

RESEARCH ARTICLE

# Technology-based instrumental activities of daily living in persons with Alzheimer's disease and related disorders

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## Funding information

Alzheimer's Association, Grant/Award Number: AARG-22-924771; National Institutes of Health, Grant/Award Number: R01AG082783; National Institute on Aging, Grant/Award Number: U54AG063546

## Abstract

**INTRODUCTION:** Instrumental activities of daily living (iADLs) increasingly involve technology (e.g., making payments online, texting). The current study examined the applicability and diagnostic accuracy of technology-based iADLs in those evaluated for Alzheimer's disease and related dementias (ADRD).

**METHODS:** A total of 264 care partners of persons undergoing comprehensive interdisciplinary evaluations completed the Functional Activities Questionnaire and 11 technology-based iADL items.

**RESULTS:** Technology-based iADLs applied to more than 80% of patients. Average dependence on technology-based items was overall less than for traditional iADLs. The addition of technology-based items to traditional iADL items slightly improved the ability to identify individuals with dementia. When considered separately, technology-based iADL items demonstrated comparable ability to distinguish between diagnostic stages.

**DISCUSSION:** Technology use is common in older adults with ADRD for a range of daily activities. Accounting for technology use increases the content validity of existing iADL measures for the modern context and yields comparable diagnostic accuracy.

## KEYWORDS

computer use, dementia diagnosis and staging, instrumental activities of daily living, internet activities, passwords, smartphone, technology

## Highlights

- Technology use is often integral to daily activity performance for individuals with Alzheimer's disease and related dementias (ADRD).
- Daily technologies, such as smartphones, were used frequently by those with ADRD.
- Many individuals were less dependent on technology activities than traditional activities.
- Adding technology questions slightly increased diagnostic accuracy for detecting dementia.

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## 1 | BACKGROUND

Digital skills are increasingly important for the performance of instrumental activities of daily living (iADLs) in the twenty-first century. For example, financial management activities rely increasingly on online account management,<sup>1</sup> social interactions are mediated by technologies such as text messaging and social media,<sup>2</sup> and shopping is increasingly done online.<sup>3</sup> Although a digital divide between younger and older adults still exists,<sup>4</sup> data increasingly suggest that this gap is narrowing,<sup>5</sup> and individuals impacted by Alzheimer's disease and related dementias (ADRD) are no exception to this trend. For example, individuals with ADRD note rates of smartphone ownership comparable to that of other older adults,<sup>6</sup> and use of these devices has been shown to be effective at enabling compensatory behaviors and interpersonal connection day to day.<sup>7</sup>

The clinical evaluation of individuals with known or suspected ADRD routinely includes an assessment of iADLs. Understanding a patient's functional status guides diagnostic staging,<sup>8,9</sup> and iADL assessment also serves as a critical outcome measure in treatment trials.<sup>10</sup> Despite such importance, many commonly used iADL measures have not been updated in the last 40–50 years to reflect how digital technology has changed daily activities.<sup>11</sup> For example, the Functional Activities Questionnaire (FAQ;<sup>12</sup>) is among the most frequently utilized iADL measure in clinical and research settings.<sup>13</sup> However, this measure was created in 1982, well before the proliferation of home computing or internet commercialization.

This lack of routine assessment of technology-based iADLs leads to a potential blindspot in understanding the lived experiences and clinical outcomes of individuals with ADRD. Are technology iADLs easier or harder to complete independently for individuals with ADRD when compared to more traditional tasks? Is the increasing pervasiveness of technology leading to more impairments in daily tasks over time, or less? Does the assessment of technology-based iADLs, sometimes (although perhaps erroneously<sup>14</sup>) perceived as more difficult for aging adults, make identification of functional impairments in ADRD populations less specific?

Measures of everyday technology use by older adults<sup>15</sup> and caregivers<sup>16</sup> have been developed, but focus narrowly on technology and cannot replace broad iADL assessments. The Amsterdam iADL Scale, which assesses a range of tasks, including aspects of technology use, has been rigorously developed and tested.<sup>17</sup> However, developing iADL item pools that can be added to existing legacy instruments in form and response method may be advantageous in situations such as multi-decade cohort studies, where replacement of existing measure risks making prior waves of data less useful.

