## UCSF UC San Francisco Previously Published Works

## Title

A comprehensive prognostic tool for older adults: Predicting death, ADL disability, and walking disability simultaneously.

**Permalink** https://escholarship.org/uc/item/1vn8b2mf

**Journal** Journal of the American Geriatrics Society, 70(10)

## **Authors**

Diaz-Ramirez, L Boscardin, W Lee, Sei <u>et al.</u>

## **Publication Date**

2022-10-01

## DOI

10.1111/jgs.17932

Peer reviewed



# **HHS Public Access**

JAm Geriatr Soc. Author manuscript; available in PMC 2023 October 01.

Published in final edited form as:

Author manuscript

JAm Geriatr Soc. 2022 October; 70(10): 2884–2894. doi:10.1111/jgs.17932.

## A Comprehensive Prognostic Tool for Older Adults: Predicting Death, ADL Disability, and Walking Disability Simultaneously

Alexandra K. Lee, PhD, MSPH<sup>1,2</sup>, L. Grisell Diaz-Ramirez, MS<sup>2</sup>, W. John Boscardin, PhD<sup>1,2,3</sup>, Alexander K. Smith, MD<sup>1,2,\*</sup>, Sei J. Lee, MD, MAS<sup>1,2,\*</sup>

<sup>1</sup>Division of Geriatrics, Department of Medicine, UCSF, San Francisco, CA

<sup>2</sup>San Francisco Veterans Affairs Healthcare System, San Francisco, CA

<sup>3</sup>Division of Biostatistics, Department of Epidemiology and Biostatistics, UCSF, San Francisco, CA

## Abstract

**Background:** Many clinical and financial decisions for older adults depend on future risk of disability and mortality. Prognostic tools for long-term disability risk in a general population are lacking. We aimed to create a comprehensive prognostic tool that predicts risk of mortality, of activities of daily living (ADL) disability, and of walking disability simultaneously using the same set of variables.

**Methods:** We conducted a longitudinal analysis of the nationally representative Health and Retirement Study (HRS). We included community-dwelling adults aged 70 years who completed a core interview in the 2000 wave of HRS, with follow-up through 2018. We evaluated 40 predictors encompassing demographics, diseases, physical functioning, and instrumental ADLs. We applied novel methods to optimize three models simultaneously while prioritizing variables that take less time to ascertain during backward stepwise elimination. The death prediction model used Cox regression and both the models for walking disability and for ADL disability used Fine and Grey competing-risk regression. We examined calibration plots and generated optimismcorrected statistics of discrimination using bootstrapping. To simulate unavailable patient data, we also evaluated models excluding one or two variables from the final model.

**Results:** In 6646 HRS participants, 2662 developed walking disability, 3570 developed ADL disability, and 5689 died during a median follow-up of 9.5 years. The final prognostic tool had 16 variables. The optimism-corrected integrated area under the curve (iAUC) was 0.799 for mortality, 0.686 for walking disability, and 0.703 for ADL disability. At each percentile of

<sup>\*</sup>Dr. A.K. Smith and Dr. S.J. Lee both contributed equally to this work as senior authors.

Author Contributions

Conflicts of Interest

All authors declare no conflicts of interest.

**Corresponding Author:** Alexandra K. Lee, PhD, MSPH, 4150 Clement St, VA181G, San Francisco, CA 94121, alexandra.lee@ucsf.edu, Twitter handle: none.

Dr. A. Lee made substantial contributions to the interpretation of data and drafting the manuscript, and gave final approval of the version to be published. Ms. Diaz-Ramirez and Dr. Boscardin made substantial contributions to the design of the study, the analysis and interpretation of data, revising the article critically for important intellectual content, and they both gave final approval of the version to be submitted. As co-last authors, Dr. S. Lee and Dr. Smith conceived and designed the study, made substantial contributions to the interpretation of data, and revised the article for important intellectual content; they both gave final approval of the version to be published.

predicted mortality risk, there was substantial spread in the predicted risks of walking disability and ADL disability. Discrimination and calibration remained good even when missing one or two predictors from the model.

**Conclusions:** Given the variability in disability risk for people with similar mortality risk, using individualized risks of disabilities may inform clinical and financial decisions for older adults.

### Keywords

Prediction; Disability; Mortality

## INTRODUCTION

Prognostic information for older adults informs long-term planning for patients, clinicians, and caregivers.<sup>1</sup> Accurate timelines for death, disability, and loss of independence are useful to help make decisions about healthcare treatments and financial planning for patients and their families. For instance, predicted life expectancy can help quantify the likelihood of benefit from long-term preventative treatments such as diabetes medications and cancer screening.<sup>1–4</sup> Predicted time until developing difficulty walking short distances can indicate a potential timeframe for becoming home-bound and needing durable medical equipment, such as a walker or wheelchair. Similarly, needing help for activities of daily living (ADLs) will require either in-home caregiving or nursing home placement. Many of these healthcare needs have major implications for patients' lifestyles and finances. Indeed, many older adults care about loss of independence as much or more than life expectancy.<sup>5</sup> Thus, accurate information on future risks of death, ADL disability, and inability to walk would be greatly valued by older adults and would help patients and their families prepare for future healthcare and financial needs.

