Effect of Subclinical Status in Functional Limitation and Disability on Adverse Health Outcomes 3 Years Later

Fredric D. Wolinsky, Douglas K. Miller, Elena M. Andresen, Theodore K. Malmstrom, J. Philip Miller, and Thomas R. Miller

Background. This article examines the effect of self-reported, baseline subclinical status (i.e., independent but adaptive performance) for functional limitation and disability on adverse health outcomes.

Methods. Nine hundred ninety-eight African-American men and women aged 49–65 years received in-home evaluations at baseline, and 853 were re-evaluated 3 years later. Baseline subclinical status was ascertained for five lower body tasks and seven activities of daily living (ADLs) and instrumental ADLs (IADLs). Outcomes included difficulty with lower body limitations, ADLs/IADLs, physical performance, physician visits, hospitalization, nursing home placement, and mortality.

Results. The baseline proportion of subclinical status evidence for the five lower body items was 0.33 (standard deviation [SD] = 0.20), and for the seven ADLs/IADLs was 0.20 (SD = 0.30). Significant independent effects of subclinical status for lower body limitations were observed on physician visits and hospitalization. Significant independent effects of subclinical status for ADLs/IADLs were observed on ADLs/IADLs and physician visits.

Conclusions. Subclinical status for functional limitation and disability independently predicts several subsequent adverse health outcomes, although the effects of the latter (ADLs/IADLs) are stronger. Interventions to reduce frailty should focus on self-reported subclinical status as an early warning system.
function and ADL/IADL difficulties. To examine the potential for modification of the subclinical status effects on these outcomes, sensitivity analyses are used to replicate the first set of models within three strata based on the aggregate level of baseline lower body function and ADL/IADL difficulties.

**Methods**

**Sample**

The sampling design of the AAH has been described elsewhere (5,6). The AAH includes 998 African Americans who were born from 1936 through 1950 and who lived in a poor, inner-city area previously studied by the investigative team (8), or the near northwest suburbs. To recruit equal numbers of participants from both strata, unequal sampling proportions were set; therefore, analysis of probability-weighted data is reported. Beyond age, inclusion criteria involved the ability and willingness to sign informed consent, self-reported black or African American race, and Mini-Mental State Examination (MMSE) score ≥ 16 (only 15 participants scored < 20) (9). Baseline evaluations averaged 2.5 hours and occurred in the participant’s home between September 2000 and July 2001. The response rate was 76%. Thirty-six-month follow-up evaluations also occurred in the participant’s home and averaged 2.0 hours. Of the 998 original participants, 853 were successfully reinterviewed at 36 months, and there were 51 deaths. Thus, the reinterview rate for surviving participants was 90%.

**Subclinical Status**

Participants were asked a comprehensive series of standard lower body function, ADL, and IADL questions. If the participant expressed any difficulty or was unable to perform the function or task, she was considered to be limited (or have disability) in that lower body function, ADL, or IADL item. If the participant reported having no difficulty in performing the target function or task, the two follow-on subclinical status questions [method and frequency (1)] were asked. Subclinical status was assessed for five lower body functions (walking one-half mile, climbing steps, stooping/crouching/kneeling, using fingers to grasp or handle, and lifting or carrying something as heavy as 10 pounds) and seven ADLs/IADLs (bathing and showering, dressing, getting in and out of bed and chairs, preparing meals, doing light housework, doing heavy housework, and managing medications). Participants reporting no task difficulty, but who changed the method or decreased the frequency of performing it (or both), were defined as having subclinical status on that item.

Construction of a summary measure across the subclinical status items is a bit complicated because a simple count of the lower body or the ADL/IADL items for which the participant reported subclinical status must be adjusted for the number of status assessments that were made. Therefore, the proportion of assessments for which subclinical status was reported in each of these two domains is used. This proportion is determined by dividing the number of tasks for which the participant reported changing the method or frequency of performance by the number of tasks assessed (of a maximum of five for lower body function and seven for ADLs/IADLs). For example, if a participant reported difficulty for three of the seven ADLs/IADLs and changed the method or frequency of performance for two of the remaining four ADLs/IADLs, the proportion of subclinical status evidence was 0.50.