To help address these needs and explore issues around measurement of iADLs in the twenty-first century, the current study sought to (1) assess the applicability of a newly developed item pool of technology-based iADL items in a sample of older adults referred for evaluation of ADRD; (2) compare the degree of dependence caregivers perceive for technology-based and traditional iADL item groupings; and (3) explore whether adding technology-based iADL items changes the sensitivity and specificity of iADL measures to ADRD. We hypoth-

### RESEARCH IN CONTEXT

1. **Systematic review:** Following a literature review, the authors identified that many of the most commonly used instrumental activities of daily living (iADL) measures do not include technology-based items. Although specialized instruments have been developed and are cited, these measures are not widely adopted in clinical research.
2. **Interpretation:** Technology adoption was widespread in older adults presenting for evaluation of Alzheimer's disease and related dementias (ADRD), although a digital divide still exists for some participants. Assessing technology use in daily tasks is important in the modern world and may increase sensitivity to dementia staging.
3. **Future directions:** The pace of technological change does not seem to be slowing, with broad impacts on daily tasks. There is a need to develop measures of daily functioning that accurately capture older adults' use of technology in daily tasks.

esized that although technology-based iADLs may be less applicable than traditional iADL items, device use and online financial management would be applicable to the majority of the sample. Furthermore, we hypothesized that dependence for tech iADLs would be less than that of traditional iADLs.<sup>16</sup> Finally, we hypothesized that assessment of technology iADLs would yield comparable diagnostic accuracy to ADRD stage.

## 2 | METHODS

### 2.1 | Approvals and diversity considerations

Issues related to the racial, ethnic, and other forms of diversity, equity, and inclusion were addressed by (1) not excluding any participants because of demographic factors; (2) creating a translated and back-translated Spanish-language version of our item pool because Spanish is the most frequently encountered non-English language in our clinic catchment area; and (3) assessing demographic factors, including age, education, gender, and race/ethnicity on applicability of technology-based iADLs as described below.

### 2.2 | Participants, materials, and procedures

Participants were the care partners of 264 older adults referred for a comprehensive evaluation at a university-based interprofessional memory clinic ( $n = 100$  in an item development and validation study;  $n = 164$  from an ongoing clinical research database). Please see Table 1 for the characteristics of the care partners. Participants completed

**TABLE 1** Demographic and clinical characteristics of the sample.

	M	SD	%
<b>Patient descriptives</b>			
Age (years)	76.2	7.4	
Education (years)	15.6	3.1	
Gender (% female)			53.4
<b>Ethnicity</b>			
Non-Hispanic			90.3
Hispanic			9.7
<b>Race</b>			
Asian			1.9
Black/African American			3.0
Native Hawaiian/Other Pacific Islander			1.5
White			91.7
<b>Clinical Staging</b>			
No cognitive disorder			12.9
Mild cognitive impairment			34.5
Dementia			51.9
<b>Care partner characteristics</b>			
<b>Relationship</b>			
Spouse/significant other			58.7
Daughter/daughter-in-law			26.1
Son/son-in-law			9.8
Grandchild			1.2
Friend			4.2
<b>Frequency of contact</b>			
Every day			72.0
Several times a week			12.5
Several times a month			12.5
At least once a month			2.2
Rarely			0.8

Note: N for total sample = 264.

the FAQ<sup>12</sup> and a series of 11 technology-based iADL items described below. The patient's completed comprehensive evaluations with resultant diagnosis and staging was made based on current diagnostic criteria (e.g.,<sup>8,9</sup>). Descriptive data for the sample are found in Table 1.

### 2.2.1 | Functional Activity Questionnaire

Care partners completed the 10 FAQ items (hereafter referred to as *traditional iADL*) via a tablet administered research electronic data capture (RedCAP)<sup>18</sup> survey at the time of the intake interview or neuropsychological evaluations. Psychometric properties of the FAQ in individuals with ADRD are explored in depth elsewhere.<sup>13</sup> Briefly, each iADL on the FAQ was rated by the care partner on a scale from 0 (normal performance) to 3 (fully dependent). In addition, care partners

could rate an item as "not applicable/never did" for items never performed by the person. They could also rate an item as "unknown" if the care partner was unsure how they were doing with each activity.

### 2.2.2 | Technology-based iADL items

Eleven technology-related items were generated by three of the authors (J.F.B., M.K.S., and A.M.K.) on the basis of their clinical and research experience working with technology use in older adults with ADRD. Items were generated to capture the following. (1) *Digital device use*: items queried remembering passwords, texting, emailing, and visiting websites; these items do not have a direct comparator on the existing FAQ. (2) *Use of specific technologies for daily tasks* covered specifically by the FAQ (cooking with a microwave vs the existing FAQ item, which combines stove, coffee, and heating water tasks, play digital games/puzzles vs hobbies/skills assessed more generally). (3) *Digital approaches for financial/commerce activities* (online purchases, credit card use, access bills online, manage online accounts) intended to contrast with financial management items on the FAQ that are a mixture of approach agnostic (i.e., managing bills without specifying if paper or computer-based bills are used) or explicitly paper-based (i.e., writing checks).