To date, prognostic information for relatively healthy older adults without serious illnesses has largely been limited to predicting mortality,<sup>6–9</sup> with no prediction tools for long-term risk of ADL disability and walking disability. However, given highly limited clinical encounter time, it is crucial to not further burden healthcare providers by having different tools for each outcome. Thus, it is important to build prediction models using an approach that considers the clinical time needed to assess that variable in addition to its predictive capacity.<sup>10</sup> Additionally, patient data is sometimes unavailable, so it is important to enable predictions even with one or two missing predictors.<sup>11</sup>

The objective of this study was to create prediction models for risk of death, risk of walking disability, and risk of ADL difficulty for adults aged 70 using a single set of predictor variables that minimized the amount of clinical time needed to assess each predictor while also allowing for unavailable predictors. This comprehensive prognostic tool would enable patients, providers, and caregivers to plan for future caregiving needs based on the likelihood of death, ADL disability, and walking disability.

## METHODS

#### **Study Population**

The Health and Retirement Study (HRS) is an ongoing longitudinal cohort study that is nationally representative of U.S. adults aged 50 years. Core surveys are conducted primarily via telephone every two years, with new birth cohorts recruited approximately every 6 years.<sup>12</sup> Following the death of a participant, exit interviews are conducted with the participant's next of kin. Our baseline was the HRS core interview in 2000. We included community-dwelling HRS participants aged 70 years at time of interview. We incorporated data from each core survey through 2018 as well as data from the exit interview for participants who died prior to 2018. All HRS participants provided informed written consent.

A total of 19,560 HRS participants completed the core interview in 2000. Of these participants, 7,506 were 70, and, of those, 7,100 were community-dwelling. For the mortality cohort, we excluded participants with any missing predictors since all predictors had <2% missingness (n=454), resulting in a final sample size of 6,646 to predict mortality. To predict ADL *disability*, we excluded HRS participants who had missing information on ADLs at baseline (n=15) and participants who reported an ADL *disability* at baseline (defined as requiring help with at least one ADL) (n=728). We included participants who, at baseline, reported no difficulties with any ADL or reported an ADL *difficulty* without requiring help (n=6357). We then excluded participants who did not have any follow-up core interviews but did not die during follow-up (n=23), and participants with missing predictors (n=333), resulting in a sample size of 6,001. To predict walking disability, we excluded participants who did not have any follow-up core interview but did not die during follow-up (n=25) or who were missing information on walking at baseline (n=12), participants who did not have any follow-up core interview but did not die during follow-up (n=24), and participants with missing values in predictors (n=400), resulting in a sample size of 6,409.

#### Outcomes

We obtained date of death from the National Death Index for deaths through 2011, the Medicare Master Beneficiary Summary File for deaths through 2018, and the HRS dataset to capture any deaths missing from either national file through 2018. With linkage using social security numbers, NDI has 97% sensitivity for death prior to 2011; <sup>13,14</sup> the Medicare Master Beneficiary Summary File has 99% of death days validated.<sup>15</sup> Participants who died after the HRS interview wave in 2018 were censored at the date of the last core interview (05/15/2019).

We identified HRS participants with incident ADL disability using both the core interview waves (2002–2018) and the exit interview for deceased participants. For the core interviews, ADL disability was defined as a self- or proxy-report of having difficulty and needing help with bathing, dressing, toileting, transferring, or eating. The date of ADL disability was assigned as the midpoint between the last core interview at which the participant/proxy reported no ADL disability and the first core interview at which the participant/proxy reported ADL disability. For the exit interviews, ADL disability was defined as next of kin's

report of disability with bathing, dressing, toileting, eating, and transferring during the last three months of life. The date of ADL disability from the exit interview was defined as three months prior to death, or, if available, the number of days prior to death that disability began, as reported by the next of kin. HRS participants who did not die and did not report ADL disability at either a core interview or the exit interview were censored at their last core interview.

Incident walking disability was defined as the first report of needing help to walk across a room from either the core interview waves (2002–2018) or the exit interview. The date of incident walking disability was assigned using an analogous method as the date of ADL disability, outlined above.

#### **Predictor Variables**

Based on our group's prior experience with mortality prediction,<sup>7–9,16</sup> we a priori included a set of 40 predictors from each participant's baseline core interview. These predictors included: demographic characteristics (age, sex, marital status, living alone), BMI, smoking history, drinking, pain, urinary incontinence, self-rated hearing, diseases (any history of cancer, diabetes, high blood pressure, stroke, heart failure, any heart problems, lung disease, arthritis), six instrumental activities of daily living (IADLs, preparing hot meal, shopping, using telephone, using a map, taking medications, managing money), doing volunteer work in the past year, some difficulty with ADLs (bathing, transferring, dressing, eating, toileting), any falls in past 2 years, and physical functioning (walking several blocks, difficulty climbing stairs, sitting for 2 hours, stooping/kneeling/crouching, reaching arms above shoulders, lifting or carrying 10 pounds, pushing/pulling large object, getting out of chair, picking up a dime from a table) (Supplemental Table S1). We did not include race/ethnicity in our set of predictor variables to avoid 'race-based medicine'.<sup>17</sup>

To determine the time cost for each predictor, we used the automated reading function of Microsoft Excel. We measured the time it took Excel's automated reader to read verbatim each question from HRS (as listed in Supplemental Table S1) and used the number of seconds as the time-cost for each predictor.<sup>10</sup>

#### **Statistical Analysis**

We examined baseline characteristics of HRS participants, stratified by death during followup. We also examined baseline characteristics in the cohorts for incident ADL disability and incident walking disability. We accounted for the complex survey design and generated weighted means and percentages.

