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Can measures of physical performance in mid-life improve the clinical prediction of disability in early old age? Findings from a British birth cohort study

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ABSTRACT

Background: Poor performance in physical tests such as grip strength and walking speed is a risk factor for disability in old age, although whether such measures improve the discrimination of clinical prediction models when traditional clinical risk factors are already known is not clear. The prevalence of disability in mid-life is relatively low and hence screening in this age group may present an opportunity for early identification of those at increased future risk who may benefit most from preventative interventions.

Methods: Data were drawn from two waves of the Medical Research Council National Survey of Health and Development. We examined whether several chronic conditions, poor health behaviours and lower scores on three measures of physical performance (grip strength, chair rise speed and standing balance time) at age 53 were associated with self-reported mobility and/or personal care disability at age 69. We used the area under the curve statistic (AUC) to assess model discrimination.

Results: At age 69, 44% (826/1855) of participants reported mobility and/or personal care disability.

Our final clinical prediction model included sex, knee osteoarthritis, taking 2+ medications, smoking, increased BMI and poor performance in all three physical tests, with an AUC of 0.740 compared with 0.708 for a model which did not include the performance measures.

Conclusion: Measures of physical performance in midlife improve discrimination in clinical prediction models for disability over 16 years. Importantly, these and similar measures are also potential targets of future diet, exercise and pharmacological intervention in mid-life.

1. Introduction

Disability becomes increasingly common in old age with 45% of adults aged 65 and above in the UK reporting disability, most commonly related to mobility (Department of Work and Pensions, 2015). Mobility disability has been shown to progress hierarchically with problems with functional tasks such as walking and climbing stairs often preceding difficulty with activities of daily living (ADLs) such as personal care (Dunlop et al., 1997; Kingston et al., 2012; Wloch et al., 2016); the cost of paid help for older people with ADL disability in the United States has been estimated at $23.7 billion (LaPlante et al., 2002). Clinical prediction models have been developed for identifying individuals at risk of disability, although these have typically been based on assessments during the seventh decade or above, by which time disability may already be manifest (Nueesch et al., 2015; Covinsky et al., 2006; Clark et al., 2012; den Ouden et al., 2013).

Lower physical performance assessed using simple measures such as grip strength and walking speed has been associated with incident or progressive disability in 22 studies and summarised in a systematic review (den Ouden et al., 2011). These studies again typically used baseline assessments at older ages, with an exception that weaker grip strength in men at mean age 54 has been associated with increased risk of disability 25 years later (Rantanen et al., 1999).There is limited evidence, however, on whether these associations translate into improvements in the clinical prediction of individuals' future risk of disability. A previous study at mean age 75 years found that walking speed increased the area under the curve statistic (AUC) for incident disability over 3 years when added to history of one or more common diseases,

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BMI, systolic blood pressure and hospitalisation in the previous year (Perera et al., 2016).

Mid-life is increasingly recognised as an important time to make assessments of overall health, for example to address risk factors for future cardiovascular disease as carried out in primary care in the UK between ages 40–74 (Robson et al., 2016). In addition, findings from a life course investigation of grip strength suggest that mid-life is the period of adulthood when individuals reach a broadly stable peak level of physical performance prior to decline with age (Nahhas et al., 2010; Dodds et al., 2014). Physical performance measures are a key component of the conditions of sarcopenia and frailty and interest in the use of such measures in the clinical setting is growing (Dodds and Sayer, 2015). Mid-life, when age-related disability is less common, might provide a key opportunity for the assessment of future disability risk including the use of physical performance measures. However, as described existing clinical prediction models have been developed in older samples and include risk factors such as a history of hip fracture (Nueesch et al., 2015) which are less prevalent in mid-life.

Using data from a British birth cohort study, the Medical Research Council National Survey of Health and Development (NSHD) (Kuh et al., 2011, 2016), our aims were to test whether poorer scores on three measures of physical performance at age 53 were associated with higher risk of mobility or personal care disability 16 years later independently of variables already routinely collected in primary care, and if so whether these measures improved the discrimination of a clinical prediction model for disability.

2. Methods

2.1. Participants

We used data from the NSHD, a socially stratified sample of 5362 singleton births in one week of March 1946 in mainland Britain that have been followed up 24 times across life including in 1999 (at age 53) when physical performance measures were first assessed, and most recently in 2015 (at age 69) (Kuh et al., 2011, 2016). At age 69, study members still alive and with a known current address in mainland Britain (n = 2698) were invited to have a home visit; 2149 (79.7%) completed a visit, 55 (2.0%) completed a postal questionnaire instead and 494 (18.3%) did not participate (Kuh et al., 2016). Of the original cohort, 1026 (19.1%) had died, 578 (10.8%) were living abroad, 22 (0.4%) asked for their participation to be restricted to postal contacts, 621 (11.6%) had previously withdrawn from the study, and 417 (7.8%) had been lost to follow-up.

