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Extended, continuous measures of functional status in community dwelling persons with Alzheimer’s and related dementia: infrastructure, performance, tradeoffs, preliminary data, and promise

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Highlights for Reviewers
- We describe the development of a mobile health platform designed for daily measures of functional status in ambulatory, community dwelling subjects, including those who have Alzheimer’s disease or related neurodegenerative disorders.
- We use Smartwatches and Smartphones to measure subject overall activity and outdoor location (to derive their lifespace).
- These clinically-relevant measures track a subject’s functional status.
- Functional status metrics are integrated with medical information and caregiver reports, which are used by a caregiving team to guide referrals for physician/APRN/NP care.
• We provide a comparison with existing similar systems.
• We provide real-world data from current subject enrollees demonstrating system accuracy and reliability.
• We describe the underlying considerations of this system so that interested organizations can adapt and scale our approach to their needs.
• We provide a potential agenda to guide development of future systems.

ABSTRACT

Background
The past decades have seen phenomenal growth in the availability of inexpensive and powerful personal computing devices. Efforts to leverage these devices to improve health care outcomes promise to remake many aspects of healthcare delivery, but remain in their infancy.

New Method
We describe the development of a mobile health platform designed for daily measures of functional status in ambulatory, community dwelling subjects, including those who have Alzheimer’s disease or related neurodegenerative disorders. Using Smartwatches and Smartphones we measure subject overall activity and outdoor location (to derive their lifespace). These clinically-relevant measures allow us to track a subject’s functional status in their natural environment over prolonged periods of time without repeated visits to healthcare providers. Functional status metrics are integrated with medical information and caregiver reports, which are used by a caregiving team to guide referrals for physician/APRN/NP care.

Comparison with Existing Methods
We describe the design tradeoffs involved in all aspects of our current system architecture, focusing on decisions with significant impact on system cost, performance, scalability, and user-adherence.

Results
We provide real-world data from current subject enrollees demonstrating system accuracy and reliability.

Conclusions
We document real-world feasibility in a group of men and women with dementia that Smartwatches/Smartphones can provide long-term, relevant clinical data regarding individual functional status. We describe the underlying considerations of this system so that interested organizations can adapt and scale our approach to their needs. Finally, we provide a potential agenda to guide development of future systems.

Keywords
Alzheimer’s disease, dementia, functional status, smartphone, smartwatch, activity, lifespace
INTRODUCTION

New ways to measure functional status are essential to evaluate future treatments for Alzheimer’s disease (AD) and other neurodegenerative processes. Currently, measures of functional status rely on self- or caregiver-provided status reports (SOTBRH 1959; Mahoney & Barthel 1965; Jette et al., 2014; Ottenbacher et al., 1996; among others) or brief physical tests (Reuben & Siu 1990; Guralnik et al., 1994; Brown et al., 2000; among others) that are potentially biased, infrequently obtained, and cannot capture detailed patterns of daily behavior. Yet, daily patterns of behavior are a rich source of information regarding functional status and play an important role in quality of life.

The rapid advance in availability, affordability, versatility, and computing power of handheld and wearable electronics makes it feasible for the first time to obtain clinically relevant disease measures from community-dwelling persons on a daily basis. For example, remote monitoring of medication adherence (Hale et al., 2016) or relevant clinical metrics (e.g., blood pressure, weight; Agboola et al., 2015; Hudson et al., 2005) have improved clinical outcomes for patients with congestive heart failure (review, Kitsiou et al., 2015). Remote blood glucose monitoring has demonstrated efficacy in helping patients achieve and sustain target blood sugar levels (Greenwood et al., 2015). However, clinical effectiveness of telemedicine-based approaches is not an assured bet (Steventon et al., 2016). Blood pressure, heart rate, and weight monitoring, combined with telephone calls from health coaches, did not lower 180 day readmission rates for persons admitted with heart failure (Ong et al., 2016), or improve functional status (Karhula et al., 2015). A similar telehealth strategy was demonstrated effective only in a subgroup of subjects with higher ejection fractions and lower scores on screening instruments for depression (Koehler et al., 2012). These experiences emphasize that successful telehealth interventions tend to judiciously measure specific and limited outcomes, focus on a specific clinical population, and ensure that end-users receive ample instruction to successfully collect data.

