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Do Physical Activity, Smoking, Drinking, or Depression Modify Transitions from Cognitive Impairment to Functional Disability?

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Abstract

BACKGROUND—Individual-level modifiers can delay onset of limitations in basic activities of daily living (ADLs) among cognitively impaired individuals. We assessed whether these modifiers also delayed onset of limitations in instrumental ADLs (IADLs) among individuals at elevated dementia risk.

OBJECTIVES—To determine whether modifiable individual-level factors delay incident IADL limitations among adults stratified by dementia risk.

METHODS—Health and Retirement Study participants aged 65+ without activity limitations in 1998 or 2000 (N=5,219) were interviewed biennially through 2010. Dementia probability, categorized in quartiles, was used to predict incident IADL limitations with Poisson regression. We estimated relative (risk ratio) and absolute (number of limitations) effects from models including dementia, individual-level modifiers (physical inactivity, smoking, no alcohol consumption, and depression) and interaction terms between dementia and individual-level modifiers.

RESULTS—Dementia probability quartile predicted incident IADL limitations (relative risk for highest versus lowest quartile=0.44; 95% CI: 0.28–0.70). Most modifiers did not significantly increase risk of IADL limitations among the cognitively impaired. Physical inactivity (RR=1.60; 95% CI: 1.16, 2.19) increased the risk of IADL limitations among the cognitively impaired. The interaction between physical inactivity and low dementia probability was statistically significant

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(p=0.009) indicating that physical inactivity had significantly larger effects on incident IADLs among cognitively normal than among those with high dementia probability.

CONCLUSION—Physical activity may protect against IADL limitations while smoking, alcohol consumption and depression do not afford substantial protection among the cognitively impaired. Results highlight the need for extra support for IADLs among individuals with cognitive losses.

Keywords

epidemiology; cognition; disability

INTRODUCTION

Limitations in instrumental activities of daily living (IADLs) increase caregiver burden and risk of institutionalization.[1, 2] Cognitive impairment both increases the risk of incident IADL limitations[3] and exacerbates the financial and caregiver burden associated with such limitations.[4, 5] Several individual behaviors and resources are known to influence the onset of disability in cognitively healthy older adults[6–10], but it is not known whether these modifiable factors have similar effects for individuals with cognitive impairments.[11]

In a previous study, we reported that the impact of cognitive impairment on the risk of incident limitations in *basic* activities of daily living (ADLs), such as independent dressing and bathing, is substantially reduced by modifiable factors including not smoking and moderate alcohol consumption.[12] However, because IADLs are generally more cognitively demanding than ADLs[13], individual-level factors may not prevent IADL limitations among those with cognitive impairment.[14] In other words, ADLs tend to be defined by physical capacities, for which individual-level modifiers like smoking have clear relevance (such as decreased lung capacity). The link to such individual-level modifiers may or may not hold for IADLs, because the skills involved in IADLs pertain more directly to facilities of logic, thought, or reasoning. Sustaining healthy behaviors is challenging for everyone and may present even larger burdens for individuals with cognitive impairments and their caregivers. As a result, it is extremely valuable for clinicians and families to understand the potential benefits of improved risk profiles. Clinicians and families can then focus their efforts on those modifiers which may have the greatest impact on the patient's function and understand what types of benefits are feasible. Additionally, if these individual-level factors do not exhibit strong effects on incident IADL limitations, this will suggest that clinicians and families may need to provide direct support for IADLs.

Using data from the Health and Retirement Study (HRS), we expanded upon our previous research to examine whether four individual-level factors–low physical activity, not consuming alcohol, smoking, and depression–were associated with incident IADL limitations regardless of cognitive function; in other words, do these factors have benefit among those with cognitive impairment or are they relevant for the onset of IADL limitations only among those with high cognitive function? We focused on these factors because, unlike demographic characteristics like age or gender, these factors can be modified or treated. Given the cognitive demands of most IADL tasks, we hypothesized that

these individual-level factors would have large benefits for individuals with low dementia probability, but fewer benefits for individuals with high dementia probability.

MATERIALS AND METHODS

HRS has been described in detail previously.[15, 16] In brief, this is a nationally representative cohort of Americans aged 50 years or older and their spouses. We restricted our analyses to those participants enrolled in HRS and aged 65 years or older in 1998; we use data from biennial follow-ups through 2010.

HRS was approved by the University of Michigan Health Sciences Human Subjects Committee. These analyses were determined to be exempt by the Harvard School of Public Health Office of Human Research Administration.

Outcome Assessment

During the biennial interviews, participants were asked to report if they had difficulty in five IADLs in the past 30 days. These activities included using a phone, managing money, taking medication, shopping for groceries, and preparing hot meals, items selected from the Lawton and Brody index.[17] Development and validation of these items is described in more detail in HRS documentation[18] and subsequent research. For example, all items were shown to predict two-year mortality in a subsample of HRS.[19] Participants reported “yes,” “no” or “do not do” to each of these items. For consistency with prior work, we used the RAND variable for any activity limitation,[20] which sums reported activity limitations in the five IADLs and ranges from 0 to 5. “Don’t do” and “refused” are treated as no limitation in the RAND coding. Those who reported any activity limitations in 1998 or 2000 were excluded from our analyses, so we could evaluate predictors of incident limitations. Sensitivity analyses indicated results were similar when respondents were censored at first report of “don’t do” or “refused” for any item and when the food preparation and managing money items were excluded from the outcome definition.