Ethical approval for this most recent follow-up was obtained from the NRES Queen Square Research Ethics Committee (14/LO/1073) and the Scotland A REC (14/SS/1009). Written, informed consent was obtained from study members for each component of the data collection.

2.2. Outcomes

The disability questions used within the NSHD are based on the Office of Population Censuses and Surveys (OPCS) of Disability in Great Britain (Wloch et al., 2016; Martin et al., 1988; Kuh et al., 1994). For the current study, we used the presence of any criteria from two domains of the survey at age 69: mobility (referred to as locomotion in the survey) and personal care, assessed using responses to questions asked during the home visit (or in the postal questionnaire for those participants who were unable to undergo a visit (n = 55)). Participants were classified as having a disability if they met the OPCS criteria for mobility and/or personal care disability, as described in Appendix A.

2.3. Candidate predictors for disability at 69

We were not aware of an existing clinical prediction model for disability with baseline age 53 (or similar) that we could validate in the present study. We therefore chose variables from the two major categories used in existing models at older ages which were also likely to be routinely collected in primary care (Nueesch et al., 2015; Covinsky et al., 2006; Clark et al., 2012; den Ouden et al., 2013): chronic conditions and behavioural risk factors. We did not include existing disability at age 53 as a candidate predictor (or exclude the small proportion of individuals with existing disability from our main analyses) as we considered it unlikely to be routinely assessed in primary care.

Chronic conditions comprised reported doctor diagnosed hypertension, cardiovascular disease, cancer and diabetes, knee osteoarthritis (defined using American College of Rheumatology criteria and based on reported symptoms of pain and stiffness and a clinical assessment (Wills et al., 2012)), and severe respiratory symptoms (based on the MRC's standardised questions (Medical Research Council, 1976) and classified as report of one or more of the following: a wheezy or whistling chest most days or nights; usually bringing up phlegm or coughing in the morning or during the day or night in winter for at least three months each year; or more than one chest illness in the past three years that kept them off work or indoors for a week or more). We also included regularly taking two or more prescribed medications, assessed by self-report.

For behavioural risk factors, we classified smoking status as never, ex-smoker or current. Body mass index (BMI) was calculated from height and weight measured using standard protocols, and was grouped into below 25, 25–30 and above 30 kg/m^2.

We used three candidate measures of physical performance: grip strength, measured in the seated position using an electronic dynamometer with two trials in both arms and the maximum value used in analyses. Chair rise time was the time taken in seconds to go from a seated position to standing with straight legs and back and then sit down again, 10 times as fast as possible. We converted chair rise times to speed (10 divided by the time taken), such that higher scores indicate better performance. Standing balance was the time in seconds (up to a maximum of 30) that a participant could stand on one leg with their eyes closed. We expressed performance in each measure as sex-specific fifths (for the cut-points used see Table A-1) and included a sixth category for those unable to complete the test for health reasons.

2.4. Statistical analyses

Of the 2204 study members assessed at age 69, 2178 (98.8%) had data on mobility and personal care disability and of these 2053 (94.3%) had been assessed at age 53. Of these, 1885 (91.8%) had data available for all the candidate predictors. A further 249 participants had complete data at 53 but were known to have died before age 69.

We developed each predictive model for disability in three stages, with a level of significance of $P < 0.05$ required for a predictor to be retained in the next stage. Firstly, we assessed univariable associations between each candidate predictor and disability, removing predictors which did not reach statistical significance. Secondly, we ran separate multivariable logistic regression models for each group (chronic conditions, behavioural risk factors and physical performance) of the remaining candidate predictors. We used a backwards elimination process, performing likelihood ratio tests to check whether each predictor within each group remained associated, again removing those which did not reach statistical significance. Finally, we combined the remaining predictors from the chronic conditions group with those from the behavioural risk factor or physical performance groups, as well as running a model with remaining predictors from all three groups combined. We again used a backwards elimination process to select a final set of predictors for each combination of groups. We included gender in all multivariable models.

We used changes in the AUC to assess if the addition of extra predictors led to an improvement in model discrimination. We undertook internal validation to assess whether the AUC in our final model was inflated by optimism in model development. To do this we reran our

model fitting procedure in 200 bootstrap samples. We then calculated AUC values for the prediction of disability in the original sample using each of the 200 models developed in the bootstrap samples (Moons et al., 2012).

We also calculated the number of individuals correctly reclassified, termed the net reclassification index (NRI) (Steyerberg et al., 2010), following the addition of physical performance measures in our final model and using a predicted risk cut-point of 40%.

We considered a priori that the physical performance measures might have the greatest benefit for assessing risk of disability among those without existing health problems. We therefore divided the sample into two groups: those with and without clinically manifest illness at 53, defined as having any of the chronic conditions described in the previous section, and/or taking two or more medications. We then repeated our analyses separately in both groups.

