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Functional Impairment and Decline in Middle Age

A Cohort Study

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Background: Difficulties with daily functioning are common in middle-aged adults. However, little is known about the epidemiology or clinical course of these problems, including the extent to which they share common features with functional impairment in older adults.

Objective: To determine the epidemiology and clinical course of functional impairment and decline in middle age.

Design: Cohort study.

Setting: The Health and Retirement Study.

Participants: 6874 community-dwelling adults aged 50 to 56 years who did not have functional impairment at enrollment.

Measurements: Impairment in activities of daily living (ADLs), defined as self-reported difficulty performing 1 or more ADLs, assessed every 2 years for a maximum follow-up of 20 years, and impairment in instrumental ADLs (IADLs), defined similarly. Data were analyzed by using multistate models that estimate probabilities of different outcomes.

Results: Impairment in ADLs developed in 22% of participants aged 50 to 64 years, in whom further functional transitions were common. Two years after the initial impairment, 4% (95% CI, 3% to 5%) of participants had died, 9% (CI, 8% to 11%) had further ADL decline, 50% (CI, 48% to 52%) had persistent impairment, and 37% (CI, 35% to 39%) had recovered independence. In the 10 years after the initial impairment, 16% (CI, 14% to 18%) had 1 or more episodes of functional decline and 28% (CI, 26% to 30%) recovered from their initial impairment and remained independent throughout this period. The pattern of findings was similar for IADLs.

Limitation: Functional status was self-reported.

Conclusion: Functional impairment and decline are common in middle age, as are transitions from impairment to independence and back again. Because functional decline in older adults has similar features, current interventions used for prevention in older adults may hold promise for those in middle age.

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To live independently, people must be able to perform basic activities of daily living (ADLs), such as bathing, dressing, and transferring out of a bed or chair. Older adults who have difficulty performing these activities, or "functional impairment," have decreased quality of life and increased risk for acute care use, nursing home admission, and death (1–3). For these reasons, slowing or preventing the progression to functional impairment is a key focus of care for older adults.

Many people think of functional impairment as a problem affecting adults aged 65 years and older, especially the oldest old. Yet, functional impairment also is common in middle age. About 15% of community-dwelling adults aged 55 to 64 years have difficulty performing basic daily activities (4), compared with 20% to 25% of those aged 65 years and older (5). Despite the high prevalence of functional impairment in middle-aged adults, little is known about its epidemiology or clinical course in this younger age group, including the extent to which it shares common features with functional impairment in older adults. Some have hypothesized that midlife functional impairments may be more transient and related to acute injuries or single diseases compared with those that develop later in life (6), which often result from a gradual, multifactorial process without a clear precipitating event (7, 8). However, previous studies in middle-aged adults often focused on prevalent functional impairment and did not distinguish between long-standing deficits due to congenital conditions or trauma and those that are newly acquired in middle age and may have different risk factors and characteristics (9–12).

Understanding the epidemiology and course of functional impairment in middle age is key in developing appropriate strategies to manage this condition in our aging population and address the rising societal costs of long-term care (1). If loss of function in middle age has a clinical course and risk factors similar to those of late-life functional impairment, existing interventions to address functional loss in older adults might potentially be adapted for this younger age group. Conversely, different risk factors and progression may require a different clinical approach.

We used nationally representative longitudinal data to determine the incidence of functional impairment in adults aged 50 to 64 years, explore the course of functional decline in this age group, and identify risk factors for functional impairment in middle age.

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Web-Only
Supplement
Interactive sunburst graphic
(http://go.annals.org/functionalimpairment)

METHODS

Participants

We analyzed data from participants in the Health and Retirement Study (HRS), a nationally representative longitudinal study of changes in the health and wealth of Americans older than 50 years (13). New participants have been enrolled every 6 years since the study began in 1992, so it remains representative of the U.S. population older than 50 years. Participants are interviewed every 2 years by telephone; face-to-face interviews are conducted for those unable to access a telephone or too ill to participate by phone.

Our analytic cohort included participants who were aged 50 to 56 years when they enrolled in the 1992, 1998, or 2004 survey waves. Of 8430 participants aged 50 to 56 years at enrollment, we excluded 1280 who reported difficulty performing either ADLs or instrumental ADLs (IADLs) at the baseline interview, 252 who did not complete any follow-up interviews, and 24 who had missing ADL or IADL information at baseline. We analyzed data from the remaining 6874 participants at intervals of approximately 2 years until 2014.

The institutional review boards of the University of California, San Francisco, and the San Francisco Veterans Affairs Medical Center approved the study.

Measures

Functional Impairment

We first examined 2 outcomes: the cumulative incidence of the first episode of ADL impairment in middle age and cumulative incidence of the first episode of IADL impairment. To assess cumulative incidence, we determined the proportion of participants who developed ADL or IADL impairment between the ages of 50 to 64 years, accounting for death as a competing risk (14, 15).

At baseline and each follow-up assessment, participants reported whether they had difficulty performing each of 5 ADLs (bathing, dressing, transferring, toileting, and eating) and 5 IADLs (managing money, managing medications, shopping for groceries, preparing meals, and making telephone calls). Those who reported difficulty in performing an activity were asked whether they required help from another person to perform that activity. We defined ADL impairment as difficulty in performing 1 or more ADLs; we defined IADL impairment similarly. For participants enrolled in 1992, we considered 1994 as the baseline assessment, because ADL and IADL measures in 1992 differed from those used subsequently. We determined date of death from the National Death Index and interviews with family members.