In this manuscript, we describe an integrated hardware and software system (Figure 1 for block diagram) to monitor individual activity and lifespace. These clinical metrics are highly relevant in the care of persons with moderate to advanced dementia who have or are at risk of developing functional loss. We devote particular attention to important trade-offs necessary to meet cost, usability, accuracy, and reliability criteria. We describe our initial experiences using this system to collect these data in a cohort of ambulatory adults with mild, moderate, and severe Alzheimer’s disease, and using these measurements to predict functional status changes. Finally, we present novel data describing the day-to-day variability in these functional measures as they relate to dementia stage and caregiver status.

MATERIALS AND METHODS

System considerations. Persons afflicted by progressive neurodegenerative diseases show an extensive range of phenotypic involvement. Cognitive or functional losses may be only apparent after extensive and highly focused testing in the earliest disease
stages; conversely, moderate to severe disease stages may be accompanied by marked functional loss. Care needs for persons with dementia will thus significantly differ depending upon disease stage. For example, in persons with preclinical signs of neurodegenerative diseases, assessment of day-to-day behaviors strongly associated with cognition, such as language, may provide an early indication of AD or a similar process (Austin et al., in press). Most of these individuals will have preserved functional status, and may not derive benefit from detailed assessment of daily activity and lifespace. However, for persons with moderate to severe AD, functional decline may have severe ramifications, including institutionalization (Smith et al., 2001; Spruytte et al., 2001, among others) and death (Covinsky et al., 2003; Lunney et al., 2003, among others). We thus chose to design our system specifically to assess measures of functional status relevant to community-dwelling (rather than nursing home dwelling) individuals with moderate to severe dementia.

Another design choice we decided to implement was to create a system that required the least amount of effort possible from its subjects. Taking a lead from the pharmacotherapy literature, it is well-established that people have difficulty adhering to medication regimes where drugs are taken more than once a day (Claxton et al., 2001). We argue that data collection methods that may be embedded into routine day-to-day habits thus have the greatest possibility of success, particularly over prolonged time frames. This consideration has also been a feature of other successful programs attempting to measure daily aspects of defined behaviors (Kaye et al., 2012; Kumar et al., 2014; Scheuller et al., 2014).

Device considerations. To collect data measuring functional status required (1) sensors to measure activity and outdoor position, and (2) telecommunication channels to transmit these data to a central server. Smartphones are particularly appealing devices to perform some of these tasks, given their robust GPS capabilities, and their multiple communication services (GSM, WiFi, and BlueTooth). Smartphone technology has also advanced considerably since their first introduction in 1999. Their major disadvantages include overall device size/weight. Also, smartphones are not easily wearable unless extra care is taken to use a holster; a complication that might prove problematic for caregivers helping persons with Alzheimer’s disease dress, and who might be resistant to unfamiliar articles of clothing. Similarly, SmartWatches are also appealing devices to perform data collection tasks. SmartWatches contain triaxial accelerometers, and are thus able to sense activity. These devices also have accompanying software (usually Bluetooth) that mates them to specific SmartPhones, simplifying system integration tasks. Further, SmartWatches have a familiar form factor, making their acceptance by persons with Alzheimer’s disease easier, and increasing the likelihood that they will be worn for prolonged periods of time. SmartWatch disadvantages include fewer commercial product choices, short battery life, and status as a technology not as advanced as that for Smartphones.

We ultimately chose the MotoG 32 Gb (Motorola) Smartphone and SmartWatch2 SW (Sony) to measure activity and outdoor position. Factors that led to these decisions included MotoG cost compared to its major competitors (Samsung Galaxy, Apple
iPhone), and the MotoG’s support for low-power Bluetooth. This decision did involve a trade-off regarding battery life (which is longer in Galaxy Smartphones) and processor power (thus limiting our Smartphone’s use as a gaming platform). Similarly, the Sony SmartWatch had the most favorable price point compared with its competitors. The SmartWatch2 has an aesthetically pleasing form factor similar to what one would expect from a traditional watch, and can be programmed to look like either an analog or digital wristwatch. The Smartwatch is also light (to prevent skin abrasion, whose risk increases with age and age-associated loss of subdermal adipose cushioning), waterproof and dust-resistant. Of note, it also uses an Android operating system, and thus can take advantage of many Google-developed application program interfaces (APIs).

