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/m², 10% were current smokers and 45% were physically active. The most frequent health conditions were respiratory diseases (49%) and

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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 ($z$-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). IL-6 were the only blood markers of the 31 evaluated that predictor ($z$-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 ($z$-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 $z$-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/](http://www.sealedenvelope.com/trials/bwhhsmodel/). Box 1 explains details of calculation of predicted risks. While a ‘healthy’

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

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Model without blood markers</th>
<th></th>
<th>Model with blood markers</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>OR</td>
<td>95% CI</td>
<td>$z$ score</td>
<td>OR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Age, per 10 years</td>
<td>2.40</td>
<td>(2.06–2.79)</td>
<td>11.29</td>
<td>2.36</td>
</tr>
<tr>
<td>Physical activity</td>
<td>0.56</td>
<td>(0.47–0.68)</td>
<td>9.99</td>
<td>0.61</td>
</tr>
<tr>
<td>Healthy diet</td>
<td>0.71</td>
<td>(0.51–0.97)</td>
<td>2.14</td>
<td>0.72</td>
</tr>
<tr>
<td>Smoker, former</td>
<td>1.46</td>
<td>(1.18–1.81)</td>
<td>3.53</td>
<td>1.46</td>
</tr>
<tr>
<td>Smoker, current</td>
<td>1.31</td>
<td>(0.84–2.05)</td>
<td>1.19</td>
<td>1.18</td>
</tr>
<tr>
<td>Systolic BP, per 10 mmHg</td>
<td>0.95</td>
<td>(0.91–0.99)</td>
<td>2.35</td>
<td>0.94</td>
</tr>
<tr>
<td>Medication use, per 1 drug</td>
<td>1.18</td>
<td>(1.11–1.26)</td>
<td>5.30</td>
<td>1.16</td>
</tr>
<tr>
<td>Arthritis</td>
<td>1.72</td>
<td>(1.44–2.06)</td>
<td>5.96</td>
<td>1.72</td>
</tr>
<tr>
<td>Depression</td>
<td>1.84</td>
<td>(1.41–2.39)</td>
<td>4.56</td>
<td>1.88</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>1.62</td>
<td>(1.18–2.22)</td>
<td>2.97</td>
<td>1.59</td>
</tr>
<tr>
<td>Hip fracture</td>
<td>1.84</td>
<td>(1.26–2.69)</td>
<td>3.15</td>
<td>1.77</td>
</tr>
<tr>
<td>CRP, per 1 ln (mg/l)</td>
<td>1.16</td>
<td>(1.01–1.32)</td>
<td>2.06</td>
<td>1.60</td>
</tr>
<tr>
<td>IL-6, per 1 ln (pg/ml)</td>
<td>1.60</td>
<td>(1.38–1.82)</td>
<td>2.14</td>
<td>0.92</td>
</tr>
<tr>
<td>IL-6, per 1 ln (pg/ml)$^2$</td>
<td>0.72</td>
<td>(0.67–0.77)</td>
<td>2.14</td>
<td>0.73</td>
</tr>
<tr>
<td>Model performance$^b$</td>
<td>Median</td>
<td>Range</td>
<td>Median</td>
<td>Range</td>
</tr>
<tr>
<td>$z$-Index</td>
<td>0.733</td>
<td>(0.732–0.733)</td>
<td>0.743</td>
<td>(0.742–0.747)</td>
</tr>
<tr>
<td>Hosmer–Lemeshow $P$ value</td>
<td>0.466</td>
<td>(0.442–0.476)</td>
<td>0.474</td>
<td>(0.446–0.498)</td>
</tr>
</tbody>
</table>

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

$^b$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-SD) instrument.
A 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...
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

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 \( \pi_j \) of locomotor disability in the \( j \)th woman with \( k \) different risk factor levels \( x_j \) is derived from logit \( \logit(\pi_j) = \beta_0 + \sum_{i=1}^{k} (\beta_i \cdot x_{ij}) \) with \( \beta_i \) being the \( i \)th beta-coefficient estimated from the prediction model.
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://wwwsealedenvelope.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://wwwsealedenvelope.com/trials/bwhhsmodel/).
- Model showed adequate discriminatory ability and external validity; addition of blood markers from major biological pathways did not improve the performance.

### Acknowledgements

We thank all participants of BWHHS and ELSA, the general practitioners and their staff who have supported data collection. We are grateful to Sealed Envelope Ltd for the implementation of the online calculator.

### Conflicts of interest

None declared.

### Funding

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All participants provided written informed consent.

Local Research Ethics Committees, and for all the ELSA waves from the National Research and Ethics Committee.

**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.

**Supplementary data**

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

**References**

Recent syncope and unexplained falls are associated with poor cognitive performance

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Abstract

Objective: to compare cognitive performance in participants with and without syncope and unexplained falls in a large population representative sample aged 50 years or older.

Methods: participants of the Irish longitudinal study on ageing (TILDA) were studied. Participants with a history of syncope and/or unexplained falls in the past 12 months were compared with those with no reported events. Cognitive performance was measured using the Montreal cognitive assessment (MoCA) score. Multivariate linear regression analysis controlling for potential confounders was performed to compare cognitive function by syncope and falls status.

Results: five thousand eight hundred and forty-six participants were analysed, median age 62 years (inter-quartile range = 14), and 54% were female. Five hundred and forty-nine (9.4%) had a syncopal event and/or an unexplained fall in past 12 months. One hundred and two (1.8%) subjects had two-plus syncopal events in the same period. There was a significant association between syncope/falls history and lower MoCA score, following adjustment for all confounders ($B = −0.4; −0.69, −0.11; P = 0.006$). Higher syncope burden was also associated with lower performance; however, this was largely explained by confounders. There was no age interaction with these findings.

Conclusion: participants who experienced syncope and/or non-accidental falls in the previous year have poor global cognitive performance compared with case–controls. There was no effect of age on our results. Further investigation of the association between syncope burden, unexplained falls and cognitive decline is required to establish a relationship between these disorders.

Keywords: syncope, neurocardiovascular instability, cognition, epidemiology, older people

Introduction

The role of vascular risk factors in the pathogenesis of cognitive disorders has gained research momentum in recent years [1]. This is partially driven by the projected increase in the burden of cognitive disorders, secondary to dramatic changes in ageing demographics worldwide [2]. Late-life hypotension and orthostatic hypotension are both reported to be associated with reduced cognitive function from cross-sectional and longitudinal studies [3, 4].

Syncope is defined as a sudden loss of consciousness due to transient global cerebral hypoperfusion characterised by rapid