Functional Trajectories

Studies in older adults suggest that functional status is dynamic and follows complex trajectories. Although some persons have persistent functional impairment after an initial episode, many others improve but are at high risk for recurrence (7, 16). Moreover, both groups are subject to worsening functional status over time (7, 16, 17).

To evaluate trajectories of functional change in participants who had incident ADL impairment, we examined several functional outcomes during follow-up. At 2-year follow-up, we examined 4 outcomes: recovery of functional independence, persistent functional impairment, further functional decline, and death. We defined ADL recovery as returning to ADL independence, persistent ADL impairment as having similar or improved function relative to the initial episode of impairment, and ADL decline as having worsened function relative to the initial episode of impairment. Using the same categories, we also examined the worst functional outcomes during the 10 years after the initial impairment.

Other Measures

Sociodemographic characteristics included self-reported age, sex, race/ethnicity, marital or partnership status, educational attainment, household income, and household net worth. Income for the previous 12 months was based on a comprehensive list of before-tax income. Net worth was calculated by summing assets and subtracting debts.

Measures of health status included self-reported medical conditions. We defined visual impairment as self-rated fair or poor eyesight despite best correction and hearing impairment as self-rated fair or poor hearing or use of a hearing aid. Other measures included cognitive impairment, assessed by using a modified version of the Telephone Interview for Cognitive Status (with impairment defined as a score of <5 on a scale of 0 to 35) (18); depression, assessed by using the 8-item Center for Epidemiologic Studies Depression Scale (with clinically significant depressive symptoms defined as a score of ≥3 on a scale of 0 to 8) (19, 20); and body mass index, calculated from self-reported weight and height.

Measures of health-related behaviors included self-reported alcohol use (21), smoking status, and frequency of physical activity (with infrequent activity defined as participation in activity once a week or less) (22). Measures of access to health care included health insurance and financial barriers to health care (defined as delay in filling a prescription or taking a medication because of cost). Measures of the physical environment included the self-reported condition of one's housing and safety of one's neighborhood.

Statistical Analysis

We used descriptive statistics to examine the characteristics of participants as well as those of functional impairment episodes. These analyses included the prevalence of impairment in 1, 2, 3, 4, or 5 ADLs and the most common pairings of ADL deficits in participants with 2 impairments; analyses for IADLs were performed similarly. These and the following analyses were adjusted for the complex HRS survey design to provide nationally representative estimates.

To calculate the cumulative incidence of the first ADL impairment episode between the ages of 50 and

64 years, we used a survival analysis framework. We defined the baseline as age 50 and the event time as the age of onset of ADL impairment. Participants who enrolled after age 50 were considered to have a delayed entry time. Because assessments occurred every 2 years, the date of onset of ADL impairment could not be observed exactly. We estimated the event time to be midway between the date when impairment was first reported and the date of the previous assessment. We censored participants who ended their observation period or were lost to follow-up; those who missed the first follow-up but had a subsequent assessment were retained in analyses (**Appendix**, Approach to Missing Data, available at Annals.org). To account for the competing risk for death, we used competing-risks survival analysis (23). We applied a similar analytic framework to determine the cumulative incidence of IADL impairment and impairments in individual ADLs and IADLs.

To determine the predicted trajectories of functional impairment over time, we used multistate survival modeling. In brief, multistate models describe the probability that participants transition among 3 or more states and may be used to characterize longitudinal trajectories in data sets in which participants enroll at different ages and are followed for different periods (24). We used a 6-state Markov model to examine the probability of transitioning between different states of functional impairment, by using the SPACE (Stochastic Population Analysis for Complex Events) programs for SAS (SAS Institute) (25). We defined states by using a summed ADL score. For each ADL, the score could take a value of 0 (independent), 1 (difficulty performing that ADL), or 2 (need for help performing that ADL). The maximum score for all 5 ADLs therefore ranged from 0 to 10. We defined 6 states by categorizing the ADL scores as 0, 1, 2, 3, 4 or more, and a final absorbing state for death. We chose the 6-state model for its clinical relevance and to ensure adequate frequencies of observed transitions among all possible states.

We first used the multistate model to determine the probability at each age of transitioning between each state. We next used these transition probabilities to simulate functional outcomes every 2 years through age 76 for 1 million microsimulated participants who were independent at study entry at age 50. Using an analytic framework similar to that used for the cumulative incidence analyses, we then calculated the percentage of participants who had a first episode of ADL impairment before age 65. For persons with incident impairment, we calculated the percentage who had functional recovery, persistence, decline, or death at 2 and 10 years after the initial impairment. We defined ADL recovery as returning to ADL independence (ADL score of 0), persistent ADL impairment as having the same ADL score as the initial episode of impairment or an improved (but nonzero) score, and ADL decline as an increase in ADL score relative to the initial episode of impairment. We performed survey-weighted bootstrapping (with 100 resampled data sets and 100 000 microsimulations per data set) to calculate 95% CIs for these estimated probabilities.

We identified risk factors for functional impairment by using competing-risks regression (**Appendix**, Analyses of Risk Factors for Functional Impairment). We performed similar analyses for IADLs. Analyses were performed with Stata 14.2 (StataCorp) and SAS 9.4.