Once the final wording was agreed upon by the authors, items were translated into Spanish by one of the authors (D.A.G.) and then independently back-translated by two additional Spanish-speaking ADRD professionals who then met to resolve any discrepancies and finalize the wording. All technology-based items were rated on the same 0–3 response scale as the original FAQ items.

### 2.2.3 | Data and instrument availability

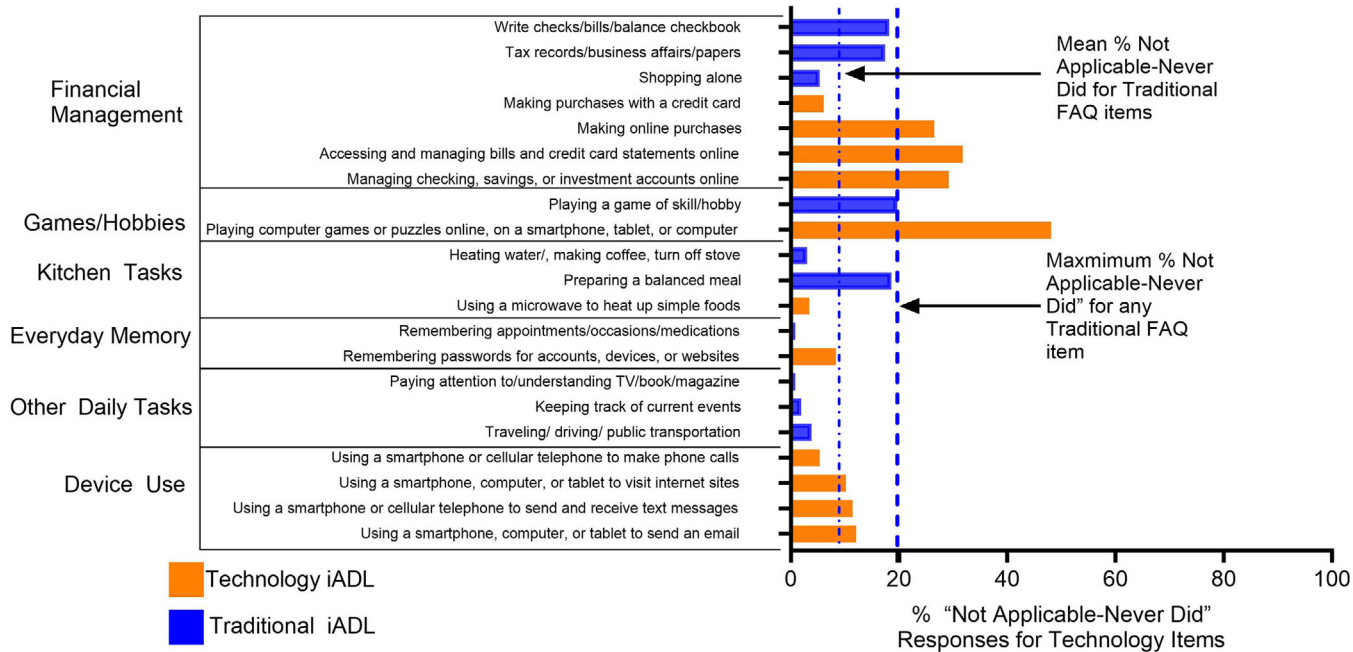
The de-identified data utilized in this publication, as well as Spanish and English technology item pools, are available at <https://osf.io/t9y5k/>.

## 3 | RESULTS

### 3.1 | Applicability of technology-based iADL items

Figure 1 contrasts the percent of technology items rated as not applicable/never did relative to the traditional FAQ items in thematic groupings as outlined earlier. Microwave use (3.8%), followed by using a smartphone to make calls (5.3%), using a credit card for purchases (6.1%), and having to remember a password (8.3%) were the technology items least frequently endorsed as not applicable. In contrast, online/computerized game play was considered not applicable for 48.1% of respondents.