Power considerations. An ongoing concern throughout our design process was to maximize battery life. Our minimum goal was to collect at least one day’s worth of data on all devices on a single charge session. Subjects could recharge the devices overnight, and use them the following day for data collection. To accomplish these battery life goals we had to accept a number of trade-offs regarding system data collection and transmission performance. These issues were particularly prominent with the Smartwatch, which by design has to maintain a low-power Bluetooth connection with the Smartphone when in operation. Smartwatch tasks included activity detection through the triaxial accelerometer. After extensive testing, we ultimately determined that the Smartwatch could not adequately sample the three components of acceleration, transmit these data to the Smartphone without regularly falling short of our battery life target. We thus had to trade-off a time series of three-dimensional accelerometer components (our data gold standard) for calculated step count (performed by the watch processor using a hardware-implemented step count sensor). This tradeoff in turn limited the extent to which we were able to classify overall activities, but did not detract from our ability to detect activity onsets and offsets.

Power issues were lesser, but still relevant, considerations for data collected by the Smartphone. Most significantly, we noted poor battery life performance when the Smartphone was kept in environments with no available GSM or WiFi communications channels; this situation likely arose from repeated efforts by the phone to acquire these channels for data transmission. We also set the GPS to pull location coordinates either every 15 seconds, or when the Smartphone detected movement of at least one meter, when outside the home. Data collection under these conditions was more than adequate for complete reconstruction of subject daily lifespace.

Device operating system considerations. Clearly, device operating system considerations are strongly tied to our chosen devices as above. While iOS is an elegant operating system, there are many issues associated with iOS that make it unsuitable for our development effort. iOS development accounts, while relatively inexpensive (99-299 per year USD) are not free, and thus add to development costs. iOS also has been described as a “walled garden” whereby access to the sensors necessary to perform our data acquisition tasks requires explicit permission (by application signing) from Apple, a process that is both time-consuming and not
ultimately guaranteed for success. For these reasons, the Android OS was by far our best choice.

Regardless of OS choice, we were required to adopt an approach to ongoing OS updates. While many Android updates did not affect data collection functionalities, there were occasional instances where OS update broke tested and validated code (e.g., changes in power management between Android ‘Lollipop’ 5.0 and Android ‘Marshmallow’ 6.0 significantly influenced how the system handled accelerometer queries). We considered a number of strategies, including locking the phones into Android 5.0 and changing the phone OS (“rooting”) to undo the power management changes. Tradeoffs with these two options are significant: locking the phone OS immediately solves the problem, but leads to future problems when the current code set is incompatible with future hardware platforms. Since Google supplies no Android bootloaders, the bootloaders available for this task have uncertain provenance, and may introduce significant security vulnerabilities into the codebase. We thus elected to modify our codebase in response to changes in Android OS, regardless of the extent of changes we might need to make.

Device/data security considerations. Since lifespace data can easily be examined to determine home GPS coordinates, which in turn may be used to determine home address, our data is thus regulated by the Health Insurance Portability and Accountability Act of 1996 (HIPAA). We thus encrypt all data stored on the Smartphone. However, encryption significantly slowed both how fast the app could load, and (more significantly), how fast the app could run on the Smartphone. To address these issues, we changed the code so that data most frequently read and written by the app was placed into a memory buffer for faster access.

For all data collection, transfer, databasing, and analysis operations, we identify subjects through their study ID number to maintain anonymity. No subject-supplied identifying information is associated with any functional monitoring data. A separate server hosted by Salesforce.com maintains subject identifying information, including the table associating subject names, addresses, and other private information to subject ID number.