We followed a multi-step process to build the prediction models for our three outcomes of death, ADL disability, and walking disability simultaneously. We used Cox proportional hazards regression for the death prediction model, incorporating the strata, clusters, and survey weights (via SAS's SURVEYPHREG) to account for the complex survey design. We used Fine and Grey competing risk regression, with death as the competing risk, for the ADL disability prediction model and the walking disability prediction model, using survey weights and robust sandwich variance to account for the complex survey design. We applied statistical methods we previously developed to conduct backwards elimination on three

prediction models simultaneously and accounting for the time needed to assess a predictor using the time-cost information criterion (TCIC).<sup>10,18</sup> Briefly, the TCIC is an alternative to the BIC used to evaluate model fit, and the TCIC favors the variable that takes less time to assess when two variables have identical predictive abilities. Backwards elimination was conducted on all three models simultaneously by applying the TCIC to each model at each backwards elimination step and finding the lowest average TCIC across the three models.<sup>18</sup> We used 3 restricted cubic splines with 4 knots for age and BMI. To evaluate discrimination of the final models, we used integrated area under the curve (iAUC) using the inverse probability of censoring weighting method.<sup>19</sup> Because Fine and Grey regression does not allow for the computing of the iAUC, we applied Wolbers et al. adaptation of iAUC to the competing risks setting, where death status is switched to censored and the time-to-event is equal to the longest possible time-to-event that any respondent was followed.<sup>20</sup> With this adaptation, we used Cox regression to calculate the iAUC for the models of ADL disability and walking disability.

We conducted internal validation to evaluate if our models were overfit. We created 100 bootstrapped samples to generate an optimism-corrected iAUC.<sup>21-23</sup> We created calibration plots by creating deciles of predicted risk and plotting the average predicted risk of each decile against the average observed risk in that decile.

To demonstrate the results of our prediction models, we created groups of individuals based on their predicted 10-year mortality risk (percentiles 23–27, 48–52, and 73–77). We first generated the predicted 10-year risk of ADL difficulty and the predicted 10-year risk of walking disability for all respondents within each group of 10-year mortality risk. To display the spread of predicted risks of ADL disability and walking disability within a given group of 10-year mortality risk, we created boxplots of predicted risk of 10-year ADL disability and predicted risk of 10-year walking disability.

To create models that accommodate unavailable predictors in the clinical setting, we created 105 models that dropped either one or two predictors from the final model, keeping age and gender in all models.<sup>11</sup> For each model, we re-estimated the coefficients. We examined statistics of discrimination as well as calibration plots for the best- and worst-performing models as identified by the TCIC.

For all models, we examined discrimination by subgroups of age (<80 years vs. >80 years), sex, and race/ethnicity (Non-Hispanic Black, Non-Hispanic White, Hispanic ethnicity or other race).

All analyses were performed in SAS Version 15.1 (SAS Institute Inc., Cary, North Carolina) or R version 4.1.0 (The R Foundation for Statistical Computing).

## RESULTS

There were 6646 HRS participants included in this study. Over a median of 9.5 years of follow-up, 5689 (weighted: 85%) died. Among the 6001 without ADL disability at baseline, 3570 (weighted: 59%) developed ADL disability during follow-up. Among the 6409 without walking disability at baseline, 2662 (weighted: 41%) developed walking disability during

follow-up. The average age was 77.5 years, 59% were female, 86% were non-Hispanic white, 34% lived alone, and 40% had difficulty walking several blocks (Table 1).

The final models to predict death, incident ADL disability, and incident walking disability included 16 predictors: age, sex, BMI, smoking history, living alone, stroke, cancer, diabetes, heart failure or other heart problems, lung disease, high blood pressure, eating difficulty, difficulty preparing meals, difficulty managing money, difficulty pushing/pulling large object, and difficulty walking several blocks (Table 2). These 16 predictors had an estimated clinical assessment time of 99.2 seconds. After optimism correction via bootstrapping, the iAUC for predicting mortality was 0.799 (0.789–0.810), the iAUC for predicting ADL disability was 0.703 (0.681–0.713), and iAUC for predicting walking disability was 0.686 (0.665–0.700). Calibration was good in all three prediction models, with high concordance between deciles of predicted risk and observed risk (Figure 1).

Within each level of predicted mortality risk, there was a wide range in predicted risks of ADL disability and of walking disability (Figure 2). Among persons with a median ( $\pm 2$  percentiles) predicted mortality risk, the predicted 10-year ADL disability risk was 37% at the 25<sup>th</sup> percentile and 52% at the 75<sup>th</sup> percentile; the predicted 10-year walking disability risk was 24% at the 25<sup>th</sup> percentile and 34% at the 75<sup>th</sup> percentile. At all percentiles of predicted mortality risk, the median risk of ADL disability was higher than the median risk of walking disability.

To simulate unavailable predictors in a clinical setting, we evaluated 14 models missing one predictor (forcing in age and gender) and 91 models missing two predictors. Discrimination was similar; all models with missing predictors had an iAUC within 0.01 of the full model (Table 3). Calibration was good in all models (Supplemental Figure S1).

There were small differences in iAUC across subpopulations as defined by age (<80 vs. 80 years), sex, and race/ethnicity that are unlikely to be clinically meaningful (Supplemental Table S2). Overall, the iAUCs were somewhat lower for women compared to men (difference in iAUC =~0.05); the difference tended to be slightly smaller for mortality compared to ADL or walking disability. For age, discrimination for mortality was very slightly better among adults 80 years vs. <80 years (iAUC difference ~0.01), while discrimination for ADL disability and walking disability was better in adults <80 years vs. 80 years (iAUC difference: 0.02 – 0.06). Discrimination was slightly lower in Non-Hispanic Blacks compared to both Hispanic ethnicity/other race and non-Hispanic white (~0.04 difference).

