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Field Application of Digital Technologies for Health Assessment in the 10,000 Families Study

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ABSTRACT

Background: We field tested new-to-market portable, digital applications to assess hearing, pulmonary, and cognitive function to determine the feasibility of implementing these applications across a range of age groups in the pilot phase of the 10,000 Families Study (10KFS), a new Minnesota family–based prospective cohort study.

Methods: We followed manufacturer recommended protocols for audiometry (SHOEBOX Inc), spirometry (NuvoAir), and the digital clock drawing test (dCDT; Digital Cognition Technologies Inc).

Results: These digital devices were low cost and readily implemented in a 2.5-hour health fair visit with minimal training (2–3 hours) of study staff. To date, we have performed these measurements on 197 eligible 10KFS participants during an in-person clinic visit. A total of 37 children (age 4–17 years), 107 adults (18–64 years), and 53 seniors (≥65 years) were eligible to undergo hearing and pulmonary assessments. Children were less likely to successfully complete the hearing test (76%) compared with adults (86%) and seniors (89%). However, successful completion of the pulmonary assessment was high across all groups: 100% of children and seniors and 98% of adults. The dCDT was performed among those over the age of 40, and completion rates were 92% for those aged 41–64 and 94% for those ≥65 years.

Conclusions: Our field testing indicates these digital applications are easy and cost-effective to implement in epidemiologic studies.

Impact: Digital applications provide exciting opportunities to collect data in population studies. Issues related to data privacy, data access, and reproducibility of measurements need to be addressed before deploying digital applications in epidemiologic studies.

See all articles in this *CEBP Focus* section, "Modernizing Population Science."

Introduction

Chronic disease epidemiology is increasingly focused on identification of subclinical alterations in phenotypes that can serve both as early markers of disease and as surrogate endpoints to facilitate etiologic studies aimed at identification of novel risk factors for chronic diseases (1). Innovations in the collection of health data using mobile, digital platforms have the potential to transform the conduct of epidemiologic studies in this regard. Portable digital technology applications expand the range of settings in which biophysical measures can be obtained and also allow for rapid and sensitive measurement of subclinical biophysical characteristics that may be useful to predict and prevent overt clinical disease in later life. Here, we describe the feasibility and field implementation of three digital applications to assess hearing, pulmonary, and cognitive function that demonstrates the promise of using these technologies in a broad range of settings beyond the traditional clinic setting.

Many physical measurements, such as weight and blood pressure, are routinely and easily performed in epidemiologic studies. However, other measures, such as pulmonary function and hearing tests, require specialized equipment (e.g., spirometers for pulmonary function; refs. 2, 3) and environments (e.g., sound proof environments for hearing tests; ref. 4) for reliable assessments in epidemiologic studies. In addition, epidemiologic studies typically employ central reading centers where measurement specialists train all study personnel at multiple field centers to carry out individual measures, oversee ongoing quality control, and provide standardized mechanisms to review both data quality and interpret the data collected. Technologic innovation has produced applications compatible with commonly used personal mobile technology to facilitate data collection in these domains in diverse settings that minimize the need for having reading centers by incorporating several quality control measures within the digital applications. In this regard, the audiometry application from ShoeBox Inc. has been shown to compare well with the traditional gold standard method for performing audiometry in a relatively noisy environment without the use of soundproof rooms (5). The spirometry application (NuvoAir Inc.) has also been shown to have comparable performance to traditional methods of performing spirometry (6, 7). In addition, both devices have regulatory approvals from the Food and Drug Administration (FDA) or the European Commission for use in a clinical setting. Despite the demonstrated validity of these instruments in clinical settings, they have not been extensively evaluated for use in epidemiologic studies in field settings that are substantially different from a traditional clinic setting and where trained specialists in audiometry and spirometry may not be available.