For the traditional FAQ items "not applicable/never did" was selected from a low of 0.8% (for the items assessing paying attention to media or remembering appointments) to a high of 19.7% for the items assessing playing a game. In general, items assessing game



**FIGURE 1** Percentage of responses to technology items (in orange) and traditional iADL items (blue) rated as "not applicable/never did." Dashed lines indicate the mean and maximum percentage "not applicable/never did" responses for the traditional FAQ items. FAQ, Functional Activities Questionnaire; iADL, instrumental activities of daily living.

play and finances were most likely to be not applicable for both the digital and traditional iADL items. Viewed as the converse, the applicability of technology-based iADLs items was over 80% for items assessing microwave, credit card, email, internet, smartphone, texting, and password use; items assessing online financial activities (account management, statement management, and online purchases) were applicable in roughly two thirds of patients, and online game play was applicable in about half of respondents. Because the online game play item was not applicable in nearly half the sample, it was dropped from further analysis.

With this change, the average respondent was rated as having 82.84% of digital items applicable (SD = 22.12%; range 10%-100%), whereas on average, 87.84% of traditional iADL items were rated as applicable (SD = 12.79%; Range, 20%-100%).

### 3.2 | The relationship of applicability of technology-based iADLs with demographic, care partner, and clinical variables

We next examined demographic and care partner relationship predictors of the percent of technology-related items endorsed as applicable with multiple regression. Predictors included care partner variables (relationship with the patient (spouse vs other), frequency of contact (daily vs other) as well as the patient's demographic factors (age, gender, education (expressed in years), race/ethnicity (non-Hispanic White vs other), and clinical staging (no cognitive diagnosis, mild cognitive impairment [MCI], or dementia).

**TABLE 2** Results of regression predicting percentage of tech items that were applicable to a participant, by patient demographic and care partner factors.

Effect	B	SE	P
Intercept	107.65	16.95	0.001
Patient factors			
Clinical staging <sup>a</sup>	-4.84	1.95	0.014
Race/ethnicity <sup>b</sup>	-4.49	4.09	0.274
Age	-0.49	0.19	0.009
Years of education	1.95	0.45	<0.001
Care partner factors			
Relationship <sup>c</sup>	6.28	3.99	0.117
Frequency of contact <sup>d</sup>	-3.59	4.07	0.378

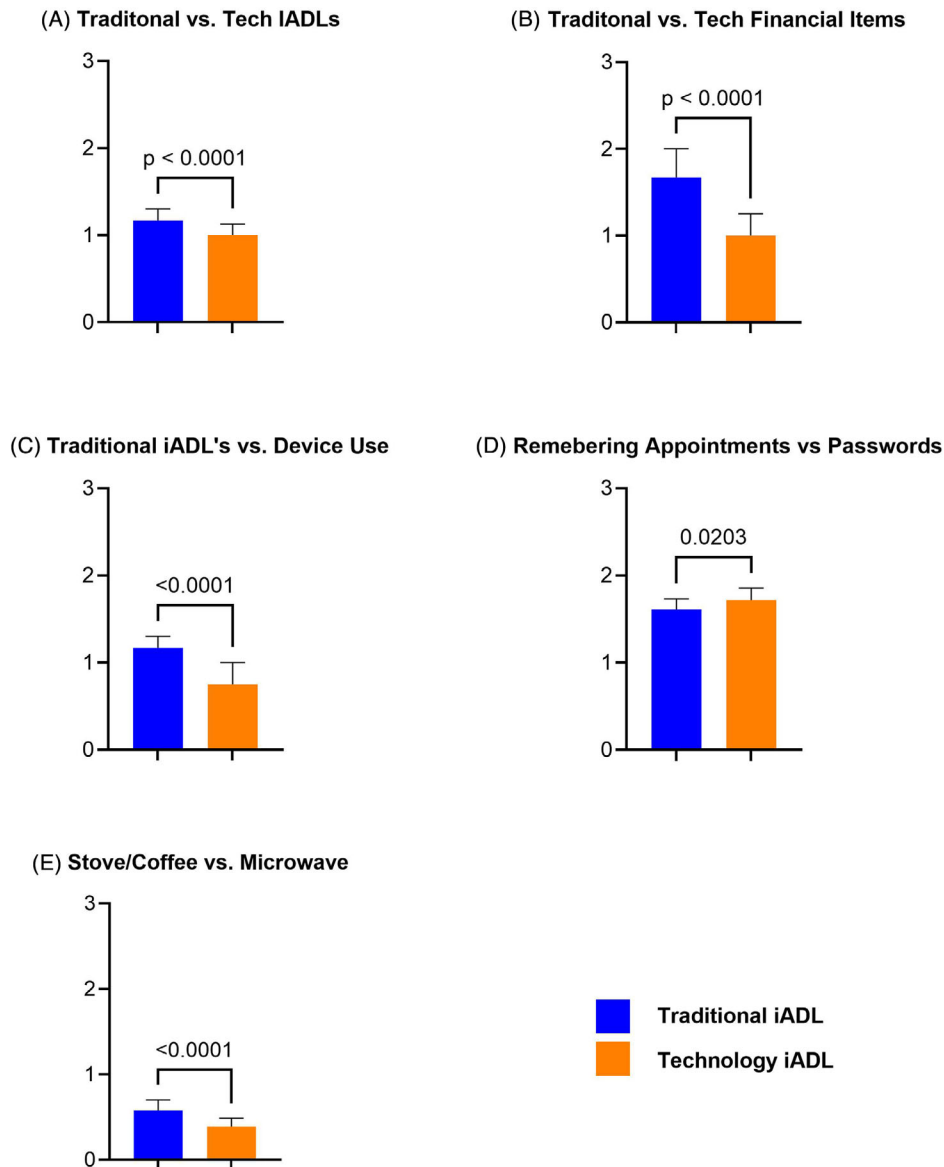
<sup>a</sup>2 = Normal cognition, 3 = MCI, 4 = Dementia.

