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Incident disability in older adults: prediction models based on two British prospective cohort studies

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Abstract

Objective: to develop and validate a prediction model for incident locomotor disability after 7 years in older adults.
Setting: prospective British cohort studies: British Women's Heart and Health Study (BWHHS) for development and the English Longitudinal Study of Ageing (ELSA) for validation.
Subjects: community-dwelling older adults.
Methods: multivariable logistic regression models after selection of predictors with backward elimination. Model performance was assessed using metrics of discrimination and calibration. Models were internally and externally validated.
Results: locomotor disability was reported in BWHHS by 861 of 1,786 (48%) women after 7 years. Age, a history of arthritis and low physical activity levels were the most important predictors of locomotor disability. Models using routine measures as predictors had satisfactory calibration and discrimination (*c*-index 0.73). Addition of 31 blood markers did not increase the predictive performance. External validation in ELSA showed reduced discrimination (*c*-index 0.65) and an underestimation of disability risks. A web-based calculator for locomotor disability is available (http://www.sealedenvelope.com/trials/bwhhsmodel/).
Conclusions: we developed and externally validated a prediction model for incident locomotor disability in older adults based on routine measures available to general practitioners, patients and public health workers, and showed an adequate discrimination. Addition of blood markers from major biological pathways did not improve the performance of the model. Further replication in additional data sets may lead to further enhancement of the current model.

Keywords: *aged, locomotor disability, clinical prediction rule, older people*

Introduction

Life expectancy has been increasing in recent decades, and the proportion of people above 65 years has risen in the United Kingdom (UK) from 5.3% in 1911 to 16.4% in 2011 [1]. Ageing is associated with multimorbidity [2], which often results in disability and loss of independence, reduces quality of life [3] and increases the risk of mortality [4]. Interventions such as physical activity programs can have a positive effect on disability in older adults [5, 6]. Nevertheless, rising numbers of older disabled adults will increase demand on the limited resources of health-care systems [7]. Accurate identification of older people at high risk of disability would help to efficiently target preventive programs to these people, help plan long-term care and treatments, and enable a more efficient design for randomised trials of interventions to prevent the onset of disability [8].

Although a considerable amount of aetiological research has been undertaken to identify risk factors for disability in older adults [9–13], studies constructing prediction models for incident disability in the general population are scarce. Most studies used small to moderate samples or lacked external validation [11, 13, 14]. Several studies found associations between different biological pathways such as inflammation, coagulation, liver or kidney disease as measured by serum blood markers and disability [15–17], but it is unclear how much these blood markers add to more readily available clinical measures. To the best of our knowledge, no model to

predict locomotor disability exists for community-dwelling older adults in the general UK population.

We used data from two UK population-based prospective studies to develop and validate a prediction model [18–20] that can be used to predict incident locomotor disability in older adults based on routine measures and tested the potential benefit of adding blood markers that proxy major biological pathways associated with disability [17].

Materials and methods

The multivariable prediction models were developed in the British Women's Heart and Health Study (BWHHS), and their performance was assessed by calibration and discrimination [19, 20]. The English Longitudinal Study of Ageing (ELSA) was used for external validation in another population [18].

Development of the prediction model in BWHHS

Study sample

We used data from the BWHHS, a prospective cohort study of women aged between 60 and 79 years who were randomly selected from general practice lists in 23 towns in England, Scotland and Wales [21]. Between 1999 and 2001, baseline data were collected in 4,286 women using self-completed questionnaires, interviews by a research nurse, physical examinations and review of primary care medical records. In 2003 and 2007, follow-up data on outcomes using self-reported questionnaires were collected.

Disability outcome

Participants were considered to suffer from locomotor disability if they reported difficulty with going up or down stairs, bending down, straightening up, keeping balance, going out of the house or walking 400 yards [17, 22]. Questions about locomotor disability were asked at baseline and after 3 and 7 years. The primary outcome was locomotor disability at 7 years and—as a secondary analysis—at 3 years.

Baseline variables

The selection of potential predictors was based on published evidence of risk factors for our primary outcome and comprised age, health conditions, lifestyle factors, medication use and available blood markers from major biological pathways [13, 17, 22–24]. Details are provided in Supplementary data, Appendix S1 available in *Age and Ageing* online. We included 31 blood markers that proxy the following pathways: inflammation, coagulation, liver, renal and other metabolic disorders. Blood markers were measured at baseline and details of measurement procedures are reported elsewhere [17, 25, 26].