In sensitivity analyses, we reran all models excluding those with prevalent mobility disability at age 53 and a small number (n = 25) known to have personal care disability, using OPCS criteria (Kuh et al., 1994). We also repeated our analyses using a combined outcome of disability at age 69 or death prior to follow-up, as we considered it likely that many of those who had died would have developed disability prior to death (Murphy et al., 2011). We performed all analyses using Stata version 14.0 (StataCorp, 2015).

3. Results

3.1. Characteristics of the sample

The main sample for the present study comprised 1885 participants (52.2% female) with disability outcome data as shown in Table 1. At age 53, 145 (7.7%) participants had existing disability and 877 (46.5%) had clinically manifest illness. A small number of participants (n = 75, 4%) were unable to complete one of the physical performance tests due to health reasons and a further 22 participants were unable to complete ≥ two tests.

3.2. Prevalence of disability and associations with candidate predictors

At age 69, 825 (43.8%) participants reported mobility and/or personal care disability, the latter being less common (8.0%) and typically occurring with mobility disability (Fig. 1). Female participants, those with chronic conditions (except cancer and diabetes), two or more medications, behavioural risk factors, poor physical performance and existing disability at age 53 were more likely to be disabled at age 69 as shown in Table 1. These risk factors were correlated: for example, those with clinically manifest illness at 53 were more likely to be female, have behavioural risk factors, poor physical performance and existing disability than those without (see Table B-1).

3.3. Predictive models for disability

In the main analyses for disability using the whole sample, the univariable analyses led to the removal of cancer and diabetes from the chronic conditions group, followed by the removal of hypertension in the multivariable model. Each of the three groups of remaining candidate predictors had similar discrimination, with AUC in the range 0.670–0.697 as shown in the first three rows of column A in Table 2.

There were modest increases in discrimination by combining different groups of candidate predictors, with the highest discrimination (AUC 0.740) seen in the model combining all three. In this model (shown in Table 3) eight variables remained following the selection process: sex, knee osteoarthritis, taking two or more medications, smoking, BMI and all three physical performance measures. The AUC statistics from the models developed in the 200 bootstrap samples were similar to the main findings: median 0.733 (range 0.722–0.738), suggesting low over-optimism in our model development.

The addition of all three physical performance measures to the routine variables was associated with an NRI of 4.1% as shown in Table B-2. We also reran our final model using each physical performance measure separately and found that the improvement in discrimination was less marked; the AUC values ranged between 0.718 for grip strength and 0.727 for chair rise speed.

The predictive models among the groups with and without clinically manifest illness are shown in columns B and C of Table 2, respectively. The overall pattern of results was similar to that seen in the whole sample. The physical performance measures remaining in the combined models varied: chair rise time remained in both groups; whereas grip strength remained in the group with clinically manifest illness and standing balance remained in the group without.

3.4. Sensitivity analyses

In the sample excluding those with prevalent disability at age 53 (n = 1740) there was no change in either the pattern of the AUC values or the variables in the prediction model combining all three groups of candidate predictors. When death was included alongside disability (n = 2134) the same pattern of results as for disability alone was found except diabetes was associated with an increased risk of disability or death during follow-up. There was also no change in the pattern of the AUC values although two additional variables, respiratory symptoms and cardiovascular disease, remained significantly associated in the final model.

4. Discussion

4.1. Summary of findings

We investigated the clinical prediction of disability across 16 years from mid-life into early old age using data from a British birth cohort study. We found a model using information which is routinely collected in a primary care setting, specifically knee osteoarthritis, taking two or more prescribed medications, smoking status and BMI had reasonable discrimination for disability risk. This was further improved by the addition of three physical performance measures: grip strength, chair rise speed and standing balance.

4.2. Comparison with existing studies

The prevalence of mobility disability in our sample (43%) at age 69 was similar to that in two other British samples of similar mean age (Nueesch et al., 2015). As far as we are aware our study is the first clinical prediction model for disability in early old age to have used a baseline assessment in mid-life. The presence of chronic conditions (or taking prescribed medications as a proxy) was a risk factor for disability and such conditions have previously formed part of clinical prediction models from other studies (Nueesch et al., 2015; Covinsky et al., 2006; Clark et al., 2012; den Ouden et al., 2013; Perera et al., 2016). Fewer studies have included behavioural risk factors such as those that we used: BMI (Covinsky et al., 2006; Perera et al., 2016) and smoking history (Nueesch et al., 2015).

The three measures of physical performance, grip strength, chair rise speed and standing balance time, all remained as statistically significant predictors and were associated with improvements in the AUC. As far as we are aware this is the first time that these three measures have been tested in this way. den Ouden et al. (2013) found that a combination of grip and leg extensor strength measurement remained in a clinical prediction model for ADL disability over 10 years' follow-up in a sample of mean age 61 years, although they did not report the associated change in model discrimination. Perera et al. (2016) showed that walking speed improved the AUC of a clinical prediction model for both bathing/dressing dependence and mobility difficulty, over 3 years' follow-up at mean ages 72 and above.