## DISCUSSION

In this study, we created a comprehensive prognostic tool for the general older adult US population to predict risk of mortality, incident ADL disability, and incident walking disability. This comprehensive prognostic tool uses one parsimonious set of variables, and verbally asking about all predictors takes <2 minutes. Statistically, this state-of-the art prognostic tool used three recently developed methods that enabled variable selection for three outcomes simultaneously, while also considering the time-cost of each variable in

addition to its predictive power.<sup>10,11,18</sup> Our models had good discrimination and calibration with little evidence of overfitting, and the models performed well even when one or two predictors were unavailable.

This prognostic tool fills an important gap in the literature to predict patient-centered outcomes of ADL disability and walking disability for older adults in the US. Currently, a few validated calculators predict life expectancy and long-term mortality risk in the general older adult population,<sup>6,8,9</sup> but long-term calculators for disability are lacking. Existing short-term disability prediction models predict 2-year disability in adults 70,<sup>24</sup> 6-month disability in acutely ill older adults,<sup>25</sup> and NH placement among older adults with caregivers.<sup>26</sup> However, for long-term planning, it is crucial to have information on >5-year risks of ADL disability and walking disability. The long-term risks will improve patients' understanding of their time remaining before loss of independence and will help them prepare for future caregiving needs and financial costs.

Long-term mortality risk and predicted life expectancy inform numerous clinical decisions where the benefit of treatment may take years to accrue.<sup>1,2</sup> If the expected time to benefit for a given treatment is longer than a patient's life expectancy, then the patient may be more likely to experience harms from side-effects than to experience benefits of treatment. For instance, statins have a 2.5-year lag-time to benefit for older adults, meaning that if a person is unlikely to live more than 2.5 years, statins are unlikely to prevent a major myocardial event in the future but may result in immediate muscle soreness.<sup>27</sup> Similarly, screening for breast and colorectal cancers are not recommended for older adults with a life expectancy <10 years,<sup>3,4</sup> and reducing HbA1c in diabetes may not reduce clinical complications until at least 5 years later.<sup>28</sup> Thus, mortality prediction tools play an important role in informing clinical decisions for many preventive treatments.

Our results showed higher discrimination for mortality compared to ADL disability and walking disability. There are several possible contributing factors. First, disability may be harder to predict than mortality. Some prior prediction models for disability had good discrimination, but they only predicted short-term (2 year) disability,<sup>24,25</sup> which is likely easier to predict than long-term disability. Other prediction models for disability within certain disease conditions, such as multiple sclerosis, have also had moderate discrimination.<sup>29,30</sup> Second, disability is inherently 'noisy:' it often fluctuates over time and can be dependent on the presence of environmental modifications, such as grab bars for toileting and bathing.

We noted a large spread in predicted risks of ADL disability and walking disability at the same predicted risk of mortality, demonstrating that risk of disability does not directly correlate with risk of mortality. This leads to different situations that may result in different decisions. For example, let's consider two people with the same 34% 10-year risk of mortality, but differing risks of ADL disability and walking disability: Nancy, a 75yo female, and Mark, a 73yo male. Nancy lives with her spouse, has difficulty managing money, a history of cancer, heart problems but not heart failure, and a BMI of 35. Her 10-year risk of ADL disability is 56% and her 10-year risk of walking disability is 34%. In contrast, Mark lives alone, has difficulty pushing a large object and has hypertension (but no other

diseases) with a BMI of 29. Mark's 10-year risk of ADL disability is 30% and his 10-year risk of walking disability is 20%. Given Mark's relative health and low risk of disability, Mark prefers to continue living alone in his two-story home, and his family agrees this is a reasonable decision. On the other hand, Nancy and her spouse, after considering the prognostic information on 10-year risks of mortality, ADL disability, and walking disability, decide to move to a senior independent living community, where they can easily transition to assisted living when they need help with daily tasks. As we can see from these vignettes, the risk of mortality is one of several concerns that are central to decision making for older adults. We believe our new comprehensive prognostic tool will inform and improve important conversations about long-term planning with older adults.

While our new prognostic tool provides important estimates of long-term disability risk, further research is needed to determine how best to communicate this information to patients and families. Current literature on communicating life expectancy to patients has found mixed results. One study showed patients prefer to know the prognostic information to prepare and make the most of the time they have.<sup>31</sup> In contrast, other studies found that many older adults are uncomfortable explicitly discussing life expectancy but are open to discussing changing health priorities, including reducing screening and preventative treatments, in the context of advanced age and health status.<sup>32,33</sup> To improve communication about prognosis, research should determine when information on long-term disability risk is most likely to influence and improve decision-making, and a patient-centered, sensitive approach for discussing this important information should be developed.

Our study has notable strengths. First, we developed our prediction models in a large, nationally representative dataset, indicating our models should be generalizable to all older adults in the US. Second, we used a novel approach to predict all three outcomes simultaneously with the same set of predictors while prioritizing variables that take less time to measure, thus minimizing the clinical burden of collecting data. Finally, we allowed for flexibility in clinical use by allowing for one or two missing predictors with minimal decrements to discrimination and calibration.

This study also has limitations. First, we likely were not able to capture all instances of ADL disability and walking disability before death, despite incorporating reports of these conditions from the exit interview, resulting in a slight underestimate of incident ADL disability and walking disability in this cohort. However, this under-ascertainment is unlikely to be differential by participant characteristics, and thus we don't believe this notably influenced our prediction models. Second, while HRS is a large study representative of the US with oversampling for Black and Hispanic adults, other racial/ethnic minority groups are not well represented. Validation of discrimination and calibration in other racial/ ethnic minority groups, such as Asians, Pacific Islanders, and Indigenous people would be beneficial.