Statistical analysis

Women with locomotor disability at baseline were excluded from all analyses. We used multivariable logistic regression models accounting for the clustered sampling of women within towns. Continuous variables were transformed using natural logarithms as appropriate and entered as linear terms in the regression models unless there was evidence for a departure from linearity compared with quadratic or cubic transformations using likelihood ratio tests. We explored interactions between health conditions and medication use and between blood pressure and use of cardiovascular medication. Missing data in candidate predictors were addressed using multiple imputation with all candidate covariates in the imputation model to create 10 imputations. We started with all non-laboratory candidate predictors and performed backward elimination to remove variables with $P > 0.05$ to obtain prediction models without blood markers. In a second step, we examined whether addition of blood markers improved the prediction of the previous models by a backward elimination to remove blood markers with $P > 0.05$. Calibration was examined by plotting observed proportions against predicted risks and Hosmer–Lemeshow P values. Discrimination was examined by receiver operation characteristics (ROC) curves and concordance (c) index, which is equivalent to the area under ROC curves. Internal validation to assess optimism in model performance was done using bootstrapping: we compared c-indices from models developed in 200 bootstrap samples to c-indices in the same models applied to the original sample [18, 20].

External validation of the prediction model in ELSA

We externally validated our models in the ELSA, a longitudinal study from a representative sample of the English population aged 50 and older [27]. Baseline data were collected in 2002/03 from a total of 12,099 respondents using self-completed questionnaires, face-to-face interviews and clinical measurements. After 8 years, data on locomotor disability were obtained using self-completed questionnaires [28]. We assessed calibration and discrimination of the model constructed based on BWHHS data with the original coefficients in all ELSA data and in ELSA restricted to women only. We also used ELSA to test whether gender is an independent predictor of locomotor disability using a likelihood ratio test. All P values are two sided.

Results

Development of the prediction model in BWHHS

Two thousand three hundred and seventy-seven women in the BWHHS [17] reported no locomotor disability at baseline and were included (Supplementary data, Appendix S2 available in *Age and Ageing* online). Women were on average 68 years old with a BMI of 26.9 kg/m^2, 10% were current smokers and 45% were physically active. The most frequent health conditions were respiratory diseases (49%) and

arthritis (37%). One thousand seven hundred and eighty-six women were followed up after 7 years and 861 (48%) reported locomotor disability. Variables contained a median of 2% missing observations (range: 0–12%). Blood markers used for model development are shown in Supplementary data, Appendix S3 available in *Age and Ageing* online.

The strongest predictors (according to z-values) for locomotor disability after 7 years were age, low physical activity and a history of arthritis (Table 1). In models without and with blood markers predicted risks corresponded to observed proportions ($P = 0.47$, Figure 1). Discrimination in models without blood markers was satisfactory (c-index 0.73). Prediction models for locomotor disability after 3 years (Supplementary data, Appendix S4 available in *Age and Ageing* online) or for a composite of locomotor disability and death after 7 years were very similar (Supplementary data, Appendix S5 available in *Age and Ageing* online). CRP and IL-6 were the only blood markers of the 31 evaluated that were retained, and when added to the prediction model, the c-index increased to 0.74 (Table 1). Internal validation showed only slight decreases of the c-index, indicating a very low over-optimism in model development (Supplementary data, Appendix S6 available in *Age and Ageing* online).

External validation in ELSA

Given the minimal increase in the prediction ability of adding blood markers to the models, we only replicated the prediction models without blood markers. In ELSA, 5,635 participants had no locomotor disability at baseline and of these 3,194 (57%) with 8 years of follow-up were included. Participants had a mean age of 61, 49% were women, 76% were physically active, 14% had arthritis and only 7 (0.2%) had a hip fracture (Supplementary data, Appendix S2 available in *Age and Ageing* online). Of these, 1,430 (45%) developed locomotor disability after 8 years. Figure 1 shows the performance of the BWHHS prediction model in ELSA. Discrimination was lower than in BWHHS (c-index 0.65), and calibration suggested that predicted risks of locomotor disability were lower than observed risks for all risk categories ($P < 0.001$). Discrimination and calibration were similar when the model was applied to female ELSA participants only (Supplementary data, Appendix S7 available in *Age and Ageing* online). We also examined prediction models with and without gender as additional predictor of locomotor disability in ELSA (Supplementary data, Appendix S7 available in *Age and Ageing* online). Although gender was an independent predictor ($P < 0.001$), the c-index in the model with gender as an additional predictor was comparable to the model with original predictors as selected in BWHHS only (0.68 versus 0.67). Calibration was adequate in all models ($P > 0.40$).