Table 1
Candidate predictors and existing disability at age 53 by outcome status at age 69.

	No disability		Disability		Death		P-values[a]	
	(n = 1060)		(n = 825)		(n = 249)			
	n	(%)	n	(%)	n	(%)	Disability	Disability or death
Female sex	461	(43.5)	523	(63.4)	105	(42.2)	< 0.001	< 0.001
Disability present at 53	17	(1.6)	128	(15.5)	59	(23.7)	< 0.001	< 0.001
Hypertension	148	(14.0)	168	(20.4)	61	(24.5)	< 0.001	< 0.001
Cardiovascular disease	24	(2.3)	50	(6.1)	34	(13.7)	< 0.001	< 0.001
Knee osteoarthritis	51	(4.8)	125	(15.2)	28	(11.2)	< 0.001	< 0.001
Respiratory symptoms	132	(12.5)	166	(20.1)	73	(29.3)	< 0.001	< 0.001
History of cancer	24	(2.3)	25	(3.0)	9	(3.6)	0.3	0.2
Diabetes	14	(1.3)	17	(2.1)	21	(8.4)	0.2	0.001
≥2 medications	175	(16.5)	282	(34.2)	106	(42.6)	< 0.001	< 0.001
Clinically manifest illness[b]	402	(37.9)	475	(57.6)	172	(69.1)	< 0.001	< 0.001
Smoking							< 0.001	< 0.001
Never smoker	337	(31.8)	247	(29.9)	48	(19.3)		
Ex-smoker	559	(52.7)	383	(46.4)	104	(41.8)		
Current smoker	164	(15.5)	195	(23.6)	97	(39.0)		
BMI (kg/m^2)							< 0.001	< 0.001
< 25	410	(38.7)	228	(27.6)	78	(31.3)		
25–30	499	(47.1)	338	(41.0)	96	(38.6)		
> 30	151	(14.2)	259	(31.4)	75	(30.1)		
Grip strength fifths[c]							< 0.001	< 0.001
Q1 – top	265	(25.0)	145	(17.6)	34	(13.7)		
Q2	232	(21.9)	148	(17.9)	44	(17.7)		
Q3	213	(20.1)	172	(20.8)	43	(17.3)		
Q4	194	(18.3)	164	(19.9)	46	(18.5)		
Q5 – bottom	149	(14.1)	175	(21.2)	73	(29.3)		
Unable	7	(0.7)	21	(2.5)	9	(3.6)		
Chair rise speed fifths[c]							< 0.001	< 0.001
Q1 – top	275	(25.9)	130	(15.8)	32	(12.9)		
Q2	264	(24.9)	141	(17.1)	42	(16.9)		
Q3	193	(18.2)	145	(17.6)	39	(15.7)		
Q4	184	(17.4)	182	(22.1)	42	(16.9)		
Q5 – bottom	132	(12.5)	185	(22.4)	64	(25.7)		
Unable	12	(1.1)	42	(5.1)	30	(12.0)		
Standing balance fifths[c]							< 0.001	< 0.001
Q1 – top	293	(27.6)	135	(16.4)	31	(12.4)		
Q2	268	(25.3)	203	(24.6)	53	(21.3)		
Q3	212	(20.0)	140	(17.0)	39	(15.7)		
Q4	207	(19.5)	243	(29.5)	47	(18.9)		
Q5 – bottom	67	(6.3)	77	(9.3)	51	(20.5)		
Unable	13	(1.2)	27	(3.3)	28	(11.2)		

[a] Comparing those with no disability to those with outcome(s) shown.
[b] Defined as having one or more of the chronic conditions shown, and/or taking two or more medications. BMI, body mass index.
[c] For the cut-points for each fifth, please see Table A-1. Note the unable category refers to those unable to complete the test for health reasons.

4.3. Interpretation of findings

We showed an increase in the AUC following the addition of physical performance measures. The AUC is a measure of overall model discrimination although it does not relate to a specific risk cut-point. This can be important in a clinical situation, where it may be desirable to classify an individual as at risk of disability or not (Cook, 2007). We therefore calculated the NRI using a risk cut-point of 40% and found that the addition of physical performance measures led to only around 4 per 100 individuals being correctly reclassified.

We considered possible explanations for the small increase in model discrimination. Poor physical performance is related to the presence of other risk factors used in the model such as chronic conditions (Welmer et al., 2012) (Table A-1); indeed the majority of disability occurred in those with clinically manifest illness at baseline (Table 1). It is also recognised that although higher levels of physical performance might act as a reserve which helps to prevent future disability that develops over several years, they have a weaker relationship with the development of disability of more rapid onset such as that following stroke (Onder et al., 2005).

