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Baseline Disability in Activities of Daily Living Predicts Dementia Risk Even After Controlling for Baseline Global Cognitive Ability and Depressive Symptoms

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Abstract

Objectives—Late-life disability in Activities of Daily Living (ADL) is theorized to be driven by underlying cognitive and/or physical impairment, interacting with psychological and environmental factors. While we expect that cognitive deficits would explain associations between ADL disability and dementia risk, the current study examined ADL as a predictor of future dementia after controlling for global cognitive status.

Methods—The population-based Cache County Memory Study (CCMS; N=3547) assessed individuals in four triennial waves (average age 74.9, years of education 13.36; 57.9% were women). Cox proportional hazards regression models assessed whether baseline ADL disability (presence of 2+ Instrumental ADL and/or 1+ Personal ADL) predicted incident dementia after controlling for *APOE* status, gender, age, baseline cognitive ability (Modified Mini-mental State Exam, 3MS-R; adjusted for education level), and baseline depressive symptoms (Diagnostic Interview Schedule).

Results—Over the course of study, 571 cases of incident dementia were identified through in-depth cognitive assessment, ending in expert consensus diagnosis. Results from Cox models suggest that ADL disability is a statistically significant predictor of incident dementia (adjusted Hazard Ratio=1.83, $p<.001$), even after controlling for covariate.

Conclusions—Findings suggest that ADL disability offers unique contributions in risk for incident dementia, even after controlling for global cognitive status. We discuss how physical impairment and executive function may play important roles in this relationship, and how ADL is useful, not just a diagnostic tool at, or after dementia onset, but as a risk factor for future dementia, even in individuals not impaired on global cognitive tests.

Keywords

Activities of Daily Living; Dementia risk; Disability

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INTRODUCTION

Dementia is a significant public health challenge, and risk factors have been extensively examined. Multiple review articles (Chen *et al.*, 2009; Daviglus *et al.*, 2010; McCullagh *et al.*, 2001) suggest that genetic factors (e.g. the *APOE* ϵ 4 allele), demographic characteristics (e.g. ethnicity, age), health behaviors (e.g. smoking), and physical health and performance variables (e.g. comorbidities) are associated with dementia risk. Additionally, research suggests that psychological factors, such as depressive symptoms predict dementia onset, although depression may be an early manifestation of dementia, or share a common etiology rather than being an independent risk factor (Panza *et al.*, 2010). Activities of Daily Living (ADL) disability has also been linked to dementia (Barberger-Gateau *et al.*, 1999; Fitz and Teri, 1994), however ADL disability is, itself, an outcome based on complex interactions between cognitive, psychological, physical, and environmental factors. This study explores the relationship between ADL disability and incident dementia risk. We will review the components of ADL disability and observe the role of baseline ADL in dementia risk after controlling for known risk factors including baseline global cognitive status and depressive symptoms.

Sources of ADL Disability

Biopsychosocial models of the disablement process (Verbrugge and Jette, 1994) suggest that disability occurs when a person's capabilities do not meet the demands of the physical and/or social environment. While disability can occur at any age and be caused by a number of factors, when applied to late life the models describe how illness leads to impairments in body systems and eventually how limitations in these systems interact with social and psychological factors to lead to loss of independence. In gerontological research, disability is typically assessed via ability to perform ADL. Basic or Personal Activities of Daily Living (BADL or PADL; Katz *et al.*, 1963) include self-care functions (eating, bathing, dressing, toileting), while Instrumental Activities of Daily Living (IADL; Lawton and Brody, 1969) involve more complex tasks required for independent living (using transportation, shopping, preparing meals, laundry).