Measures of cognitive function in epidemiologic studies have primarily used the Mini Mental Scale Examination (MMSE) and the traditional clock drawing test, which are very well-established tools for

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diagnosis of dementia (8, 9). Specifically, the traditional clock drawing test (CDT) is a well-accepted cognitive screening tool used in subjects with conditions such as Alzheimer disease, Parkinson disease, and others (10, 11). As a simple paper and pencil test, the CDT is quick and easy to administer, noninvasive and inexpensive, yet provides valuable clinical and diagnostic information. However, the main drawbacks of the CDT are that (i) the interpretation of the test relies on the clinician's subjective judgment of the drawing and (ii) it is not sufficiently sensitive to identify mild or subclinical impairments in cognitive function (12, 13). Administering the CDT using digital technology (i.e., the digital clock drawing test; dCDT) allows standardized machine administration and scoring of the CDT (14–16) and measures distinct components of psychomotor slowing (17, 18). The dCDT uses a digital pen that looks and feels like a normal pen but incorporates several sensors that monitor the usage of the pen when performing the traditional clock drawing test. This novel technology now allows detection of subclinical cognitive impairment that was not possible with traditional cognitive function tests (19), but has not been extensively evaluated in epidemiologic studies.

We describe the implementation of three digital applications for the measurement of hearing, pulmonary, and cognitive function in the pilot phase of a family-based prospective cohort study in Minnesota and share our experience in applying these technologies in the context of a 2.5-hour health fair visit.

Materials and Methods

The 10,000 families study (10KFS)

The pilot phase of the 10KFS, a new prospective cohort, was initiated to address research needs in Minnesota that were not adequately addressed by large national and international epidemiologic efforts. Specifically, Minnesota is home to a large rural population, the second highest Hmong population in the United States (1.2% of the Minnesota population vs. 0.08% of the national population), and one-third of the national Somali population (representing 0.6% of the Minnesota population vs. 0.02% of the national U.S. population; refs. 20–22). Although these groups suffer higher death rates from chronic diseases such as cancer, cardiovascular diseases, stroke, and chronic lower respiratory diseases, they are not adequately represented in national cohorts (23–25). The family-based design provides unique opportunities to study environmental exposures across the lifespan and evaluate the intergenerational transmission of environmental, genetic, and epigenetic risk factors. Currently, the 10KFS is in the pilot phase of the recruitment process and is not actively recruiting minority populations. During the pilot phase, all study participants were a convenience sample recruited at the Minnesota State Fair. The focus of this pilot phase was to establish robust study procedures including optimal deployment strategies for digital applications, which is the focus of this manuscript.

Figure 1 provides an overview of the 10KFS recruitment procedures and study activities. Index participants were eligible for inclusion in the study if they were an adult (≥18 years), lived in Minnesota, had the capacity to provide consent and could communicate in English (for the pilot phase of 10KFS only). Adults who visited the University of Minnesota's research building at the annual Minnesota State Fair were approached about the study by research staff and asked to complete a brief eligibility screener. If eligible, these "index participants" were sent an e-mail and two reminders asking them to invite at least one additional family member from a different generation to enrolled in the study and/or to enroll at least one of their child under age 18, if applicable. Once at least one family member of any age from a different generation was enrolled in the study, the family became eligible for study inclusion. Definition of "family" was determined by study participants. Family members were then invited to complete an online questionnaire (self-completion for individuals 18 years of age or older; parent completion for children <18 years). Adult family members also received at least one e-mail inviting them and any children to attend a health fair with the list of available health fair dates. Participants were updated via e-mail as new dates for health fairs were added. The health fair was a 2.5-hour physical exam conducted in the field by trained study personnel that included anthropometric measurements (height, weight, hip circumference, and waist circumference), blood pressure, grip strength, vision tests, pulmonary function, hearing test, cognitive function, and collection of a variety of biospecimens (blood, urine, saliva, hair, and nails). This study was approved by the Institutional Review Board at the University of Minnesota (IRB approval number: STUDY00000877).

10KFS staff training and assessment administration

A detailed description of staff training, monitoring, and assessment administration for all three digital applications is provided in Supplementary Data file S1.