To lower the possibility that an unauthorized person might attempt to reverse engineer our application to determine sensitive information, such as the IP address of our cloud server, we obfuscated the code using ProGuard (proguard.sourceforge.net/). Code obfuscation replaces code names, line numbers, and other identifying information with random character strings, making it more difficult for decompiling programs to recover useable information from the code. However, since ProGuard provides minimum obfuscation to Java programs, it will not stop a hacker with expertise and time from ultimately recovering the original program. DexGuard, a commercial version of ProGuard, can provide greater degrees of obfuscation, but may still be vulnerable to attackers with sufficient time. Preventing app reverse engineering remains a major focus of IT security professionals.
**Device upload frequency.** The Smartwatch relays step count to the Smartphone every 60 min. In the event that the Smartphone is not available for data receipt, the Smartwatch will time out and retry connecting after a 60 minute delay. All data unsuccessfully sent by Smartwatch (no matter how old) remains tagged for retransmission until successful receipt by the Smartphone is achieved. Smartwatch memory capacity holds greater than one day of step count data without difficulty. The Smartphone communicates with our cloud-based server on a daily basis. This communication can occur either through GSM (cell phone network) or Wifi connectivity. At this time, Smartphone memory capacity and battery life are relatively minor issues with regard to data upload to our service, which is performed on a daily basis. This decision is based on our battery life concerns. When batteries with longer lives are developed, we could increase the frequency of data pushes to our servers to create a more real time picture of these functional activities.

**Data upload and upload security considerations.** We iterated through a number of different solutions regarding data upload to our servers until we arrived at the best choice. Initially, we uploaded data directly from the Smartphones into a Dropbox ([www.dropbox.com](http://www.dropbox.com)) account. While this approach was suitable for testing small subject cohorts in a technology validation context, we immediately appreciated multiple limitations of this approach: HIPAA noncompliant, potential changes in terms of service, long-term placement of data on servers out of our control. Our first approach to address these issues were to transfer data directly to our research server using an http post. We augmented transfer security by creating a secure path (using ssh tunneling) for the data transfer. This tradeoff involved placing a ssh code library on the Smartphone (a trivial concern), and storing ssh credentials to the project server on the Smartphone. Under these conditions, if a third party found a lost Smartphone, they might be able to decompile the code, find the server username and password, and thus breech the entire system.

We ultimately implemented an enterprise service bus between the Smartphone and project server using Mulesoft ([www.mulesoft.com](http://www.mulesoft.com)). Instead of storing server credentials on the phone, we store a Mulesoft url. We transmit data from Smartphone to the Mulesoft application using a secure process (https post). The Mulesoft application (which itself exists within our firewall) in turn communicates with the project server and then clears the transmitted data. In this manner, we minimize opportunities for third parties to access our server, while maintaining appropriate security protections for data from Smartphone to cloud to server.

The major tradeoff associated with this approach is that when Mulesoft updates their host (without our prior knowledge), data transmission from Smartphone to server is interrupted. Under these conditions, the Smartphone receives notification that data transfer was unsuccessful, and data transfer is retried the following hour. At this time, there are no open source solutions to perform these tasks; organizations adopting this approach will thus have to budget for Mulesoft or similar service bus costs.
**Database considerations.** We chose to implement our database using the open source relational database MySQL (www.mysql.com) running on a server using the Ubuntu Linux (www.ubuntu.com) operating system. For this application, the Linux OS offers many advantages over other options (e.g., Windows), including an easier debugging environment, and better server integration with both Mulesoft and Salesforce platforms.

We considered encrypting data within the MySQL database. However, both the UCSF and UNMC IT security officers deemed that we were providing appropriate data security through the combination of the Mulesoft data bus and the university firewalls surrounding the server. If the server were to reside outside of the university firewall, we would then implement database encryption using AES 128 bit encryption as implemented in MySQL encryption tools (AES_ENCRYPT, https://dev.mysql.com/doc/refman/5.5/en/encryption-functions.html#function_aes-encrypt).

Decisions regarding how study data is represented in the database ultimately have marked influence on many important database performance issues, most importantly how quickly the database can be accessed for read/write operations. We chose to organize the data in three tiers: (1) raw data taken directly from the devices, (2) classified data, e.g., binned step count-outdoor location following raw data quality control, and (3) daily functional metrics, for upload to the Salesforce dashboard that our project staff used to deliver all study interventions.