Role of the Funding Source

The funding sources had no role in the study's design, conduct, or reporting.

RESULTS

Of the 6874 participants, 54% percent were men, 80% were white, and 15% had less than a high school education (**Table**). A substantial proportion of participants had their first episode of ADL impairment between the ages of 50 and 64 years. The cumulative incidence of ADL impairment increased with age, reaching 22% at age 64 (95% CI, 21% to 23%) (**Figure 1**). Difficulty in dressing was the most common ADL impairment, affecting 14% of participants during at least 1 biennial assessment through age 64 (CI, 13% to 15%) (**Figure 2**). Less common were impairments in transferring (cumulative incidence, 11% [CI, 10% to 12%]), toileting (7% [CI, 7% to 8%]), bathing (7% [CI, 6% to 8%]), and eating (3% [CI, 3% to 4%]).

Most participants with a first episode of ADL impairment had difficulty in 1 ADL (70%), with a smaller percentage having difficulty in 2 ADLs (19%), 3 ADLs (6%), 4 ADLs (4%), or 5 ADLs (1%) (**Appendix Table 1**, available at Annals.org). Among participants with 2 impaired ADLs, the most common pairing of affected activities was transferring and dressing.

Analyses of further functional transitions after the index impairment were estimated by using multistate models. Among participants who had an initial episode of ADL impairment, further functional transitions were common. Two years after an initial impairment episode, 37% (CI, 35% to 39%) of participants had fully regained ADL independence (**Figure 3**). The remainder fared worse: 50% (CI, 48% to 52%) remained at a stable or an improved (but not fully independent) level of functional impairment, 9% (CI, 8% to 11%) had worse functional status, and 4% had died (CI, 3% to 5%).

In the 10 years after the initial episode of ADL impairment, 28% (CI, 26% to 30%) of participants regained function and remained independent throughout that time. An additional 37% (CI, 35% to 39%) had 1 or more episodes of stable or improved functional impairment, 16% (CI, 14% to 18%) had 1 or more episodes of further ADL decline, and 19% died (CI, 16% to 21%).

The pattern of findings for IADLs was similar. The cumulative incidence of IADL impairment at age 64 was 19% (CI, 18% to 20%) (**Appendix Figure 1**, available at Annals.org). Difficulty in shopping for groceries was the most common impairment, affecting 10% (CI, 9% to 11%) of participants by age 64, followed by difficulty in managing money (cumulative incidence, 8% [CI, 7% to 8%]) and preparing meals (6% [CI, 5% to 7%]) (**Appendix Figure 2**, available at Annals.org). Most participants with a first episode of IADL impairment had a decline in

Table. Baseline Characteristics of 6874 Participants With and Without Incident ADL Impairment in Middle Age

Characteristic*	All Participants (*n* = 6874)†	ADL Impairment (*n* = 1192)†	No ADL Impairment (*n* = 5682)†	*P* Value
Demographic characteristics, %				
Female	46	50	45	0.011
Race/ethnicity				<0.001
White non-Latino	80	71	82	
Black non-Latino	9	14	9	
Latino	7	11	7	
Other	3	4	3	
Married or partnered	75	68	76	<0.001
Socioeconomic status, %				
Less than high school education	15	26	13	<0.001
Income quartile				<0.001
≤$32 363	25	43	22	
$32 363 to ≤$60 000	25	24	25	
$60 000 to ≤$98 192	25	20	26	
>$98 192	25	13	27	
Net worth quartile				<0.001
≤$44 500	25	41	22	
$44 500 to ≤$136 000	25	26	25	
$136 000 to ≤$345 000	25	19	26	
>$345 000	25	14	27	
Health status				
Chronic medical conditions, %				
Hypertension	29	39	27	<0.001
Stroke	2	4	1	<0.001
Diabetes	7	15	6	<0.001
Cardiac disease	7	11	7	<0.001
Lung disease	3	6	2	<0.001
Cancer	4	5	3	0.016
Arthritis	25	43	22	<0.001
Other health conditions, %				
Visual impairment	12	23	10	<0.001
Hearing impairment	11	16	10	<0.001
Mean Telephone Interview for Cognitive Status score (SD)‡§	25.0 (2.9)	24.0 (2.9)	25.1 (2.5)	<0.001
Depression, %	16	27	13	<0.001
Body mass index, %				<0.001
<18.5 kg/m^2	1	1	1	
18.5–24.9 kg/m^2	30	22	32	
25–29.9 kg/m^2	42	37	43	
≥30 kg/m^2	27	41	25	
Health-related behaviors, %				
Alcohol use, ≥3 drinks per day	12	12	12	0.95
Current smoker	23	30	22	<0.001
Infrequent physical activity	60	68	59	<0.001
Access to health care, %				
Uninsured	11	19	10	<0.001
Financial barriers to medical care	8	17	7	<0.001
Physical environment, %				
Fair or poor condition of housing‡	11	23	9	<0.001
Fair or poor safety of neighborhood	9	18	8	<0.001

ADL = activity of daily living.
* Results weighted to generate nationally representative estimates and account for the complex survey design.
† Percentages may not sum to 100% due to rounding.
‡ Includes only participants enrolled in 1998 and 2004; variable was not available at baseline for those enrolled in 1992.
§ We report mean scores rather than percentage of participants with cognitive impairment because no participants met criteria for cognitive impairment at study enrollment.

