRS is a consultant for PhysIQ and declares payment for being on the Heartline Study Executive Committee. All other authors declare no competing interests.

Data sharing

Additional data obtained within the current trial are presented in the appendix. The protocol can be shared by request to the corresponding author.

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Research in context

Evidence before this study

We searched PubMed for articles published between Jan 1, 2020, and April 1, 2023, using the search terms ((“COVID-19” OR “COVID” OR “SARS-CoV-2”) AND “detection” AND (“diagnostic” OR “diagnosis” OR “early identification” OR “alert”) AND (“wearable sensor” OR “wearable”)) with no language restrictions. We identified 55 articles. Excluding articles that focused exclusively on the technology, we considered six articles and one review, which provided consistent results in the use of wearable sensors for the early detection of SARS-CoV-2 infection, with low risk of bias. These studies confirmed that during the COVID-19 pandemic, the most effective strategy to limit the spread of the virus was early identification of infected individuals and prompt isolation. To improve this strategy, previous retrospective studies have shown that wearable technology can detect, in some people, infection-related physiological changes even before symptoms appear. Once an individual is identified as being at high risk of having an infection, home diagnostics, which are now mainstream, can be used to detect the virus and prompt isolation of the infected individual. However, although these novel tools exist, the feasibility of the pragmatic implementation of both tools in combination has not previously been published.

Added value of this study

To our knowledge, this is the first prospective trial showing the feasibility of a system that informs participants to take an at-home test when they experience physiological changes or symptoms suggestive of an acute respiratory infection. We recruited a diverse population, with 232 (52%) of 450 participants historically under-represented in biomedical research (UBR) and 137 (30%) participants UBR on the basis of race or ethnicity. Results showed that 118 (39%) of 300 participants were prompted to self-test, more frequently due to symptoms than to physiological changes. Although we showed the feasibility of combining personalised alerting with home testing using a decentralised trial design, we identified several barriers, including low participant engagement and challenges in providing adequate instructions via digital means to ensure that all participants understood the trial purpose.

Implications of all the available evidence

Numerous digital health innovations are now capable of early acute respiratory infection warning, potentially prompting individuals to test and confirm their infection status, and serving as supplementary public health tools for future pandemics. Our study’s decentralised format lays the groundwork for future at-home testing studies, including the collection of participant-provided wearable data and self-reported symptoms, and closing the loop by returning actionable information to the participant. Nevertheless, substantial refinements in terms of operational streamlining and further scientific development of the algorithm are necessary before clinical implementation.

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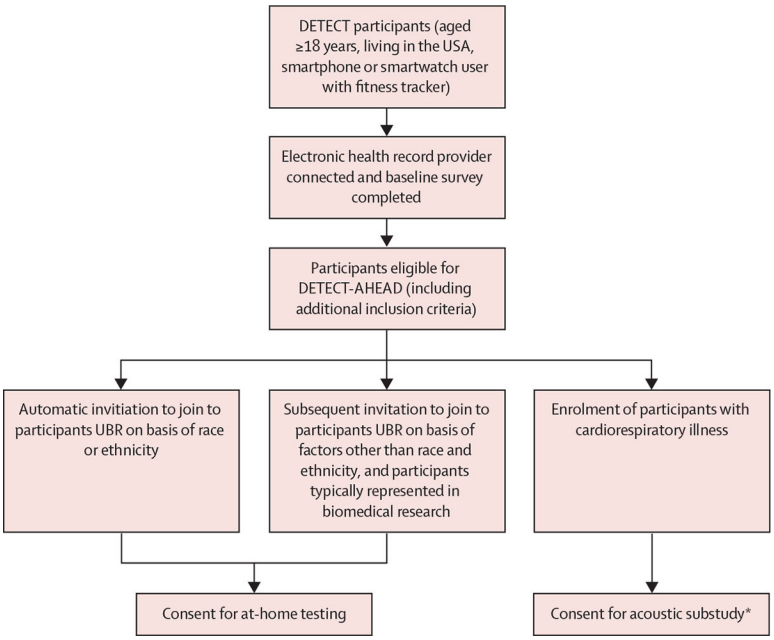

Figure 1: DETECT-AHEAD participant selection process

Selection process of participants in the DETECT-AHEAD substudy from participants in the parent study DETECT, including characteristics for eligibility and invitation to join the study. UBR=under-represented in biomedical research. *Not reported here.