As indicated in Figure 1, ADL disability is an outcome based on physical and/or cognitive constraints (Leveille *et al.*, 2004) as well as environmental barriers and/or psychological risk or protective factors (Verbrugge and Jette, 1994). For example, if people are unable to prepare their own meals independently (an IADL), it may be because of severe arthritis limiting hand movement (a *physical* impairment), or because of *cognitive* deficits restricting their ability to perform tasks in sequence. Research supports that ADL disability is consistently linked with the ability to perform basic physical tasks (Fauth *et al.*, 2007; 2008; Gill *et al.*, 1995; Hairi *et al.*, 2010) as well as global cognitive abilities (multiple cognitive abilities included in one assessment) and specific cognitive abilities (Fauth *et al.*, 2008; Reed *et al.*, 1989). Environmental, psychological and motivational characteristics may play a lesser, but measureable role in ADL disability. For example, people with functional limitations may become unable to prepare their meal in a home that requires lengthy trips up a staircase to a kitchen or has a stove that is difficult to turn on (*environmental* barriers). Characteristics of one's home environment (e.g. safety; Cho *et al.*, 1998) and neighborhood (e.g. negative street characteristics; Beard *et al.*, 2009; substandard housing; Clark and George, 2005) predict disability outcomes for older individuals. Finally, individuals may be more or less able to prepare meals based on their motivation to ignore pain, or complete the task (other *psychological* factors). Psychological factors such as motivation play a clear role in determining people's willingness to complete ADL tasks that are challenging (Resnick, 1999). Depressive symptoms consistently predict ADL disability both cross-sectionally (Hairi *et al.*, 2010) and longitudinally (Li and Yeates, 2009; Schillerstrom *et al.*, 2008), with

evidence that changes over time in both depressive symptoms and ADL disability are closely intertwined processes (Fauth *et al.*, 2012; Taylor and Lynch, 2004) and somewhat reciprocal in relationship (Ormel *et al.*, 2002).

The Current Study

Currently, associations between ADL disability and dementia are typically identified by observing ADL disability as a diagnostic tool (e.g. one criterion in a clinical dementia diagnosis), or as an indicator of decline over the course of dementia (Fitz and Teri, 1994; Peres *et al.*, 2008). That is, ADL disability is associated with dementia because it is assessed as an outcome of the dementia process. Specifically, individuals with dementia or preclinical dementia first experience disability in the more complex IADL (Barberger-Gateau *et al.*, 1999) although may experience PADL disability in later stages (Fields *et al.*, 2010).

This study does not use ADL to diagnose dementia or to examine how dementia impacts ADL decline; rather we assess the extent to which ADL disability in older adults *without dementia* predicts *subsequent incident dementia*. Restated, ADL disability is utilized here as a risk factor for the onset of future dementia (i.e. the outcome of analyses is “yes they developed dementia”, or “no they did not develop dementia”), not as a way to track dementia progression or rate of functional change over time. We would, of course, expect that a relationship exists between ADL disability and risk for dementia onset because preclinical cognitive impairment can be a common cause of both ADL disability and future dementia diagnosis. Unique to this study, however, is that we control for baseline global cognitive function (amalgam of multiple cognitive abilities) and other factors. By doing so, we test whether global cognitive function is the “common cause” for both ADL disability and subsequent dementia onset, or if non-cognitive aspects of ADL (e.g. physical impairment, emotional and environmental resources and barriers) or cognitive factors not captured in our global cognitive assessment (e.g. executive function; Woodford & George, 2007) remain key indicators in determining dementia risk. Because emotional well-being and depressive symptoms are linked to cognitive impairment and dementia (Wilson *et al.*, 2002), we also control for depressive symptoms.

We hypothesize that ADL disability will predict dementia risk, even after controlling for global cognitive status and depressive symptoms. Specifically, we propose that ADL function will predict future dementia onset net of global cognitive status and depressive symptoms because of the physical frailty and executive function components of ADL disability. Research supports the idea that incident dementia is predicted by physical frailty (Buchman *et al.*, 2008a) and specific physical abilities such as poorer grip strength and gait (Buchman *et al.*, 2008b; Rosano *et al.*, 2005; Wang *et al.*, 2006), and physical frailty is a key contributor to ADL. Likewise, executive function is the ability to plan and execute goals, including processes of reasoning and judgment (Lezak, 1995), and it has been found to be more sensitive than global cognitive tests at predicting cerebral events such as postoperative delirium (Greene *et al.*, 2009) as well as ADL impairment (Johnson *et al.*, 2007), but is not assessed in our global measure of cognitive status.