<sup>b</sup>1 = Non-Hispanic White, 2 = Other.

<sup>c</sup>2 = Spouse 3 = Other.

<sup>d</sup>1 = Daily, 2 = Other.

The overall model was statistically significant ( $F(6, 253) = 7.193, p < 0.001, R^2 = 0.15$ ), with results presented in Table 2. In terms of individual predictors, younger patient age ( $t = -2.62, p = 0.009$ ), lower cognitive impairment stage ( $t = -2.47, p = 0.014$ ), and greater patient education ( $t = -4.15, p < 0.001$ ) predicted more technology items being rated as applicable, whereas care partner frequency of contact or relationship did not significantly predict applicability of technology items.



**FIGURE 2** Comparison of average degree of dependence for traditional (blue bars) and technology-based (orange bars) instrumental activities of daily living. Bars represent means and 95% confidence intervals, and the  $p$ -values presented are based upon  $t$ -test values presented in text.

### 3.3 | Relative level of dependence for traditional versus technology-based iADLs

When considered as a whole, mean dependence ratings for technology-based iADL items were, on average, less than those reported for traditional iADL items ( $t(263) = 4.29, p < 0.001; d = 0.26$ ; Figure 2A).

Within the financial domain, the mean dependence rating of digital financial management (using credit cards, online purchases, accessing bills online, managing accounts online) was lower than for the traditional financial management items (writing checks, tax records, shopping alone;  $t(247) = 6.70, p < 0.0001; d = 0.43$ ; Figure 2B).

In terms of device use, average dependence for the mean of items assessing device use (using smartphones, computers, or cellular telephones to do routine tasks such as send text messages, make calls, visit the internet, or check email) was again less than the mean of tradi-

tional iADL management as a whole ( $t(253) = 4.77, p < 0.0001; d = 0.29$ ; Figure 2C).

However, specific item pairs also demonstrate divergent patterns. For example, individuals were rated as being more dependent for remembering passwords than remembering appointments and dates ( $t(236) = -2.34, p = 0.010; d = -0.15$ ; Figure 2D). In contrast, the dependence for using a microwave was less than the item that queries heating water/stove use ( $t(233) = 4.10, p < 0.0001; d = 0.26$ ; Figure 2E).

### 3.4 | Level of dependence of technology-based and traditional iADLs by diagnostic stage

Mean and SDs of the traditional and technology items are presented in Table 3 by diagnostic stage. Multivariate analysis of variance

**TABLE 3** Mean traditional versus technology iADL dependence by diagnostic stage.

Diagnostic stage	Traditional items		Tech items	
	Mean	Standard deviation	Mean	Standard deviation
No cognitive disorder (n = 34)	0.47	0.53	0.35	0.40
Mild cognitive impairment (N = 91)	0.75	0.63	0.63	0.58
Dementia (N = 137)	1.70	0.74	1.57	0.80

(MANOVA) was conducted to explore these differences, with the independent variable being diagnostic stage and two dependent variables (mean dependence for technology and traditional iADL measures). An overall effect for diagnostic stage was noted ( $F(2, 258) = 32.36$ ,  $p < 0.001$ ; Wilk's lambda = 0.60). Post hoc comparisons revealed that for both digital and traditional daily activities, there were statistically significant differences in the expected direction with individuals with no cognitive diagnosis requiring less assistance on average than individuals with MCI; in turn, both groups required less assistance with technology and traditional iADLs than individuals with dementia (all post hoc contrasts  $p < 0.05$ ).