Exposure Assessment

We used imputed dementia probability as our measure of cognitive functioning in this study. Methods for calculating this score have been described in detail elsewhere.[21] In brief, participants able to complete cognitive interviews were assessed via immediate and delayed recall of a 10-word list and a modified Telephone Interview for Cognitive Status. If a participant was too impaired to participate in cognitive interviews, proxies completed the Jorm Informant Questionnaire for Cognitive Decline[22–24] and a single item memory impairment question. Additionally, a subset of HRS participants completed a multi-instrument memory assessment. To impute dementia probabilities, the proxy and participant assessments were combined and calibrated against dementia diagnosis according to DSM-III-R and DSM-IV criteria (C statistic = 94.3%). The dementia probability has a theoretical range from 0 (no chance individual has dementia) to 1 (individual certain to have dementia) and an actual range in our data of $4.38*e^{-13}$ to 0.99.

For the purpose of these analyses, the dementia probabilities were divided into four categories based on the quartile cutpoints of the dementia probability distribution in the first

exposure wave (2000). The reference group for all analyses was the highest dementia probability quartile. The other dementia categories were modeled as three indicator variables and interactions between modifiers and each indicator variable were used to test whether effects differed by dementia probability. In all analyses, dementia probability was assessed in the wave prior to IADL assessment. We also performed sensitivity analyses in which participants were categorized into two groups based on a cutpoint of the 90th percentile of the dementia probability distribution at baseline. The effects of our modifiers were similar to those seen in our main analyses (see supplemental material).

Assessment of Individual Level Modifiers

We assessed whether physical inactivity, not consuming alcohol, smoking, or depression accelerated onset of IADL limitations among individuals in the highest dementia probability category. We slightly modified the RAND version[20] of these variables to account for changes in questions over time and to create dichotomous variables consistent with our previous work.[12, 25] We dichotomized physical activity as active versus inactive. Since the questions on physical activity changed over time, in 1998, 2000, and 2002, we defined "active" as vigorous activity 3 or more times per week. From 2004 onwards, we defined active as vigorous activity 1 or more times per week. Although this is a lower level of physical activity, this category was the closest to the category used in earlier questionnaires. We dichotomized alcohol consumption as moderate drinking (more than zero and fewer than two drinks per day) versus not drinking. Due to the small number of heavy drinkers (2 or more drinks per day) in this cohort, we were not able to examine interactions between heavy drinking and dementia probability and excluded heavy drinkers from our analyses of alcohol consumption. To calculate drinks per day, the number of drinks consumed on days the participant drinks was multiplied by the number of days per week the participant reported drinking and the result was divided by seven. Current smoking status was a binary variable (yes/no). We dichotomized depressive symptoms as depressed versus not depressed, defined as reporting three or more depressive symptoms in the past two weeks using a modified 8-item Centers for Epidemiologic Studies-Depression scale. All modifiers were assessed in the wave prior to outcome assessment.

Covariates

We adjusted for both time-constant and time-varying confounders. Our time-constant confounders were assessed in 1998 and included: age (centered, continuous), centered age squared (continuous), gender, race (black versus other), southern birthplace, years of education (linear spline model with discontinuities at completion of high school and completion of college plus an indicator variable for GED completion), mother's and father's education (=<8 years, >8 years), and height (gender-specific baseline quartiles). Our time-varying confounders were all assessed in the wave prior to the exposure and included: marital status (divorced/separated, widowed, never married, married), log of household size-adjusted wealth (continuous), body mass index (continuous), self-reported comorbidities (high blood pressure, diabetes, cancer, lung disease, heart disease, stroke, psychiatric problems, and arthritis), low income (dichotomized using a cutpoint of $12,031, the 25th percentile of household-size adjusted income at baseline), our individual level modifiers, and interview wave. Participants missing any covariate at baseline were excluded from all

analyses. If a covariate or modifier value was missing during follow-up, we carried forward the last known value of the covariate or modifier.

Statistical Analysis

Our outcome was the count of IADL limitations at each wave which allowed us to model the total number of limitations experienced by an individual. Poisson regression models were used to estimate the relative risk of reporting IADL limitations for each dementia probability category. Participants were censored from analyses after developing any IADL limitation, last interview, death, or at the first wave of missing information on dementia probability or IADL limitations.

We used two approaches to determine if the individual-level factors had differential effects on the risk of incident IADL limitations for participants in each of the dementia categories. First, we included an interaction term between each dementia category and each modifier (in separate models for each modifier). This tests whether the modifier has different *relative* effects on the development of IADL limitations depending upon the participant's dementia probability. To correct for overdispersion and clustering, we used sandwich variance estimators.[26] These analyses were performed using PROC GENMOD in SAS 9.3 using the covb option and with weights described below.