Hearing assessments

Audiometry application

Hearing assessments were performed using the SHOEBOX Pro mobile audiometry application (Shoebox Inc). The SHOEBOX audiometry application allows for customization of test tones and frequencies. We used the "Automatic Pure Tone Test" mode to evaluate hearing at seven frequencies; 500, 1,000, 2,000, 3,000, 4,000, 6,000, and 8,000 Hz. The hearing assessment consisted of a two-choice play task, which would generate a sound above or below the participant's hearing threshold when the objects were touched (some objects remained silent). The participant then sorted the object according to whether a sound was heard, by dragging it into the appropriate bin on the screen. The system also performed masking in situations of asymmetric hearing loss and automatically flagged frequencies with questionable results. The stimuli were presented with DD450 Transducers (RadioEar) and mobile-based hearing tests were performed with an Apple iPad Air (iOS 8; Apple). Unilateral hearing loss was defined as the pure tone average >25 decibels across all four frequencies 500, 1,000, 2,000, and 4,000 Hz in either ear while bilateral hearing loss was defined as the pure tone average >25 decibels in both ears across all four frequencies (26).

Study participants

Hearing assessments were performed on all 10KFS participants ≥4 years. The "Child" test was administered to all participants 4–11 years old and the "Adult" test was administered to all participants 12 years and older.

Pulmonary function

Spirometry application

Pulmonary function was assessed using the Air Next Spirometer (NuvoAir AB), a small portable device (dimensions: 79 × 56 × 20 mm; weight: 50 grams) that was connected to a study specific smartphone or a tablet [Apple iPAD with IOS ver. 8.0 (Apple)] at the headphone jack. The Air Next device included a lithium battery, designed to have a half-life of 2 years (or 1,000 spirometry measurements) and was attached to a disposable turbine mechanism (FlowMIR; Medical International Research, Roma, Italy) with a cardboard mouthpiece to perform the spirometry measurements. To perform spirometry, the participant exhaled air into the turbine to measure the forced expiratory volume in one second (FEV_1),

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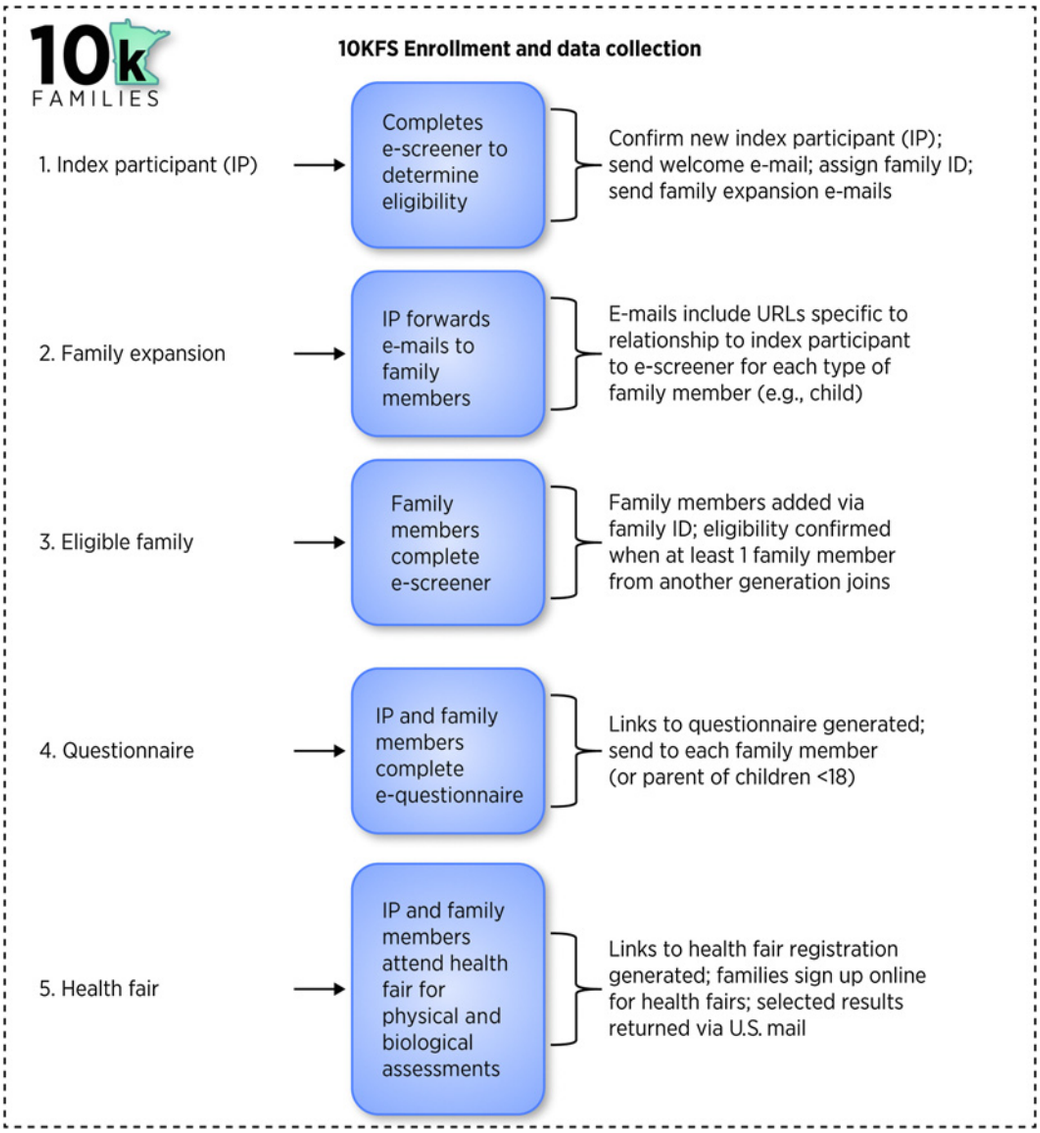