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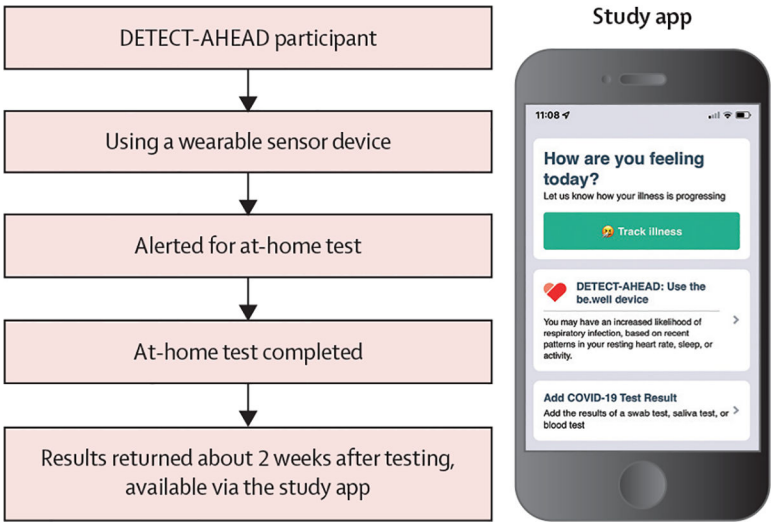

Figure 2: Study-provided devices used in the DETECT-AHEAD trial

Devices provided in the DETECT-AHEAD trial were a wearable device to monitor physiological signals (Fitbit Sense; all participants) and a home diagnostic kit (Alveo be.well test kit and app; groups 1 and 2) to detect acute respiratory infection (SARS-CoV-2 or respiratory syncytial virus). The study app was connected to the wearable sensor device and allowed the participant to self-report symptoms. The study app also alerted the participant and invited them to complete an at-home test, and then provided the results of the test. Group 1 received alerts to test on the basis of physiological data or self-reported symptoms; group 2 received alerts on the basis of self-reported symptoms only. Group 3 did not receive alerts and did not have at-home testing capability.

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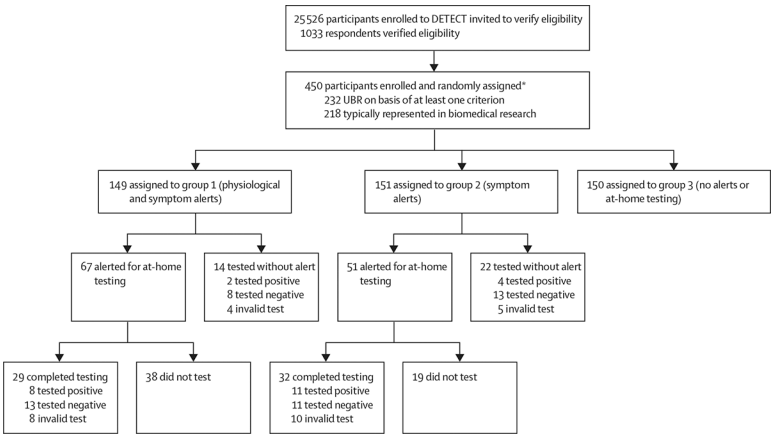

Figure 3: Trial profile and testing results

UBR=under-represented in biomedical research. *Of 450 participants who enrolled in the study, 399 ordered the Fitbit Sense smartwatch and 372 (162 of whom were UBR) connected its data to the study platform.