Online calculator

Results were used to create an online calculator that predicts risks of locomotor disability available at http://www.sealedenvelope.com/trials/bwhhsmodel/. Box 1 explains details of calculation of predicted risks. While a 'healthy'

Table 1. Multivariable prediction models for locomotor disability after 7 years ($n = 1,786$)

Predictors	Model without blood markers			Model with blood markers		
	OR	95% CI	z score	OR	95% CI	z score
Age, per 10 years	2.40	(2.06–2.79)	11.29	2.36	(2.04–2.73)	11.60
Physical activity	0.56	(0.47–0.68)	−5.99	0.61	(0.50–0.73)	−5.07
Healthy diet	0.71	(0.51–0.97)	−2.14	0.72	(0.51–1.01)	−1.88
Smoker, former	1.46	(1.18–1.81)	3.53	1.46	(1.18–1.80)	3.46
Smoker, current	1.31	(0.84–2.05)	1.19	1.18	(0.78–1.78)	0.78
Systolic BP, per 10 mmHg	0.95	(0.91–0.99)	−2.35	0.94	(0.90–0.98)	−2.68
Medication use, per 1 drug	1.18	(1.11–1.26)	5.30	1.16	(1.09–1.23)	4.90
Arthritis	1.72	(1.44–2.06)	5.96	1.72	(1.42–2.08)	5.56
Depression	1.84	(1.41–2.39)	4.56	1.88	(1.45–2.42)	4.83
Cardiovascular disease	1.62	(1.18–2.22)	2.97	1.59	(1.16–2.20)	2.84
Hip fracture	1.84	(1.26–2.69)	3.15	1.77	(1.22–2.57)	2.99
CRP, per 1 ln(mg/l)				1.16	(1.01–1.32)	2.06
IL-6, per 1 ln(pg/ml)				1.60	(1.14–2.26)	2.71
IL-6, per 1 ln(pg/ml)^2				0.92	(0.82–1.03)	−1.45
Model performance[a]	Median	Range		Median	Range	
c-Index	0.733	(0.732–0.733)		0.743	(0.742–0.747)	
Hosmer–Lemeshow P value	0.466	(0.442–0.476)		0.474	(0.446–0.498)	

95% CI, 95% confidence interval; BP, blood pressure; CRP, C-reactive protein; IL-6, interleukin-6; OR, odds ratio.

[a]Median and ranges across 10 imputations.

Participants were considered physically active if they reported moderate to vigorous exercise for at least 2 h per week. Participants were considered to follow a healthy diet if they reported to consume at least 4-5 portions of fruits or vegetables per day. Smoking was self-reported and classified as current, former or never smoker. Alcohol consumption was self-reported and was classified into never, occasional (1-2 times a month or on special occasions only) and regular (daily on most days or weekends only). Use of cardiovascular medication (aspirin, blood-pressure and lipid-lowering medication) was classified according to BNF codes. Self-reported arthritis: osteoarthritis, rheumatoid arthritis or any other form. Cardiovascular disease: myocardial infarction, angina, stroke, claudication, deep vein thrombosis, pulmonary embolism or aortic aneurysm. Hip fracture is self-reported by participants. Depression was considered present if participants reported being moderately or extremely anxious or depressed on the respective question of the European Quality of Life (EQ-5D) instrument.