Second, using the "margins" command in Stata 12, we computed the expected number of IADL limitations if everyone in the population was in the low, mild, moderate, or high dementia probability categories and had either the "beneficial" or "adverse" value of the modifier. This estimates the *absolute* effect of each modifier for each dementia probability category. The average number of expected incident IADL limitations was calculated using coefficients estimated in Poisson regression models with interaction terms and the actual population distribution of other covariates.

We used inverse probability weights (IPWs) to account for time-varying confounders, selective survival, and attrition.[27] The IPWs use lagged covariate values, so our first "exposure" wave was 2000 and our first "outcome" wave was 2002. We constructed weights for dementia probability category, modifier status, survival and participation in HRS. The weights and the HRS sampling weight from 1998 were multiplied together to create a final weight for each participant; the final weight reflects the inverse of the probability that the individual was alive and participated in the outcome wave and had the dementia category and modifier values he or she actually had, given his or her past dementia probability, modifier and covariate history. Weights were stabilized[27] and truncated at the 98th percentile to minimize outlier influence.

We used identical methods to those describe above for sensitivity analyses with the alternative operationalization of the exposure (cutpoint at the 90th percentile of the dementia probability distribution at baseline). Due to concerns that some IADL instructions may be gender specific, we also performed additional sensitivity analyses excluding managing money and preparing hot meals and found similar results to those shown here (not shown).

From the 10,367 individuals aged 65 or older in 1998, we excluded the 3391 participants who reported prevalent IADL limitations in 1998 or 2000 or who did not answer any of the questions on IADL limitations in 1998. We also excluded 747 participants who did not answer the question on IADL limitations in 2002 and 453 participants for whom cognitive measures were not available in 1998 or 2000. Finally, we excluded 355 participants missing baseline covariate information, leaving 5219 participants for our analyses.

RESULTS

Among respondents with the highest probability of dementia at baseline, 63.% were physically inactive, 77.7% did not consume alcohol and 13.6% were depressed. In comparison, among respondents with low dementia probability 48.1% were physically inactive, 69.4% did not consume alcohol and 8.1% were depressed (Table 1). Individuals with the highest probability of dementia reported the highest mean number of limitations at each wave (Table 2).

The low dementia probability category was associated with lower risk of incident IADL limitations (relative risk=0.44, 95% CI: 0.28–0.70). Compared to high dementia probability, mild (relative risk=0.35; 95% CI: 0.27–0.45) and moderate probability of dementia (relative risk=0.53; 95% CI: 0.44–0.65) were also associated with significantly lower risk of incident IADL limitations (results not shown in tables). Physical inactivity (relative risk=1.50; 95% CI: 1.20, 1.87) significantly predicted a higher risk of incident IADL limitations. The association between depression and incident IADL limitations did not reach conventional thresholds for statistical significance but suggested a harmful effect (relative risk=1.29; 95% CI: 0.99, 1.69, p-value =0.06).

Table 3 shows the association between our dementia probability categories and the risk of incident IADL limitations, the association between each modifier and incident IADL limitations, and the interaction between each dementia probability category and each modifier. In these models, an interaction coefficient of 1 indicates the modifier has the same relative effect on IADL limitations in those with high dementia probability as in those with low dementia probability. If the interaction coefficient is less than 1, it indicates the modifier effect is lower (less harmful) among those with low dementia probability; conversely, if the interaction coefficient is greater than 1, it indicates the modifier effect is higher (more harmful) among those with low dementia probability.

Physical inactivity predicted higher increased risk of incident IADL limitations among those with high dementia probability (RR=1.60; 95% CI: 1.16, 2.19). The interaction between physical inactivity and low dementia probability was over 1 and statistically significant (RR=2.28, 95% CI: 1.05, 4.93) indicating that the estimated relative harm of physical inactivity is greater among those with the lowest dementia probability than among those with the highest probability of dementia.

The three other modifiers we examined – not consuming alcohol, smoking, and depression – were not significantly associated with increased risk of IADL limitations among those with high dementia probability. The interaction terms between these modifiers and most of our

dementia categories were not statistically significant, so there was also no evidence that the relative harm of these modifiers differed by dementia probability. Although the interaction between the moderate dementia probability and depression was statistically significant (RR=1.81, 95% CI: 1.03, 3.17), the effect was not seen for other dementia probability categories and showed no consistent pattern across levels of dementia probability.

We also estimated the absolute impact of the modifiers on the risk of incident IADL limitations for individuals in different dementia categories, by calculating predicted number of incident IADL limitations in each group. Respondents in the high dementia probability category who were physically active were predicted to develop an average of 0.25 incident IADL limitations over the next two years (Figure 1). Those in the high dementia probability category who were physically inactive were expected to develop 0.39 limitations over the next two years. Therefore, physical inactivity increased the average number of incident IADL limitations by 0.15 for the most cognitively impaired category (p-value for difference = 0.007). Among people in the low dementia probability category, physical inactivity was associated with an extra 0.14 new IADL limitations at each wave (p-value for difference =0.004). Consistent with the multiplicative models, alcohol use, smoking, and depression had little benefit on an absolute scale for individuals in the highest dementia probability quartile (figures 1b–1d).

