Journal of Gerontology: MEDICAL SCIENCES
2000, Vol. 55A, No. 1, M43–M52

Preclinical Mobility Disability Predicts Incident Mobility Disability in Older Women

Linda P. Fried,[1,2] Karen Bandeen-Roche,[3] Paulo H. M. Chaves,[2,4] and Brent A. Johnson[3]

[1]Department of Medicine, The Johns Hopkins University School of Medicine and [2]Department of Epidemiology and [3]Department of Biostatistics, The Johns Hopkins University School of Hygiene and Public Health, Baltimore, Maryland.
[4]Universidade do Estado do Rio de Janeiro, Brazil.

Background. Physical disability and dependency are serious, and frequent, adverse health outcomes associated with aging and resulting from chronic disease. Reasoning has suggested that there might be a preclinical, intermediate phase of disablement which might develop in parallel with progression of underlying disease and precede and predict disability. Definition of this stage could provide a basis for screening and early intervention to prevent disability. The objective of this study was to determine preclinical functional predictors of incident mobility difficulty and provide evidence for a preclinical stage of disability.

Methods. A prospective, population-based cohort study was carried out in Baltimore, Maryland, with two evaluations 18 months apart. The participants were 436 community-dwelling women, 70–80 years of age at baseline, not cognitively impaired, and reporting difficulty in no areas, or only one area, of physical function (primarily mobility), who were participating in the Women's Health and Aging Study II. Participants were recruited from a population-based, age-stratified random sample. Incident mobility disability was studied in the subset without such disability at baseline. The main outcome measure was self-reported incident difficulty walking ½ mile or climbing up 10 steps.

Results. At baseline, 69.3% of the cohort reported no difficulty with mobility. After 18 months, 16.0 and 11.7% of this group reported incident difficulty walking ½ mile or climbing up 10 steps, respectively. Those reporting baseline task modification due to underlying health problems, our measure of preclinical disability, were at three- to fourfold higher odds of progressing to difficulty than were those without such modification. In multivariate logistic regression analyses, this self-report measure, task modification without difficulty, and objective measures of performance were independently and jointly predictive of incident mobility difficulty. Specifically, for incident difficulty walking ½ mile, self-reported task modification odds ratio (OR) = 3.67, walking speed (.5 m/s difference) OR = 2.16; for incident difficulty climbing up 10 stairs, OR for task modification = 3.84, for stair climb speed (⅓ step/s difference) = 2.08 (95% CI did not include 1 for any). Covariates, age, living alone, number of chronic diseases, depression score, knee strength, and balance by functional reach, were not significant predictors in either model.

Conclusions. Two indicators of functional changes in older women without mobility difficulty, self-report of modification of method of doing a task in the absence of difficulty and performance measures, are independent and strong predictors of risk of incident mobility disability. The self-report measure provides substantial strength in predicting risk of incident disability across the full range of performance, and may identify a vulnerable point at which other risk factors act to cause transitions to disability. Together, the preclinical indicators identify a subset of high-functioning older women who are at high risk of mobility disability, and provide a potential basis for screening for disability risk and targeting interventions to prevent mobility disability.

THE Institute of Medicine states that prevention of physical disability is a top priority for aging research (1). The primacy of this goal reflects the frequency and serious import of disability as people age, with 40% of people 65 and older limited in their ability to carry on their daily activities and over 22% of women and 15% of men dependent (2). Disability usually occurs first in mobility, and mobility difficulty predicts onset of disability in tasks essential to living independently in the community (e.g., shopping, meal preparation) and caring for oneself (e.g., bathing, dressing) (3). At least half of endstage disability in self-care tasks results from such a progressive decline in function, whereas the remainder may occur catastrophically due to a medical event (e.g., stroke) (4). Task difficulty predicts dependency (5), and both are associated with high rates of institutionalization and mortality.

These findings define a pathway of progressive disablement once mobility difficulty begins. In contrast, the pathway to the initiation of disability is not well understood, although intervening during early decline is likely an important opportunity for prevention (1). Disability results from chronic diseases and aging-specific biologic changes, modified by numerous other factors (6). However, because only a fraction of people with a given disease become disabled, defining the intermediate stages and transitional points between the two is critical to understanding who will become disabled, and why.

There are few data to define this pathway of progression to disability among those who develop it chronically. It is possible that at a threshold severity of chronic disease(s), people precipitously develop difficulty functioning without any precursors. More likely, a progressive but unnoted decline in function occurs as a result of disease progression. This early decline would be a preclinical stage of disability (7,8), analogous to the preclinical stage of disease which precedes and predicts onset of clinically manifested disease. In the case of cardiovascular diseases, preclinical disease is among the strongest predictors of the older adults who will develop clinical disease (9). If preclin-

ical disability could be, similarly, determined to predict onset of disability, it would provide insight into a critical point of transition to risk for disability and define a subset at high risk, as well as filling in the undefined component of the natural history of disability in older adults (Figure 1).

Clinically, once individuals are disabled, it is often difficult to fully remove the functional decrements; therefore, rehabilitation focuses heavily on maximizing compensation and preventing further decline. This clinical experience supports the perception that those at risk need to be identified earlier for implementation of effective prevention. To address this, Guralnik and colleagues have shown that objective measures of walking speed and balance predict dependency in older adults (10). However, because the at-risk population in that study included people both with and without difficulty initially, it is not yet known whether these measures identify *preclinical* risk among those *without* any difficulty initially. Additionally, whether self-report measures (8) could more simply and inexpensively identify those at risk of disability than would performance measures is not known.

The goal of this study was to determine whether potential self-report and performance measures of preclinical disability predict incident mobility disability in high-functioning older women. Older women constitute the vast majority of disabled older adults, and would be, potentially, the major beneficiaries of interventions to prevent such disability. Loss of mobility function has been shown to be the first area in which most older adults become disabled. This report provides the first prospective evaluation of whether self-report or performance measures of preclinical disability identify persons at risk of incident mobility disability.