These proportions are then multiplied by 10, so that the regression coefficients and odds ratios (ORs) reflect the effect associated with a 10% increase in the extent of subclinical status.

**Adverse Outcomes**

Seven adverse outcomes were measured: lower body limitations, difficulty with ADLs/IADLs, physical performance, physician visits, hospitalization, nursing home placement, and mortality. Lower body limitations were measured as the sum of five items (walking one-quarter mile, going up and down one flight of steps, stooping/crouching/kneeling, lifting 10 pounds, and pushing large objects) for which the participant reported difficulty. Similarly, ADLs/IADLs were measured as the sum of seven items (bathing, dressing, getting in and out of a chair, preparing meals, doing light housework, doing heavy housework, and managing medications) for which the participant reported difficulty. Physical performance was measured using the 0–12 Short Physical Performance Battery (SPPB) summary score developed by Guralnik and colleagues (10). The SPPB summary score is based on three components: gait speed (m/s), five repeated chair stands (s), and tandem stand with eyes open (s). Each component is scored from 0 to 4, with 0 indicating that the participant was unable or unwilling to perform, and the four remaining categories reflecting approximate quartiles in the baseline distributions. Physician visits were measured as the self-reported number that occurred in the year prior to baseline and in the year prior to the 36-month follow-up interview. The hospitalization measure reflects whether the participant was hospitalized in the year prior to follow-up. The two remaining outcomes reflect whether the participant was placed in a nursing home or died by the time of the 36-month follow-up.

**Covariates**

Numerous risk factors have been identified for ADLs/IADLs, lower body limitations, health services use, and mortality (11–14). Accordingly, several demographic, socioeconomic, and comorbidity measures were included to determine the independent effect of subclinical status in lower body function and ADLs/IADLs at baseline on the targeted adverse outcomes (5–7). Demographic characteristics included age, sex, and marital status. The socioeconomic status indicators were education and perceived income adequacy. Comorbidity was measured using markers for diabetes, cancer, heart disease, lung disease, elevated systolic or diastolic blood pressure, clinically relevant levels of depressive symptoms, and cognitive ability, using the MMSE.

In addition, to ensure that the unique effect of subclinical status is identified, the second set of models also adjusts for baseline levels of difficulties with lower body function and ADLs/IADLs. This adjustment is made by first determining the aggregate number of these limitations and then creating a set of two dummy variables reflecting that distribution. The two dummy variables reflect low (1–3) and high (4 or more) levels of baseline difficulties, with the reference or omitted category being those participants who reported no such limitations at baseline.

**Analytic Models**

Because lower body limitations, ADLs/IADLs, the SPPB, and physician visits are essentially count variables for which the traditional assumptions of multiple linear regression do not hold, residualized change score (15) multiple Poisson regression techniques were used to model these outcomes. In these models, the 36-month follow-up value of the outcome is initially regressed on its baseline value and the extent of subclinical status evidence for the lower body function and ADL/IADL domains. This step provides estimates of the crude effects of subclinical status in these two domains on changes in the outcome measure. The covariates (and, in the second set of models, the dummy variables reflecting the
aggregate distribution of lower body function and ADL/IADL difficulties are then added to these models to obtain the independent effects of the extent of subclinical status evidence in these two domains on the adverse outcomes. For all binary outcomes, similar multiple logistic regression models were used with the same sequential introduction of the covariates (16). Sensitivity analyses were conducted replicating the first set of adjusted models within each of three strata based on the aggregate level of baseline lower body function and ADL/IADL difficulties to examine the potential for modification of the subclinical status effects on these outcomes.