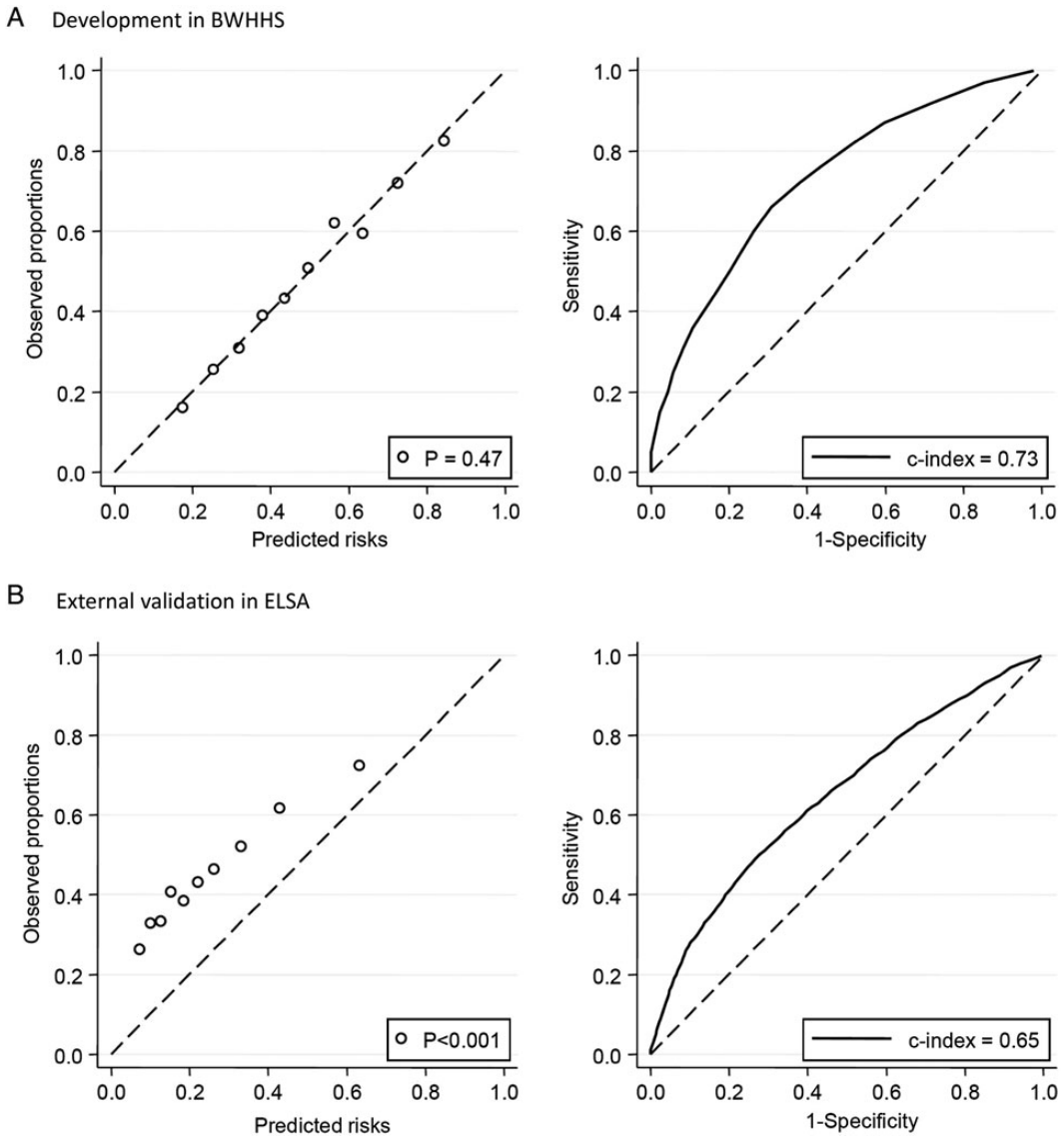


Figure 1. Performance of prediction models (without blood markers) for locomotor disability in the BWHHS after 7 years (Development, Panel A) and in the ELSA after 8 years (External validation, Panel B), which was assessed by calibration using expected and observed deciles of risks (left) and discrimination using ROC curves (right). Presented are median *P* values from Hosmer–Lemeshow tests and median *c*-indices across 10 imputations.