Methods

In this study we tested the hypothesis that among high functioning older women, there is a definable subset with preclinical functional loss who are at high risk of developing mobility disability over an 18-month period. This question was evaluated in the Women's Health and Aging Study II (WHAS II), a population-based study of 436 women who, at time of recruitment, were 70–79 years of age and among the highest functioning two thirds of community-dwelling women in this age group. The cohort was designed to be a companion study to the Women's Health and Aging I, a study of the one third most disabled older women residing in the community. Both cohorts were sampled from the same sampling frame, the Health Care Financing Administration's Medicare eligibility lists for 12 zip code areas in eastern Baltimore City and County. For WHAS II, age-stratified (70–74, 75–79) random samples were drawn by Westat, Inc., in three serial replicates from HCFA lists as of 3/1/94, 10/1/94, and 5/1/95, with enrichment at each replicate for women aging into eligibility or moving into the sampling frame. The screening and recruitment process is detailed in Figure 2. Eligibility criteria for screening were: (i) able to be contacted by telephone; and (ii) sufficient hearing and English language proficiency to be interviewed. To determine full study eligibility, those sampled were screened with an interviewer-

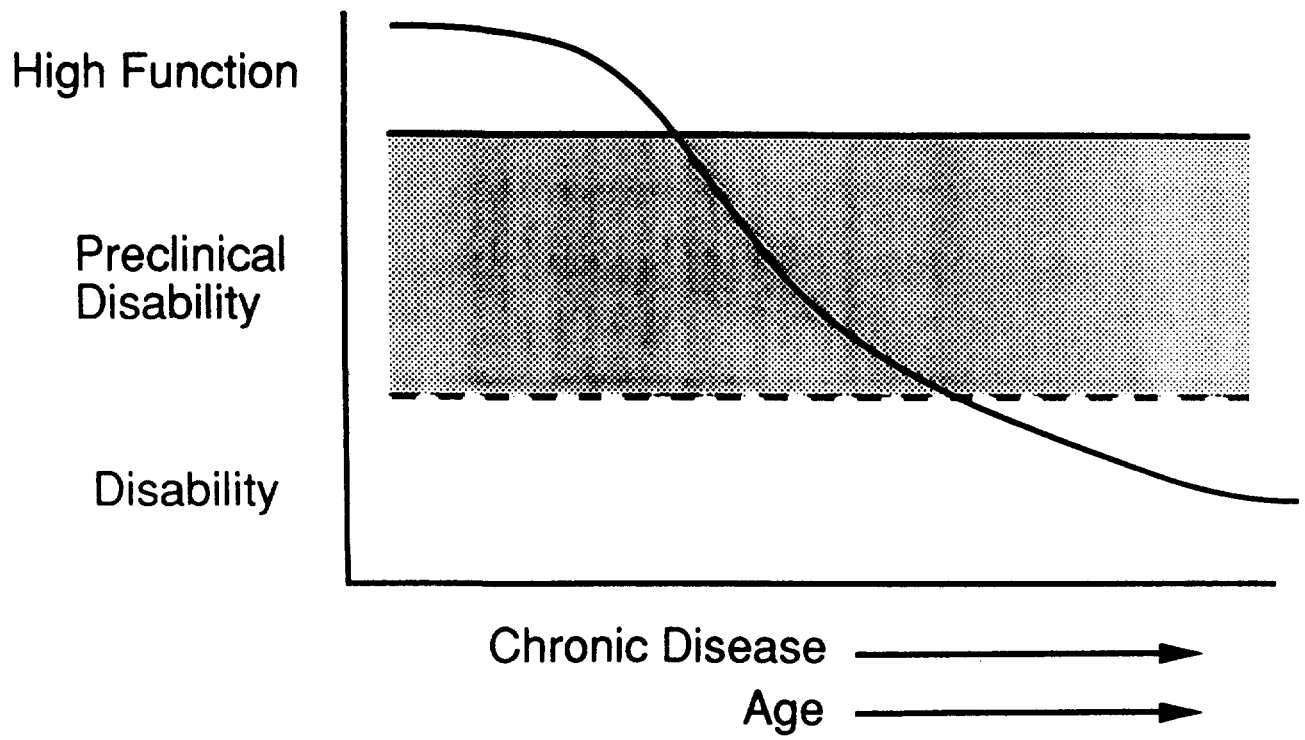

Figure 1. Conceptual representation of decline in physical function with age or as a function of chronic disease, and the potential intermediate stage of preclinical disability through which individuals may pass during a chronic progression to disablement.

administered questionnaire. For one third, screening was performed by Westat in person, in the home. Due to fiscal constraints, the remainder of screening was performed via telephone contact. National data are that telephone screening results in response rates ranging from 41–79%, with an average of 62% (11). Our overall rates for screening were 64%.

Among those screened, eligibility for participation in the full study was determined based on the following criteria: (i) self-report of difficulty in no tasks (of 15 assessed) or in only 1 domain of physical function among the following 4: mobility tasks, upper extremity tasks, household management tasks, and self-care tasks (12,13). This criteria had been shown to identify the higher functioning two thirds of older women (13); (ii) intact cognitive function, by Mini-Mental State Examination (14) scores of ≥24 on in-person interview, or scores of 80% on telephone administration of an abbreviated Mini-Mental screen, which excluded those questions which must be completed in person or were irrelevant (e.g., identification of the examination center location); and (iii) ability to participate in a 1-day clinic examination in Baltimore city. Thus, we sought high-functioning women whose cognitive function was sufficient to reveal the preclinical stage of disability through which high-functioning people may pass. Among eligible women, 49.5% agreed to participate in the extensive examination at the Johns Hopkins Hospital and to prospective follow-up. Those agreeing to participate were, notably, more highly educated and had more diseases than those who refused to participate, but did not differ significantly in disability characteristics (see Table 1).

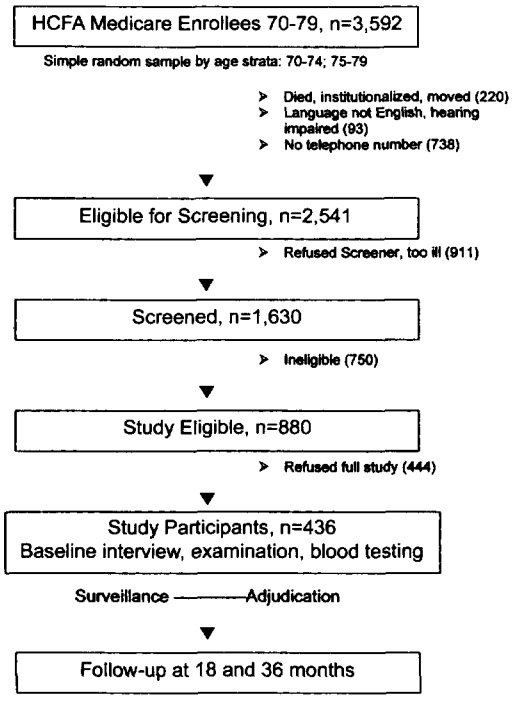

Figure 2. Sampling and recruitment design and results for the Women's Health and Aging Study II. Those recruited were selected to be among the two thirds least disabled, or most highly functioning, women living in the community who were 70–79 years of age at time of sampling.