We organized data in the 2nd tier in one-day-long bins starting at midnight. Analysis software was written in Python (www.python.org), an open-source, well-validated software environment distinguished by both its coding ease and execution speed. An advantage of Python is the number of validated toolboxes for machine learning, database connectivity, Salesforce.com connectivity, etc., including SciPy, NumPy, and Scikit, that have been created and validated by the developer community over the past decade. These off-the-shelf toolboxes allowed our group to rapidly develop our required software. Another advantage to using Python is its large developer community, making it less difficult to recruit future team members who are familiar with this language and who can examine working code to determine its function and (if needed) required modifications. The only significant trade-off entailed by Python is that its execution speed would be significantly slower than that of a system written entirely in C. However, our team strongly felt that the availability of Python tools greatly outweighed the speed increase from a C-based system, developed with much greater difficulty.

To maximize data access speed, we used Python to format and store the data in a compressed manner (called a ‘blob’). This strategy also made it very fast to access a subject’s daily functional data. The major trade-off involved in storing data by daily Python blobs is that it limits what kinds of software might be able to query the database. To form blobs, Python uses a process (called ‘pickling’) to string the different data points together into a single sequence. This process is Python-specific, meaning that other software may be unable to reconstruct the original data from the blob.
Because we collected data from individuals living across multiple time zones, and individual activity and lifespace behavior is highly dependent on their time zone, we needed to incorporate time zone information into our data time stamps. Originally, we stored data timestamps in UNIX time (number of ms since midnight 1-January-1970 Coordinated Universal time). However, UNIX time lacks information regarding the timezone that the subject resided in when data collection occurred. To incorporate timezone information, we switched from UNIX time to Python datetime objects. Major tradeoffs associated with this change include the availability of fewer programming tools to convert datetime objects to user-friendly time/date metrics, and complications in calculating time zone windows.

Data quality control/classification/analysis considerations. Our data quality control performs two tasks: identification of data points that are clearly outliers, and determining if low data point values arise from a Smartwatch/Smartphone not carried by the subject. Details regarding how these tasks are implemented and validated are beyond the scope of this text; details regarding validation of step count (Carlson et al., 2012; Rye-Hanton et al., in press) and GPS (Wan et al., 2013; Wan & Lin 2013) data have been previously published.

Prior to SmartPhone and SmartWatch deployment for this study, we also ran a beta test to determine data consistency, data accuracy, and system performance. Briefly, project staff members at both the Omaha and San Francisco sites wore a SmartWatch and kept a Smartphone with them at all times except for charging. At the end of each day of data collection, these staffers would log onto a web-based data portal that provided system-obtained step count and GPS data for that day. Staff were asked to clarify episodes where collected data did not match their experience, or where data collection might have been missed (Supplemental Figure 1). These beta tests provided early estimates for data consistency, as well as identifying specific battery life issues not appreciated during system design.

Data classification for step count and lifespace is straightforward: we sum daily step data from midnight to midnight to determine total daily step count, and we determine distance from GPS coordinate to GPS coordinate and calculate maximum distances to estimate lifespace.

There are many tradeoffs and opportunities that arise from the above approach. Since we use the Android step counter API to obtain our step counts, we do not have access to the code performing this task, and thus do not know how this specific step counting algorithm works. Prior data suggests that step counter performance from pedometers employing piezoelectric sensors can vary by body morphology (Kinnunen et al., 2011; Lipert & Jegier 2016), cadence (Park et al., 2011; Giannakidou et al., 2012), and what part of the body carried the step counter (Graser et al., 2007). Thus, our approach is suitable for performing comparisons of an individual’s performance from day-to-day, but more problematic for comparing the performances of different individuals. By contrast, lifespace estimation from GPS data is a robust process, and not significantly affected by
the addition of small travel distances (10-20 meters) that may arise from sensor noise when the Smartphone is stationary.