### 3.5 | Impact of adding technology-based iADL items on diagnostic staging

Technology-based iADL items alone distinguished between diagnostic stages similarly to the FAQ (all contrasts  $> 0.05$ ): no cognitive diagnosis versus any diagnosis (area under the curve [AUC] for tech 0.81 [95% confidence interval (CI) 0.74, 0.87] vs traditional 0.80 [95% CI 0.73, 0.87]); MCI versus dementia (AUC 0.83 [95% CI 0.78, 0.88] vs 0.83 [95% CI 0.78, 0.88]); no cognitive disorder from dementia (AUC 0.91 [95% CI 0.87, 0.96] vs 0.90 [95% CI 0.85, 0.96]).

Combined technology and traditional iADL items also yielded comparable diagnostic accuracy at distinguishing no cognitive diagnosis from any diagnosis (AUC 0.81 [95% CI 0.75, 0.88] vs 0.79 [95% CI 0.73, 0.87];  $z = -1.35$ ;  $p = 0.18$ ; Figure 3A) and individuals with MCI from dementia (AUC 0.85 [95% CI 0.80, 0.89] vs 0.83 [95% CI 0.78, 0.88];  $z = -1.82$ ;  $p = 0.07$ ; Figure 3B). The combined items slightly improved the detection of no cognitive disorder from those with dementia (AUC 0.93 [95% CI 0.88, 0.97] vs 0.90 [95% CI 0.85, 0.96]; paired sample area difference  $z = -2.07$ ,  $p = 0.03$ ).

## 4 | DISCUSSION

### 4.1 | Are technology iADLs applicable to the lives of individuals with ADRD?

Although technology-based iADL items were rated as less applicable than traditional iADL items overall, this varied by the specific technologies assessed. For example, items assessing a broad range of technology activities, including using a smartphone to send a message or make a call, checking websites, or using credit cards, applied to over 80% of

respondents, and digital financial management was applicable in nearly two thirds of respondents.

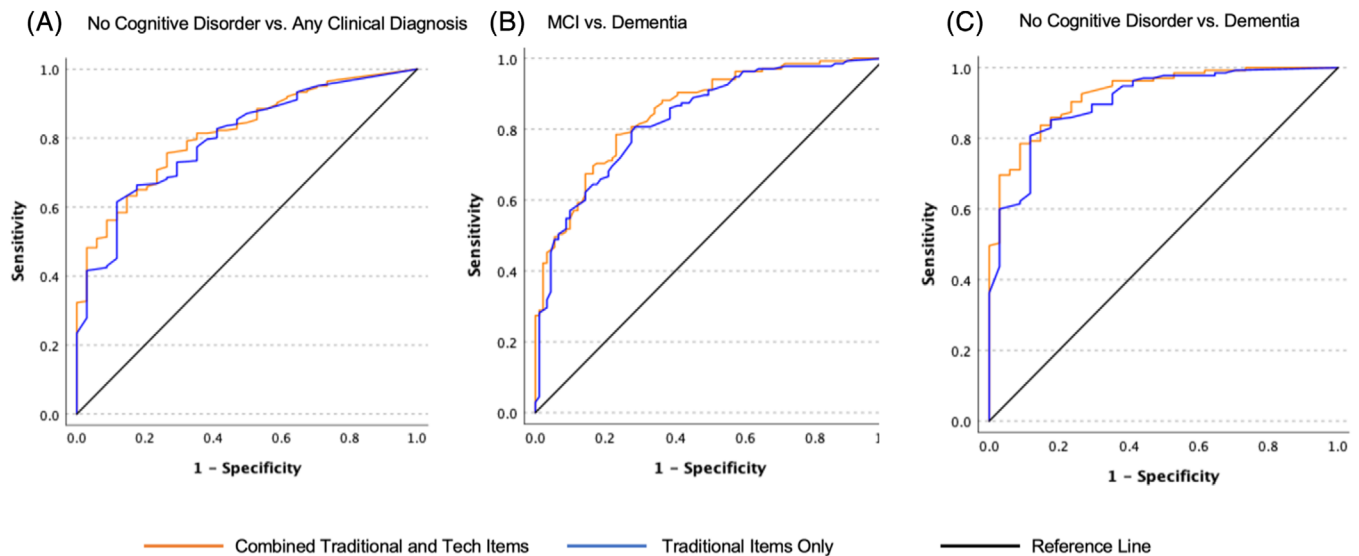
That being said, there remains a digital divide in our sample, where increasing age and decreasing education, in particular, predicted less applicability for technology-based items, a finding that mirrors broader population trends in technology adoption among older adults.<sup>5</sup> These findings suggest two broad implications.