Participants signed an approved informed consent and then received a 5–6-hour examination at baseline and a 4–5-hour examination 18 months later. Examinations at each time point were performed in the Johns Hopkins Functional Status Laboratory and included standardized questionnaires ascertaining demographic characteristics, self-report of physician diagnosis of any of 11 chronic diseases (arthritis, high blood pressure, myocardial infarction, angina, congestive heart failure, diabetes, cancer, lung disease, stroke, hip fracture, and Parkinson's disease) and visual and hearing impairment. Disease diagnoses were validated with standardized medical record review and then clinical adjudication using state-of-the-art disease algorithms (13). Mini-Mental State Exam (14) and the Geriatric Depression Scale (depressive symptomatology assessed on scale of 0–30) (15) were administered. Objective measurement of other known risk factors for disability was conducted using standardized protocols by trained technicians, and included: (i) maximal isometric strength of the knee extensor muscles, measured by hand-held dynamometer (Nicholas Manual Muscle tester; Model BK-7454, Fred Sammons, Inc., Burr Ridge, IL), with the participant seated on a hard chair and hips and knees flexed at 90 degrees. With the dynamometer placed proximal to the femoral condyles at the distal thigh, strength was measured as the peak force the examiner had to apply to break the isometric contraction. Interrater reliability of strength tests was assessed in a pilot study of 22 women; the intraclass correlation coefficient was .91 for knee extension (16). (ii) Dynamic balance was assessed by the Functional Reach test. This evaluates maximal distance (cm) able to lean forward, from an initial upright stance with the right arm at right angles to the torso and at the height of the acromion process (17).

Physical disability was ascertained by self-report of *difficulty (DIF)* performing any of 27 tasks of daily life, including mobility, upper extremity, household management, and basic self-care tasks, using the National Health Interview Survey standardized questions (18). Then, to identify early functional decrements (8), we asked each participant, regardless of whether they indicated difficulty, whether they had modified the method or had changed the frequency with which they performed the task as a result of underlying health problems. In a separate cross-sectional study, this self-report measure was shown to be associated with levels of objectively measured function that were intermediate between those with difficulty and those with neither difficulty nor this modification (8). Based on this work, persons reporting such *modification but no difficulty* in a task were characterized as, potentially, being in a stage of preclinical decline in function in that task, or preclinical disability (labeled in this article as the Modification or "MOD" group). Finally, those who reported no difficulty in a task and no such modification were considered to be a "high function" group (labeled as "HF"). Both task modification and difficulty have been shown to be reliably identified by the individual (8,19).

For functional performance, we objectively measured time to walk 4 m and time to climb up and down a flight of 14 stairs (both to 0.1 s, performed at usual pace), administered in standardized manner from a defined starting point to finishing line by trained physical therapists (13). Test-retest reliability was high, with assessments of walking speed as much as 20 weeks apart having correlations above 0.6 (20).

The outcome measure for this study was new onset of diffi-

culty (5,18) in two mobility tasks, walking ½ mile or climbing up 10 steps, by self-report at the 18-month follow-up evaluation. These two measures were selected a priori because they were the two relatively pure mobility measures with the highest rates of incident task modification and incident task difficulty at the follow-up evaluation. These rates were, respectively, 12.6 and 33% for heavy housework (which is not a pure mobility measure because it involves a number of actions besides mobility, such as pushing, lifting, bending, stooping); 11.9 and 31.4% for walking ½ mile; 7.4 and 26.3% for climbing up 10 steps; 6.9 and 19.4% for lifting and carrying 10 pounds; 6.4 and 10% for bed transfer; and 3.9 and 23.5% for walking ¼ mile (data not shown). The choice of the measures with the highest incidence rates suggests that we have chosen the mobility tasks that are first affected in the onset of disablement, and provide the greatest power in assessing associations.

Baseline frequencies of demographic and health characteristics and of self-reported functioning (HF, MOD, DIF) in each task were assessed. As functional changes (MOD or DIF) were primarily reported in mobility tasks (Table 1), subsequent analyses were limited to these tasks. We compared disease burden between the HF, MOD, and DIF groups. For each task, mean number of diseases (and standard error of mean) was determined by category of self-reported function, and 95% confidence intervals were calculated. Similar analyses were performed for the proportion with fair or poor self-reported health (other categories: excellent, very good, good).

To describe the natural history of functional change in this population, we determined transitions in function from baseline to 18 months later, both for self-reported function and observed performance. (i) Self-reports of HF, MOD, or DIF at baseline and 18 months were cross-tabulated for two of the mobility tasks in which self-report of MOD or DIF was most common at baseline: walking ½ mile and climbing up 10 steps. (ii) To describe transitions in performance, we regressed the follow-up – baseline change in walking speed on the (centered) average of a woman's baseline and follow-up walking speeds, using simple linear regression models. These models measure population average decline in speed (intercept), as well as the additional decline per 1 m/s increase in average speed (slope).

We also evaluated whether self-report changed in parallel with performance measures both for cross-validation and potential insights into relative sensitivity of the two measures. Transitions in self-reported function in walking ½ mile from baseline to the 18-month follow-up were coded in nine possible patterns (e.g., those reporting task modification at baseline and then difficulty at follow-up, or MOD-to-DIF); because of low frequencies, we merged the difficulty-to-high functioning and difficulty-to-task modification transitions. Mean speed changes for each transition were computed relative to those who had difficulty at both time points (DIF-to-DIF) as the reference, regressing change in walking speed on transitions in self-reported function, as well as baseline speed. To assess change in performance versus self-report changes, while accounting for baseline performance, we computed partial residuals from our fitted models (21). These subtracted the predicted contribution to change of one's baseline walking speed from one's observed change in speed.