RESULTS

Sample Characteristics

At baseline, the mean age of the 998 participants was 56.8 years, 42% were men, 47% were currently married, 28% were divorced or separated, 13% were widowed, and 12% were single. The mean educational attainment was 12.5 years, and 15% reported not having enough income to make ends meet. Twenty-six percent had diabetes, 7% had cancer, 10% had heart disease, 5% had lung disease, 21% had clinically relevant levels of depressive symptoms, 49% had elevated systolic and 32% had elevated diastolic blood pressure, and the mean score on the MMSE was 27.9. The mean number of lower body difficulties was 1.33 (standard deviation [SD] = 1.59; 46.5% had none), the mean number of ADLs/IADLs was 0.80 (SD = 1.46; 67.1% had none), 44% had no lower body or ADL/IADL difficulties, 31% had 1–3, and 25% had 4 or more. The mean SPPB summary score was 8.06 (SD = 3.31), and the mean number of physician visits was 4.35 (SD = 3.85).

The mean baseline proportions of the two domains of subclinical status were 0.33 (SD = .38) for lower body limitations, and 0.20 (SD = .30) for ADLs/IADLs. Figures 1 and 2 contain histograms of these distributions, which emphasize the substantial modal response at 0%, and the generally uniform distribution thereafter, with the exception of the typical heaping of count measures at the upper extremes. Note that, in the models estimated, these proportions are multiplied by 10 (resulting in means of 3.3 and 2.0 for lower body limitations and ADLs/IADLs, respectively) so that the effects will be calibrated as those associated with an additional 10% evidence of subclinical status. At the time of the 36-month follow-up, the mean number of lower body limitations was 1.45, the mean number of ADLs/IADLs was 0.94, the mean SPPB summary score was 8.45, the mean number of physician visits was 4.63, 164 participants (16%) had been hospitalized, 8 participants (0.8%) had been placed in nursing homes, and 51 participants (5.1%) had died.

Crude and Adjusted Poisson Regression Estimates

Table 1 contains the crude and adjusted Poisson regression estimates obtained from the residualized change score regressions for the lower body limitations, ADLs/IADLs, SPPB summary scores, and the number of physician visits for the models among the 853 participants re-interviewed 3 years after baseline. These coefficients reflect the change in the adverse outcome from its baseline value, and may be interpreted as the effect associated with an increase of 10% evidence of subclinical status on all assessed tasks in that domain. The first pair of columns contains the crude effects, the second pair of columns contains the effects adjusted for the covariates (i.e., Model 1), and the third pair of columns contains the effects adjusted for the covariates and the set of dummy variables reflecting baseline combined levels of lower body function and ADL/IADL difficulties (i.e., Model 2). As shown, baseline subclinical status for both lower body function and ADLs/IADLs have significant crude effects on all four outcomes. Significant adjusted effects are shown for both lower body function and ADLs/IADLs in three of the four outcomes in Model 1, with the adjusted effect for the latter on lower body limitations marginal insignificantly (p = .079). In Model 2, significant adjusted effects for subclinical status in ADLs/IADLs is found on ADLs/IADLs and physician visits, whereas the effect on lower body function difficulties remains marginally insignificant (p = .077), and the prior effect on the SPPB is no longer significant (p = .207). Baseline subclinical status for lower body function has a statistically significant effect only on physician visits. This effect is substantially smaller than that for subclinical status in ADLs/IADLs, and reduces rather than increases the number of physician visits.

Multiple Logistic Regression Analyses

Table 2 contains the crude and adjusted (Models 1 and 2) ORs obtained from multiple logistic regression of whether the participant was hospitalized in the year prior to the 36-month follow-up interview, was placed in a nursing home, or died within 3 years of baseline. Hospitalization and nursing home placement were evaluated for the 853 participants re-interviewed at the 36-month follow-up, whereas mortality was evaluated for all 998 participants. Because the proportion of subclinical status evidence for each domain has been multiplied by 10, these ORs can be interpreted as reflecting the comparison of risk associated with having a 10% increment in subclinical status evidence on the assessed tasks in the given domain. As shown, the only independent significant effect observed was that of baseline subclinical status in lower body function on subsequent hospital-
associated with an additional 10% evidence of subclinical status on all assessed tasks. Because the proportions of subclinical status evidence have been multiplied by 10, these coefficients can be interpreted as reflecting the comparison of differences.

dummy variables reflecting 0, 1–3, or 4 or more total baseline difficulties with lower body function, activities of daily living (ADLs), and instrumental ADLs (IADLs).

blood pressure, high diastolic blood pressure, clinically relevant levels of depressive symptoms, and cognitive ability. Model 2 adjusts for these factors and a set of residualized change. Model 1 adjusts for age, sex, marital status, education, perceived income adequacy, diabetes, cancer, heart disease, lung disease, high systolic blood pressure, high diastolic blood pressure, clinically relevant levels of depressive symptoms, and cognitive ability.