METHODS

Study Overview and Participants

Data come from the Cache County Memory Study (CCMS), a large population-based study of older individuals in northern Utah, approved by institutional review boards at Utah State University, Duke University, and Johns Hopkins University. Informed consent was acquired for all participants at each visit, and participants were provided \$20.00 for the initial screening, and \$50.00 for each additional in-depth visit. In 1995 residents of Cache County

aged 65+ were contacted (5,756 individuals). Ninety percent of these agreed to participate (N=5,092). Individuals provided information on a large battery of questions assessing health and health behavior, psychological and social resources, nutrition, and provided samples for genetic testing. Interviews were conducted in four triennial waves. In addition, the study utilized a comprehensive multi-stage protocol to diagnose dementia (see Breitner *et al.*, 1999 for a detailed description). In short, an in depth neuropsychological assessment was performed in the home by a nurse and research technician, with results reviewed by a geriatric psychiatrist and neuropsychologist. Participants were diagnosed with dementia using criteria defined by the Diagnostic and Statistical Manual of Mental Disorders, Third Edition-Revised (DSM-III-R; American Psychiatric Association, 1987). The DSM-III-R does not include ADL limitations as part of the diagnosis for dementia, in contrast to other diagnostic criteria such as ICD-10 (World Health Organization, 1992) and CAMDEX (Roth *et al.*, 1986) where ADL impairment is a required criterion (Erkinjuntti *et al.*, 1997). In addition, we used the DSM-III-R criteria except that we did not require a demonstrable deficit in both short-term *and* long-term memory, but allowed one or the other (Breitner *et al.*, 1999) which is more consistent with subsequent revisions of the DSM (DSM-IV; DSM-IV-TR). Thus, our criteria for diagnosis did not change over all waves of CCMS, and our modification to the DSM-III-R specification made our criteria alike to that of DSM-IV and DSM-IV-TR. Individuals with working diagnosis of dementia also completed a psychiatrist's examination, imaging and lab studies. A multidisciplinary consensus panel reviewed all available data and assigned final consensus dementia diagnoses, with additional clinical follow-up at 18 months.

Of the initial 5,092 CCMS participants, 583 developed dementia. Individuals with prevalent dementia at the initial visit of the study (N=359), and those with unknown dementia status (N=188) were excluded from the current analyses, as were those with missing data on independent variables or covariates, yielding a baseline sample of N = 4404 (571 incident dementia). Finally, because the current analyses required longitudinal data, 857 individuals with no follow-up data were excluded. The final sample for these analyses was N = 3547 (571 incident dementia). Within our final sample, we had 58.6% attrition (2078 individuals were missing follow-up at waves 3 or 4), with participant death as the main reason for dropout (48.1%). Those that dropped out of the study were compared to those that completed all 4 visits. The attrition group did not differ in terms of *APOE* status, gender, ethnicity, or depressive symptoms, but were more likely to be older ($t(3545)=-23.57$, $p<.001$), have fewer years of education ($t(3545)=7.23$, $p<.001$), have lower scores of cognitive ability ($t(3545)=16.67$, $p<.001$), and were less likely to be married ($\chi^2 = 112.72$, $p<0.01$, d.f.= 4).

Measures

Activities of Daily Living Disability—Disability was assessed via self-reported ability to independently perform ADL. Seven PADL included eating, bathing/grooming, walking long distances, mobility without cane or walker, getting up/down, toileting, and needing reminders for toileting. Eleven IADL included traveling beyond walking distance, meal preparation, laundry, light housework, heavier chores, using the telephone, shopping, grocery shopping, shopping for other things, taking medications, and managing finances. If an individual needed assistance on 1+ PADLs or 2+ IADLs, he or she was considered to have ADL disability. In the past, disability was defined as difficulty in 1+ PADL tasks (Guralnik *et al.*, 2002; Seeman *et al.*, 1996; Sun *et al.*, 2007) or 1+ IADL or PADL tasks (Ishizaki *et al.*, 2002; Konno *et al.*, 2004). Iwashina and Christie (2007) defined disability as 2 + PADLs or 2 + IADLs. For the current study we wished to utilize all ADL data (both PADL and IADL), but recognized that IADL tasks are more complex in nature, and individuals typically become IADL impaired before they become PADL impaired (Judge *et*