To determine predictors of incident mobility difficulty, we evaluated the subset who reported no mobility difficulty at baseline. Separate multiple logistic regression models evaluated the independent associations of predictor variables with incident self-reported difficulty after 18 months of follow-up in (A) walking ½ mile and (B) climbing up a flight of stairs. Predictor variables entered into the model as potential indicators of preclinical disability were: self-reported MOD (compared with HF in the same task) and walking or stair-climbing speed (inverse of time to walk 4 m or climb a flight of stairs), respectively. Also entered were covariates previously shown to be risk factors for disability: age (70–74 vs 75–80), education (≤11th grade vs 12th grade or high school graduate vs >12 years of education), living alone (versus with others), number of chronic diseases (validated), depression score, knee strength, and balance (cm by functional reach). Separate models adjusted knee strength by weight to evaluate the independent role of knee power. Odds ratios for the independent association of each predictor with incident mobility difficulty were calculated from the beta coefficients. Models were fit with and without a task modification-by-performance speed interaction; the interaction terms were not significant. Similar models were run without the two preclinical disability indicators to evaluate the strength of association of other covariates in predicting disability.

To validate observations from these models, we plotted our models' predictions of incident mobility difficulty as a function of performance speed and self-report of task modification, then compared the models' incidence estimates with "crude" incidence estimates. Fitted probabilities were determined from multiple logistic regression models (above), fixing numeric predictors at average values and household status as "not living alone." "Crude" estimates were obtained by smoothing the difficulty report data over walking speeds, separately by HF and MOD status, using the "ksmooth" function in the S-PLUS statistical programming language (22) with normal kernel and bandwidth =.8 chosen by eye to capture variation in risk by speed while eliminating trivial fluctuations (23). This procedure computes a crude incidence estimate (number of women reporting difficulty over the total number of women) within a small range of walking speeds, for each of many small ranges covering the whole range of walking speeds. In doing this, we found that risk of incident stair-climbing difficulty was well-described by our model. However, the assumption of a single odds ratio for risk with walking speed did not agree with the observed data. To address this, we refit our walking model with a linear spline (24), which joined one risk relationship among women with the top 95% of speeds and another for women with the lowest 5% of speeds. Models using other speed percentile cut points were qualitatively similar.

Results

Baseline Characteristics

Characteristics of study participants are shown in Table 1, along with the characteristics of those who were eligible but refused to participate. The study population was 70 to 80 years old at time of examination. Fifty-nine percent of the recruited cohort reported no difficulty in any of 15 tasks of daily living at baseline, whereas 31% reported difficulty in mobility tasks, 9% difficulty in upper extremity tasks, and 0.5% and 0.7% reported difficulty in household maintenance (e.g., shopping) or self-care tasks, respectively.

To assess cross-sectional face and criterion validity of the self-report measure of preclinical disability, the frequency of this self-report in the study population and its association with health status were assessed. Among those reporting no difficulty in a task, task modification (MOD) was identified at baseline with frequencies comparable to reports of difficulty with the same task (DIF) (Table 2), consistent with prior findings in a separate population (8). The mean number of diseases reported in both the MOD and the DIF groups was greater than in the HF group (Table 3). In separate analyses, 7, 18, and 20% of the HF, MOD, and DIF groups, respectively (for walking ½ mile), reported fair or poor health (data not shown). Thus, report of MOD identified a subset of those with no difficulty walking who had a worse health status than others with no difficulty in a task, the HF group.

Table 1. Women's Health and Aging Study II: Baseline Characteristics of Telephone Screenees Who (a) Agreed or (b) Refused to Participate in Full Study

	Study Participants ($N = 436$) Percent*	Study Refusers ($N = 444$) Percent*	p
Age (years)			
70–74	59.2	55.2	.43
75–80	40.8	44.8	
Race			
White	81.0	79.1	.57
African American	18.8	20.5	
Others	0.2	0.4	
Education (years)			
≤8	13.5	25.7	<.0001
9–11	14.9	25.9	
12	30.7	28.6	
>12	40.8	19.6	
Married	38.1	32.2	.08
Number of Diseases (of 11†)			
0	13.5	18.5	.13
1	36.9	33.8	
≥2	49.5	47.8	
Visual Impairment (self-report)	81.2	76.4	.09
Hearing Impairment (self-report)	16.7	11.7	.04
Difficulty in Functional Domains			
Number of functional domains with reported difficulty			
0	58.7	61.9	.36
1	41.3	38.1	
Self-reported difficulty in ≥1 tasks of			
Mobility	31.2	28.2	.36
Upper extremity	8.9	7.6	.57
Household management tasks	0.5	1.1	—
Basic self-care tasks	0.7	1.1	—
Objective Performance Measures	Mean	*SE*	Range
Walking speed (m/s)	0.999	0.013	(0.42,2.11)
Chair climbing speed (steps/s)	1.851	0.022	(0.30,5.6)
Knee strength‡	0.271	0.005	(0.04,0.55)
Depression score (GDS)	10.417	0.120	(0,23)
Functional reach (cm)	29.406	0.274	(7.33,54.73)

*Unweighted; weighted proportions similar.

†History of physician diagnosis of arthritis, high blood pressure, myocardial infarction, angina, congestive heart failure, diabetes, cancer, lung disease, stroke, hip fracture, or Parkinsons's disease.

‡Knee strength is adjusted for weight.

Transitions in Function From Baseline to Follow-up

We next evaluated transitions in mobility function in the population over 18 months, and whether transitions were greater in the preclinical MOD group than the HF group. Of those reporting at baseline that they had modified their usual method of walking ½ mile or climbing up 10 steps due to underlying health problems ("Task Modification"), 31.4% and 26.3%, respectively, reported new difficulty in these tasks 18 months later, compared to 11.9% and 7.4%, respectively, of those who were "High Function" at baseline (Table 4); for walking ½ mile, OR = 3.18, 95% confidence interval (CI) = 1.66,6.02; for climbing up 10 steps, OR = 3.98, 95% CI = 1.99,7.92. Those with

Table 2. Baseline Self-Reported Function in Tasks Dependent, to Some Degree, on Mobility—Non-/Mildly Disabled Women Aged 70–80 Years ($N = 436$)

	Baseline Self-Report of Function		
	No Difficulty		Difficulty/ Dependency
	High Function* (%)	Modification (%)	Disabled (%)
Walk ½ mile	65.9	16.6	17.5
Walk ¼ mile	84.9	8.7	6.4
Climb up 10 steps	66.3	19.1	14.7
Heavy housework	61.0	17.3	21.7
Lifting and carrying 10 lbs	81.6	7.7	10.7
Transfer from bed	84.7	6.9	8.3

*No modification.