Figure 1.
A graphical overview of the enrollment and data collection methods (questionnaire and physical measures) used in the 10,000 Families Study (10KFS).

forced vital capacity (FVC), and their ratio (FEV_1/FVC). According to manufacturer's recommendations, the device does not require instrument calibration for the life of the instrument (approximately 1,000 spirometry readings). Parameters such as age, sex, and height were entered before spirometry. The portable device used the Hankinson reference values validated in the NHANES III study to calculate the percentages of FEV_1 and FVC (27). When the participant initiated exhalation, a chronometer switched on and changed color from red to green after 6 seconds of exhalation. This allowed the examiner to visualize each curve independently to identify artifacts. In addition, a flow meter detects errors of acceptability and displays any errors on the screen with the spirometry results.

Study participants

Spirometry was performed on all 10KFS participants 5 years or older who were at least 110 cm tall. Spirometry was not performed on participants who were pregnant or had a heart attack/stroke or eye surgery within the last 6 months. All spirometry measurements conformed to American Thoracic Society/European Respiratory Society guidelines (28).

dCDT

Digital pen

To complete the dCDT test, participants were asked to draw the face of a clock with the hands set to a predesignated time (e.g., "10 after 11") first to Command and then Copy a Model Clock that was provided (29). The dCDT measures pen position on a coded paper 80 times per second enabling position detection and facilitating the distinctions between overlapping cognitive and motor components of psychomotor slowing in the CDT and allowed for the dissection of the total time to complete the dCDT into discrete segments such as time spent drawing on the paper (Ink Time) versus time spent

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not drawing (Think Time; refs. 17, 18, 30). All data was time-stamped and video recorded to facilitate making judgments regarding clock elements (e.g., discriminating hour hands and spokes, etc.) and to enhance classification accuracy. The dCDT test provides over 700 individual features, which are grouped into four categories; drawing efficiency, simple and complex motor tasks, information processing and spatial reasoning. Digital Cognition Technologies provides standardized scores in these four domains for all adults over the age of 40 years. Examples of the 700 individual features include total time needed to complete the dCDT, the percent Ink Time (time spent drawing on the paper for the command and copy conditions) and % Think Time (time spent on the test when pen is not in contact with the paper, measured from the completion of the first pen stroke to the beginning of the last pen stroke).

Study participants

The dCDT was administered to all 10KFS participants over 40 years of age. Age, gender, and handedness information were provided to obtain standardized scores for dCDT.