DISCUSSION

Results from this large, prospective cohort study suggest that not consuming alcohol, smoking, and depression have limited effects on the incidence of IADL limitations among cognitively impaired individuals. In contrast physical inactivity is associated with an increased risk of incident IADL limitations for both the high and low dementia risk groups. This paper builds on our previous work on these modifiers, cognitive impairment, and ADL limitations by examining the effect of the modifiers on IADL limitations in both cognitively normal and cognitively impaired populations.

A previous meta-analysis concluded that cognitive status influences functional outcomes,[3] but did not explore whether the impact of cognitive status on functional outcomes can be modified by individual level health behaviors. Several of the factors that we examined, including smoking,[6–10] depression,[28] and high levels of alcohol consumption,[29] have already been associated with functional decline or impairment among those with normal cognition. Fewer studies have examined effects of these modifiers among those with cognitive impairment or examined IADLs as a separate outcome from ADL limitations. A recent review of the literature on depression and disability found that of the 12 studies which measured cognition, only 6 reported that baseline or incident depression predicted disability independent of cognition.[28] However, these studies examined ADLs or a composite of ADLs and IADLs as their measure of disability. Since IADLs are typically more cognitively demanding than ADLs, we hypothesized that it was less likely that these individual-level factors would ameliorate the effects of cognitive impairment on IADL limitations.[30]

Intervention studies suggest that physical activity may improve functional outcomes among those with dementia or mild cognitive impairment.[31],[32, 33] Additionally, a previous

observational study examined the effect of physical activity on both ADL and IADLs among community-based elderly participants without dementia. They observed decreased in the risk of incident ADL (HR=0.89; 95% CI: 0.83–0.95) and IADL (HR=0.93; 95% CI: 0.89–0.99) limitations for each additional hour of physical activity.[34] However, this study did not examine whether the impact of physical activity on incident IADL limitations varied by level of baseline cognitive function. Our study expands upon these results by examining whether the impact of physical inactivity on IADL limitations varies by cognitive status. Physical inactivity increased the risk of incident IADL limitations among those with and without cognitive impairments, with evidence that the effect was stronger in relative terms among those without cognitive impairments. In addition to the relative impact of physical inactivity on the risk of IADL limitations, the magnitude of the effect estimate in absolute terms was clinically meaningful, especially given the other known benefits of physical activity on cardiovascular and cognitive health. Although apraxia and cognitive losses may inhibit the ability of the cognitively impaired person to participate in some activities, clinicians and caregivers can work together to develop activities in which the cognitively impaired person can participate.[35]

Although over 3.4 million Americans over the age of 71 are affected by MCI or dementia [36], there is no known cure and treatments have modest if any benefits. Median survival after diagnosis with dementia is 4.1 years for men and 4.6 years for women.[37] Therefore, it is of utmost importance to develop strategies to preserve quality of life and, to the extent possible, independence, for patients as long as possible. Overall, our findings highlight the tremendous challenges in helping cognitively impaired individuals maintain IADL independence. Even with behavioral modifications designed to help preserve independence in basic ADLs, patients with dementia or cognitive impairment are likely to need substantial assistance with IADLs. Unfortunately, many IADLs are not considered part of routine medical care or even home health care. For individuals with cognitive impairment, IADL limitations may lead to earlier institutionalization or major burdens on caregivers. For patients without extensive networks to help with IADLs, such limitations may pose serious threats to health and safety. Providing direct support for IADLs, alongside behavioral interventions to preserve ADL independence and treatment of other comorbidities like depression, should be a key strategy for preserving quality of life for individuals with cognitive impairment or early dementia.

We acknowledge important limitations in our study, including the potential for residual confounding by factors like physical impairments that may affect both our individual-level risk factors and incident IADL limitations. Additionally, this study examines overall number of IADL limitations and does not consider the order in which the limitations occur, the co-occurrence of ADL and IADL limitations, or back-transitions due to resolution of IADL limitations. Additionally, our study only examined the presence or absence of an IADL limitation and did not consider whether individual-level modifiers impact the severity of the IADL limitation. It is possible that these modifiers may reduce the severity of IADL limitations but our measures were not sufficiently sensitive to detect modest improvements. Also, this study only looks at four individual-level modifiers and there may be other individual-level characteristics, behaviors, and health factors for incident IADL limitations (for example, dietary factors[38] [39], social activities[40], body mass index, disease

burden, lower extremity functional limitation, low frequency of social contacts, and vision impairment [4]) which may modify the association between cognitive impairment and incidence IADL limitations. Our use of data from a large, nationally representative cohort study is a major strength of this study. Since the data were collected longitudinally over several years, we assessed cognitive status and individual-level modifiers prior to outcome assessment. Additionally, we used inverse probability weighting to control for the possibility that cognitive functioning may impact future modifier status and selective attrition. Another strength of this study was the use of imputed dementia probability categories. Although those with severe cognitive impairment often cannot complete cognitive assessments and are excluded from analyses, we used proxy reports of cognitive status to determine a subject's dementia probability category. This allowed us to retain those individuals with severe cognitive impairments.