Table 3. Association of Number of Diseases* With Self-Reported Function

	Number of Diseases		
	No Difficulty		Difficulty/ Dependency
Baseline Self-Report of Function in Tasks	High Function†	Task Modification	Disabled
Walk ½ mile	1.67 (0.07)	2.21 (0.14)‡	2.31 (0.16)
Walk ¼ mile	1.80 (0.06)	2.30 (0.22)‡	2.41 (0.26)
Climb up 10 steps	1.76 (0.07)	2.21 (0.14)‡	1.94 (0.15)
Heavy housework	1.74 (0.07)	2.20 (0.16)‡	2.06 (0.13)
Lifting and carrying 10 lbs	1.84 (0.06)	2.00 (0.23)	2.11 (0.19)
Transfer from bed	1.83 (0.06)	2.13 (0.22)	2.19 (0.21)

Note. Data are mean (*SE* of mean).

*Out of 11 diseases.

†No modification.

‡95% confidence interval for difference between High Function and Task Modification does not include 0. Comparisons not flagged were not significantly different, including tests for difference between Task Modification and Disabled.

"Difficulty" or in the High Function group at baseline also reported change over 18 months, but to lesser degrees.

We also examined transitions in walking speeds from baseline to the 18-month follow-up. Baseline speeds ranged from 0.5 to 2.1 m/s (distributions displayed on bottom of Figure 3). There was a clear trend toward slower speeds at follow-up; the mean decline was .07 m/s (95% CI = .04,.10). Moreover, there was a tendency for those who were faster at baseline to decline more severely (estimated .23 m/s additional decline per 1 m/s increase in average baseline speed, CI = .11,.35) (data not shown). Thus, there was overall change in function by both self-report and performance over the 18-month evaluation period. The major declines in walking speeds were among the groups (a) transitioning from preclinical disability (MOD) to disability (DIF) and (b) remaining disabled (DIF to DIF); these showed declines in speed over time, and they were significantly larger than for the high functioning groups ($p < .05$) (data not shown).

Prediction of Disability

We sought, centrally, to determine whether either hypothesized indicator of preclinical disability (self-report of task modification and performance-based measures of function) independently predicted incident difficulty in mobility. For this we evaluated the subsets of 331 and 350 women, respectively, who reported no difficulty in walking ½ mile or climbing up 10 steps at baseline (from Table 4). The results of two multiple logistic regression models testing this question are shown in Table 5. The two preclinical disability measures were each independently statistically significant and predictive of incident mobility difficulty, adjusting for other risk factors. Specifically, those who reported Task Modification were at 3.8- and 3.9-fold increased risk of developing disability in (A) walking ½ mile and (B) climbing up 10 stairs, respectively, after 18 months, compared to the High Function group. Walking speed and stair-climb speed were also independently predictive of difficulty in the two tasks (odds ratios = 2.0 and 2.1, respectively, for .5-m/s decreased walking speed and one-third step per second decreased stair climbing speed; these cut-points represented the interquartile ranges for speed, thus differentiating the middle half of the cohort). Each of these associations was statistically significant. Associations of other known risk factors with incident difficulty were weak and either borderline or not statistically significant. This latter finding could not be explained by a lack of power; the odds ratios for these covariates were small, with the exception of living alone. The associations of covariates with incident difficulty changed little in separate models run without the preclinical disability indicators (data not shown).

Finally, we evaluated the validity of these observations by plotting each model's predictions of incidence as a function of walking speed and self-report of task modification. Incident stair climbing difficulty was well described by the model reported in the previous paragraph. Our walking model was better fit, however, with a linear "spline," resulting in walking speed, as well as self-report of task modification, retaining statistical significance (Wald [23] chi-square test for significance of the speed spline = 11.98 on two degrees of freedom; odds ratio for MOD versus HF = 4.0 with 95% CI = 1.98,8.06). Figure 3 illustrates this final, refitted model, and, in so doing, highlights the added value for risk prediction of discriminating MOD from HF. In interpreting this figure, notice that the middle 90% of the walking speeds are 0.67–1.50 for HF, 0.65–1.49 for MOD, and 0.57–1.38 for DIFF. The MOD group had significantly higher probability of progressing to disability compared to the HF group at all walking speeds except the slowest, with remarkably uniform difference in incidence between the two groups up to about the 95th percentile of walking speed (1.50 and 1.49, respectively). Those with the fastest walking speeds were still at risk if they reported preclinical changes in function (MOD). At the slowest walking speeds, the risk of incident difficulty increased substantially. Also, it can be seen that the slowest 5% (far left side of Figure 3) has a sharp increase in probability of incident disability, suggestive of a threshold effect. However, the data in this region were too sparse in this initially high-functioning population to reliably determine MOD and HF differences with precision and so the threshold effect should be taken qualitatively rather than quantitatively. On average, prediction of disability based on walking speed was substantially enhanced along virtually the whole range of walking speeds by differentiating those who reported task modification from those who reported no modification, among those with no difficulty. Interestingly, there was no statistical interaction between self-report of task modification and either walking or

Table 4. Transitions in Function Over 18 Months—Women's Health and Aging Study II

	Self-Reported Function at 18 Months					
	Walking ½ Mile†			Climbing Up 10 Steps*		
Baseline Function	High Function††	Task Modification*	Difficulty	High Function††	Task Modification*	Difficulty
High Function†	81.6% (213)	6.5% (17)	11.9% (31)	81.1% (219)	11.5% (31)	7.4% (20)
Task Modification‡	44.3% (31)	24.3% (17)	31.4% (22)	42.5% (34)	31.3% (25)	26.3% (21)
Difficulty	17.4% (12)	10.1% (7)	72.5% (50)	21.1% (12)	19.3% (11)	59.7% (34)

*n for walking ½ mile = 400; n for climbing 10 steps = 407; missing data are due to loss to mortality (n = 7), loss to follow-up due to relocation or refusal (n = 11), or missing data at either baseline or follow-u p.

†No modification, no difficulty.

‡No difficulty.