Database creation

Eligible study participants were e-mailed a unique link to an electronic questionnaire developed in REDCap. The data from the questionnaire was entered into a MySQL database with a unique participant identifier. A database table was created for each of the mobile apps using MariaDB with the unique participant identifier serving as key. Case report forms were developed to capture data collected at the health fair that are not collected by the digital apps. The data from these were double keyed into a custom data collection system that generated queries when errors were detected. Once the data passed all checks, they were entered into an Oracle database using the participant identifier as the key. After each health fair, the data were either e-mailed to an account (pulmonary function data) or automatically downloaded from a cloud-based server and sent to a secure server where they were incorporated into the study database. Database programming was conducted using Python version 3.7.4.

Statistical analysis

Categorical data was summarized using counts and percentages while continuous data was summarized using medians and quartiles. Tests for differences between independent groups of individuals were conducted using Welch modified two-sample *t* test. All statistical analyses used R version 3.6.0.

Table 1. Demographic characteristics of participants attending a 10KFS health fair.

Characteristics	Age group (years)	
	Children (age <18; *n* = 50)	Adults (age ≥18; *n* = 160)
Age, median (quartiles)	7 (3–11)	56 (37–69)
Female, *n* (%)	23 (46)	104 (65)
Race[a], *n* (%)		
Asian	1 (2.0)	7 (4.4)
Black	1 (2.0)	2 (1.3)
Hispanic or Latino	5 (9.8)	0 (0.0)
White	49 (98.0)	150 (93.8)
Other	1 (2.0)	1 (0.6)
BMI, median (quartiles)	18 (16, 19)	25 (23, 30)
Smokers, *n* (%)	NA	27 (19)
Educational level ≤high school	NA	7 (5)

[a]Some participants identify as more than 1 race.

Results

1,084 index participants completed the eligibility screener. After recruitment of additional family members, 158 families with participants in two or more generations were eligible to participate in 10KFS. E-mails with links to online questionnaires were sent to 561 participants. Among these eligible participants, 288 participants (51% of participants who received a questionnaire) completed the online questionnaire. A total of 210 participants attended a 10KFS health fair. Most participants were white adults who had more than a high-school education (**Table 1**). 197 participants (93.8%) were eligible to perform at least one of three measurements; audiometry, pulmonary, or cognition function assessments. The remaining 13 participants were children under the age of 4 years and were not eligible to perform any of these assessments.

Hearing assessment

A total of 37 children (age 4–17 years), 107 adults (age of 18–64 years), and 53 seniors (over the age of 65) were eligible to undergo hearing assessments. Among those tested, 28 children (76%), 92 adults (86%), and 47 seniors (89%) successfully completed the hearing assessment (**Table 2**). The prevalence of hearing loss was substantially

Table 2. Hearing assessments among 10KFS participants.

Characteristics	Age group (years)		
	4–17 (*N* = 37)	18–64 (*N* = 107)	65+ (*N* = 53)
Completed assessment, *N* (%)	28 (75.7%)	92 (86%)	47 (88.7%)
Bilateral hearing loss, *N* (%)	0 (0%)	5 (5.4%)	18 (38.3%)
>25 dB 500 Hz both ears, *n* (%)	0 (0%)	4 (4.3%)	5 (10.6%)
>25 dB 1,000 Hz both ears, *n* (%)	0 (0%)	4 (4.3%)	5 (10.6%)
>25 dB 2,000 Hz both ears, *n* (%)	0 (0%)	5 (5.4%)	13 (27.7%)
>25 dB 4,000 Hz both ears, *n* (%)	0 (0%)	9 (9.8%)	30 (63.8%)
Unilateral hearing loss, *N* (%)	0 (0%)	8 (8.7%)	25 (53.2%)
>25 dB 500 Hz either ear, *n* (%)	0 (0%)	4 (4.3%)	5 (10.6%)
>25 dB 1,000 Hz either ear, *n* (%)	0 (0%)	4 (4.3%)	5 (10.6%)
>25 dB 2,000 Hz either ear, *n* (%)	0 (0%)	5 (5.4%)	13 (27.7%)
>25 dB 4,000 Hz either ear, *n* (%)	0 (0%)	9 (9.8%)	30 (63.8%)

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Table 3. Pulmonary function test results among 10KFS participants.