We found that all three measures of physical performance had independent associations with disability, similar to the recent findings for the associations of walking speed and standing balance with subsequent disability (Heiland et al., 2016). The different measures reflect the function of different physiological systems, as previously suggested by the finding in NSHD of independent associations with all-cause mortality rates (Cooper et al., 2014). We also showed that chair rise speed and standing balance time were associated with subsequent disability among those without clinically manifest illness. This suggests that these tests are either markers of pre-clinical disease or that poor function (combined with age-related functional decline) directly leads to disability.

Finally, we did not include existing disability as one of our candidate predictors. We thought it was unlikely that disability would be routinely assessed in primary care in mid-life, when there is more of a focus on chronic diseases and behavioural risk factors (Robson et al., 2016). Those in the sample with disability at 53 were at increased risk of subsequent disability, although the exclusion of this small group did not change our findings. Existing disability at age 53 also does not appear to be a particularly useful tool for detecting subsequent problems: the prevalence of disability at age 53 was low at 8%, with most cases of disability (84.5%) at age 69 therefore occurring in those without disability at the earlier time-point.

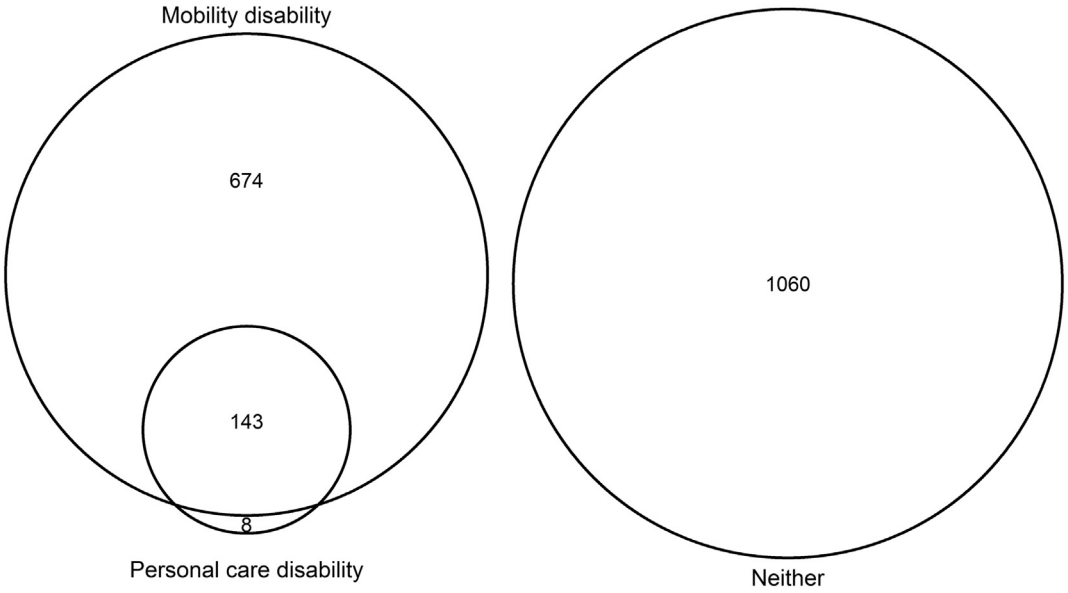

Fig. 1. Number of participants at follow-up with mobility and personal care disability.
N = 1885. Overall 817 participants (43%) had mobility disability and 151 participants (8%) had personal care disability at age 69. The combined outcome of mobility and/or personal care disability was more common in women than men, with 53% and 34% classified as disabled, respectively.

4.4. Methodological considerations

We used data from a birth cohort study which is still representative of the national-born population of the same age (Wadsworth et al., 2006; Stafford et al., 2013) and where considerable efforts have been undertaken to maintain participation at subsequent waves of data collection (Kuh et al., 2016). Nevertheless, potential limitations of this longitudinal study include loss to follow-up and missing data. Of the 2988 participants assessed at age 53, 613 were not seen at age 69 (or were not known to have died during follow-up). Of those seen at both time-points (or seen at 53 and known to have died during follow-up), 241 had missing data for one or more candidate predictor at age 53 and/or disability status at age 69, and were not included in analyses. In general, being lost to follow-up and having incomplete data were associated with the presence of chronic conditions, smoking, greater BMI and poorer physical performance. Our findings may have therefore underestimated the strength of the associations between the candidate predictors and subsequent disability.

A strength of the current study is that the baseline data were collected at age 53 (with follow-up 16 years later), whereas previous work has typically involved baseline assessment in the seventh (Nueesch et al., 2015; den Ouden et al., 2013) and eighth (Covinsky et al., 2006; Clark et al., 2012; Perera et al., 2016; Heiland et al., 2016) decades of life (with correspondingly shorter follow-up times).

We used several stages of multivariable logistic regression to produce clinical prediction models for disability. The model using routinely-collected variables (chronic conditions and behavioural risk factors) showed reasonable discrimination and this was further improved by the addition of physical performance measures. We carried out internal validation using bootstrapping, and this showed little evidence of over-optimism in our model development. It remains likely, however that our model would have lower discrimination if applied to other samples. It would be important to validate our findings in an external cohort before implementing the model in clinical practice.