First, given that technologies are continuing to evolve rapidly but are not distributed equally across society, iADL measures may be needed that account for differences in daily task demands and technologies used to address these tasks across a diverse aging population. Second, from a health disparities standpoint, these patterns raise concern for the compounding impact of digital disadvantage on other social determinants of health. Individuals with lower educational and financial status are not only at increased risk for dementia<sup>19</sup> but also have a decreased likelihood of owning/using technologies that could potentially promote independence. For example, someone with educational and other socioeconomic disadvantages, who is already at heightened risk for developing dementia, may experience the additional digital disadvantage of not having access to or the ability to set up digital approaches to financial management, a class of tasks that our data would suggest individuals can be more independent with, relative to the financial tasks queried on the FAQ (i.e., writing checks, managing papers). This disparity holds the potential to increase chances for late bills or errors, thereby decreasing independence. This is, to date, a hypothesis that has not been explored directly, but the worrisome covariance of dementia risk factors and reduced access to potentially helpful technologies warrants further study.

In terms of applicability, it is also important to note the potential influence of cohort effects, especially as increasing age predicts less applicability of technology-based iADLs. At the time of this writing in 2024, individuals in their 50's and 60s would have just been entering high school during a time when personal computer usage was beginning to emerge. These digital pioneers appear likely to presage a generation where technological familiarity increasingly represents a lifelong habit, rather than a late-life development. The extent to which these cohort effects will affect the validity of existing iADL measures in upcoming generations has not yet been explored.

### 4.2 | Relative dependence for traditional versus technology-based iADLs

A commonly encountered stereotype is that older adults and those with ADRD cannot use digital technologies.<sup>20</sup> Contrary to this



**FIGURE 3** Receiver-operating characteristic (ROC) curves for distinguishing cognitive diagnoses based on mean scores for either the traditional iADL items or the combined technology-based and traditional iADL items. iADL, instrumental activities of daily living.

stereotype, our data have demonstrated that perceived dependence for device use was generally less than that of overall dependence for traditional iADLs. These findings point to several considerations for dementia and technology researchers as well as for measuring iADLs in the twenty-first century and beyond.

Although lower rates of technology use and difficulties with technology are frequently reported in older adults,<sup>21</sup> other technologies may allow for automation that actually simplifies day-to-day tasks. As an example, our data suggest that individuals with ADRD, on average, are rated as being less dependent for digital financial management than similar questions on the FAQ.

This may reflect the ability to automatize some tasks. For example, automatic bill pay, which is typically set up once and then just monitored, may contribute to perceptions of greater independence for daily financial management. Similarly, once procedural memories for making a smartphone call are established, it may be easier to “touch” a contact than to remember a 7- or 10-digit phone number. In this way, a technologically enriched environment holds the potential to increase independence in at least some task domains, consistent with what we have termed the technological reserve hypothesis.<sup>22,23</sup>

However, there are aspects of technology use in daily activities that seem more difficult for individuals with ADRD, and are potentially digital markers of functional impairment.<sup>24</sup> For example, individuals in the current study were rated as being more dependent for remembering passwords than remembering day-to-day appointments/events. Thus, assessing digital task performance may capture subtle cognitive decline and functional impacts. In addition, digital performance may also be objectively quantified (i.e., number of password resets required or failed login attempts), providing a window into real world cognitive and functional changes.

An additional consideration is that the querying method of performing a daily task seems to matter when eliciting reports of iADL performance from care partners. For example, in our sample, legacy

financial management items were rated as more dependent on average than when digital approaches specifically were queried. Although we believe this implies, at least in part, an actual difference in daily task demands as discussed above, it also reflects differences in the specificity of items. The FAQ items query broad swaths of task performance, such as writing checks, bills, and balancing checkbooks. A care partner may rate an individual as independent on this item because bills are on autopay, may mark it as not applicable if bills are automatically paid, or may try to predict what bill pay would be like without a digital assist.