1 IADL (78%); fewer had impairment in 2 IADLs (15%), 3 IADLs (4%), 4 IADLs (2%), or 5 IADLs (2%) (**Appendix Table 2**, available at Annals.org). Difficulty in shopping and preparing meals was the most common combination of IADL impairments.

Baseline characteristics differed in people who had their first ADL impairment episode in middle age versus those who did not. Participants in whom ADL impairment developed were more likely to be women, less likely to be white, and less likely to be married and had lower socioeconomic status, including lower education, income, and net worth (**Table**). They also had worse health status, including a higher prevalence of chronic medical conditions, sensory impairments, depression, and obesity. Participants who had ADL impairment were more likely to smoke and to exercise infrequently and more likely to lack health insurance and to report financial barriers to health care. They also were more likely to report that housing conditions and neighborhood safety were fair or poor.

In multivariable analyses, the strongest predictors of ADL impairment included low income, stroke, and arthritis; additional risk factors included other chronic medical conditions, sensory impairment, depression, obesity, infrequent physical activity, lack of health insurance, and residence in a neighborhood with fair or poor safety. Risk factors for IADL impairment generally were similar (**Appendix Tables 3** and **4**, available at Annals.org).

DISCUSSION

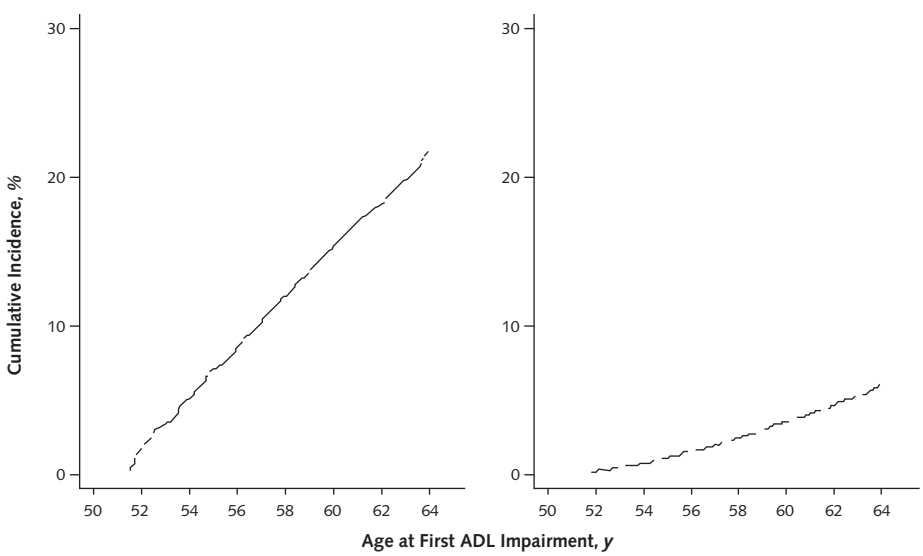
In this nationally representative study of community-dwelling adults, functional impairment and decline were common in middle age. Functional impairment developed in nearly one quarter of participants aged 50 to 64 years, nearly two fifths of whom died or had further functional decline during at least 1 period over the next 10 years, either directly or after an intervening period of functional stability or improvement. However, other patterns of functional transitions also were common, including durable return to independence. Risk factors for functional impairment spanned several domains, including sociodemographics, health status, health-related behaviors, and the physical environment.

Previous cross-sectional studies showed that functional impairment is common in middle age. However, these impairments traditionally have been viewed as transient and related to acute injuries or single diseases, in clinical distinction from the more chronic and progressive impairments in older adults (6). A growing body of research in adults aged 70 years and older is now showing that functional impairment in older adults actually is surprisingly dynamic, with difficulties in basic daily activities developing and regressing over relatively short periods (7, 16). This dynamism is believed to result from intervening events that precipitate disability, such as illness, injury, and hospitalization, followed by periods of recovery (26). This work also shows that although initial recovery from disability is common, a first episode of functional impairment is a seminal event that strongly predicts progression to more chronic impairment (7, 16, 17).

Our findings suggest that the same general patterns are true of functional impairment in middle age. Although the cumulative incidence of ADL impairment was nearly 25% by age 64, more than one third of the participants studied had recovered functional independence 2 years later. Overall, however, nearly two fifths of persons who had an initial ADL impairment episode died or had worsened functional status over time. These findings suggest that an initial episode of ADL impairment is an important prognostic marker, even in this relatively young age group.

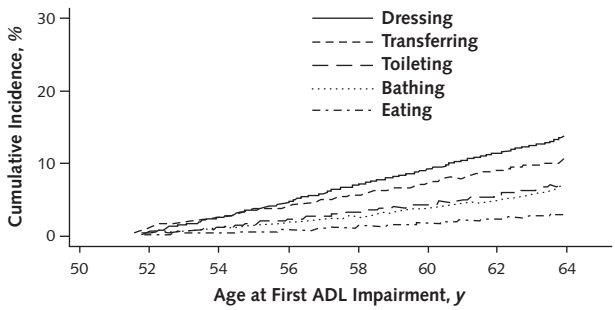
Our findings also point to key differences in the patterns of incident ADL and IADL impairment in middle-aged versus older adults. The cumulative incidences of ADL and IADL impairment were comparable in this cohort, at 22% and 19%, respectively, a finding consistent with previous cross-sectional research in middle-aged adults (27, 28). In older adults, in contrast, the prevalence of IADL impairment typically exceeds that of ADL impairment substantially (29, 30). The higher prevalence of IADL impairment in older adults is believed to reflect a hierarchical disabling process, in which loss of independence in IADLs precedes the loss in ADLs, driven largely by the effect of cognitive impairment on the ability to perform cognitively complex

Figure 1. Cumulative incidence of ADL impairment and death among middle-aged adults.