**Subjects.** We offered our functional monitoring study to a subset of subjects enrolled in the Care Ecosystem, a CMMI-supported clinical trial to determine best practices for dementia care. Details regarding this trial’s organization and protocol have been previously published (Possin *et al*., 2017). The Nebraska site enrolled 299 individuals, of which 191 were randomized to the intervention arm. Enrollment criteria required subjects to be Medicare enrolled or eligible, 45 years old or older, able to identify a caregiver (who is at least 19 years old), living in a community setting (and not a locked dementia unit or skilled nursing facility), and having a diagnosis of AD or related dementia. We approached subjects randomized to the Nebraska intervention arm who had expressed an interest in participating in functional monitoring during the subject consent phase. We initially deployed this technology to 12 subjects. As discussed above, most of the investigators who worked with subject functional monitoring data had access to no subject PHI, and all subject PHI collected by our system (GPS coordinates) was encrypted when outside of our study server.

**PRELIMINARY RESULTS**

Subjects successfully used this technology to collect data (as measured by number of days where a subject returned activity and/or location data) for a majority of days within our 5 month observation time (Figure 2). Specifically, we obtained at least one 15 minute bin of activity data for 57% of all observation days; on average, for each day we received data covering 40% of total hours (range 32%-50%). Adherence for obtaining lifespace data was even greater, with subjects returning GPS coordinates for 79% of all observation days. Of note, these rates are similar to those observed when examining individual adherence to a once-a-day drug regime (Claxton *et al*., 2001). This experience suggests that individuals with Alzheimer’s disease, a clinical population where adherence to therapies may be challenging given the memory loss characteristic of this disease process, can successfully return significant data streams describing individual activity and lifespace for prolonged periods of observation.

In Figures 3 and 4, we show the daily activity and lifespace, respectively, for 3 selected subjects over a 5 month period spanning 1 August 2016 until 31 December 2016. Subject 4404 has mild dementia secondary to Alzheimer’s disease and lives with their spouse in rural Nebraska. Subject 5778 has moderate dementia secondary to an Alzheimer’s/vascular disease overlap, and lives with their spouse in the Omaha metropolitan area. Subject 4764 has mild dementia secondary to Alzheimer’s disease, and lives with their spouse in the Omaha metropolitan area. For all subjects, communication between the SmartWatch and SmartPhone (indicated by time within the 24 hour clock not coded in grey) is usually present during daylight hours; times where we instructed subjects to wear the charged watch. While there are also periods of time at night when the SmartWatch and SmartPhone are in communication, we discount these values since we instructed subjects to take the watch off at night and recharge it
for the following day. Our current system’s inability to determine night-time activity is a major limitation that we will address in subsequent system iterations, probably by adding a sensor to determine when subjects are lying in bed. We also noted a minor interruption in GPS data collection during September because of an Android OS update pushed to the SmartPhones.

Despite the above-mentioned problems, these data clearly show the feasibility of obtaining highly textured, simultaneous data streams measuring activity and lifespace over prolonged observation periods in community-dwelling adults. Of particular note is that all of these data can be obtained using off-the-shelf, commercially available SmartPhones and SmartWatches, and can be successfully used by members of the public with only minimal, phone-based training.

**DISCUSSION/CLINICAL IMPLICATIONS**

In summary, we describe a novel system using SmartPhones and SmartWatches as activity and lifespace sensors to measure functional status in community-dwelling persons with dementia. As expected, these data streams are characterized by many episodes of data loss, arising from both user error (forgetting to charge or carry the technology) and unanticipated technical problems (broken software). However, by collecting these data for a given individual over long periods of observation, we find that we have more than enough data for the purposes of making inferences regarding individual functional status. Our efforts to interpret and further classify these data are ongoing.