The variables related to chronic conditions (knee osteoarthritis and number of medications) and behavioural risk (smoking and BMI) could be extracted from a patient's medical record or alternatively would be quick to ascertain. There are other routine variables that we could have

Table 2
Model discrimination for disability using three groups of candidate predictors, by presence of clinically manifest illness.

Group(s)	A Whole sample (n = 1885)		B With clinically manifest illness (n = 877)		C Without clinically manifest illness (n = 1008)	
	AUC	Variables	AUC	Variables	AUC	Variables
1 Chronic conditions	0.670	OA, Resp, CVD, Meds	0.652	OA, CVD, Meds	n/a	–
2 Behavioural risk factors	0.676	Smoke, BMI	0.644	BMI	0.670	Smoke, BMI
3 Physical performance	0.697	GS, CR, SB	0.693	GS, CR	0.682	CR, SB
1 & 2	0.708	*Minus* Resp	0.677	*Minus* CVD	n/a	–
1 & 3	0.720	*Minus* CVD	0.711	*Minus* CVD	n/a	–
Combined						
1, 2 & 3	0.740	OA, Meds	0.733	OA, Meds	0.708	–
		Smoke, BMI		BMI		Smoke, BMI
		GS, CR, SB		GS, CR		CR, SB
P-value*		< 0.001		< 0.001		0.001

Sex was included in all models. Clinically manifest illness was defined as having one or more of the chronic conditions or taking two or more prescribed medications at age 53. AUC, area under the curve statistic. OA, knee osteoarthritis. Resp, severe respiratory symptoms. CVD, cardiovascular disease. Meds, taking two or more prescribed medications. Smoke, smoking status. BMI, body mass index. GS, grip strength. CR, chair rise time. SB, standing balance time.

* The P-value tests the difference between the AUC statistic for the final model (groups 1, 2 and 3 combined) to that for chronic conditions and behavioural risk factors (groups 1 and 2 combined). In the case of C, those in the sample without clinically manifest illness, the P-value compares the AUC value of behavioural risk factors and physical performance (groups 2 and 3 combined) to that from behavioural risk factors alone.

Table 3
Multivariable associations in final clinical prediction model.

	Association with disability		
Variable	OR	(95% CI)	P-value
Female sex	2.25	(1.81, 2.79)	< 0.001
Knee osteoarthritis	2.32	(1.60, 3.39)	< 0.001
≥2 medications	1.81	(1.42, 2.30)	< 0.001
Smoking			< 0.001
Never smoker	1	(Ref)	
Ex-smoker	0.97	(0.77, 1.22)	
Current smoker	1.69	(1.26, 2.26)	
BMI category			< 0.001
< 25	1	(Ref)	
25–30	1.32	(1.05, 1.67)	
> 30	2.8	(2.10, 3.73)	
Grip strength fifths[a]			0.001
Q1 – top	1	(Ref)	
Q2	1.19	(0.87, 1.63)	
Q3	1.55	(1.14, 2.12)	
Q4	1.53	(1.12, 2.11)	
Q5 – bottom	1.84	(1.33, 2.56)	
Unable	3.44	(1.30, 9.13)	
Chair rise fifths[a]			< 0.001
Q1 – top	1	(Ref)	
Q2	1.05	(0.77, 1.44)	
Q3	1.45	(1.05, 2.01)	
Q4	1.79	(1.30, 2.45)	
Q5 – bottom	2.2	(1.57, 3.07)	
Unable	3.22	(1.47, 7.02)	
Standing balance fifths[a]			0.002
Q1 – top	1	(Ref)	
Q2	1.55	(1.15, 2.09)	
Q3	1.28	(0.93, 1.78)	
Q4	1.74	(1.28, 2.35)	
Q5 – bottom	1.92	(1.25, 2.97)	
Unable	2.14	(0.95, 4.82)	

N = 1885. This table provides the coefficients for the combined clinical prediction model (shown at the bottom of column A of Table 2). BMI, body mass index.

[a] For the cut-points for each fifth, please see Table A-1. Note the unable category refers to those unable to complete the test for health reasons.

included. For example, we did not include a history of depression which has previously been associated with subsequent disability in this age group (Penninx et al., 1999; Hajek and König, 2016). We did include taking two or more medications and it is likely that, to an extent, this variable will have captured conditions not included in our model. There are also other behavioural risk factors that we could have included such as diet, although these are unlikely to be routinely collected in a primary care setting. We also use categorisation of several variables although we would not expect the prediction model to be significantly different if we were to use continuous predictors instead. The physical performance measures are not currently in widespread use in clinical practice, although interest in such measures and their implementation is growing (Ibrahim et al., 2016; Studenski, 2017). This includes as part of initiatives to identify and treat the related conditions of sarcopenia (Cruz-Jentoft et al., 2014; Band et al., 2018) and frailty (British Geriatrics Society and Royal College of General Practitioners, 2015; Lee et al., 2015).