In conclusion, our comprehensive prognostic tool represents an important advance for the field. Predicting ADL disability and walking disability in addition to mortality will provide relevant information for providers, patients, and their families, to inform and improve decision-making for aging adults. To facilitate ease-of-use in busy clinical settings, we

reduced the common barriers to prediction models by minimizing time needed to assess each variable, as well as allowing for unavailable predictors. This new comprehensive prognostic tool will be available on ePrognosis to ensure easy access for clinicians and other professionals who create health and financial plans for older adults. It is our hope that this comprehensive prognostic tool will help older adults prepare better for their future physical, emotional, and financial needs, thereby improving quality of life for older adults and their families.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## ACKNOWLEDGEMENTS

We would like to acknowledge Brian Nguyen, BA, Research Assistant in the Division of Geriatrics, for his valuable contributions in organizing and facilitating this study.

#### Sponsor's Role

The sponsor was not involved in the design, methods, analysis and interpretation of the data, and preparation of the manuscript.

#### Funding:

This study was supported by grants from the NIH/NIA: R01AG047897, T32AG212000, K24AG068312, and K24AG066998.

The HRS (Health and Retirement Study) is sponsored by the National Institute on Aging (grant number NIA U01AG009740) and is conducted by the University of Michigan.

## REFERENCES

- 1. Gill TM. The central role of prognosis in clinical decision making. JAMA. 2012;307(2):199–200. doi:10.1001/jama.2011.1992 [PubMed: 22235093]
- Lee SJ, Leipzig RM, Walter LC. Incorporating lag time to benefit into prevention decisions for older adults. JAMA. 2013;310(24):2609–2610. doi:10.1001/jama.2013.282612 [PubMed: 24322396]
- Wilt TJ, Harris RP, Qaseem A, et al. Screening for cancer: Advice for high-value care from the American college of physicians. Annals of Internal Medicine. 2015;162(10):718–725. doi:10.7326/ M14-2326 [PubMed: 25984847]
- Smith RA, Andrews KS, Brooks D, et al. Cancer screening in the United States, 2018: A review of current American Cancer Society guidelines and current issues in cancer screening. CA: A Cancer Journal for Clinicians. 2018;68(4):297–316. doi:10.3322/caac.21446 [PubMed: 29846940]
- Fried TR, Bradley EH, Towle VR, Allore H. Understanding the Treatment Preferences of Seriously III Patients. New England Journal of Medicine. 2002;346(14):1061–1066. doi:10.1056/ NEJMsa012528 [PubMed: 11932474]
- Schonberg MA, Li V, Marcantonio ER, Davis RB, McCarthy EP. Predicting Mortality up to 14 Years Among Community-Dwelling Adults Aged 65 and Older. J Am Geriatr Soc. Published online 2017. doi:10.1111/jgs.14805
- Yourman LC, Lee SJ, Schonberg M a, Widera EW, Smith AK Prognostic indices for older adults: a systematic review. JAMA. 2012;307(2):182–192. doi:10.1001/jama.2011.1966 [PubMed: 22235089]
- Cruz M, Covinsky K, Widera E, Stijacic-Cenzer I, Lee S. Predicting 10 year mortality for older adults. J Am Med Assoc. 2013;309(9):875–876. doi:10.1136/bmj.f174.2.