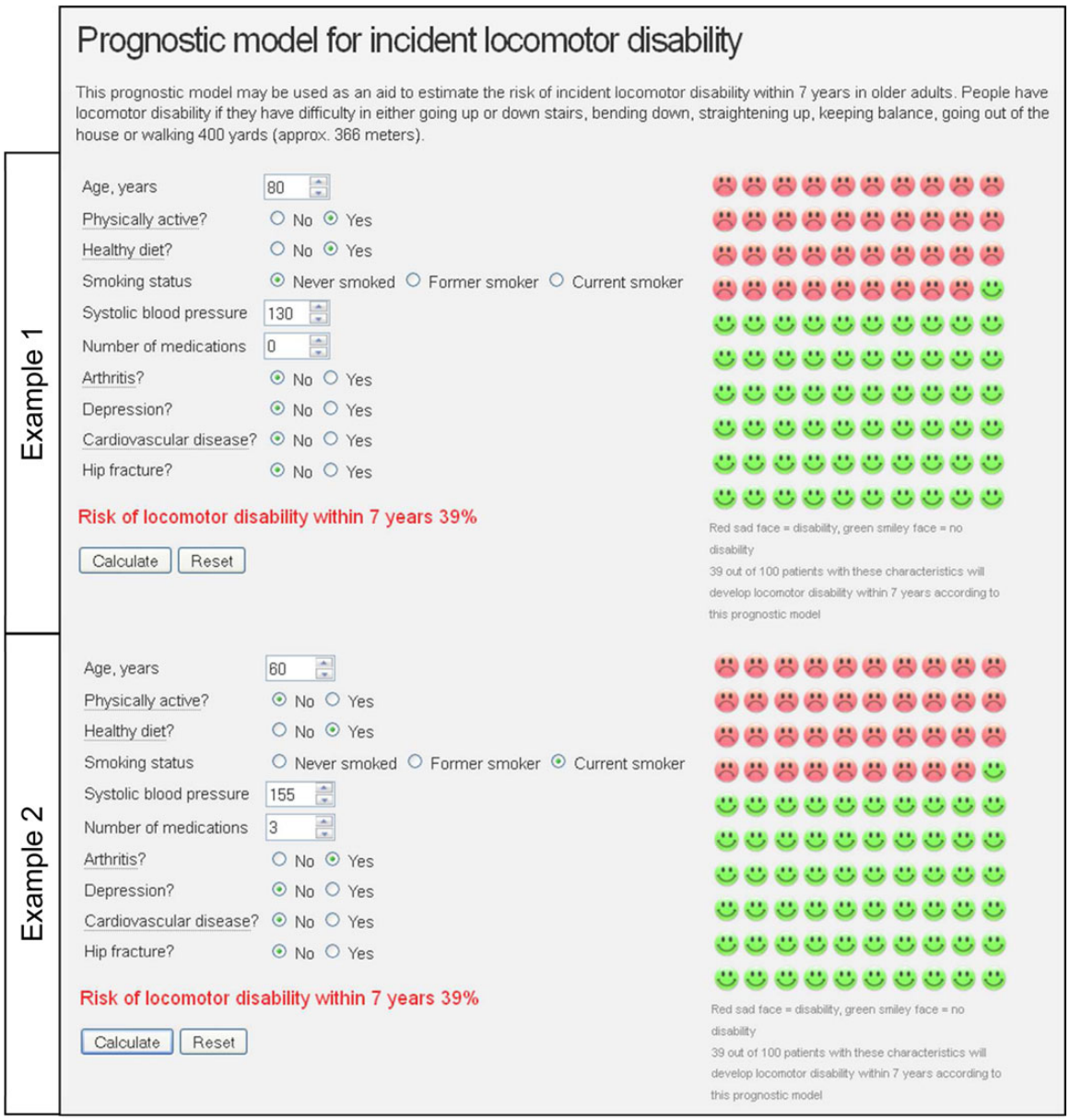
woman reaches a risk of 39% locomotor disability by the age of 80 (Example 1), a similar risk could already be present 20 years earlier with several risk factors present (Example 2). Supplementary data, Appendix S8 available in *Age and Ageing* online shows distributions of risk scores in women by locomotor disability status and corresponding predicted risks. Locomotor disability risk at 7 years predicted from models without blood markers ranged from 17% (95% CI 16–19%) in women with the 10% lowest risk scores to 82% (95% CI 80–83%) in women with the 10% highest risk scores. Accuracy of risk scores using the model without blood markers (Supplementary data, Appendix S9 available in *Age and Ageing* online) showed that higher risk score values (e.g. 70) are needed to get satisfactory power to rule in locomotor disability, but at the expense of low sensitivity of 20%.