al., 1996). Thus someone who is unable to perform 1 IADL task may be “less disabled” than someone who is unable to perform 1 PADL task. This guided our decision to use the criteria for *ADL disability* to needing assistance in 1 + PADL or 2 + IADLs. For parsimony the ADL variable will include both PADL and IADL impairment, but models will also be run separately using just PADL impairment, and just IADL impairment to compare results.

Covariates—Age, *APOE* status ($\epsilon 4$ carriers vs. $\epsilon 4$ non-carriers; Corder *et al.*, 1993; Schneider *et al.*, 2006) gender, baseline cognitive ability, and baseline depressive symptoms were included in the models. Global cognitive ability was assessed via the 3MS-R (Tschanz *et al.*, 2002), a modified version of the 3MS (Teng and Chui, 1987), which itself is derived from the Mini-Mental State exam (MMSE; Folstein *et al.*, 1975). The 3MS and 3MS-R were designed to cover a broader range of global cognitive abilities than the MMSE. Scores range from 1–100. The current 3MS-R score used in the analyses is adjusted for education level.

Depressive symptoms were assessed via the modified Diagnostic Interview Schedule (DIS; Stephens *et al.*, 2000). The modified DIS includes 3 ‘gateway questions’ assessing feelings of sadness, loss of interest or irritability. If an individual endorsed at least one gateway symptom, he or she completed the remainder of the DIS. Results from the full DIS were used to determine if an individual met the criteria for major depression according to the DSM-IV (American Psychiatric Association, 2000). In the current analyses, any individual who endorsed the presence of 1+ gateway symptoms was considered to have at least minor depressive symptoms. Our dichotomous variable distinguishes those without minor symptoms (none of the gateway items endorsed) vs. those with any level of minor or major depressive symptoms. We also ran all analyses including a trichotomous depressive symptoms variable of 0 (no symptoms), 1 (minor symptoms: endorsing one or more gateway questions but not meeting DSM-IV criteria for depression based on DIS results), and 2 (major depression as defined by DSM-IV criteria). Because the results did not differ when we used the latter specification, the dichotomous, more parsimonious, version is reported herein.

Statistical Analyses

The outcome of interest was time (in years) from initial visit to dementia onset. Those who did not develop dementia over the course of the study were right-censored as of the last measurement occasion prior to death, or to end of follow-up. Separate Kaplan Meier (KM) plots and Mantel-Cox log rank tests of equality were used to assess associations between 1) ADL disability and dementia, 2) 3MS-R quartiles and dementia, and 3) depressive symptoms and dementia. For the final model, Cox regression analysis tested whether ADL disability predicted dementia in the presence of covariates. Post hoc analyses were run separately using just PADL disability and just IADL disability to determine if these models differed from those using ADL disability (combining PADL and IADL disability together).

RESULTS

Demographic analyses of the sample revealed that 69.6% of the sample was married at baseline, 26.1% were widowed, and the remaining 4.3% were separated, divorced, or never married. The sample was mostly White (99.5%), and occupation groups were reported as 33.9% of the sample in professional/managerial positions, 22.2% in clerical/sales, 15.1% in mechanical/miscellaneous, 10.5% agricultural, 9.8% service, and 8.5% never employed. Table 1 provides the demographic characteristics for the entire CCMS sample, and separately for those reporting ADL disability and no disability at baseline. The group that reported disability (18.1% of the sample) was significantly more likely to be female ($\chi^2(1) = 54.3$, $p < 0.001$), less likely to carry *APOE* allele 4 ($\chi^2(1) = 8.3$, $p = 0.004$), more likely to

report depressive symptoms ($\chi^2(1) = 43.5, p < 0.001$), and more likely to develop incident dementia ($\chi^2(1) = 50.1, p < 0.001$). T-test comparisons revealed statistically significant differences between the ADL disability and non-disability groups such that, on average, the ADL disability group was older ($t(3545) = -22.7, p < 0.001$), had less education ($t(3545) = 8.0, p < 0.001$), lower 3MS-R score ($t(3545) = 17.4, p < 0.001$), and fewer years to dementia onset ($t(569) = 6.3, p < 0.001$).