- Lee SJ, Boscardin WJ, Kirby KA, Covinsky KE. Individualizing life expectancy estimates for older adults using the gompertz law of human mortality. PLoS ONE. 2014;9(9):e108540. doi:10.1371/ journal.pone.0108540
- Lee SJ, Smith AK, Grisell Diaz-Ramirez L, et al. A Novel Metric for Developing Easy-to-Use and Accurate Clinical Prediction Models The Time-cost Information Criterion. Medical Care. 2021;59:418–424. www.lww-medicalcare.com [PubMed: 33528231]
- Aliberti MJR, Kotwal AA, Smith AK, Lee SJ, Banda S, Boscardin WJ. Pre-estimating subsets: A new approach for unavailable predictors in prognostic modeling. J Am Geriatr Soc. 2021;69(9):2675–2678. doi:10.1111/jgs.17278 [PubMed: 34002370]
- 12. Health and Retirement Study. Produced and distributed by the University of Michigan with funding from theNational Institute on Aging (grant numbers U01AG009740, RC2AG036495, and RC4AG039029). Ann Arbor, MI.
- Calle EE, Terrell DD. Utility of the National Death Index for Ascertainment of Mortality among Cancer Prevention Study II Participants. American Journal of Epidemiology. 1993;137(2):235– 241. doi:10.1093/oxfordjournals.aje.a116664 [PubMed: 8452128]
- Levin MA, Lin HM, Prabakar G, McCormick PJ, Egorova NN. Alive or dead: Validity of the Social Security Administration Death Master File after 2011. Health Services Research. 2019;54(1):24–33. doi:10.1111/1475-6773.13069 [PubMed: 30520023]
- Research Data Assistance Center (RESDAC). Death Information in the Research Identifiable Medicare Data. Published 2018. Accessed February 10, 2022. https://resdac.org/articles/deathinformation-research-identifiable-medicare-data
- Lee SJ, Lindquist K, Segal MR, Covinsky KE. Development and validation of a prognostic index for 4-year mortality in older adults. Jama. 2006;295(7):801–808. doi:10.1001/jama.295.7.801 [PubMed: 16478903]
- Cerdeña JP, Plaisime M v, Tsai J. From race-based to race-conscious medicine: how anti-racist uprisings call us to act. The Lancet. 2020;396(10257):1125–1128. doi:10.1016/ S0140-6736(20)32076-6
- Diaz-Ramirez LG, Lee SJ, Smith AK, Gan S, Boscardin WJ. A Novel Method for Identifying a Parsimonious and Accurate Predictive Model for Multiple Clinical Outcomes. Computer Methods and Programs in Biomedicine. 2021;204. doi:10.1016/j.cmpb.2021.106073
- Uno H, Cai T, Tian L, Wei LJ. Evaluating prediction rules for t-year survivors with censored regression models. J Am Stat Assoc. 2007;102(478):527–537. doi:10.1198/016214507000000149
- 20. Wolbers M, Koller MT, Witteman JCM, Steyerberg EW. Prognostic models with competing risks methods and application to coronary risk prediction. Epidemiology. 2009;20(4):555–561. doi:10.1097/EDE.0b013e3181a39056 [PubMed: 19367167]
- Noma H, Shinozaki T, Iba K, Teramukai S, Furukawa TA. Confidence intervals of prediction accuracy measures for multivariable prediction models based on the bootstrap-based optimism correction methods. Statistics in Medicine. 2021;40(26):5691–5701. doi:10.1002/sim.9148 [PubMed: 34302372]
- 22. Steyerberg EW, Harrell FE, Borsboom GJJM, et al. Internal Validation of Predictive Models: Efficiency of Some Procedures for Logistic Regression Analysis. Vol 54.; 2001.
- Harrell FE, Lee KL, Mark DB. Multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. Stat Med. 1996;15(4):361–387. doi:10.1002/(SICI)1097-0258(19960229)15:4<361::AID-SIM168>3.0.CO;2-4 [PubMed: 8668867]
- Covinsky KE, Hilton J, Lindquist K, Dudley RA. Development and validation of an index to predict activity of daily living dependence in community-dwelling elders. Med Care. 2006;44(2):149–157. doi:10.1097/01.mlr.0000196955.99704.64 [PubMed: 16434914]
- Aliberti MJR, Covinsky KE, Apolinario D, et al. 10-minute targeted geriatric assessment predicts disability and hospitalization in fast-paced acute care settings. Journals of Gerontology - Series A Biological Sciences and Medical Sciences. 2019;74(10):1637–1642. doi:10.1093/gerona/glz109 [PubMed: 31056669]

- Wolff JL, Mulcahy J, Roth DL, et al. Long-Term Nursing Home Entry: A Prognostic Model for Older Adults with a Family or Unpaid Caregiver. J Am Geriatr Soc. 2018;66(10):1887–1894. doi:10.1111/jgs.15447 [PubMed: 30094823]
- 27. Yourman LC, Cenzer IS, Boscardin WJ, et al. Evaluation of Time to Benefit of Statins for the Primary Prevention of Cardiovascular Events in Adults Aged 50 to 75 Years. JAMA Internal Medicine. 2021;181(2):179. doi:10.1001/jamainternmed.2020.6084 [PubMed: 33196766]
- Rodriguez-Gutierrez R, Gonzalez-Gonzalez JG, Zuñiga-Hernandez JA, McCoy RG. Benefits and harms of intensive glycemic control in patients with type 2 diabetes. The BMJ. 2019;367:1–20. doi:10.1136/bmj.l5887
- Pellegrini F, Copetti M, Sormani MP, et al. Predicting disability progression in multiple sclerosis: Insights from advanced statistical modeling. Multiple Sclerosis Journal. 2020;26(14):1828–1836. doi:10.1177/1352458519887343 [PubMed: 31686590]
- Law MTK, Traboulsee AL, Li DKB, et al. Machine learning in secondary progressive multiple sclerosis: an improved predictive model for short-term disability progression. Multiple Sclerosis Journal - Experimental, Translational and Clinical. 2019;5(4). doi:10.1177/2055217319885983
- Ahalt C, Walter LC, Yourman L, Eng C, Pérez-Stable EJ, Smith AK. "Knowing is better": Preferences of diverse older adults for discussing prognosis. Journal of General Internal Medicine. 2012;27(5):568–575. doi:10.1007/s11606-011-1933-0 [PubMed: 22127798]
- Schoenborn NL, Boyd CM, Lee SJ, Cayea D, Pollack CE. Communicating about Stopping Cancer Screening: Comparing Clinicians' and Older Adults' Perspectives. Gerontologist. 2019;59:S67– S76. doi:10.1093/geront/gny172 [PubMed: 31100135]
- Schoenborn NL, Lee K, Pollack CE, et al. Older adults' views and communication preferences about cancer screening cessation. In: JAMA Internal Medicine. Vol 177. American Medical Association; 2017:1121–1128. doi:10.1001/jamainternmed.2017.1778 [PubMed: 28604917]