Cumulative incidences of ADL impairment (*left*) and death (*right*) between the ages of 50 and 64 y were determined by using competing-risks survival analysis to account for the competing risk for death. Analyses were adjusted to account for the complex survey design. ADL = activity of daily living.

Figure 2. Cumulative incidence of ADL impairment among middle-aged adults.



Cumulative incidences of individual ADL impairments between the ages of 50 and 64 y were determined by using competing-risks survival analysis to account for the competing risk for death. Analyses were adjusted to account for the complex survey design. ADL = activity of daily living.

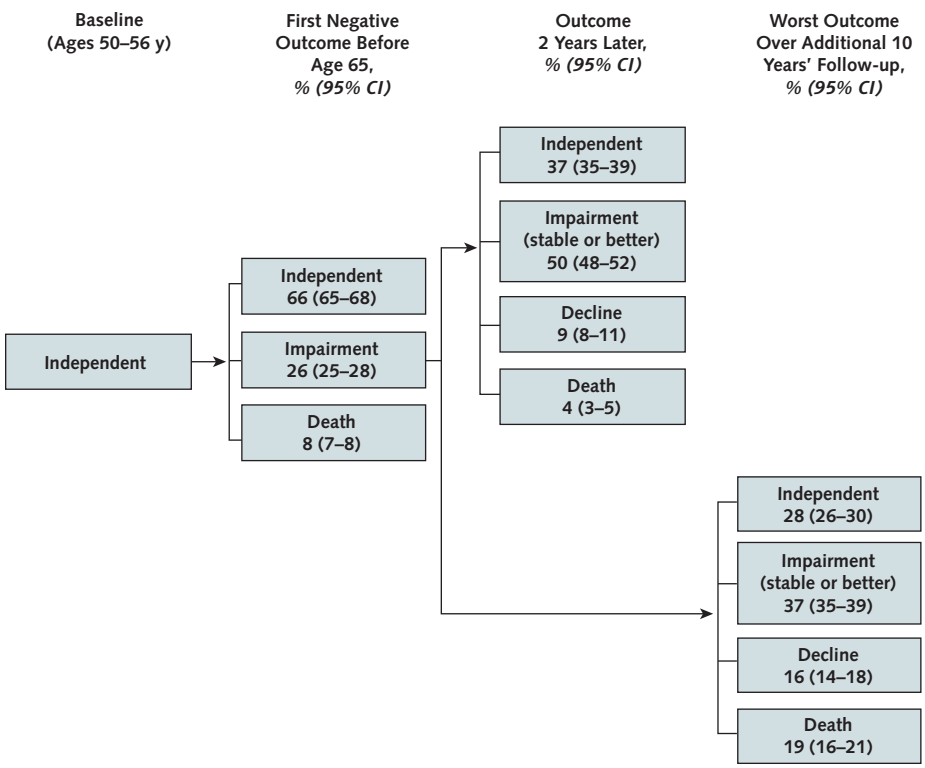
IADL tasks (6, 31). The lower burden of IADL impairment in this middle-aged cohort may reflect the low prevalence of cognitive impairment.

Our findings also reveal differences in the onset of individual ADL impairments in middle-aged versus older adults. Dressing impairment had the highest cumulative incidence and the earliest age of onset in this cohort, followed by functional loss in transferring, toileting, bathing, and eating; previous cross-sectional studies of middle-aged adults showed similar findings (28, 32). In contrast, research in adults aged 70 years and older shows that bathing typically is the first ADL to become impaired, followed by dressing, transferring, toileting, and eating (33–35). It is unclear why dressing and transferring difficulties precede bathing difficulty in middle-aged adults, because these tasks require similar abilities, including upper and lower extremity strength and mobility (35, 36). However, these findings suggest that interventions to address functional impairment in middle age must be tailored to meet the specific functional needs of this age group, which may differ from those of older adults.

Our findings further point to key similarities, as well as important differences, between risk factors for functional problems in middle age and those in older age. Risk factors shared across age groups include low income, chronic medical conditions, sensory deficits, depression, obesity, and low physical activity (31, 37). However, other classic risk factors for functional impairment in older age, including sex, cognitive decline, and low body mass index, were not in this cohort.

Several factors may explain these differences. Previous research showed that older women report more functional problems than do men and that this disparity may be related to a higher burden of disabling conditions among older women, including osteoporosis, os-

Figure 3. Predicted functional outcomes among middle-aged adults.



Probabilities (and corresponding 95% CIs) of different functional outcomes among middle-aged adults, estimated by using a multistate model. The predicted probability of a first episode of ADL impairment in the multistate model (26%) differed slightly from that in the competing-risks model (22%). ADL = activity of daily living.

teoarthritis, and depression (38–42). However, sex differences in disability may not emerge until age 65, when differential risk factors reach a critical mass (41). The prevalence of cognitive impairment in this middle-aged cohort was too low to examine its association with functional outcomes; the same was true of low body mass index.