A KM plot showed (without the inclusion of covariates) that the relationship between the survival functions of ADL disability vs. no disability groups was fairly constant over time, meeting the proportional hazards assumption (see Figure 2). The associated log rank test of equality was significant ($p < 0.001$), indicating that those with ADL disability were at higher risk for dementia, compared to those without ADL disability. Similarly, the KM plot for the 3MS-R score quartiles displayed relationships between the survival functions to be fairly constant over time, and the log rank was also significant ($p < 0.001$), indicating that those with lower baseline global cognitive ability were also at higher risk for dementia. However, the KM plot for depressive symptoms (symptoms present or not) did not display clear distinction between groups in terms of dementia risk (log rank n.s.; $p = 0.7$).

These three variables were all carried forward into a Cox regression analysis, along with known dementia risk factors as covariates: age, gender, and *APOE* status (education was adjusted for in the 3MS-R score, and was therefore not included as a separate covariate). Because age is a known predictor of dementia risk and we wished to control for it, all Cox regression models were stratified by age quartile, in addition to including age as a covariate in the model. The advantage to this approach is that birth cohort effects are minimized because parameters are estimated separately within birth cohort quartiles, then aggregated into final results (Cleves *et al.*, 2008). Therefore results for age should be interpreted as the effect of an additional year of age on dementia risk *within* a given quartile.

Table 2 displays the multivariate Cox regression results. Having the *APOE* $\epsilon 4$ allele yielded an 80% higher risk of dementia compared to those without the allele, and every point reduction in 3MS-R score yielded an 8% increase of developing dementia. After controlling for gender, age, *APOE*, education adjusted 3MS-R, and the presence of depressive symptoms, ADL carried an 83% higher risk of developing incident, compared to those without baseline ADL disability.

Post hoc analyses explored whether IADL or PADL had differential associations with dementia risk. The presence of 2+ IADL occurred for 14.2% of the sample and 1+ PADL occurred for 11.4% of the sample at baseline, with high levels of co-occurrence ($\chi^2(1) = 989.52, p < .001$). Cox regression models (including above covariates) yielded highly similar outcomes to each other and to models using the combined ADL variable; baseline PADL disability yielded a 76% higher risk of dementia than those without PADL disability, and baseline IADL disability yielded a 75% higher risk of dementia than those without IADL disability. Due to high levels of agreement across all models, only results for the combined ADL models are presented in the current study.

CONCLUSION

Late-life ADL disability is influenced by physical and cognitive abilities and to a lesser extent by psychological and environmental factors. In addition, ADL is associated with dementia-related outcomes. One would expect that if an individual's ADL disability is rooted in his or her cognitive deficit, the link between ADL and subsequent dementia would be explained by the common underlying cause of cognitive impairment. The current study, however, examined whether or not ADL disability status predicted future dementia after

controlling for baseline global cognitive status (and other known risk factors, including baseline depressive symptoms). In our study, ADL disability remained a significant predictor of dementia risk, even after controlling for baseline cognitive status, suggesting that 1) non-cognitive influences on the ADL/dementia association may be important; and/or 2) cognitive influences not captured in the 3MS-R global cognitive assessment may influence the ADL/dementia association.