Many groups have implemented systems to measure adult functional status over prolonged periods of observation. These systems often rely on motion sensors placed in strategic locations throughout an individual’s living quarters. Circadian patterns of activity, as well as the indoor place where this activity is occurring, have been successfully measured in both assisted living facility (Kaye et al., 2012) and skilled nursing facility (Skubic et al., 2014) settings. A major strength of these systems is their reliability of data acquisition, since they require no effort on the subject’s part. Use of more advanced data processing algorithms (Petersen et al., 2012) and additional sensor modalities (Popescu et al., 2008; Liu et al., 2012) further allow these systems to discriminate between multiple individuals, and more finely hone estimates of clinically important metrics (such as gait speed). However, all of these systems require subjects to remain within spaces monitored by sensors, and do not provide data when subjects leave the home. Other groups have addressed this problem by providing subjects with wearable sensors (Ertin et al., 2011; Sarker et al., 2014), or using sensor functions intrinsic to SmartPhones (Schueller et al., 2014). Not surprisingly, major strengths of these systems are their ability to follow subjects throughout the community. However, adherence to these systems constitutes a subject burden, which may lead to skipped periods of data acquisition or even loss of all data if the subject becomes disenchanted with the benefit proposition that the technology affords.
Data describing individual functional status of community-dwelling adults over long periods of time yet with fine temporal and spatial resolution has previously not been available to either investigators or clinicians. On first examination, the above data appears to have rich implications for both clinical science and practice. For example, we note that subject 4404 continues to have an extensive lifespace despite the diagnosis of mild Alzheimer’s disease. Despite incomplete data collection, we have sufficient data to infer that this subject’s caregiver provides structure and out-of-house activities on a month-by-month basis, including visits to the couple’s children in Omaha, and vacations at their lake house in northern Nebraska. We further determined after interviewing the caregiver that the subject’s overall activity status over our 5 months of observation was acceptable. Of note, our approach regularly missed about 2 hours of activity between 6:30 AM and 8:30 AM (where we observe 4404 activity onset); by caregiver report, the subject needed a reminder to wear the watch every morning, and this reminder usually occurred at their breakfast. As discussed previously, we may be able to better account for this kind of error with the presence of a bed sensor. In this case, functional monitoring provides quantitative data supporting the caregiver’s assertion that the subject’s functional status remains stable and is appropriate to support their day-to-day activities.

Subject 5778 provides a different situation. Here, monitoring suggests that the subject’s lifespace has significantly shrunk, with only one foray outside of the home over a 4 month period of observation. However, this subject’s activity is robust, with regular movement over their 12 hours spent awake. This subject also has sharp activity onsets (occurring at 0800) and offsets (occurring at 20:00), suggesting that either the subject or caregiver is providing significant structure while at home. Thus, while this subject’s lifespace in absence of other information is concerning, further knowledge of simultaneous activity status provides clinical assurance that this small lifespace may be due to an external factor (such as lack of transportation) rather than difficulties dressing, moving, and motivating the subject to travel.

Subject 4764 illustrates a specific situation where functional monitoring may improve clinical outcomes. By QDRS, this subject has mild dementia, and should thus demonstrate minimal functional limitations. However, we quantify 4764’s activity over the 5 months of observation at below mean levels determined from all subjects with mild AD. Further, we note that lifespace for 3 of the 5 observation months is attenuated. These features suggest that subject 4764 may be at risk for functional loss at an earlier onset of the disease process compared to subject 4404, who has a similar degree of cognitive loss. Management options at this time might include a more detailed assessment by an occupational or physical therapist for functional deficits, and a program of restorative therapy to stabilize function at current levels.

A major limitation of our current system is the inability to better localize individual activity within the home, which we term ‘homespace.’ As described above, there are already a number of successful homespace systems currently in operation. Unfortunately, none of the current motion sensor based technologies are easily integrated into the
SmartPhone/SmartWatch framework we use for activity and lifespace acquisition. We have thus been testing a system using low power BlueTooth-based estimotes, RSSI triangulation, signal processing, and decision tree algorithms to provide within-room localization. Preliminary data suggests that this system’s performance exceeds that of journal-based entries for subjects within their home. Our group hopes to integrate this homespace system into future iterations of our functional monitoring approach.