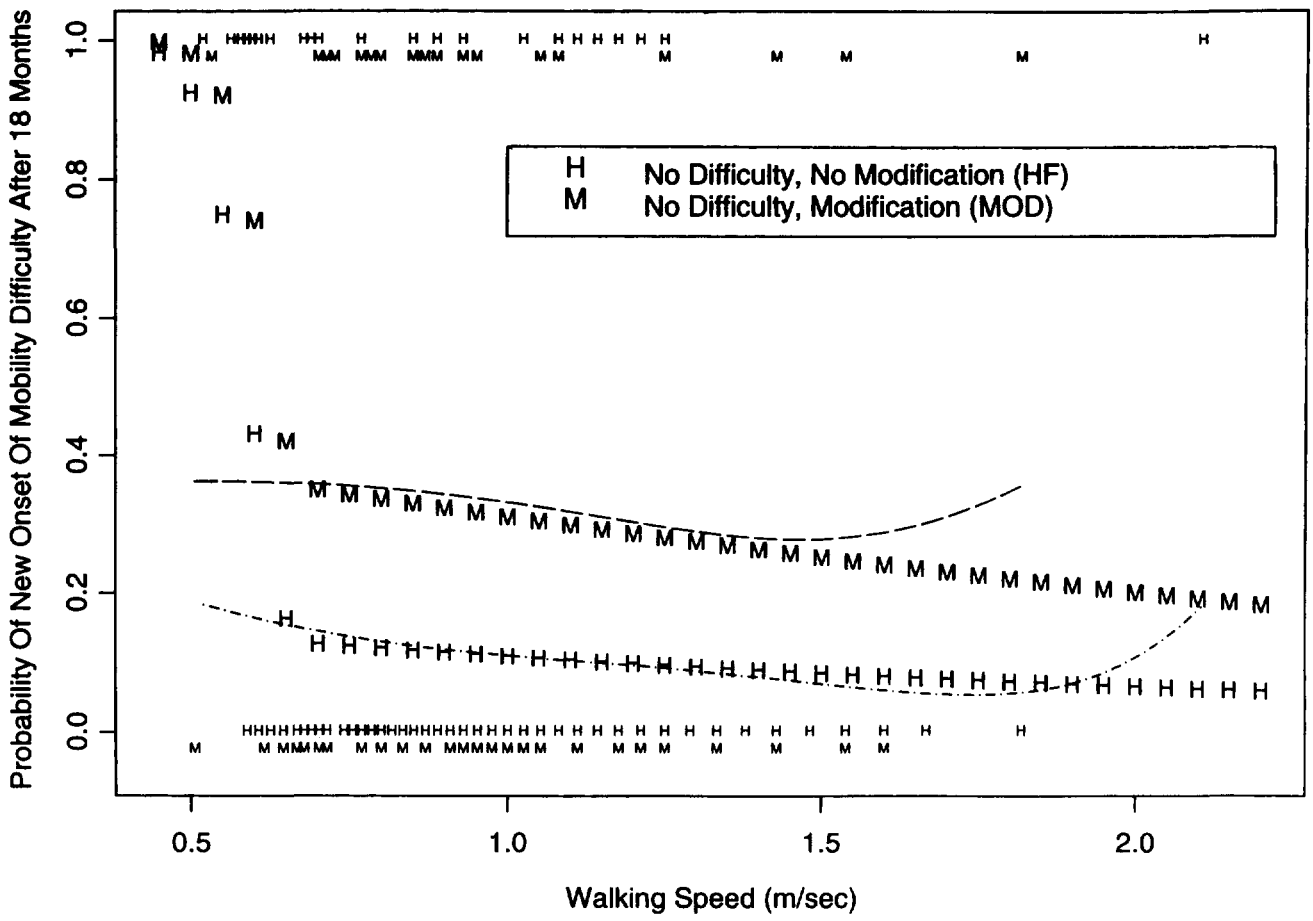

Figure 3. Association of baseline walking speed and self-reported task modification with incident difficulty walking half mile 18 months later. Fitted probabilities (curves labeled with large "H" and "M" for High Function and Task Modification groups, respectively) were determined from multiple logistic regression models as described in Methods, fixing household status as "living alone" and all other model covariates other than the preclinical disability measures at average values. Small "H" and "M" at top and bottom of the figure denote the actual report of difficulty at 18 months (0 = no, 1 = yes) among women who reported no difficulty at baseline. Dashed and dot-dash lines are "crude" incidence estimates as smoothed from the actual data, as described in Methods. The inclusion of a linear "spline" in the regression model at the slowest 95th percentile point in walking speed permits displaying the differences in probabilities for the slowest 5% versus the remaining group. With this approach, it can be seen that the slowest 5% (far left side of figure) has a sharp increase in probability of incident disability, suggestive of a threshold effect.

stair climbing speed, regardless of modeling approach. This is supported by Figure 3. The two types of preclinical disability measures provide independent information in predicting future mobility disability.

Discussion

The results from this study confirm prior reports that preclinical declines in function can be identified by self-report (8) and objective performance (10) measures, and provide the first prospective evidence that these measures identify a subset at high risk of developing difficulty in mobility tasks in the near future. Both the self-report and performance indicators of preclinical disability contribute independent information as to who is at risk, and jointly provide substantially enhanced characterization of the probability of onset of new disability in mobility over the short term. These findings provide the first evidence for the predictive validity of self-reported preclinical disability, thus offering methodologic support for the meaningfulness of this measure. Clinically, this information can provide a new basis for identifying those at risk of mobility difficulty. Having methods to identify those at risk early in the course of functional decline could provide a basis for early screening and more effective interventions to prevent disability and dependency in older adults.

Almost half of the high-functioning women in this study population who became disabled in mobility over 18 months initially described preclinical disability in mobility tasks (Table 4): from 42 to 51% of the study population who developed difficulty were in this preclinical stage 18 months before. This stage appears to be one, therefore, that many pass through—although not all. It is also a stage that is more transitional than are the High Function or Difficulty groups, although both groups reported transitions over 18 months. Individuals in this preclinical stage of disability were identified by report of modification of their method of performing mobility tasks so as to compensate for the impact of underlying health changes, while

Table 5. Prediction of Incident Disability in Mobility After 18 Months—Women's Health and Aging Study II

	Risk of Difficulty After 18 Months in			
	Model A—Walking ½ Mile*		Model B—Climbing up 10 Stairs*	
Baseline Characteristics	OR	95% CI	OR	95% CI
Task modification, but no difficulty in tasks†	3.77	1.91,7.47	3.86	1.83,8.17
Walking speed (m/s)‡	2.04	1.02,4.09	—	—
Stair climb speed (step/s)‡	—	—	2.05	1.37,3.06
Age	1.27	0.69,2.35	0.96	0.48,1.94
Education	0.85	0.56,1.29	0.92	0.57,1.47
Living alone	0.72	0.38,1.39	0.53	0.25,1.11
Number of chronic diseases§	1.03	0.78,1.35	1.00	0.74,1.35
Depression score	1.10	0.97,1.25	0.99	0.84,1.16
Knee strength (per kg)¶	1.05	0.99,1.11	1.00	0.93,1.07
Balance: functional reach (per cm)	1.02	0.96,1.08	1.02	0.95,1.09

*Multivariate logistic regression analyses: Model A, with difficulty at 18 months walking ½ mile as outcome measure, $n = 331$; Model B, with difficulty at 18 months climbing 10 stairs, $n = 350$.