Characteristics	Age group (years)			Diagnosed with asthma		
	4–17 ($n = 37$)	18–64 ($n = 107$)	65+ ($n = 53$)	No ($n = 163$)	Yes ($n = 20$)	P^a
% predicted FEV_1: mean (SD)	66 (20)	98 (16)	97 (19)	96 (20)	84 (18)	0.02
% predicted FVC: mean (SD)	84 (17)	105 (17)	103 (22)	103 (20)	97 (14)	0.10
% predicted FEV_1/FVC: mean (SD)	88 (12)	93 (11)	95 (13)	93 (12)	88 (14)	0.16
PEF (L/min): mean (SD)	3.63 (1.63)	6.78 (2.17)	5.38 (2.33)	6.06 (2.37)	5.78 (2.24)	0.62

[a]*P*-value tests for differences between people with and without asthma.

higher among seniors (>65 years) as compared with children and younger adults (**Table 2**).

Pulmonary function

Successful completion of spirometry was achieved in all 37 children (100%), 105 adults (98%), and 53 seniors (100%; **Table 3**). With the exception of predicted % FEV_1 in children, all average predicted values for FEV_1, FVC, and FEV_1/FVC were within the normal range (**Table 3**). Among the children tested, 70% ($n = 26$) had predicted FEV_1 <80% and 38% ($n = 14$) had predicted FVC <80%. The prevalence of predicted FEV_1 or predicted FVC <80% was much lower in adults (<15%). FEV_1 was significantly lower among asthmatics as compared with those without asthma (84% vs. 96%; $P = 0.02$; **Table 3**).

Cognitive function

Among those tested, 54 adults (92%) and 50 seniors (94%) successfully completed the dCDT (**Table 4**). The simple and complex motor task domain was nominally different by age, with those 41–62 years old more likely to be outside the standardized range for both the Command mode (55.6% vs. 36% in seniors; $P = 0.07$) and Copy mode (48.1% vs. 28% in seniors; $P = 0.06$; **Table 4**). There was no difference in the total time, % Ink time, or % Think time across both age groups for both the command and copy conditions.

Discussion

We have described the feasibility of implementing these low cost app-based digital measures for hearing assessment, pulmonary function and cognitive function in 10KFS using study personnel who received minimal training in these applications before the study. We also highlight the various advantages and challenges of these digital measures over traditional approaches.

A major advantage of all digital applications used in 10KFS was the availability of automated quality-control measures incorporated into these applications that simplified standardized data collection without the need for central reading centers or specialized training in individual areas. For example, the automated data collection mode within the SHOEBOX application automatically performed masking (i.e., noise intentionally introduced in one ear while the other ear is being

Table 4. dCDT results among 10KFS participants.

Characteristics	Age group (years)		*P*
	41–64 ($n = 59$)	65+ ($n = 53$)	
Completion rate, *n* (%)	54 (91.5%)	50 (94.3%)	
dCDT score	79.22 (61.85–93.64)	81.41 (59.79–89.84)	0.20
dCDT classification			0.81
Class 0 (within normal limits): *n* (%)	31 (57.4%)	29 (58%)	
Class 1 (indeterminate): *n* (%)	11 (20.4%)	8 (16%)	
Class 2 (outside normal limits): *n* (%)	11 (22.2%)	13 (26%)	
Drawing efficiency [*n* (%) outside normal range]			
Command mode	20 (37%)	12 (24%)	0.22
Copy mode	8 (14.8%)	16 (32%)	0.07
Simple and complex motor tasks [*N* (%) outside normal range]			
Command mode	30 (55.6%)	18 (36%)	0.07
Copy mode	26 (48.1%)	14 (28%)	0.06
Information processing [*N* (%) outside normal range]			
Command mode	14 (25.9%)	17 (34%)	0.49
Copy mode	17 (31.5%)	13 (26%)	0.69
Spatial reasoning [*N* (%) outside normal range]			
Command mode	12 (22.2%)	13 (26%)	0.83
Copy mode	14 (25.9%)	18 (36%)	0.37
Command mode total time (sec) [mean (SD)]	35.74 (16.94)	36.72 (14.81)	0.75
Command mode % ink time (%) [mean (SD)]	43.58 (7.88)	43.26 (8.55)	0.84
Command mode % think time (%) [mean (SD)]	56.42 (7.88)	56.74 (8.55)	0.84
Copy mode total time (sec) [mean (SD)]	28.11 (9.13)	29.21 (14.75)	0.65
Copy mode % ink time (%) [mean (SD)]	48.57 (6.53)	49.03 (6.82)	0.72
Copy mode % think time (%) [mean (SD)]	51.43 (6.53)	50.97 (6.82)	0.72