Discussion

Using data from two population-based prospective studies in older British adults, we showed that a model containing easily measured predictors, available to general practitioners during routine medical evaluation, had a reasonable prediction capacity and validity to identify incident disability. We also provide an online calculator that could be implemented in primary care with minimal resources. The strongest predictors in our model were older age, low physical activity and a history of arthritis. Additional information on 31 blood markers covering major biological pathways had a minimal incremental benefit. The additional cost and logistics associated with these blood markers therefore do not justify their inclusion. Discrimination of the model in an

Box 1 Calculation of predicted risks of incident locomotor disability.

An online calculator to predict risks of locomotor disability is available from http://www.sealedenvelope.com/trials/bwhhsmodel/.



Calculation of risks

The predicted risk π_j of locomotor disability in the jth woman with k different risk factor levels x_j is derived from logit $(\pi_j) = \beta_0 + \Sigma_{i=1 \text{ to } k} (\beta_i * x_{ij})$ with β_i being the ith beta-coefficient estimated from the prediction model.

external sample was lower, which coincides with our internal validation suggesting very low over-optimism. Calibration suggested an underestimation of disability risks in the external sample. However, good discriminatory capacity is more important than good calibration, as the model aims at identifying people with higher disability risks to prioritise allocation of preventive care programs to those with the greatest need.

Strengths of our study include the wide range of potential predictors available, the long follow-up of 7 years in the BWHHS and the validation of our models in an external sample. We found a reduced predictive capacity of our models in ELSA, which might be due to differences in measurements of some important predictors and in the prevalence of other characteristics such as alcohol consumption or

respiratory conditions. The performance of these models other populations in- and outside the United Kingdom remains to be determined, and updating the model with adjustments for baseline risks or predictor weights might help to improve performance in external populations [18, 29]. Further strengths are relatively low missing data and the use of imputation in baseline characteristics to further improve this. However, one-fourth of the women without baseline locomotor disability died or was lost to follow-up, and was excluded, which might have resulted in an underestimation of disability risks. Our prediction models were developed in women only, which may limit the application of our models to men or mixed populations and may explain the lower performance in the external mixed cohort. However, when we assessed gender as additional predictive factor, the increase in the discriminatory capacity was minimal. Some variables reported to predict disability (e.g. cognitive function and muscle strength) [11, 30] were not available in the BWHHS and could have improved performance. However, the wide range of predictors included means it is unlikely that we have missed variables that would increase performance substantially. For an unmeasured predictor to substantially increase the prediction capacity, the variable would need not only to be strongly associated with disability but also to be minimally correlated with the predictors already included. Women who died could not be assessed for locomotor disability and were excluded from the main analyses, which could have introduced selection bias. However, the performance of our model was similar for a composite of locomotor disability or death. Accuracy of the derived risk scores was limited, regardless of cut-offs chosen. Thus, rather extreme cut-off values in the risk scores are needed to rule in or rule out locomotor disability with sufficient certainty for clinical practice. However, it is important to note that the discriminatory capacity of our model (*c*-index 0.71–0.74) is within the range of values reported for the widely used Framingham risk score used for risk prediction of coronary heart disease [31].

To our knowledge, this is the first report to develop and validate a prediction model for incident locomotor disability [18–20]. All factors, which were retained in our prediction model, have previously been reported to predict disability. Variability of alcohol consumption in women in the BWHHS is lower than in comparable studies [32]. This might explain why we found low physical activity a stronger predictor, while previous studies suggested alcohol use to be predictive [33]. Unlike other studies that included cases with (mild) disability at baseline, we restricted our sample to participants free of locomotor disability at baseline and were able to predict incident locomotor disability. Various cut-offs to denote different levels of severity of disability have been used. Our prediction models had a discrimination capacity similar to other prediction models, but calibration and validation have not been reported in other prediction models for disability [11, 33].