Finally, we found that functional impairment was multifactorial, with risk factors including sociodemographics, health status, and health-related behaviors. This finding is important, because many geriatric models of care that address functional impairment are multicomponent interventions that target individual patients' many risks and needs. Our findings suggest that a similar approach may be appropriate for middle-aged adults. Indeed, proven geriatric models of care have been delivered successfully to vulnerable middle-aged adults (43, 44). Novel care models that improve functioning in low-income older adults (45) may hold similar promise for low-income middle-aged adults.

This study has several limitations. Function was measured by self-report rather than objective criteria. However, self-reported function is an important patient-centered measure (46) that strongly predicts adverse outcomes (2, 47, 48). We excluded persons who lacked follow-up data; participants with greater functional impairment may have more difficulty completing follow-up interviews, potentially leading to underestimation of functional outcomes and affecting generalizability. However, HRS researchers conduct in-person interviews with participants unable to complete interviews by phone because of illness or functional limitations, which may mitigate this problem. Finally, because assessments occurred every 2 years, shorter periods of functional impairment may have been missed, leading to underestimation of functional outcomes.

In conclusion, we found that functional impairment was common in middle age and that nearly two fifths of persons with impaired function died or had further functional decline. Risk factors for functional impairment spanned several domains, including socioeconomic status, health status, and health-related behaviors. These findings challenge traditional thinking that functional impairment in middle age is merely a transient phenomenon and point to common features between functional impairment in middle-aged adults and that in older persons. At the same time, functional impairments in middle age have characteristics distinct from those in older age, including a relatively lower cumulative incidence of IADL versus ADL impairment and differing patterns of impairment in individual ADLs. Taken together, these findings suggest that interventions commonly used to prevent functional decline in older adults may hold promise for adults in middle age but must be tailored to meet their unique needs.

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Note: Drs. Brown and Steinman are employees of the San Francisco Veterans Affairs Medical Center.

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Reproducible Research Statement: *Study protocol:* See **Supplement 1** (available at Annals.org). *Statistical code:* See **Supplement 2** (available at Annals.org). *Data set:* Publicly available from the HRS Web site at http://hrsonline.isr.umich.edu/.

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Appendix: Supplemental Statistical Analyses and Results

Approach to Missing Data

Participants who missed 1 or more assessments were retained in cumulative incidence analyses. We took this approach because excluding persons with missing assessments likely would have led to biased outcome assessments. Persons with ADL or IADL impairments may be more likely to miss follow-up interviews, so excluding these participants might underestimate functional outcomes and affect generalizability. Furthermore, rates of missingness were relatively low during the 14-year follow-up for the cumulative incidence analyses: 90.2% of participants completed all assessments during the follow-up, 6.6% missed only 1 assessment, 2.5% missed 2 assessments, 0.6% missed 3 assessments, and 0.1% missed 4 assessments. With regard to the specific assessments missed, of the 6874 participants 396 were lost at the first follow-up. Of these 396 persons, 313 had data at 1 or more subsequent assessments. Of the remaining 83 participants who had missing data at all subsequent assessments, all died before age 65 and were categorized as having a competing risk for death. Of the 83 participants who died, 69 died before the year 4 assessment, 7 died between years 4 and 6, 3 died between years 6 and 8, and 4 died between years 8 and 10.

Analyses of Risk Factors for Functional Impairment

To identify risk factors for ADL and IADL impairment, we first compared characteristics of participants who lost ADL (or IADL) function with those who did not, by using the *t* test and the Rao–Scott test, a design-adjusted version of the Pearson chi-square test. We then used competing-risks regression to determine the adjusted subdistribution hazard ratios for the association of these potential risk factors with each outcome in the presence of death as a competing risk. We assessed predictors upon study enrollment. Most variables in the models were drawn from the RAND HRS Data Files (RAND Corporation), which use high-quality multiple imputation to address missing data; additional variables that are not available in the RAND data set were drawn from HRS data files, in which missing data are not imputed. The overall percentage of missingness for the final multivariable models was less than 10% (9.9% for the ADL impairment model and 7.3% for the IADL impairment model). We built the multivariable models for each outcome by using backward elimination, sequentially removing covariates with a *P* value of 0.05 or greater. We forced into the final model sociodemographic variables, including study wave, sex, race/ethnicity, education, income, and net worth. Because measures for physical activity changed in 2004, we included an interaction term to determine whether the relationship of these measures to outcomes varied by study wave. The interaction term was not significant in any of the models. To test the proportional hazard assumption, we refit the final models by using Cox proportional hazards regression.

Proportional Hazards Analyses

In the Cox regression final models for ADL and IADL impairment, we found a departure from the proportional hazards assumption. This departure mainly was a result of the predictor "arthritis" in the ADL impairment model and "study wave" in the IADL impairment model. We refit new models in which we stratified by these predictors and retested the proportional hazards assumption. In the new stratified models, the proportional hazards assumption was met. In addition, we compared the estimates for the hazard ratios in the stratified models with those in the model without stratification, and they were similar. Thus, we concluded that the departure from the proportional hazards assumption did not affect our estimates, and we used the aforementioned predictors in the final models.