No. of Physician Visits

<table>
<thead>
<tr>
<th>Lower body limitations</th>
<th>Crude Regression Coefficients</th>
<th>Model 1 Adjusted Regression Coefficients</th>
<th>Model 2 Adjusted Regression Coefficients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coefficient</td>
<td>0.032</td>
<td>0.019</td>
<td>0.014</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.015, 0.049</td>
<td>0.001, 0.038</td>
<td>0.005, 0.032</td>
</tr>
<tr>
<td>p value</td>
<td>.001</td>
<td>.042</td>
<td>.139</td>
</tr>
<tr>
<td>ADLs and IADLs</td>
<td>0.059</td>
<td>0.039</td>
<td>0.018</td>
</tr>
<tr>
<td>Coefficient</td>
<td>0.038, 0.081</td>
<td>0.016, 0.063</td>
<td>0.006, 0.041</td>
</tr>
<tr>
<td>95% CI</td>
<td>.001</td>
<td>.001</td>
<td>.146</td>
</tr>
<tr>
<td>p value</td>
<td>.001</td>
<td>.001</td>
<td>.001</td>
</tr>
<tr>
<td>Physical Performance Scale</td>
<td>-0.011</td>
<td>0.000</td>
<td>0.003</td>
</tr>
<tr>
<td>Coefficient</td>
<td>-0.019, -0.003</td>
<td>-0.008, -0.009</td>
<td>-0.006, 0.011</td>
</tr>
<tr>
<td>95% CI</td>
<td>-0.016</td>
<td>-0.017</td>
<td>-0.021, 0.005</td>
</tr>
<tr>
<td>p value</td>
<td>.001</td>
<td>.001</td>
<td>.001</td>
</tr>
<tr>
<td>No. of Physician Visits</td>
<td>0.021</td>
<td>0.033</td>
<td>0.033</td>
</tr>
<tr>
<td>Coefficient</td>
<td>-0.030, -0.013</td>
<td>-0.042, -0.023</td>
<td>-0.043, -0.023</td>
</tr>
<tr>
<td>95% CI</td>
<td>-0.065, 0.088</td>
<td>0.066, 0.090</td>
<td>0.068, 0.093</td>
</tr>
<tr>
<td>p value</td>
<td>.001</td>
<td>.001</td>
<td>.001</td>
</tr>
</tbody>
</table>

Notes: Other than the two subclinical status performance measures, the crude effect model only includes the baseline value of the dependent variable to reflect rezidualized change. Model 1 adjusts for age, sex, marital status, education, perceived income adequacy, diabetes, cancer, heart disease, lung disease, high systolic blood pressure, high diastolic blood pressure, clinically relevant levels of depressive symptoms, and cognitive ability. Model 2 adjusts for these factors and a set of dummy variables reflecting 0, 1–3, or 4 or more total baseline difficulties with lower body function, activities of daily living (ADLs), and instrumental ADLs (IADLs). Because the proportions of subclinical status evidence have been multiplied by 10, these coefficients can be interpreted as reflecting the comparison of differences associated with a further 10% evidence of subclinical status on all assessed tasks.

CI = confidence interval.

Sensitivity Analyses

As indicated above, the models shown in Tables 1 and 2 were replicated within each of three strata based on the aggregate level of baseline lower body function and ADL/IADL difficulties. With the exception of the mortality models, there were 392 participants in the no baseline difficulties analytic group, 259 participants in the 1–3 baseline difficulties analytic group, and 211 participants in the 4 or more baseline difficulties analytic group. Because statistical power is substantially reduced in each of these strata (and therefore the confidence intervals become large), the focus is on whether the point estimates (regression estimates) for the subclinical status measures vary appreciably from one strata to the next. The results (not shown) indicate that they do not. That is, although the effects of subclinical status in ADLs/IADLs are noticeably stronger among those participants with no lower body or ADL/IADL difficulties at baseline, regression estimates comparable to those observed in the pooled analysis were observed in the 1–3 and 4 or more baseline difficulty analytic groups as well. Thus, no evidence of effect modification was observed.