4.5. Conclusions

The prevention of disability in old age is a major priority and hence tools to identify those at risk are required. We have shown that measures of physical performance in midlife improve discrimination in clinical prediction models for disability over 16 years, although the resulting proportion of individuals correctly reclassified was low. Future work could validate our findings in different samples, replicate in other age groups and investigate whether repeat measures over time improve discrimination. Physical performance measures are also potential targets of future diet, exercise and pharmacological intervention in mid-life.

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Conflicts of interest

None of the authors have any conflicts of interest to declare.

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Data used in this publication are available to bona fide researchers upon request to the NSHD Data Sharing Committee via a standard application procedure. Further details can be found at http://www.nshd.mrc.ac.uk/data doi:https://doi.org/10.5522/NSHD/Q101; doi:https://doi.org/10.5522/NSHD/Q102; doi:https://doi.org/10.5522/NSHD/Q103.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.exger.2018.06.001.

References

Band, M.M., Sumukadas, D., Struthers, A.D., et al., 2018. Leucine and ACE inhibitors as therapies for sarcopenia (LACE trial): study protocol for a randomised controlled trial. Trials 19 (1), 6.

British Geriatrics Society, Royal College of General Practitioners, 2015. Fit for Frailty Part 2: Developing, Commissioning and Managing Services for People Living With Frailty in Community Settings. Available at: http://www.bgs.org.uk/campaigns/fff/fff2_full.pdf.

Clark, D.O., Stamp, T.E., Tu, W., Miller, D.K., 2012. A comparison and cross-validation of models to predict basic activity of daily living dependency in older adults. Med. Care 50 (6), 534–539.

Cook, N.R., 2007. Use and misuse of the receiver operating characteristic curve in risk prediction. Circulation 115 (7), 928–935.

Cooper, R., Strand, B., Hardy, R., Patel, K., Kuh, D., 2014. Physical capability in mid-life and survival over 13 years of follow-up: British birth cohort study. BMJ 348, g2219.

Covinsky, K.E., Hilton, J., Lindquist, K., Dudley, R.A., 2006. Development and validation of an index to predict activity of daily living dependence in community-dwelling elders. Med. Care 44 (2), 149–157.

Cruz-Jentoft, A.J., Landi, F., Schneider, S.M., et al., 2014. Prevalence of and interventions for sarcopenia in ageing adults: a systematic review. Report of the International Sarcopenia Initiative (EWGSOP and IWGS). Age Ageing 43 (6), 748–759.

Department of Work and Pensions, 2015. Family Resources Survey 2014/15. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/531242/family-resources-survey-2014-15.pdf (Accessed August 15, 2016).

Dodds, R., Sayer, A.A., 2015. Sarcopenia and frailty: new challenges for clinical practice. Clin. Med. 15 (6).

Dodds, R.M., Syddall, H.E., Cooper, R., et al., 2014. Grip strength across the life course: normative data from twelve British studies. PLoS One 9 (12), e113637.

Dunlop, D.D., Hughes, S.L., Manheim, L.M., 1997. Disability in activities of daily living: patterns of change and a hierarchy of disability. Am. J. Public Health 87 (3), 378–383.

Hajek, A., König, H.-H., 2016. Longitudinal predictors of functional impairment in older adults in Europe – evidence from the survey of health, ageing and retirement in Europe. PLoS One 11 (1), e0146967.

Heiland, E.G., Welmer, A.-K., Wang, R., et al., 2016. Association of mobility limitations with incident disability among older adults: a population-based study. Age Ageing 45 (6), 812–819.

Ibrahim, K., May, C., Patel, H.P., Baxter, M., Sayer, A.A., 2016. Roberts H. A feasibility study of implementing grip strength measurement into routine hospital practice (GRImP): study protocol. Pilot Feasibility Stud. 2 (1), 27.

Kingston, A., Collerton, J., Davies, K., Bond, J., Robinson, L., Jagger, C., 2012. Losing the