Results of Multivariable Models

In multivariable analyses, the strongest predictors of ADL impairment included low income (lowest vs. highest income quartile), stroke, and arthritis. Each of these characteristics was associated with approximately a twofold increased risk for ADL impairment. Additional risk factors for ADL impairment included other chronic medical conditions (hypertension, diabetes, and chronic lung disease), vision and hearing impairment, depression, obesity, infrequent physical activity, lack of health insurance, and residence in a neighborhood with fair or poor safety (Appendix Table 3).

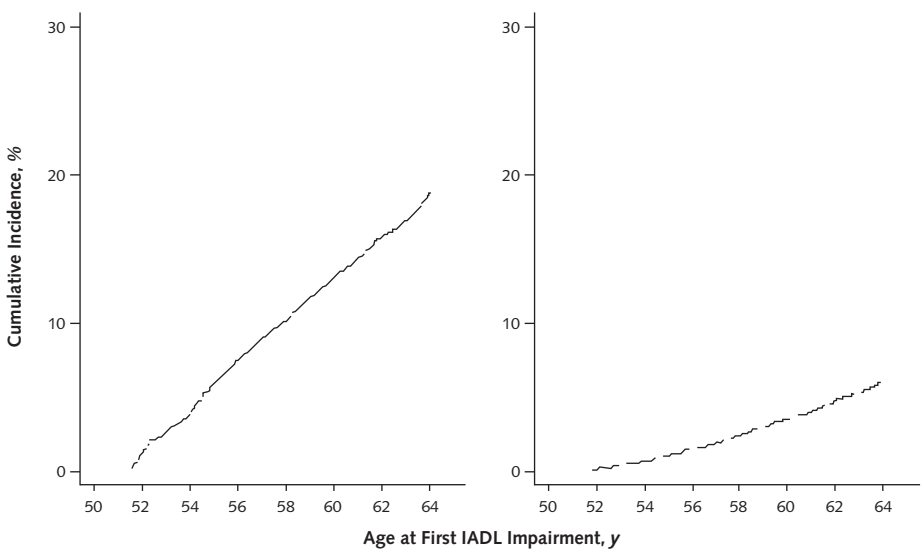
Risk factors for IADL impairment generally were similar to those for ADL impairment (Appendix Table 4). In sensitivity analyses including all potential predictors of ADL and IADL impairment in the final multivariable models, results were similar (results not shown).

Appendix Table 1. Characteristics of First Episode of ADL Impairment in Middle-Aged Adults

Characteristic*	Participants With ADL Impairment (n = 1143), %
Number of ADL impairments	
1	70
2	19
3	6
4	4
5	1
Most common ADL pairings	
Transferring and dressing	34
Bathing and dressing	16
Transferring and toileting	14
Dressing and toileting	14
Dressing and eating	9

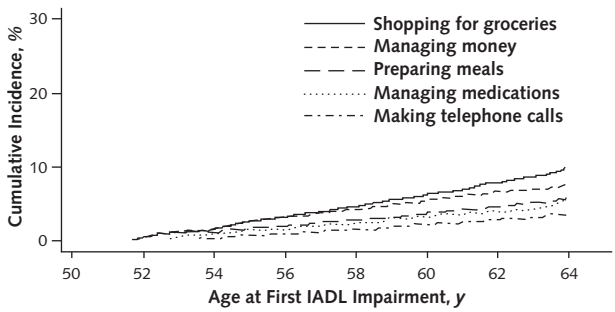
ADL = activity of daily living.
* Results weighted to generate nationally representative estimates and account for the complex survey design.

Appendix Figure 1. Cumulative incidence of IADL impairment and death among middle-aged adults.



Cumulative incidences of IADL impairment (*left*) and death (*right*) between the ages of 50 and 64 years were determined by using competing-risks survival analysis to account for the competing risk for death. Analyses were adjusted to account for the complex survey design. IADL = instrumental activity of daily living.

Appendix Figure 2. Cumulative incidence of IADL impairment among middle-aged adults.



Cumulative incidences of individual IADL impairments between the ages of 50 and 64 years were determined by using competing-risks survival analysis to account for the competing risk for death. Analyses were adjusted to account for the complex survey design. IADL =instrumental activity of daily living.

Appendix Table 2. Characteristics of First Episode of IADL Impairment in Middle-Aged Adults

Characteristic*	Participants With IADL Impairment (n = 1011), %†
Number of IADL impairments	
1	78
2	15
3	4
4	2
5	2
Most common IADL pairings	
Preparing meals and shopping	44
Managing medications and managing money	17
Managing money and shopping	12
Using the telephone and managing money	7
Using the telephone and shopping	4

IADL = instrumental activity of daily living.
* Results weighted to generate nationally representative estimates and account for the complex survey design.
† Percentages may not sum to 100% due to rounding.