†Compared with no difficulty, no modification group.

‡For walking speed, differential risk for women who differ in speed by 0.5 m/s; for climbing 10 stairs, differential risk for women who differ in speed by .3 step/s. These units correspond to the interquartile ranges for speed, thus differentiating the middle half of the cohort. Stair climb speed not entered into model for walking ½ mile; walking speed not entered into model for climbing up 10 stairs.

§Risk associated with each additional disease, out of 11 diseases.

¶Average of best scores, right and left legs.

having no difficulty with the task(s). We hypothesize that these modifications may well successfully minimize the effects of impairments on function and thus slow decline or maintain function—in the short run—so that no difficulty with task performance is perceived. That such compensation is reasonably successful is suggested by the similar number of diseases, but difference in self-report of function, between the Task Modification and Difficulty groups.

The report of preclinical disability identified a vulnerable subset of older women who are in a highly transitional stage and at almost fourfold increased risk of mobility disability, compared to those reporting no difficulty and no compensations. Subsets in such rapid transition may represent an optimal target group for intervention to prevent disability, given that they are a high risk group and may be particularly responsive to altered risk factors. The biologic and environmental bases for such change remain to be defined, in order to develop appropriate interventions. However, these data suggest that maximizing effective compensations in the nondisabled population may prove useful in disability prevention. Several approaches could be considered. Those who were reporting preclinical changes at baseline and then progressed to mobility difficulty over 18 months may have had less effective compensations than those who remained stable in their function. Alternatively, progression of disease could have overwhelmed compensations in place. Attention should be focused on this question, as well as on those who may not be implementing such compensations but might benefit from them. Perhaps those in the High Function group who developed incident mobility difficulty were in that latter category. Alternatively, they could have had a catastrophic change in health status that precluded compensation. This remains to be determined. Those who decline may already be utilizing their reserve capabilities and therefore have little available to prevent progression in the face of other decrements. Perhaps the transition to disability occurs when additional declines in health overwhelm the compensations being employed. If so, clinical attention to those in the task modification group to minimize progression of disease severity or onset of new health problems might prove an effective strategy for prevention of frank difficulty in tasks of daily life. Additionally, understanding why a large proportion of this group reports improvement will provide further insight into opportunities for prevention.

The potential limitations of this study are, primarily, related to the generalizability of its findings beyond populations who match the characteristics of those in the study. Because we were primarily dependent on telephone screening for recruitment of the cohort, recruitment rates were substantially lower than can be achieved by in-person, in-home recruitment, resulting in a study population that is not as representative as the latter would provide. Clearly, the study participants recruited were more highly educated than those who refused. To account, to the degree possible, for such differences among screenees, analyses in this study were adjusted for education. To explore how the recruited cohort references to the national population of women 70–79 years of age, we contrasted them with women in this age group evaluated in the 1994 U.S. National Health Interview Survey. The age distribution of those recruited in this study is virtually identical to that in the NHIS. Educational level distributions in the NHIS population were similar to that of those recruited for this study at the low end, but there was a lower proportion of highly educated in the NHIS group; specifically: 0–8 years, 16.9%; 9–11 years, 15.1%; 12 years, 41.5%; and >12 years, 25.7% in NHIS (compare with Table 1). The most notable differences between our cohort and the national sample are that the NHIS cohort had less disease and disability: 38.8% reported no diseases and 75.4% reported no difficulty in the 15 tasks screened for in this study. These differences suggest that this study recruited a cohort that was more highly educated and with more disease and mobility disability than a national sample. The effect of this on our findings could be (a) to have a more diseased MOD group with greater rates of transition, or (b) to include in the HF group women with more chronic disease than would be found in a national sample, potentially making our estimates of risk associated with preclinical disability measures (Table 5) conservative. Overall, we suggest that it is highly unlikely that the associations found here are an artifact of refusal characteristics.

Thus, this study assessed a high-functioning population who were better educated and had more chronic disease than the general population of study eligibles. These differences may have led to a higher prevalence of preclinical disability than would be found in the general population. The differences in educational level might, hypothetically, also lead to differences in the proportion who transitioned to difficulty via a preclinical stage and might lead to slower rates of functional decline than in the general population, if effective compensations delay de-

cline. In addition, our estimates of transitions partially include regression to the mean effects due to having screened for high-functioning people. Thus, these results might not be wholly generalizable, especially to lower educated groups. However, given that the analyses in Table 5 found a strong association of preclinical disability with incident disability after adjusting for educational level, this suggests that the predictive association reported here is not spurious and provides meaningful insight into risk in like populations. Overall, the importance of these findings lies in being able to preferentially identify which populations decline in function and do so via a preclinical pathway.

Prior studies have reported that performance on objective measures of function predicts dependency (10,25,26). In this study, both performance measures and self-report measures were independent predictors of incident mobility *difficulty*, an outcome measure of substantial import as a health outcome and which precedes dependency (5). Each preclinical measure provided information about risk even when the other was in an optimal risk range. However, for walking speed, the relationship of performance measures with disability was primarily for those with relatively slow speeds. Because participants in this study tended to have high walking speeds, this interpretation should be considered more qualitative than quantitative. For those with faster or moderate walking speeds, the relationship of speed with incident mobility difficulty was weak. The conclusion from this observation is that walking speed is not a very sensitive indicator of preclinical decline. Stair-climb speed was a more sensitive predictor of incident difficulty climbing stairs than walking speed was of difficulty walking.

The observation that changes in self-reported function from HF to MOD or DIF did not have commensurate significant changes in performance also suggests that the preclinical self-report measure might be more sensitive to very early change in function in a high-functioning cohort than are performance measures; this is supported by the spline analysis for walking speed. This finding could also occur if individuals were likely to perform optimally, rather than in their usual manner, during standardized, laboratory-based performance tests.

Notably, the strength of prediction associated with both indicators of preclinical decline in function was substantially greater than that of other known risk factors for disability evaluated in our models. This observation could be a consequence of the characteristics of those willing to be screened and recruited into this study, perhaps overselecting for those with less severe decrements in these risk factors. It does, however, raise questions as to whether the covariate risk factors in Table 5 may become important when a group is already at high risk, i.e., those with preclinical declines in function.