In summary, we demonstrate that an inexpensive, easy-to-use system based on commercially available telecommunications products such as SmartWatches and SmartPhones, with appropriate software, cloud, and analytic infrastructure, can be a powerful tool to measure day-to-day functional status in community-dwelling individuals who have Alzheimer’s disease or other processes resulting in cognitive and functional loss. The modular nature of this system suggests that the scaling required to provide this service to larger clinical populations is fully within the realm of possibility (particularly by harnessing the power of SmartPhones that caregivers and subjects are already carrying for their personal use). This approach provides data measuring individual functional status at very fine temporal and spatial precision. Simple data visualization tools allow trained clinicians to infer the subject’s functional status, and this inference is robust to missed data points. The success of this effort strongly justifies further research and development to improve data acquisition (particularly for times when individuals may not be wearing the SmartWatch, such as while asleep), further refine data visualization and inference algorithms, and develop stronger connections to currently-available clinical information technology systems. We also note that the availability of data examining physical activity and lifespace in large populations of community-dwelling adults will also be of considerable interest to investigators in a variety of non-healthcare focused fields, as well as powerful information upon which to base public healthcare policy. For example, urban planners trying to determine if available open spaces meet people’s needs would benefit from knowing patterns of activity and lifespace within a community. These patterns would also provide important information to entrepreneurs interested in locating a business or shop. In a healthcare policy context, these data would provide baselines of physical activity that could be used to predict future community healthcare utilization (particularly for exercise-sensitive conditions such as diabetes, heart disease, and emphysema), incentivize positive health behaviors, and ultimately provide political decision-makers with data justifying financial support for programs that change health behaviors.

AUTHOR CONTRIBUTIONS
AKS, AMB, KLP, BLM, SJB developed our study concepts and oversaw project tasks. BZ, GN, JJ, GS, MS identified, created, validated, and tested required project hardware and software. KG, MS, ADB, TLB coordinated and oversaw system deployment to subjects. BZ, AKS, SJB performed data analysis. SJB, AKS prepared the manuscript.
CONFLICTS OF INTEREST
SJB, AKS: have been granted US patent 9106718 (“Lifespace data collection from discrete areas”) describing the underlying technology of our functional monitoring approach, particularly with focus on lifespace data collection/analysis.
ADB, TLB: none.

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Figure 1. Current system architecture. Arrowheads indicate direction of data flow. The system SmartPhone both collects lifespaced data and relays data from the activity sensors to the cloud for analysis.
Figure 2. Representative data adherence plots for 4 subjects, 1-Aug-2016 through 9-Jan-2017. A-D. Step count and GPS data obtained per day. Points touching x-axis indicate day where no data received. Blue traces are activity data from SmartWatch; green traces are GPS data from Smartphone. Overall, we have activity data for 57%, GPS data for 69% of observation days. E. Percent days with both step count and GPS data.
Figure 2. Representative activity rasters. Clock times are military, starting/ending at midnight. Each concentric circle represents one day of data collection. For subjects 4404 and 4764 the first day of data collection (1 August 2016) is depicted in the innermost circle; the last day of data collection (31 December 2016) is depicted in the outermost circle; month markers are provided on the vertical axis. For subject 5778 we show one month of data collection beginning 3 September 2016 and ending 3 October 2016. Step count values as shown above and coded per color map.

Figure 3. Representative activity rasters. Clock times are military, starting/ending at midnight. Each concentric circle represents one day of data collection. For subjects 4404 and 4764 the first day of data collection (1 August 2016) is depicted in the innermost circle; the last day of data collection (31 December 2016) is depicted in the outermost circle; month markers are provided on the vertical axis. For subject 5778 we show one month of data collection beginning 3 September 2016 and ending 3 October 2016. Step count values as shown above and coded per colormap.
**Figure 3.** Representative lifespace trajectories over a 4-5 month observation period for subjects with mild to moderate dementia. Two subjects reside in Omaha metropolitan area (B,C); one in rural Nebraska (A). Note relatively substantial lifespace trajectories in subjects A and C, but quite limited lifespace in subject B. Each monthly lifespace calculated from GPS positions obtained over at least 20 days of the given month. GPS trajectories in red points; each plane depicts another month of data. Data collection occurred between 1 August 2016 and 31 December 2016. In September, an Android OS update temporarily broke data collection code, artifactually shrinking lifespaces for all subjects. Subject home depicted by the thin vertical line. Distance calibration provided next to each plot.