CONCLUSION

We found a strong association between dementia probability and incident IADL limitations. Physical inactivity was associated with an increased risk of incident IADL limitations regardless of cognitive status. However, not consuming alcohol, smoking, and depression did not have major impacts on IADLs among individuals with cognitive impairments. Given the increased cognitive demands of IADLs, it may be difficult to use some of the individual-level factors examined in this study to ameliorate the impact of cognitive impairment on IADL limitations. In addition to supporting continued physical activity among the cognitively impaired, direct support for IADLs may also be an important component of providing health care to individuals with cognitive impairment or dementia.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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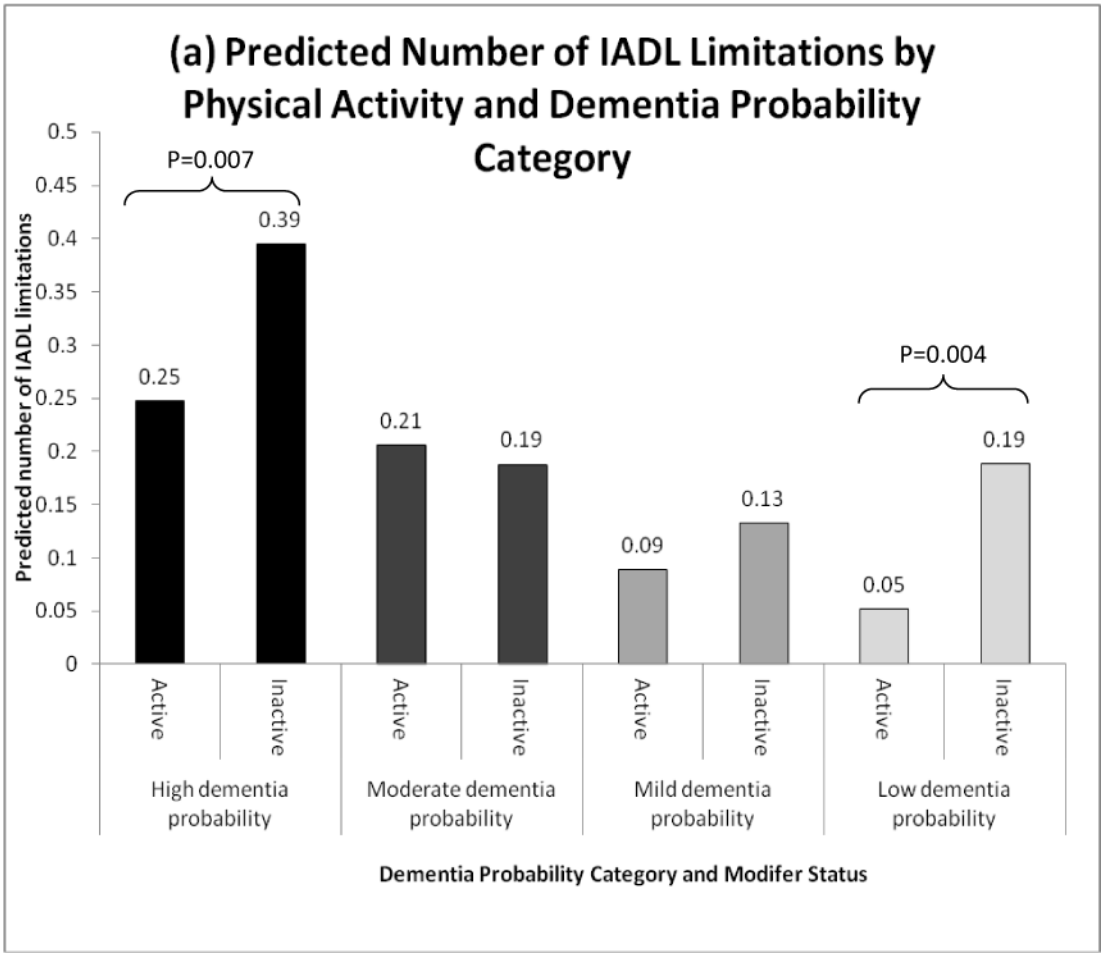