DISCUSSION

The contributions to the literature in this article involve extensions in (i) the follow-up period over which the effect of subclinical status has been demonstrated, and (ii) the range of adverse outcomes affected by subclinical status. In terms of the former, previous studies by Fried and colleagues (4,17) and Wolinsky and colleagues (7) reported that subclinical status was a robust predictor of selected functional limitations and disability at 18 and 24 months, respectively. The results presented here extend the reach of the effects of subclinical status to 36 months. In terms of the range of affected outcomes, previous reports by Fried and colleagues (4,17) and Wolinsky and colleagues (7) were limited to four functional limitations (walking one half mile, going up and down one flight of stairs, stooping/crouching/kneeling, and lifting or carrying 10 pounds) and one ADL item (doing heavy housework). The results presented here extend the range of adverse outcomes for which statistically significant independent effects of subclinical status have been identified to five lower body functional limitations, seven ADLs/IADLs, the number of physician visits, and hospitalization. Thus, the effects of subclinical status on subsequent adverse health outcomes are more enduring and widespread than previously reported.

The magnitudes of these effects, however, are modest. Indeed, the maximal contrast would involve comparing a participant with 0% subclinical status evidence in either domain versus one with 100% subclinical status evidence, which would be equivalent to 10 times the adjusted Poisson regression estimates shown in Table 1 (which are calibrated at a 10% difference comparison). For the lower body function and ADL/IADL outcomes, the maximal contrast represents an increase of only one fifth to one half of an additional lower body or ADL/IADL limitation over 3 years. That amount, however, is approximately similar in magnitude to the baseline prevalence for these outcomes, and thus should not be considered trivial. Similarly, the same maximal contrast for the subclinical status in ADLs/IADLs translates into 0.8 more physician visits and a 74% increase in the likelihood of being hospitalized. Thus, the main effect of subclinical status in disability appears to involve future demands on the health care delivery
system, most likely in an attempt to stabilize the disablement process.

Before discussing the implications of these results, four issues warrant attention. First, these results were obtained from a probability-based, representative community sample of African American men and women who were 49–65 years old at the time of their baseline interviews (5–7). In contrast, the pioneering works of Fried and colleagues (4,17) were based on older adults, most of whom were white women who enjoyed high levels of physical and cognitive abilities. This raises the question of whether the results reported here generalize to other middle-aged minority and majority groups. Of course, further research using more diverse samples is needed to definitively resolve that question. What is more likely, however, is that given the earlier onset and increased burden of functional limitation, disability, and resultant health services use among disadvantaged minorities (18–20), the more enduring and widespread effects of subclinical status in functional limitation and disability was simply more palpable in this sample of middle-aged African American men and women.

Second, no independent effects of subclinical status in functional limitations or disability were observed on nursing home placement and mortality. This finding is most likely due to the limited statistical power for these outcomes. Indeed, only 8 participants were placed in a nursing home during the 3-year follow-up window, and only 51 participants died during that time.

To avoid over-fitting event history models, it is generally recommended that there be 10 events (nursing home placements or deaths) for each predictive term in the logistic regression equation (21–23). These data do not meet that minimum, and this likely explains why the significant crude effect of subclinical status for ADLs/IADLs on mortality is fully decomposed by the introduction of the covariates.

Third, the effects of subclinical status in the ADL/IADL domain are stronger, more widespread, and consistent with expectations compared to the less robust and selective effects of subclinical status in the functional limitation domain. This is understandable. In traditional models of the disablement process, the primary pathway is from impairments to functional limitations to disability to subsequent outcomes (3). Thus, the effects of subclinical status in the functional limitation domain are subject to mediation by those in the disability domain.