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Table 1:

Demographics of participants

	Group 1 (physiological and symptom alerts; n=149)	Group 2 (symptom alerts; n=151)	Group 3 (control; n=150)
Age, years			
18–44	62 (42%)	72 (48%)	56 (37%)
45–64	61 (41%)	58 (38%)	70 (47%)
≥65	26 (17%)	21 (14%)	24 (16%)
Gender			
Female	88 (59%)	92 (61%)	84 (56%)
Male	61 (41%)	53 (35%)	65 (43%)
Other	0	6 (4%)	1 (1%)
UBR	79 (53%)	71 (47%)	82 (55%)
UBR on basis of race or ethnicity	45 (30%)	46 (30%)	46 (31%)
Asian	10 (7%)	15 (10%)	14 (9%)
Black or African American	5 (3%)	13 (9%)	8 (5%)
Other (including American Indian or Alaskan Native, Middle Eastern, north African, Hispanic, Latino, Spanish, Hawaiian, Pacific Islander, and multiple races or ethnicities)	30 (20%)	18 (12%)	24 (16%)
UBR on basis of socioeconomic status (education or income level)	4 (3%)	8 (5%)	6 (4%)

In an exploratory analysis, we evaluated the differences among the two interventional groups (groups 1 and 2) and the control group (group 3). UBR=under-represented in biomedical research.

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Table 2:

Physiological and symptom alerts received

	Group 1 (physiological and symptom alerts; n=149)	Group 2 (symptom alerts; n=151)	p value group 1 *vs* group 2
Participants never alerted	82 (55%)	100 (66%)	0·047
Alerted to test (physiological data)	26 (17%)	..	..
Alerted to test (symptoms)	41 (28%)	51 (34%)	0·24
Alerted to test (total)	67 (45%)	51 (34%)	0·047
Completed symptom survey in 7 days from wearable sensor alert	8 (5%)	..	..
Completed symptom survey in 7 days from symptom alert	41 (28%)	51 (34%)	0·24
Completed symptom survey in 7 days from any alert	49 (33%)	51 (34%)	0·87

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Table 3:

EHR data and participants positive for acute respiratory infection

	Group 1 (physiological and symptom alerts; n=149)	Group 2 (symptom alerts; n=151)	Group 3 (control; n=150)
Participants with at least one EHR entry	148 (99%)	149 (99%)	147 (98%)
Participants with at least one EHR entry after DETECT-AHEAD enrolment	85 (57%)	82 (54%)	71 (47%)
Participants with at least one EHR entry for SARS-CoV-2 after DETECT-AHEAD enrolment	20 (13%; 3 positive only, 12 negative only, 5 both)	22 (15%; 2 positive only, 18 negative only, 2 both)	15 (10%; 1 positive only, 13 negative only, 1 both)
Participants with an EHR entry for SARS-CoV-2 among those who received an alert	11 (7%; 2 positive only, 4 negative only, 5 both)	8 (5%; 1 positive only, 6 negative only, 1 both)	..
Participants who received an alert, with at least one SARS-CoV-2 test result in EHR in the 2 weeks after the alert	2 (1%; 1 positive only, 1 negative only)	6 (4%; 1 positive only, 5 negative only)	..
Participants who received an alert, with a SARS-CoV-2 test result in EHR only outside the 2 weeks after the alert	9 (6%; 1 positive only, 4 negative only, 4 both)	2 (1%; 2 negative only)	..
Participants who did not receive an alert, with at least one SARS-CoV-2 test result in EHR	9 (6%; 8 negative only, 1 both)	14 (9%; 1 positive only, 12 negative only, 1 both)	15 (10%; 1 positive only, 13 negative only, 1 both)
Participants who received an alert, tested at home, and had a SARS-CoV-2 test result in EHR in the 2 weeks after the alert	2 (1%; 1 concordant positive, 1 concordant negative)	1 (<1%; 1 concordant positive)	..

One participant who received an alert tested positive for respiratory syncytial virus using the Alveo be.well at-home test kit. EHR=electronic health record.

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