Furthermore, we note that current definitions of impairment and dependence in daily activities do not consistently account for the impact of approach, compensatory mechanisms, or automation. However, as technologies that increasingly automate daily tasks (e.g., self-driving automobiles; “smart” home systems that automate daily routines) become used, it may prove important to reconsider what is meant by independence in daily tasks. Clearly, more work is needed to thoughtfully develop and define functional ability in an increasingly digital world. Although not fully realized,<sup>25</sup> our results highlight that technological innovations remain both an opportunity to support independence in ADRD and a potential challenge for defining, assessing, and staging of the disease.

### 4.3 | Diagnostic accuracy of technology-based iADLs

The current results provide initial evidence that adding technology iADL items to the measurement of daily activities does not diminish and, indeed, may modestly increase the sensitivity and specificity of caregiver-reported iADL assessment. Although we note that the DeLong method of AUC comparison may be sensitive to small differences in ROC curves,<sup>26</sup> it is clear that the assessment of technology-based iADLs did not diminish the diagnostic sensitivity of iADL

measurements, as the AUCs (and their corresponding CIs) largely overlapped when considered as individual scales or a combined scale. There was a concern of diminished sensitivity as some older adults experience difficulties with technology even in the absence of cognitive decline,<sup>27</sup> and thus functional impairment in the digital domain might be insensitive to ADRD staging. Although this was not observed in the current sample, further exploration is needed of daily task performance across more diverse samples and, as noted above, likely revisited as cohorts with varying degrees of digital nativeness reach the age when ADRD tends to develop.

#### 4.4 | Limitations and future directions

The current work included a modest sample size, and the findings need further validation in more diverse samples, including explicit evaluation of the Spanish-language item pool. In addition, future work is needed to develop and refine item pools to capture modern iADLs, particularly with input from relevant stakeholders in diverse samples. To this end, we note that the current item pool does not capture technology impacts on transportation (i.e., GPS navigation<sup>11</sup>; self-driving features of cars; use of ride-share services), and this should be included in future studies. We do recommend that future work consider collaborating specifically with older adults and those with ADRD in developing technology-based iADL items more specifically. It may also be important to specify the method (digital or analog) that is being referenced when developing future iADL item sets. This may become particularly important as novel technologies automate broader swaths of daily tasks. Further work is also needed to understand the psychometric properties of technology-based iADL items across language, racial/ethnic, age, and education groups, as well as properties of item sets to help discern optimum measurement of iADLs across the disease spectrum. Finally, we note that this study focused on caregiver-rated iADL performance; however, self-perceived difficulties with technology should be studied to see if they provide an even more-sensitive indicator of daily difficulties early in the disease course. In this way, the current results are a start but not the end of an evolving conversation about what it means to be experiencing functional impairment in the digital age.

## 5 | CONCLUSION

Technology is rapidly changing how older adults and those with ADRD perform a host of iADLs. Our current findings suggest that a range of technologies are broadly applicable to the lives of individuals with ADRD and highlight how measurement of these skills can inform how individuals are functioning in a technology-enriched environment. Furthermore, assessing technology-based iADLs provides comparable diagnostic accuracy in the identification of individuals with late-life cognitive disorders. Finally, these data encourage considerations on approaches to refine and improve upon existing iADL measures to

validly capture the rapidly evolving technological landscape of those living with ADRD.

#### ACKNOWLEDGMENTS

We thank the participants for their participation in this study. Portions of these data were presented previously at the Alzheimer's Association International Conferences in 2023 and 2024. The current study was supported by the Alzheimer's Association (AARG-22-924771) and the National Institutes of Health (NIH; R01AG082783). Andrew Kiselica is supported by a Career Development Award by the National Institute on Aging (NIA) of the NIH under Award Number U54AG063546, which funds NIA-Imbedded Pragmatic Alzheimer's and AD-Related Dementias Clinical Trials Collaboratory (NIA IMPACT Collaboratory). The content of this report does not necessarily represent the official views of the funding agencies.

#### CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest. Author disclosures are available in the [Supporting information](#).

#### CONSENT STATEMENT

Participants in the item development study provided written informed consent and no consent was required for the participants in the subsequent retrospective clinical database study; all study procedures for both data sets were approved by the institutional review board at the University of Texas at Austin and in accordance with the 1964 Declaration of Helsinki and its later amendments.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

**How to cite this article:** Bengé JF, Ali A, Chandna N, et al. Technology-based instrumental activities of daily living in persons with Alzheimer's disease and related disorders. *Alzheimer's Dement.* 2024;16:e70022. <https://doi.org/10.1002/dad2.70022>