Finally, it should be noted that the effects of subclinical status in lower body limitations and ADLs/IADLs on physician visits and hospitalization are in the opposite direction. Indeed, the former appear to be counterintuitive, whereas the latter are more consistent with general expectations. Two plausible explanations may help to reconcile this apparent anomaly. On the one hand, subclinical status in lower body function may serve as an access barrier for physician visits, and less frequent physician use may reduce the risk of hospitalization. On the other hand, the onset of (or increases in) difficulties with ADLs (especially those that are more cognitively demanding) initially increases the demand for health services (reflecting diagnostic and evaluation activity), followed by a triage and selection process (associated with forgoing subsequent treatment) after recovery is deemed unlikely (24–30). In this study of middle-aged adults, it is unlikely that the initial increase in service demand has given way to the triage and selection processes. Further evaluation of these explanations, however, is beyond the scope of this article.

These issues notwithstanding, the results reported here have important implications for health policy. To reduce frailty, interventions should focus on self-reported subclinical status as "an early warning system." This is entirely consistent with the recent Institute of Medicine report (31) that distinctly targets as a national priority the reduction of frailty among older adults. Inasmuch as existing interventions focus on difficulty (rather than subclinical status), their success may be minimized because their target is recovery rather than prevention. Thus, given the relative ease of ascertaining subclinical status and its ability to predict the onset of multiple adverse outcomes, health policy should seize the opportunity to move the focus on interventions further upstream in the disablement process to more effectively address prevention rather than recovery.

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**Table 2. Crude and Adjusted Odds Ratios Obtained From Logistic Regression Models of the Effect of the Baseline Subclinical Status Proportion Measures on Hospitalization, Nursing Home Placement, and Mortality 3 Years Later (N = 853 for Hospitalization and Nursing Home Placement; N = 998 for Mortality)**

<table>
<thead>
<tr>
<th>Dependent Variables</th>
<th>Crude Odds Ratios</th>
<th>Model 1 Adjusted Odds Ratios</th>
<th>Model 2 Adjusted Odds Ratios</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lower Body ADLs/IADLs</td>
<td>Lower Body ADLs/IADLs</td>
<td>Lower Body ADLs/IADLs</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>Odds ratio</td>
<td>0.944 (1.147)</td>
<td>0.914 (1.126)</td>
</tr>
<tr>
<td></td>
<td>95% CI</td>
<td>0.892 (1.000)</td>
<td>0.856 (1.038)</td>
</tr>
<tr>
<td></td>
<td>p value</td>
<td>.050 .004</td>
<td>.007 .004</td>
</tr>
<tr>
<td>Nursing home placement</td>
<td>Odds ratio</td>
<td>0.965 (1.266)</td>
<td>0.988 (1.127)</td>
</tr>
<tr>
<td></td>
<td>95% CI</td>
<td>0.945 (1.695)</td>
<td>0.738 (1.325)</td>
</tr>
<tr>
<td></td>
<td>p value</td>
<td>.793 .114</td>
<td>.938 .508</td>
</tr>
<tr>
<td>Mortality</td>
<td>Odds ratio</td>
<td>0.984 (1.167)</td>
<td>0.977 (1.075)</td>
</tr>
<tr>
<td></td>
<td>95% CI</td>
<td>0.902 (1.295)</td>
<td>0.888 (1.205)</td>
</tr>
<tr>
<td></td>
<td>p value</td>
<td>.724 .004</td>
<td>.634 .217</td>
</tr>
</tbody>
</table>

Note: Model 1 adjusts for age, sex, marital status, education, perceived income adequacy, diabetes, cancer, heart disease, lung disease, high systolic blood pressure, high diastolic blood pressure, clinically relevant levels of depressive symptoms, and cognitive ability. Model 2 adjusts for these factors and a set of dummy variables reflecting 0, 1–3, or 4 or more total baseline difficulties with lower body function, activities of daily living (ADLs), and instrumental ADLs (IADLs). Because the proportions of subclinical status evidence have been multiplied by 10, these coefficients can be interpreted as reflecting the comparison of differences associated with an additional 10% evidence of subclinical status on all assessed tasks.
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