Overall, these findings indicate that there are two types of indicators of preclinical disability, by self-report and performance measures. The self-report measure, in particular, is a compelling predictor of risk of mobility disability in persons with moderate or high levels of performance. Preclinical disability appears to identify a very transitional group which may be more vulnerable to changes in health status than others who are not disabled. These data suggest new avenues for screening for those at high risk of disability, and potential approaches for interventions to prevent disability by preventing worsening of disease and by enhancing compensations in those at risk of developing mobility disability. Given the natural history of chronic, progressive disability, preventing mobility difficulty should decrease the subsequent rates of difficulty and dependency in tasks essential to independent living and self-care.

ACKNOWLEDGMENTS

This work was supported by National Institute on Aging Grant RO1 AG11703-01A1 and by NIH-NCRR, OPD-GCRC grant RR00722. Dr. Bandeen-Roche is a Brookdale National Fellow. Dr. Chaves was supported by the Brazilian Federal Agency for Post-Graduate Education (CAPES). The authors thank Dr. Carla Maffeo and Ms. Donna Davis for data on expected telephone recruitment and comparable national estimates. We thank Drs. Scott Zeger and Joseph Margolick for their critical and constructive review of the manuscript.

Address correspondence to Linda P. Fried, MD, MPH, Professor, Medicine and Epidemiology, 2024 E. Monument Street, Suite 2-600, Baltimore, MD 21205. E-mail: lfried@welch.jhu.edu

REFERENCES

1. Lonergan ET, Krevans JR. Special Report. A national agenda for research on aging. *N Engl J Med.* 1991;324:1825–1828.
2. Guralnik JM, Simonsick EM. Physical disability in older Americans. *J Gerontol.* 1993;48(Special Issue):3–10.
3. Harris T, Kovar MG, Suzman R, et al. Longitudinal study of physical ability in the oldest-old. *Am J Public Health.* 1989;79:698–702.
4. Ferrucci L, Guralnik JM, Simonsick E, et al. Progressive versus catastrophic disability: a longitudinal view of the disablement process. *J Gerontol Med Sci.* 1996;51A:M123–M130.
5. Gill TM, Robinson JT, Tinetti ME. Difficulty and dependence: two components of the disability continuum among community-living older persons. *Ann Int Med.* 1998;128:96–101.
6. Fried LP, Guralnik JM. Disability in older adults: evidence regarding significance, etiology, and risk. *J Am Geriatr Soc.* 1997;45:92–100.
7. Fried LP, Herdman SJ, Kuhn KE, Rubin G, Turano K. Preclinical disability: hypothesis about the bottom of the iceberg. *J Aging Health.* 1991: 3;285–300.
8. Fried LP, Bandeen-Roche K, Williamson JD, et al. Functional decline in older adults: expanding methods of ascertainment. *J Gerontol Med Sci.* 1996;51A:M206–M214.
9. Kuller LH, Shemanski L, Psaty BM, et al. Subclinical disease as an independent risk factor for cardiovascular disease. *Circulation.* 1995:92; 720–726.
10. Guralnik JM, Ferrucci L, Simonsick EM, Salive ME, Wallace RB. Lower-extremity function in persons over the age of 70 years as a predictor of subsequent disability. *N Engl J Med.* 1995;332:556–561.
11. *1997 Proceedings of the American Statistical Association Section on Survey Research Methods*, 707–712.
12. Fried LP, Ettinger WH, Lind B, Newman AB, Gardin J, for the Cardiovascular Health Study (CHS) Collaborative Research Group. Physical disability in older adults: a physiological approach. *J Clin Epidemiol.* 1994; 47:747–760.
13. Fried LP, Kasper JD, Guralnik JM, Simonsick EM. The Women's Health and Aging Study: an introduction. In: *The Women's Health and Aging Study: Health and Social Characteristics of Older Women with Disability.* Guralnik JM, Fried LP, Simonsick EM, Kasper JD, Lafferty ME, eds. NIH Pub. No. 95-4009. Bethesda, MD: National Institutes of Health, National Institute on Aging; 1995:1–8.
14. Folstein MF, Folstein SE, McHugh PR. "Mini-Mental State." A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res.* 197;12:189–198.
15. Norris JT, Gallagher D, Wilson A, Winograd CH. Assessment of depression in geriatric medical outpatients: the validity of two screening measures. *J Am Geriatr Soc.* 1987;35:989–995.
16. Rantanen T, Guralnik JM, Izmirlian G, et al. Association of muscle strength with maximum walking speed in disabled older women. *Am J Phys Med Rehab.* 1998;77:299–305.
17. Duncan PW, Weiner DK, Chandler J, Studenski S. Functional reach: a new clinical measure of balance. *J Gerontol Med Sci.* 1990;45:M192–M197.
18. Fitti JE, Kovar MG. The Supplement on Aging to the 1984 National Health Interview Survey. *Vital & Health Statistics—Series 1: Programs & Collection Procedures.* 1987:1–115.19.

19. Rathouz P, Kasper J, Zeger S, Ferrucci L, Bandeen Roche K, Fried LP. Short-term consistency in self-reported physical functioning among elderly women: The Women's Health and Aging Study. *Am J Epidemiol.* 1998;147:764–773.
20. Ferrucci L, Guralnik JM, Salive ME, et al., for the Women's Health Aging Study Research Group. Effect of age and severity of disability on short term variation in walking speed. *J Clin Epidemiol.* 1996;49:1089–1096.
21. Larsen W, McCleary S. The use of partial residual plots in regression analysis. *Technometrics.* 1972;14:781–790.
22. Statistical Sciences, Inc. *S-PLUS for Windows Users' Manual,* Version 4.0. Seattle: Statistical Sciences; 1997.
23. Smith P. Splines as a useful and convenient statistical tool. *Am Statistician.* 1979;33:57–62.
24. Santner TJ, Duffy DE. *The Statistical Analysis of Discrete Data.* New York: Springer Verlag; 1989:296–298.
25. Gill TM, Robinson JT, Tinetti ME. Predictors of recovery in activities of daily living among disabled older persons living in the community. *J Gen Int Med.* 1997;12:757–762.
26. Gill TM, Williams CS, Mendes de Leon CF, Tinetti ME. The role of change in physical performance in determining risk for dependence in activities of daily living among non-disabled community-living elderly persons. *J Clin Epidemiol.* 1997;50:765–772.

Received January 12, 1999
Accepted July 13, 1999
Decision Editor: William B. Ershler, MD