Past research also links emotional factors with both ADL disability and dementia risk, for example increased depressive symptoms are associated with poorer ADL function (Hairi *et al.*, 2010; Li and Yeates, 2009; Schillerstrom *et al.*, 2008) and increased risk for dementia (Wilson *et al.*, 2002). In our sample, chi-square tests revealed that the ADL disability group was more likely to report the presence of depressive symptoms, but KM plots and Cox regression models did not find baseline depressive symptoms to be related to dementia risk. Nonetheless, we controlled for the presence of depressive symptoms in these analyses, and ADL disability remained a strong predictor of dementia. Our results indicate depressive symptoms are not likely to be the driving factor behind the ADL/dementia risk association, suggesting that physical impairment, environmental resources/barriers, or cognitive tasks not included in our global cognitive assessment are likely to be the more important factors in ADL impairment that predict subsequent dementia risk. Our inability to identify depressive symptoms as predictive of future dementia may be related to measurement issues, or may indicate that earlier depressive symptoms do not, in fact, predict subsequent dementia. The DIS and its three “gateway questions” (see methods section for details) may not have captured the same kind of variability found in measures of depressive symptoms that mark the presence or frequency of a long list of depressive symptoms (e.g. the Center for Epidemiologic Studies Depression Scale, Radloff, 1977; or Geriatric Depression Scale, Yesavage *et al.*, 1982). Research has found differences in terms of sensitivity across these three measures of depression and depressive symptoms (Blank *et al.*, 2004). In addition, only 5% of our sample reported depressive symptoms at baseline, thus statistical power to detect associations may be low. Alternatively, the lack of statistically significant associations in the current analyses may be explained by the fact that our study measures associations between baseline depressive symptoms and future dementia onset. Perhaps associations between depressive symptoms and dementia are stronger when they are assessed concurrently.

There are several possible mechanisms supported by research explaining how physical features of ADL impairment are related to dementia risk after controlling for global cognitive status and depressive symptoms. First, underlying preclinical dementia factors could be driving baseline physical impairment. In other words, the same pathology that eventually causes dementia may also cause reductions in physical abilities associated with daily functioning. In older individuals without Parkinson’s disease, Schneider and colleagues (2006) found that neurofibrillary tangles in the substantia nigra were related to gait ability, an example of how preclinical cognitive impairment may share etiology in brain pathology with physical performance tasks. An alternative explanation is that there is specific pathology impacting ADL disability that simply exacerbates dementia progression. For example, vascular problems may lead to poorer health and physical function (Ettinger *et al.*, 1994) but also place a person at greater risk for Alzheimer’s disease (Kivipelto *et al.*, 2001). We also acknowledge that mechanisms for how ADL impairment impacts dementia risk may differ depending on the source of the ADL impairment. For example vascular problems may be a driving factor in subsequent dementia if a stroke or diabetes has caused the initial ADL disability, whereas other processes factors may be operating if the initial ADL impairment was caused by a fall, general frailty, or other pathology. ADL impairment is an outcome that can result from multiple pathways, and the same can be said for dementia. Thus while our study demonstrates the potential for ADL to serve as a predictive

measure for dementia onset, we cannot presume that all ADL impairment, all dementia, and the associations between the two will fall along the same pathway or mechanism.

Likewise, as suggested above, cognitive abilities not captured in the global 3MS-R, such as executive function, may contribute to both baseline ADL impairment and subsequent dementia risk. Even by controlling for *global* cognitive impairment, we have not ruled out the possibility that some kind of cognitive impairment is still an underlying feature of both ADL impairment and future dementia onset. Executive function, in particular, should be further examined as a “common cause” risk factor.

Strengths, Limitations and Future Directions

The unique characteristics of the CCMS sample and design allow us to measure ADL disability and other covariates prior to dementia onset, and also to study dementia outcomes without relying on clinical settings for recruiting participants, however the sample has low levels of ethnic minority participants, and findings may not be generalizable to ethnic minority populations. Future studies should utilize epidemiological samples from diverse populations to observe whether these same relationships emerge, and whether the different components of ADL disability carry comparable levels of risk for dementia. We also acknowledge that at baseline, the mean score of the 3MS-R in our sample was 91 out of 100, reflecting a possible ceiling effect. While this measure likely discriminated among individuals with cognitive impairment and those without, future studies should include global cognitive measures that are designed to be sensitive at discriminating cognitive ability among non-impaired individuals with higher levels of cognitive function. Also, while this is a longitudinal study, only baseline predictors were used. Future research should observe how changes in ADL, cognitive ability, and depression work together to predict dementia. Finally, although it was only part of our descriptive analyses of the sample and not central to our research question, future research should more closely examine our finding that carriers of the *APOE4* allele were more likely to be in the non-disabled group at baseline. Prior research has revealed mixed findings, sometimes suggesting that *APOE4* is a risk factor for functional disability, even after controlling for cognitive status (Albert *et al.* 1995), but other times finding no association between *APOE* and ADL function (Melzer *et al.*, 2005; Tzuo *et al.*, 2009). The fact that our study found differences across ADL impaired and ADL non-impaired groups, but in the opposite direction to that of Albert and colleagues needs further examination.