Appendix Table 3. Risk Factors for Incident ADL Impairment in Middle-Aged Adults

Characteristic*	Outcome Frequency†		Adjusted Subhazard Ratio (95% CI)‡
	ADL Impairment (*n* = 1192)	No ADL Impairment (*n* = 5682)	
Study wave, %			
Enrolled 1992	23	24	Reference
Enrolled 1998	41	34	1.30 (1.11–1.53)
Enrolled 2004	36	42	0.99 (0.81–1.21)
Female, %	50	45	1.07 (0.91–1.25)
Race/ethnicity, %			
White non-Latino	71	82	Reference
Black non-Latino	14	9	1.05 (0.87–1.28)
Latino	11	7	1.21 (0.95–1.54)
Other	4	3	1.20 (0.79–1.83)
Married or partnered, %	68	76	
Less than high school education, %	26	13	1.14 (0.95–1.36)
Income quartile, %			
≤$32 260	43	22	1.92 (1.46–2.52)
$32 260 to ≤$60 000	24	25	1.39 (1.08–1.79)
$60 000 to ≤$98 192	20	26	1.24 (0.95–1.64)
>$98 192	13	27	Reference
Net worth quartile, %			
≤$44 500	41	22	1.26 (0.95–1.67)
$44 500 to ≤$136 000	26	25	1.16 (0.88–1.54)
$136 000 to ≤$345 000	19	26	1.09 (0.84–1.43)
>$345 000	14	27	Reference
Chronic medical conditions, %			
Hypertension	39	27	1.18 (1.02–1.37)
Stroke	4	1	2.25 (1.57–3.25)
Diabetes	15	6	1.45 (1.17–1.78)
Cardiac disease	11	7	
Lung disease	6	2	1.57 (1.09–2.26)
Cancer	5	3	
Arthritis	43	22	2.02 (1.70–2.40)
Visual impairment, %	23	10	1.33 (1.11–1.59)
Hearing impairment, %	16	10	1.31 (1.09–1.59)
Mean Telephone Interview for Cognitive Status score (SD)	24.0 (2.9)	25.1 (2.5)	
Depression, %	27	13	1.43 (1.21–1.69)
Body mass index, %			
<25 kg/m^2	23	33	Reference
25–29.9 kg/m^2	37	43	1.17 (0.98–1.40)
≥30 kg/m^2	41	25	1.69 (1.40–2.03)
Alcohol use, ≥3 drinks per day, %	12	12	
Current smoker, %	30	22	
Infrequent physical activity, %	68	59	1.33 (1.11–1.58)
Uninsured, %	19	10	1.31 (1.10–1.55)
Financial barriers to medical care, %	17	7	
Fair or poor condition of housing, %	23	9	
Fair or poor safety of neighborhood, %	18	8	1.38 (1.12–1.69)

ADL = activity of daily living.
* Results weighted to generate nationally representative estimates and account for the complex survey design. Final column shows only the variables retained on backward elimination, except for sex, race/ethnicity, and net worth, which were forced into the final model. All variables assessed at study enrollment.
† Percentages may not sum to 100% due to rounding.
‡ Subhazard ratios adjusted for all listed variables and calculated by using competing risks regression to account for the competing risk for death.

Appendix Table 4. Risk Factors for Incident IADL Impairment in Middle-Aged Adults

Characteristic*	Outcome Frequency, %†		Adjusted Subhazard Ratio (95% CI)‡
	IADL Impairment (*n* = 1011)	No IADL Impairment (*n* = 5863)	
Study wave			
Enrolled 1992	21	24	Reference
Enrolled 1998	39	34	1.25 (1.04–1.49)
Enrolled 2004	40	41	1.26 (1.02–1.54)
Female	46	45	1.06 (0.91–1.24)
Race/ethnicity			
White non-Latino	70	82	Reference
Black non-Latino	16	8	1.14 (0.91–1.43)
Latino	11	7	1.16 (0.89–1.51)
Other	4	3	1.27 (0.74–2.18)
Less than high school education	29	13	1.43 (1.19–1.73)
Income quartile			
≤$32 260	45	22	2.62 (1.90–3.61)
$32 260 to ≤$60 000	25	25	1.76 (1.29–2.41)
$60 000 to ≤$98 192	20	26	1.72 (1.28–2.31)
>$98 192	10	27	Reference
Net worth quartile			
≤$44 500	44	22	1.51 (1.10–2.07)
$44 500 to ≤$136 000	27	25	1.42 (1.03–1.96)
$136 000 to ≤$345 000	17	26	1.17 (0.84–1.63)
>$345 000	12	27	Reference
Chronic medical conditions			
Hypertension	40	27	1.18 (1.00–1.39)
Stroke	5	1	2.25 (1.53–3.31)
Diabetes	15	6	1.47 (1.13–1.90)
Lung disease	6	2	1.66 (1.15–2.38)
Arthritis	38	23	1.58 (1.35–1.85)
Visual impairment	26	10	1.60 (1.34–1.92)
Hearing impairment	18	10	1.39 (1.13–1.72)
Depression	29	13	1.48 (1.23–1.77)
Body mass index			
<25 kg/m^2	27	32	Reference
25–29.9 kg/m^2	37	42	1.00 (0.80–1.26)
≥30 kg/m^2	35	26	1.28 (1.04–1.58)
Current smoker	35	21	1.33 (1.08–1.64)
Infrequent physical activity	67	59	
Uninsured	20	10	
Fair or poor safety of neighborhood	18	8	

IADL = instrumental activity of daily living.
* Results weighted to generate nationally representative estimates and account for the complex survey design. Final column shows only the variables retained on backward elimination, except for sex and race/ethnicity, which were forced into the final model. All variables assessed at study enrollment.
† Percentages may not sum to 100% due to rounding.
‡ Subhazard ratios adjusted for all listed variables and calculated by using competing risks regression to account for the competing risk for death.