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tested) in situations of asymmetric hearing loss, flagged frequencies with questionable results, and repeated the process multiple times at different frequencies and intensities to ensure reproducibility of measurements without any manual intervention. The spirometry application automatically performed all quality checks recommended by the American Thoracic Society/European Respiratory Society (28), checked for artifacts in the individual lung function curves, estimated reliability of spirometry measurement, and did not require regular instrument calibration. The digital pen provided video recording of the entire measurement for standardized interpretation of the dCDT. The availability of these real-time quality-control measures allows technicians with little background in the specific measurements to be trained to reliably perform these measurements. In the 10KFS, we trained undergraduate and graduate students with minimal background in hearing assessments, pulmonary function, and cognitive function to perform these measurements at the health fairs. These built-in quality-control measures along with the portability of these instruments also allow deployment of these applications in a variety of field settings. Although in 10KFS, these applications have been predominantly used only in the context of a structured clinic visit, we have recently used these applications successfully at mobile health fairs and home visits.

The low cost of these applications is another advantage. For example, the SHOEBOX application has an annual cost of $2,400/device. Although the cost of the SHOEBOX application itself is not substantially cheaper than other audiometry equipment, the ability to perform hearing assessments without the need for a specialized sound-proof room is a major cost saving for performing hearing assessments. The Air Next spirometer costs around $250/device with the disposable turbines costing around $1.50/turbine. The Air Next spirometers are approximately a tenth of the cost of a regular spirometer although they last for much shorter duration (1,000 measurements) as compared with a standard spirometer that can last for several years. In addition, the ability to perform these measurements without the use of reading centers is a major cost savings in using these digital applications.

The digital pen was used in 10KFS under a shared research agreement with Digital Cognition Technologies Inc. The major advantage of this application as compared with the traditional pen and paper method is the ability to identify features in the clock drawing test that are not possible using the traditional method. So, although this application is likely to cost more than the pen–paper-based method it provides far richer quantitative data and the potential for detecting mild cognitive impairment that is not possible with the traditional method. In addition, the automated algorithm used for interpretation of the dCDT greatly reduces the need for highly trained specialists to interpret the results and thereby could result in additional cost savings.

Despite the numerous advantages of digital applications, some potential pitfalls need to be addressed prior to widespread implementation in epidemiologic studies. Because all digital applications have only been recently introduced, their performance characteristics may not be fully evaluated. In 10KFS, we specifically chose digital applications that were supported by substantial published data that demonstrated their accuracy compared with traditional gold standard measurements (6, 7, 31). While we did not formally validate the performance of these digital applications compared with traditional methods of assessing the various physical measures, we evaluated whether the percentage of abnormal values obtained by these digital applications were similar to the percentage of abnormal results obtained using traditional methods in other studies. The prevalence of bilateral hearing loss in all 10KFS participants (11%) was similar to the national prevalence of bilateral hearing loss among those older than 12 years (12.7%; ref. 31). Although the audiometry application performed well, the relatively low audiometry completion rates among children (76%) suggests that children were not sufficiently interested or engaged in completing the audiometry assessment even though the child-specific version of the audiometry application was available. Our experience suggests that the children needed extra motivation to even start performing the audiometry assessment and even if they started the audiometry assessment, they were more likely to stop before completion as they did not find the test interesting as opposed to having technical issues related to the audiometry application. A majority of the adults who did not complete the hearing assessments had well documented hearing impairment and used hearing aids on a regular basis.