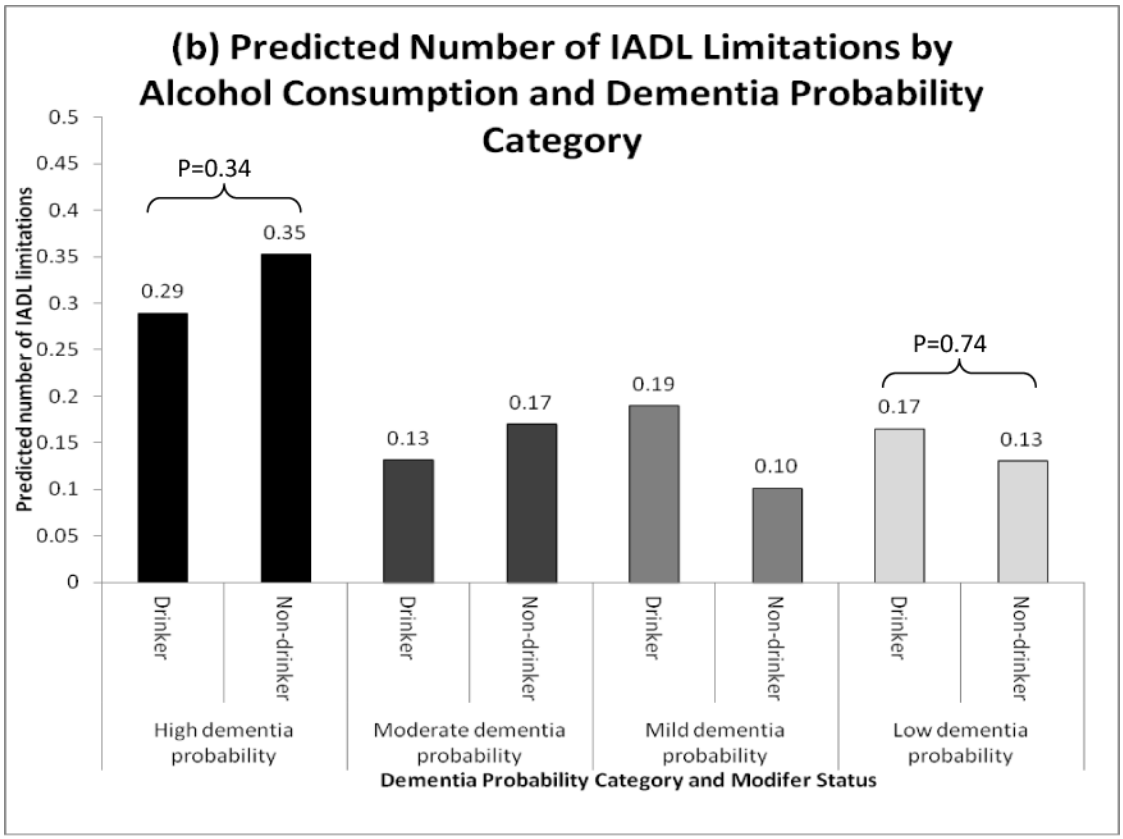

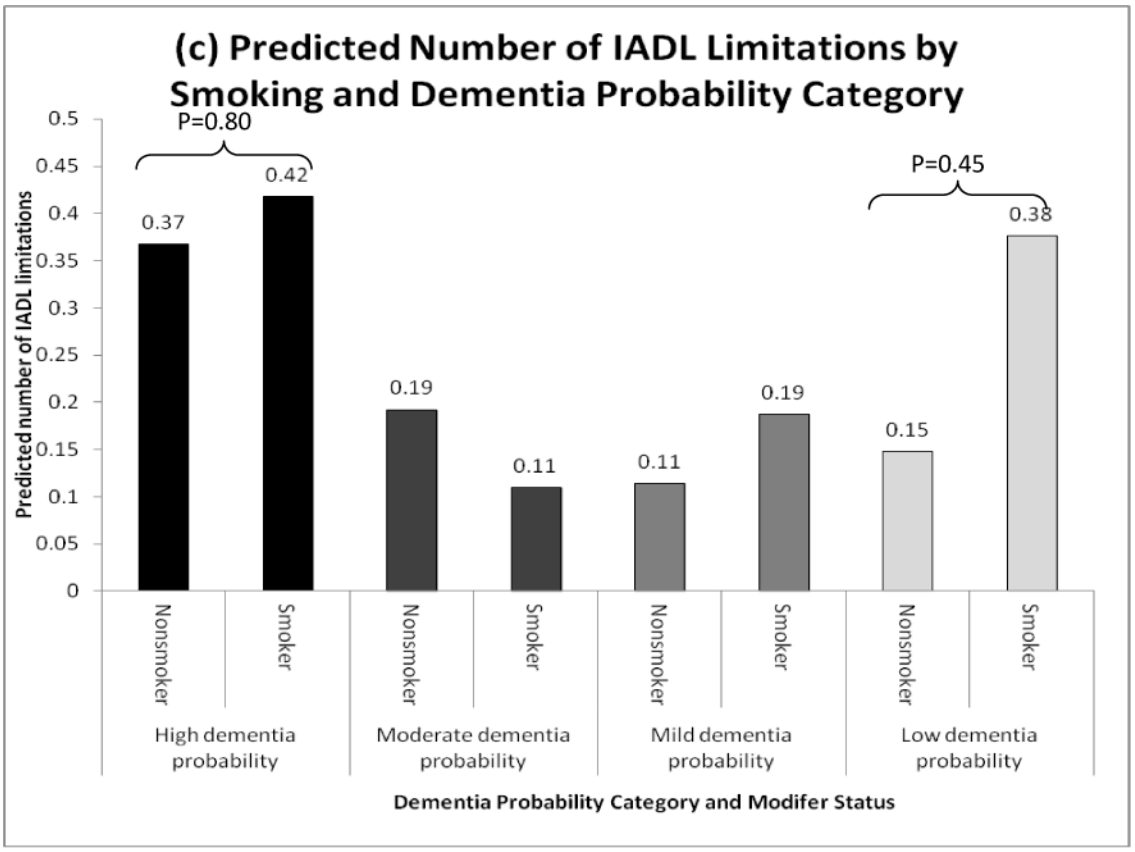

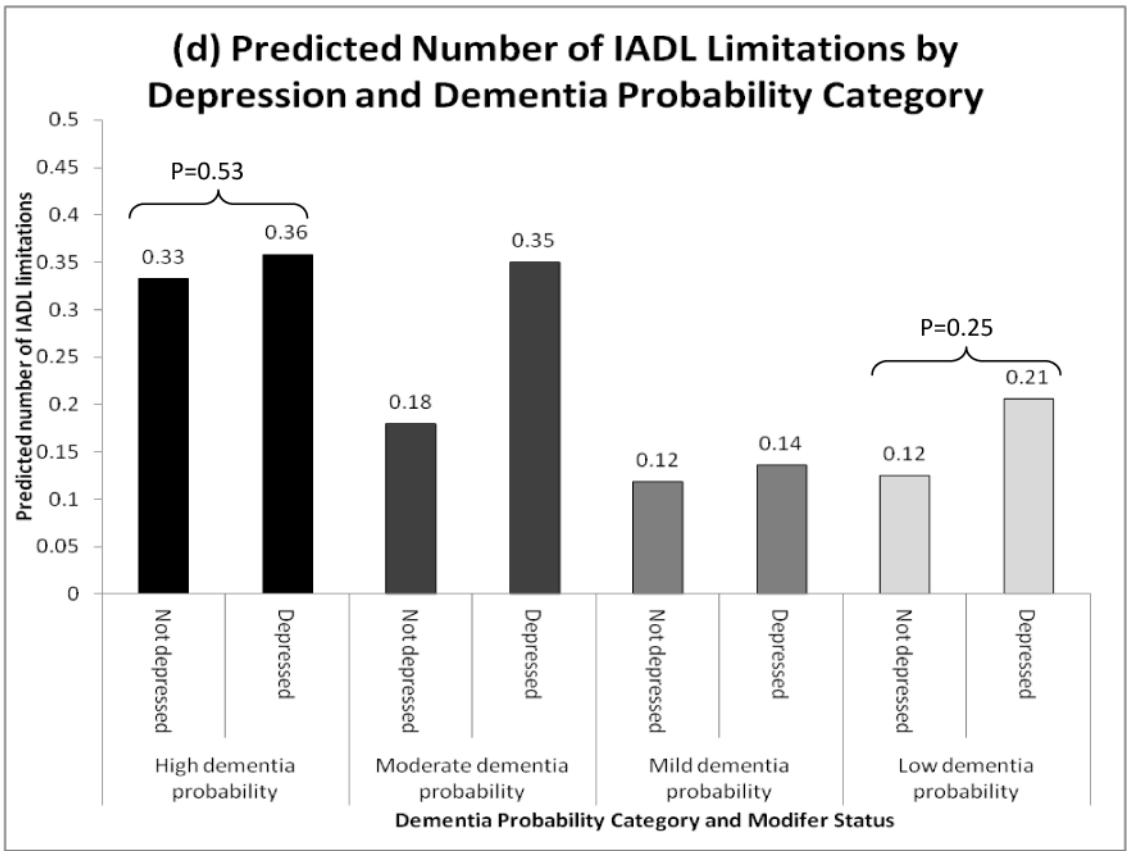

Figure 1.

Predicted number of incident IADL limitation per wave, by modifier and dementia probability category, with statistical significance tests for differences in absolute effects for those in the highest and lowest dementia probability categories.

Legend: IADL limitations were assessed each wave (every two years). We adjusted for the following potential time-constant confounders: age, age squared, sex, race, southern birthplace, education, mother's and father's educations, and height. Additionally, we adjusted for the following time-varying confounders using an inverse probability weighting approach: marital status, log of household size-adjusted wealth, body mass index, a summary score of self-reported comorbidities, and our modifiers.

Table 1

Baseline characteristics of those included in the analysis of dementia probability category and any incident IADL limitation by dementia probability category at baseline.