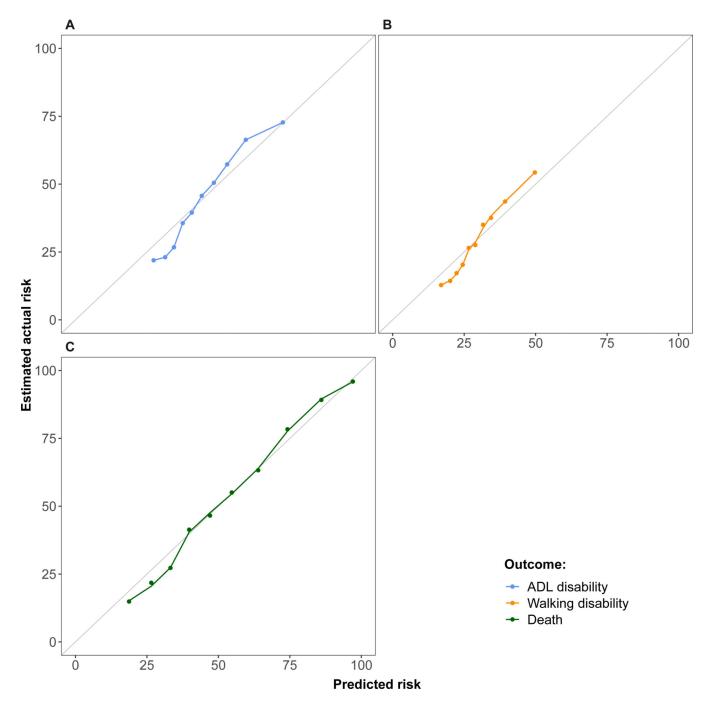
## **KEY POINTS**

- We created a comprehensive prognostic tool that accurately predicts longterm risk of mortality, walking disability, and ADL disability in adults 70years.
- At a similar level of mortality risk, the risk of walking disability and ADL disability differed substantially between individuals, demonstrating the need for personalized predictions of each outcome.

## WHY DOES THIS MATTER?

This comprehensive prognostic tool will provide invaluable information on long-term risk of disability and mortality for older adults and their families as they plan for future healthcare and caregiving needs.

Lee et al.



**Figure 1.** Calibration Plots for 10-year Risk of ADL Disability, Walking Disability, and Death. For each calibration plot, one dot represents a decile (one-tenth) of participants. The X axis is the observed risk of the outcome and the Y axis is the estimated risk from the model. In an ideal calibration plot, all dots would be exactly on the 45degree line, indicating that the observed risk is the same as the predicted risk. Panel A [blue line] is for ADL Disability, Panel B [orange line] is for Walking Disability, and Panel C [dark green line] is for Mortality.

Lee et al.

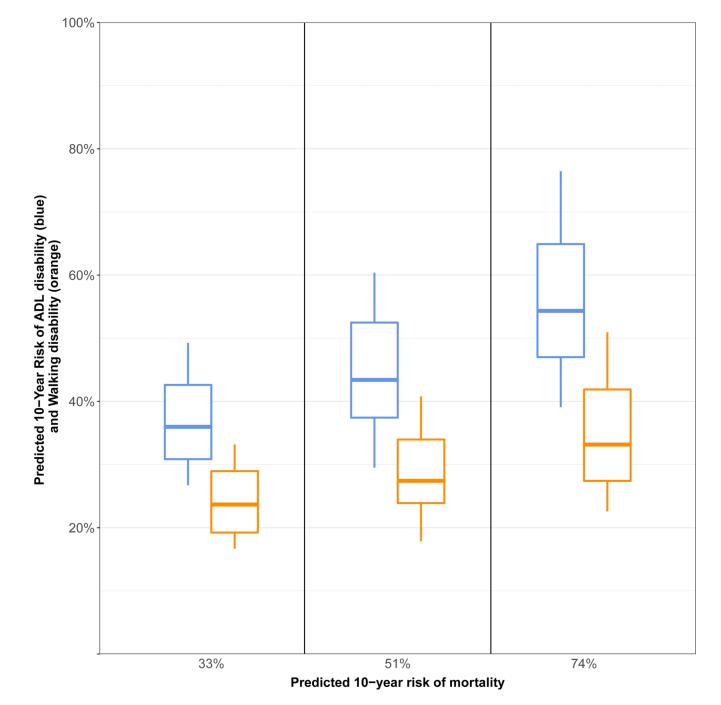


Figure 2. Boxplots of Predicted 10-year Risk of ADL disability and Walking disability by Predicted Risk of Mortality

For each boxplot, the horizontal lines are the  $25^{\text{th}}$  percentile, median, and  $75^{\text{th}}$  percentile of predicted disability risk; the whiskers are the  $5^{\text{th}}$  and  $95^{\text{th}}$  percentiles. The percentiles of predicted disability risks are not weighted. The predicted 10-year risk of mortality of 33% corresponds to the  $23^{\text{rd}} - 27^{\text{th}}$  percentiles of predicted mortality risk. The 10-year mortality risk of 51% corresponds to the  $48^{\text{th}}-52^{\text{nd}}$  percentiles of mortality risk. The 10-year mortality risk of 74% corresponds to the  $73^{\text{rd}} - 27^{\text{th}}$  percentiles of predicted mortality risk.

#### Table 1.

Baseline Characteristics of Adults Aged 70 in HRS, by Mortality Status during follow-up, n=6,646.

	Overall	Died	Alive
	n=6,646	n=5,689	n=957
Age, mean ± SD	$77.5\pm6.34$	$78.2\pm6.42$	$73.5\pm3.46$
Female	59.0	57.2	69.1
Race/Ethnicity			
Non-Hispanic White	85.7	85.8	85.4
Non-Hispanic Black	7.9	8.2	5.9
Other	6.4	6.0	8.7
BMI, mean $\pm$ SD	$25.9\pm5.25$	$25.8 \pm 5.32$	$26.4\pm4.87$
Smoking			
Current smoker	8.4	9.0	4.5
Former smoker	46.4	47.9	38.2
Hypertension	52.3	54.5	39.8
Heart Failure	4.6	5.3	0.8
Stroke	9.8	11.0	2.7
Lung Disease	9.3	10.6	1.7
Cancer	15.8	16.9	9.7
Diabetes	15.1	16.5	7.5
Pain	28.2	29.7	20.1
Lives alone	34.0	35.2	27.3
IADL Difficulty			
Preparing hot meals	8.4	9.7	0.8
Managing money	7.9	9.0	1.3
Reading map	11.7	12.1	9.5
Taking medications	4.2	4.7	1.1
Some difficulty eating	3.9	4.6	0.3
Some difficulty pushing large object	37.3	40.2	21.4
Some difficulty walking several blocks	39.5	43.2	18.6
Did volunteer work in past year	29.7	27.4	42.8
Proxy respondent	9.4	10.1	5.5

Data are weighted percent except when noted as mean  $\pm$  standard deviation.