We developed a prediction model to identify older people at high risk of developing incident locomotor disability, because these people are likely to need more care when living at home or even admission to residential care. Our prediction model is intended to help target limited resources for individual or community interventions to the most relevant people. For example, interventions such as progressive resistance training [5] require a substantial commitment from the patient, the care giver and often physical resources (gym or clinic). Further studies will be needed to determine whether individuals at high risk of disability identified by our web-based risk score benefit from physical training, social or other interventions, and whether use of health-care resources are optimised. The risk score may also minimise resource allocation to people at very low risk of developing disability.

Our prediction model is based on information that can be obtained during a routine physician appointment or that is available to people themselves without the need for a physician to administer it. However, before experimental studies are conducted to evaluate its utility in primary care settings and public health work, further replication of this model is needed in additional samples that may serve to refine the predictive capacity of the current model [18, 29]. To facilitate the evaluation of the prediction model, we have implemented a web-based calculator for locomotor disability risk (see http://www.sealedenvelope.com/trials/bwhhsmodel).

Key points

- Prediction model for incident disability in older adults based on routine measures was developed and validated.
- The model is available via a web-based calculator (http://www.sealedenvelope.com/trials/bwhhsmodel/).
- Model showed adequate discriminatory ability and external validity; addition of blood markers from major biological pathways did not improve the performance.

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Conflicts of interest

None declared.

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Ethical approval

Ethical approval was granted for the BWHHS from the London Multi-Centre Research Ethics Committee and 23 Local Research Ethics Committees, and for all the ELSA waves from the National Research and Ethics Committee. All participants provided written informed consent.

Supplementary data

Supplementary data mentioned in the text are available to subscribers in *Age and Ageing* online.