The average FEV_1, FVC, and FEV_1/FVC among adult 10KFS participants were similar to the average values for adults in other population studies (2, 3). The frequency of reduced FEV_1 (<80% predicted) among young adults (18–64 years) is similar to previously published studies (prevalence of FEV_1 <80% predicted: 10% in 10KFS vs. 4%–13% in a previous study; ref. 32), while the prevalence of FEV_1/FVC <70% was slightly lower than those reported in other populations of young adults (4% in 10KFS vs. 3%–8% in a previous study; ref. 3). In contrast, the percent of children in 10KFS who had reduced FEV_1 (70%) was substantially higher as compared with prevalence of reduced FEV_1 among predominantly non-Hispanic white children in other studies (9%–14%; refs. 33, 34). The mean FEV_1 among children in 10KFS was also substantially lower (66%) as compared with children in other studies (101%; refs. 33, 34). Thus, the overall performance of the spirometry application was acceptable for adults. However, although children were sufficiently engaged during spirometry assessment and the spirometry application was designed to work in children older than 5 years, the exceptionally high rates of abnormal FEV_1 in children suggests that additional training of study personnel is essential for successful completion of spirometry in children using this digital application. Recently, we retrained all study personnel on appropriate procedures for conducting spirometry with specific focus on spirometry procedures in children. We also instituted a procedure to report any unacceptable spirometry results (after first 3 readings) to the health fair coordinator so that specific attention is paid to retraining the participants before additional spirometry readings are attempted. These efforts have improved spirometry quality and completeness in children to levels observed in adults.

We also compared values obtained from the dCDT among 10KFS participants with dCDT data available from the Framingham Heart Study and found that the total time to completion, % Ink Time and % Think Time were all very similar to those reported in the Framingham Heart Study for both the command and copy conditions (35). Because the four domains reported by the digital pen application are composite scores developed by the company, comparable data for these domains are not available in other studies.

Because utilizing digital applications necessitates storing research data in proprietary clouds owned by the application developers, it is essential to ensure no private identifiable information is uploaded to the cloud servers that is not directly under the control of study investigators. In this regard, we worked with commercial vendors for the digital pen and NuvoAir to provide the required information (e.g., age without divulging the date of birth). Another related issue is the ability to obtain all the raw data from the cloud for data analysis. All

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applications provide processed data that is ready for data analysis in an easy to understand format for individual participants. However, research studies typically require the raw data for both quality assurance and developing novel methods of data analysis. Restrictions on access to raw data is highly variable across different companies with some companies providing free access to raw data as a part of their annual subscription or research agreement, for example, SHOEBOX Inc and Digital Cognition Technologies Inc, while others (e.g., NuvoAir) charge additional fees to access the raw data. Hence, studies need to fully understand and account for access to the raw data prior to implementing digital applications in their research.

Finally, we deliberately chose digital applications that had regulatory approvals or were in the process of obtaining those approvals. This increased the likelihood that we would be able to standardize these measurements over several years as any changes to these digital applications would again go through the regulatory approval process thereby providing researchers a reasonable idea of the changes made to the digital applications.

Finally, these digital applications were evaluated in a predominantly non-Hispanic white English-speaking population. As 10KFS establishes procedures for robust recruitment of minority populations, additional barriers to successfully utilizing these digital applications in non-English speaker minority populations may be identified.

In summary, digital applications provide new opportunities to include measurements of physical data that were previously unaffordable in the context of large epidemiologic studies. Future applications include using these highly portable, affordable, and reliable devices to perform physical measurements remotely without the need for an in-person clinic visit. In addition, novel digital applications for other biological functions such as electrocardiograms, sleep, physical activity, and diet will provide opportunities to obtain detailed measurements of subclinical alterations that are currently not practical to collect in large population studies.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

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Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): B. Thyagarajan, M.A. Roesler, E. Cassidy, L.G. Spector

Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): B. Thyagarajan, H.H. Nelson, C. Reilly, L.G. Spector, D.A. Lazovich

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