ability in activities of daily living in the oldest old: a hierarchic disability scale from the Newcastle 85+ study. PLoS One 7 (2), e31665.
Kuh, D.J., Wadsworth, M.E.J., Yusuf, E.J., 1994. Burden of disability in a post war birth cohort in the UK. J. Epidemiol. Community Health 48, 262–269.
Kuh, D., Pierce, M., Adams, J., et al., 2011. Cohort profile: updating the cohort profile for the MRC National Survey of Health and Development: a new clinic-based data collection for ageing research. Int. J. Epidemiol. 40 (1), e1–e9.
Kuh, D., Wong, A., Shah, I., et al., 2016. The MRC National Survey of Health and Development reaches age 70: maintaining participation at older ages in a birth cohort study. Eur. J. Epidemiol. 31 (11), 1135–1147.
LaPlante, M.P., Harrington, C., Kang, T., 2002. Estimating paid and unpaid hours of personal assistance services in activities of daily living provided to adults living at home. Health Serv. Res. 37 (2), 397–415.
Lee, L., Heckman, G., Molnar, F.J., 2015. Frailty: identifying elderly patients at high risk of poor outcomes. Can. Fam. Physician 61 (3), 227–231.
Martin, J., Meltzer, H., Elliot, D., 1988. OPCS Surveys of Disability in Great Britain, Report 1: The Prevalence of Disability among Adults. HMSO, London.
Medical Research Council, 1976. Questionnaire on Respiratory Symptoms and Instructions for Interviewers.
Moons, K.G.M., Kengne, A.P., Woodward, M., et al., 2012. Risk prediction models: I. Development, internal validation, and assessing the incremental value of a new (bio) marker. Heart 98 (9), 683–690.
Murphy, T.E., Han, L., Allore, H.G., Peduzzi, P.N., Gill, T.M., Lin, H., 2011. Treatment of death in the analysis of longitudinal studies of gerontological outcomes. J. Gerontol. A Biol. Sci. Med. Sci. 66 A (1), 109–114.
den Ouden, M.E.M., Schuurmans, M.J., Arts, I.E.M.A., van der Schouw, Y.T., 2011. Physical performance characteristics related to disability in older persons: a systematic review. Maturitas 69 (3), 208–219.
den Ouden, M.E.M., Schuurmans, M.J., Mueller-Schotte, S., van der Schouw, Y.T., 2013. Identification of high-risk individuals for the development of disability in activities of daily living. A ten-year follow-up study. Exp. Gerontol. 48 (4), 437–443.
Nahhas, R.W., Choh, A.C., Lee, M., et al., 2010. Bayesian longitudinal plateau model of adult grip strength. Am. J. Hum. Biol. 22 (5), 648–656.
Nueesch, E., Pablo, P., Dale, C.E., et al., 2015. Incident disability in older adults: prediction models based on two British prospective cohort studies. Age Ageing 44, 275–282.
Onder, G., Penninx, B.W.J.H., Ferrucci, L., Fried, L.P., Guralnik, J.M., Pahor, M., 2005. Measures of physical performance and risk for progressive and catastrophic disability: results from the Women's Health and Aging Study. J. Gerontol. A Biol. Sci. Med. Sci. 60 (1), 74–79.
Penninx, B.W.J.H., Leveille, S., Ferrucci, L., Van Eijk, J.T.M., Guralnik, J.M., 1999. Exploring the effect of depression on physical disability: longitudinal evidence from the established populations for epidemiologic studies of the elderly. Am. J. Public Health 89 (9), 1346–1352.
Perera, S., Patel, K.V., Rosano, C., et al., 2016. Gait speed predicts incident disability: a pooled analysis. J. Gerontol. A Biol. Sci. Med. Sci. 71 (1), 63–71.
Rantanen, T., Guralnik, J.M., Foley, D., et al., 1999. Midlife hand grip strength as a predictor of old age disability. JAMA 281 (6), 558–560.
Robson, J., Dostal, I., Sheikh, A., et al., 2016. The NHS Health Check in England: an evaluation of the first 4 years. BMJ Open 6, e008840.
Stafford, M., Black, S., Shah, I., et al., 2013. Using a birth cohort to study ageing: representativeness and response rates in the National Survey of Health and Development. Eur. J. Ageing. http://dx.doi.org/10.1007/s10433-013-0258-8.
StataCorp, 2015. Stata Statistical Software: Release 14.
Steyerberg, E.W., Vickers, A.J., Cook, N.R., et al., 2010. Assessing the performance of prediction models: a framework for some traditional and novel measures. Epidemiology 21 (1), 128–138.
Studenski, S., 2017. Utility of brief cognitive and physical assessments in clinical care. J. Am. Geriatr. Soc. 72 (1), 59–60.
Wadsworth, M., Kuh, D., Richards, M., Hardy, R., 2006. Cohort profile: the 1946 National Birth Cohort (MRC National Survey of Health and Development). Int. J. Epidemiol. 35 (1), 49–54.
Welmer, A.-K., Kareholt, I., Angleman, S., Rydwik, E., Fratiglioni, L., 2012. Can chronic multimorbidity explain the age-related differences in strength, speed and balance in older adults? Aging Clin. Exp. Res. 24 (5), 480–489.
Wills, A.K., Black, S., Cooper, R., et al., 2012. Life course body mass index and risk of knee osteoarthritis at the age of 53 years: evidence from the 1946 British birth cohort study. Ann. Rheum. Dis. 71 (5), 655–660.
Wloch, E.G., Kuh, D., Cooper, R., 2016. Is the hierarchy of loss in functional ability evident in midlife? Findings from a British birth cohort. PLoS One 11 (5), e0155815.