References

1. Census. Population Estimates for the United Kingdom. www.ons.gov.uk: Office of National Statistics 2011.
2. Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. Lancet 2012; 380: 37–43.
3. Bowling A, Seetai S, Morris R, Ebrahim S. Quality of life among older people with poor functioning. The influence of perceived control over life. Age Ageing 2007; 36: 310–5.
4. Dale C, Prieto-Merino D, Kuper H *et al*. Modelling the association of disability according to the WHO International Classification of Functioning, Disability and Health (ICF) with mortality in the British Women's Heart and Health Study. J Epidemiol Community Health 2012; 66: 170–5.
5. Liu CJ, Latham NK. Progressive resistance strength training for improving physical function in older adults. Cochrane Database Syst Rev 2009; 3: CD002759.
6. Smith SM, Soubhi H, Fortin M, Hudon C, O'Dowd T. Managing patients with multimorbidity: systematic review of interventions in primary care and community settings. BMJ 2012; 345: e5205.
7. Pickard L. Informal Care for Older People Provided by Their Adult Children: Projections of Supply and Demand to 2041 in England. www.pssru.ac.uk. London, UK: Personal Social Services Research Unit 2008.
8. Kent DM, Rothwell PM, Ioannidis JP, Altman DG, Hayward RA. Assessing and reporting heterogeneity in treatment effects in clinical trials: a proposal. Trials 2010; 11: 85.
9. Buchman AS, Boyle PA, Leurgans SE, Evans DA, Bennett DA. Pulmonary function, muscle strength, and incident mobility disability in elders. Proc Am Thorac Soc 2009; 6: 581–7.
10. Odding E, Valkenburg HA, Stam HJ, Hofman A. Determinants of locomotor disability in people aged 55 years and over: the Rotterdam Study. Eur J Epidemiol 2001; 17: 1033–41.
11. Tas U, Steyerberg EW, Bierma-Zeinstra SM, Hofman A, Koes BWVerhagen AP. Age, gender and disability predict future disability in older people: the Rotterdam Study. BMC Geriatr 2011; 11: 22.
12. Tas U, Verhagen AP, Bierma-Zeinstra SM *et al*. Incidence and risk factors of disability in the elderly: the Rotterdam Study. Prev Med 2007; 44: 272–8.
13. Tas U, Verhagen AP, Bierma-Zeinstra SM, Odding E, Koes BW. Prognostic factors of disability in older people: a systematic review. Br J Gen Pract 2007; 57: 319–23.
14. den Ouden ME, Schuurmans MJ, Mueller-Schotte S, van der Schouw YT. Identification of high-risk individuals for the development of disability in activities of daily living. A ten-year follow-up study. Exp Gerontol 2013; 48: 437–43.
15. Cook WL. The intersection of geriatrics and chronic kidney disease: frailty and disability among older adults with kidney disease. Adv Chronic Kidney Dis 2009; 16: 420–9.
16. Claessen H, Brenner H, Drath C, Arndt V. Gamma-glutamyltransferase and disability pension: a cohort study of construction workers in Germany. Hepatology 2010; 51: 482–90.
17. Nuesch E, Dale CE, Amuzu A *et al*. Inflammation, coagulation and risk of locomotor disability in elderly women: findings from the British Women's Heart and Health Study. Eur J Epidemiol 2012; 27: 633–45.
18. Altman DG, Vergouwe Y, Royston P, Moons KG. Prognosis and prognostic research: validating a prognostic model. BMJ 2009; 338: b605.
19. Moons KG, Royston P, Vergouwe Y, Grobbee DE, Altman DG. Prognosis and prognostic research: what, why, and how? BMJ 2009; 338: b375.
20. Royston P, Moons KG, Altman DG, Vergouwe Y. Prognosis and prognostic research: developing a prognostic model. BMJ 2009; 338: b604.
21. Lawlor DA, Bedford C, Taylor M, Ebrahim S. Geographical variation in cardiovascular disease, risk factors, and their control in older women: British Women's Heart and Health Study. J Epidemiol Community Health 2003; 57: 134–40.
22. Ebrahim S, Wannamethee SG, Whincup P, Walker M, Shaper AG. Locomotor disability in a cohort of British men: the impact of lifestyle and disease. Int J Epidemiol 2000; 29: 478–86.
23. Wannamethee SG, Ebrahim S, Papacosta O, Shaper AG. From a postal questionnaire of older men, healthy lifestyle factors reduced the onset of and may have increased recovery from mobility limitation. J Clin Epidemiol 2005; 58: 831–40.
24. Ebrahim S, Adamson J, Ayis S, Beswick A, Gooberman-Hill R. Locomotor disability: meaning, causes and effects of interventions. J Health Serv Res Policy 2008; 13(Suppl. 3): 38–46.
25. Gaunt TR, Lowe GDO, Lawlor DA, Casas JP, Day INM. A gene-centric analysis of activated partial thromboplastin time and activated protein C resistance using the Human CVD focused genotyping array. Eur J Hum Genet 2013; 21: 779–83.
26. Jefferis BJ, Lowe GD, Welsh P *et al*. Secondhand smoke (SHS) exposure is associated with circulating markers of inflammation and endothelial function in adult men and women. Atherosclerosis 2010; 208: 550–6.
27. Marmot M, Banks J, Blundell R, Lessof C, Nayroo J, eds. Health, Wealth and Lifestyle of the Older Population in England: The 2002 English Longitudinal Study of Ageing. London: Institute for Fiscal Studies, 2002.
28. Angleman SB, Harris TB, Melzer D. The role of waist circumference in predicting disability in periretirement age adults. Int J Obes (Lond) 2006; 30: 364–73.
29. Moons KG, Altman DG, Vergouwe Y, Royston P. Prognosis and prognostic research: application and impact of prognostic models in clinical practice. BMJ 2009; 338: b606.

30. Rajan KB, Hebert LE, Scherr PA, Mendes de Leon CF, Evans DA. Disability in basic and instrumental activities of daily living is associated with faster rate of decline in cognitive function of older adults. J Gerontol A Biol Sci Med Sci 2013; 68: 624–30.
31. Tzoulaki I, Liberopoulos G, Ioannidis JP. Assessment of claims of improved prediction beyond the Framingham risk score. JAMA 2009; 302: 2345–52.
32. Ebrahim S, Lawlor DA, Shlomo YB *et al*. Alcohol dehydrogenase type 1C (ADH1C) variants, alcohol consumption traits, HDL-cholesterol and risk of coronary heart disease in women and men: British Women's Heart and Health Study and Caerphilly cohorts. Atherosclerosis 2008; 196: 871–8.
33. Tas U, Verhagen AP, Bierma-Zeinstra SM, Hofman A, Pols HAKoes BW. Course and prognostic factors of disability in community-dwelling older people with mild disability: the Rotterdam Study. Australas J Ageing 2012; 31: 28–33.

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