#### Table 2.

#### Hazard Ratios from the Final Prediction Models

	Hazard Ratio (95% Confidence Interval)					
Predictor	Death [Cause-specific HR]	ADL disability [Sub- distribution HR]	Walking disability [sub- distribution HR]			
Age						
Spline 1	1.12 (1.08 – 1.15)	1.04 (1.00, 1.09)	1.05 (1.00, 1.11)			
Spline 2	0.97 (0.83 – 1.13)	1.09 (0.89, 1.33)	1.04 (0.84, 1.28)			
Spline 3	1.00 (0.64 – 1.57)	0.75 (0.44, 1.30)	0.78 (0.45, 1.38)			
Male gender	1.56 (1.43 – 1.69)	0.81 (0.74, 0.87)	0.79 (0.71, 0.87)			
BMI						
Spline 1	0.91 (0.88 - 0.93)	1.00 (0.97, 1.04)	1.02 (0.98, 1.06)			
Spline 2	1.19 (1.08 – 1.30)	1.01 (0.89, 1.15)	0.96 (0.84, 1.10)			
Spline 3	0.68 (0.51 - 0.90)	0.97 (0.66, 1.44)	1.14 (0.76, 1.71)			
Smoking (ref: never)						
Former	1.19 (1.11 – 1.27)	1.02 (0.94, 1.10)	0.98 (0.89, 1.08)			
Current	1.66 (1.40 – 1.96)	0.93 (0.80, 1.08)	0.84 (0.71, 0.99)			
Diabetes	1.38 (1.11 – 1.72)	1.18 (1.06, 1.32)	1.11 (0.97, 1.26)			
Ever have cancer	1.21 (1.13 – 1.31)	1.11 (1.00, 1.23)	1.06 (0.94, 1.19)			
Heart Problems or Heart Failure (ref: none)						
Heart problems but not heart failure	1.23 (1.15 – 1.31)	1.01 (0.94, 1.10)	0.98 (0.89, 1.08)			
Heart failure	1.58 (1.36 – 1.84)	0.87 (0.67, 1.14)	0.89 (0.71, 1.13)			
High blood pressure	1.18 (1.10 – 1.27)	1.08 (1.00, 1.17)	1.02 (0.93, 1.12)			
Lung disease	1.72 (1.56 – 1.90)	0.96 (0.82, 1.12)	0.80 (0.68, 0.95)			
Stroke (ref: never)						
Stroke without remaining problems	1.23 (1.09 – 1.39)	1.25 (1.04, 1.50)	1.31 (1.09, 1.58)			
Stroke with remaining problems	1.02 (0.83 – 1.26)	1.23 (0.95, 1.61)	1.16 (0.93, 1.44)			
Lives alone	1.10 (1.04 – 1.17)	0.88 (0.81, 0.95)	0.98 (0.89, 1.08)			
Difficulty preparing hot meals	1.39 (1.14 – 1.69)	1.27 (0.99, 1.64)	1.24 (1.00, 1.53)			
Difficulty managing money	1.34 (1.18 – 1.51)	1.46 (1.23, 1.74)	1.30 (1.06, 1.59)			
Some difficulty eating	1.38 (1.11 – 1.72)	1.41 (0.89, 2.23)	1.29 (0.94, 1.75)			
Difficulty pushing large object	1.24 (1.13 – 1.35)	1.12 (1.03, 1.21)	1.10 (0.99, 1.21)			
Difficulty walking several blocks	1.40 (1.29 – 1.51)	1.20 (1.09, 1.32) 1.27 (1.15, 1.40)				
iAUC (95% Confidence Interval)	0.803 (0.790 - 0.816)	0.709 (0.690 - 0.728)	0.694 (0.672 - 0.716)			
Optimism corrected iAUC (95% Confidence Interval)	0.799 (0.789 – 0.810)	0.703 (0.681 - 0.713) 0.686 (0.665 - 0.700)				

iAUCs calculated using inverse probability of censoring weighting to provide 95% confidence intervals.

## Table 3.

Discrimination of Prediction Models with 1 or 2 Unavailable Predictors Compared to the Full Prediction Models

Best- and worst-case scenarios	Missing information	Discrimination (iAUC)			
		Mortality	ADL Disability	Walking Disability	Average across Outcomes
No missing predictors (reference)	None (Full model, 16 predictors)	0.803	0.709	0.692	0.734
Best-case scenario for 1 missing predictor	Difficulty eating	0.802	0.708	0.690	0.733
Worst-case scenario for 1 missing predictor	Difficulty walking several blocks	0.798	0.709	0.696	0.726
Best-case scenario for 2 missing predictors	Difficulty eating, stroke	0.800	0.707	0.689	0.732
Worst-case scenario for 2 missing predictors	Difficulty walking several blocks, lung disease	0.793	0.700	0.684	0.726