Characteristic	Dementia Probability Category at Baseline			
	High Dementia Probability (N= 1305)	Moderate Dementia Probability (N= 1304)	Mild Dementia Probability (N= 1305)	Low Dementia Probability (N= 1305)
Age (mean, std)	76.5 (6.4)	72.6 (5.5)	72.0 (5.2)	70.2 (4.6)
Gender (% male)	55.5	56.2	33.4	23.4
Race (% black)	14.8	8.8	8.5	6.3
Southern birthplace (%)	15.9	14.0	12.3	10.7
Years of education (mean, std)	11.2 (3.2)	12.5 (2.7)	12.8 (2.6)	13.4 (2.4)
Mother had ≥8 years of education (%)	43.1	50.8	55.1	58.0
Father had ≥8 years of education (%)	38.2	43.8	45.9	49.6
Marital status				
Married (%)	57.4	68.9	64.5	64.2
Divorced/separated (%)	5.4	5.4	5.8	8.2
Widowed (%)	34.0	21.7	25.9	24.4
Never married (%)	3.1	4.0	3.8	3.1
Physically inactive (%)	63.0	54.5	51.3	48.1
Not drinking (%)	77.7	71.2	70.0	69.4
Current smoking (%)	7.6	8.4	9.7	9.6
Current depression (%)	13.6	11.4	8.8	8.1
Low household-size adjusted income (%)	30.5	18.1	15.3	14.4
Body mass index (mean, std)	26.0 (4.2)	26.5 (4.2)	26.6 (4.8)	26.2 (4.5)
Number of comorbidities (mean, std)	1.7 (1.2)	1.6 (1.2)	1.6 (1.2)	1.4 (1.1)

Table 2

Distribution of dementia probability categories and total number of people reporting incident IADL limitations by year.

Dementia Probability Category	Year					Number of people reporting incident IADL limitations (n)	Mean number of limitations reported among those reporting limitations (n, std)
	2002	2004	2006	2008	2010		
High dementia probability (n)	1305	1094	1002	869	699	1085	2.20 (1.44)
Moderate dementia probability (n)	1304	1114	896	690	572	482	1.64 (1.09)
Mild dementia probability (n)	1305	1081	885	724	529	307	1.49 (0.94)
Low dementia probability (n)	1305	956	623	449	324	179	1.63 (1.16)
Number of people reporting incident IADL Limitations (n)	524	512	400	290	327	2053	
Mean number of limitations reported (n, std)	1.90 (1.29)	1.81 (1.25)	1.88 (1.30)	1.91 (1.26)	2.14 (1.46)		1.91 (1.31)

List of abbreviations: IADL = instrumental activities of daily living; std = standard deviation

Note: The number of people declines from left to right because of censoring due to incident IADL limitations, death, or dropout.

Table 3

Association between dementia probability category and incident IADL limitations including interactions between dementia probability and individual health factors.

	OR	95%	CI	p-value
Physical Activity				
No Physical Activity	1.60	1.16	2.19	<0.01
Low dementia probability	0.21	0.12	0.38	<0.01
Low dementia probability *No Physical activity	2.28	1.05	4.93	0.04
Mild dementia probability	0.36	0.21	0.62	<0.01
Mild dementia probability *No Physical activity	0.94	0.50	1.74	0.83
Moderate dementia probability	0.83	0.54	1.29	0.41
Moderate dementia probability *No Physical activity	0.57	0.34	0.96	0.03
Drinking				
Not Drinking	1.22	0.79	1.88	0.39
Low dementia probability	0.57	0.16	2.01	0.38
Low dementia probability *Not Drinking	0.65	0.17	2.48	0.53
Mild dementia probability	0.66	0.32	1.34	0.25
Mild dementia probability *Not Drinking	0.44	0.21	0.93	0.03
Moderate dementia probability	0.45	0.25	0.82	<0.01
Moderate dementia probability *Not Drinking	1.06	0.57	1.97	0.85
Smoking				
Smoking	1.00	0.36	2.74	0.79
Low dementia probability	0.40	0.24	0.68	<0.01
Low dementia probability *Smoking	2.24	0.33	15.01	0.41
Mild dementia probability	0.31	0.24	0.40	<0.01
Mild dementia probability *Smoking	1.44	0.37	5.61	0.60
Moderate dementia probability	0.52	0.42	0.53	<0.01
Moderate dementia probability *Smoking	0.50	0.11	2.38	0.39
Depression				
Depression	1.08	0.79	1.47	0.63
Low dementia probability	0.37	0.24	0.58	<0.01
Low dementia probability *Depression	1.53	0.70	2.77	0.28
Mild dementia probability	0.36	0.27	0.48	<0.01
Mild dementia probability *Depression	1.06	0.41	2.77	0.90
Moderate dementia probability	0.54	0.41	0.71	<0.01
Moderate dementia probability *Depression	1.81	1.03	3.17	0.04

Note: The reference group for all analyses presented above is the highest dementia probability group. Therefore, the OR for each modifier (e.g., no physical activity, smoking) provides the estimated effect of that modifier among individuals in the highest dementia probability group. The asterisks indicate coefficients for the interaction term between the dementia probability group and the modifier.