We have presented general, but powerful results to suggest that ADL disability is a strong predictor of future dementia, even after controlling for global cognition and depression. While there were many people with baseline ADL impairment that did not develop dementia over the course of the study, we propose that, net of covariates included in the model, identifying that there was an 83% higher risk for developing dementia among those with baseline ADL impairment is not trivial. We suggest that future studies expand upon these results by further teasing apart the role of specific cognitive tasks (e.g. executive function) and the role of underlying physical impairment and pathology. Currently, researchers consider mild cognitive impairment as a “warning sign” or risk factor for future dementia. The current study suggests that we should also consider ADL impairment not only as a diagnostic tool for dementia, or a way to determine dementia stages post-diagnosis, but as part of the risk profile for future dementia, even in individuals who are not impaired on global cognitive tests. While ADL disability alone does not indicate that future dementia will occur, ADL function may serve additional utility when added to a larger battery of variables used to determine dementia risk.

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Figure 1.
ADL Disability predicts Dementia Risk

Figure 2.

Survival Function for Prototypical Participant (75 year old male, not a *APOE* 4 carrier, 13 years of education & average 3MS-R score of 91.47): Plotted with and without ADL disability at baseline.

Table 1

Basic Descriptive Characteristics of the Sample

	ADL Disabled at Initial Visit				Total	
	No		Yes			
N (%)	2905 (81.9%)		642 (18.1%)		3547 (100%)	
	N	%	N	%	N	%
Female Gender	1598	55.0	455	70.9	2053	57.9
<i>APOE</i> allele 4 is Present	853	32.8	173	26.9	1126	31.7
Depressive Symptoms*	118	4.1	67	10.5	185	5.2
Developed Incident Dementia	408	14.0	163	25.4	571	16.1
	Mean	SD	Mean	SD	Mean	SD
Age (years)*	73.79	5.9	80.0	7.8	74.9	6.7
Education (years)	13.54	2.9	12.55	2.8	13.36	2.9
Cognitive Ability (3MS-R)*†	92.31	5.4	87.67	8.8	91.47	6.4
Years-to-Right Censoring	7.78	3.7	4.96	3.6	7.32	3.8
Years-to-Dementia	6.01	3.3	4.17	2.9	5.52	3.3

Notes:

* measurement at baseline;

† adjusted for education; For all categorical measures, Chi-square differences between the ADL disability and no disability groups indicates statistically significant ($p < 0.010$). For all continuous measures, t-tests between the ADL disability and no disability groups scores indicates statistically significant ($p < 0.001$).

Table 2**Multivariate Cox Proportional Hazards Regression Model**

Variables in the Equation	B	SE	Wald	df	Sig.	Exp (B)	95.0% CI for Exp(B)	
							Lower	Upper
Gender (Female)	0.06	0.09	0.51	1	0.48	1.07	0.90	1.27
Age	0.02	0.02	1.67	1	0.20	1.02	0.99	1.05
<i>APOE</i> allele 4	0.59	0.09	46.87	1	0.00	1.80	1.52	2.14
3MS-R [*]	-0.08	0.01	178.82	1	0.00	0.92	0.91	0.93
Depressive Symptoms	-0.26	0.20	1.71	1	0.19	0.77	0.53	1.14
ADL Disability	0.61	0.11	30.62	1	0.00	1.83	1.48	2.27

Note: for all variables, measurements occurred at baseline.

^{*} Education Adjusted 3MS-R score