External validation and further exploration of fall prediction models based on questionnaires and daily-life trunk accelerometry

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Abstract

Background: Ambulatory measurements of trunk accelerations can provide valuable insight into the amount and quality of daily life activities. Such information has been used to create models that aim to identify individuals at high risk of falls. However, external validation of such prediction models is lacking, yet crucial for clinical implementation. We externally validated three previously described fall prediction models developed by van Schooten and colleagues (1), which were based on 1) questionnaires, 2) daily life trunk accelerations, 3) a combination of both, in a new cohort of older people.

Methods: Complete questionnaires and one week of trunk acceleration data were obtained in 263 community-dwelling people (mean age 71.8 years, 68.1% female). A 12-month fall record was obtained prospectively using fall diaries and monthly telephone contact, while for the consistency with original models, we only focus on 6 months of fall records. In addition, we tested if the models' accuracy would improve when we included only people who fell during walking. To validate models, we first used the coefficients and optimal cut-offs from original cohort, then recalibrated the original models, as well as optimized parameters based on our new cohort.

Results: Among all participants, 37.6% experienced at least one fall in the past 6 months, and 39.9% experienced falls during 6-month follow-up. When using the original coefficients and cut-offs, all models showed moderate accuracy (0.50-0.75), poor precision (0.20-0.56), poor sensitivity (0.22-0.58), good specificity (0.59-0.89) and moderate model performance (AUC: 0.50-0.68). In addition, calibration of the original models did not improve model performance. Using coefficients and cut-offs optimized on the external cohort also did not improve results (accuracy: 0.53-0.66, precision: 0.27-0.53, sensitivity: 0.53-0.66, specificity: 0.53-0.66, AUC: 0.53-0.73). Last, the odds ratios in our cohort indicated that gait characteristics except for index of harmonicity ML did not improve fall prediction.

Conclusions: Prediction of fall risk in our cohort was not as effective as in the original cohort. We found that all three models were overfitted, and recalibration as well as optimized model parameters resulted in

limited increase in accuracy. Our results suggest that fall prediction models are highly specific to the cohort studied and highlight the need for large representative cohorts, preferably with an external validation cohort.

Keywords: Wearable devices; Activity monitoring; Aged; Locomotion; Accidental falls; Verification

1. Introduction

Falls among older adults are a major cause of disability and death. Each year, one in three older adults aged 65 years or over experience at least one fall (2, 3). Therefore, early identification of fall risk is necessary for timely intervention. Fall risk can be estimated by questionnaires, functional tests in a clinical setting or in a biomechanical laboratory, but all these methods have limited predictive value (4). Specifically, questionnaires have low reliability due to the subjective bias of the participants or testers (5-8). Clinical gait tests, such as Berg Balance scale, Timed Up and Go and POMA, cannot quantify fall risk well, especially in frail elderly populations (9-11). Gait tests in a biomechanics laboratory do not reflect exposure to environmental and task-related hazards(12, 13).

Wearable sensors allow for ambulatory monitoring of the quantity and quality of daily-life activities. Several studies have shown that daily-life gait quality characteristics, assessed with a single sensor, are able to discriminate fallers from non-fallers. Examples of such characteristics are local dynamic stability, variability of gait, frequency domain parameters, and gait smoothness (14-17). However, only a few research teams focus on developing fall risk prediction models based on daily-life activities in community environment (15-18). Among these, three predictive models from van Schooten and colleagues (1) had moderate to good predictive ability for falls happening in the next 6 months, and demonstrated that daily life accelerometry contributed substantially to the identification of individuals at risk of falls (areas under curve (AUC) of 0.68, 0.71 and 0.82 respectively). These models were logistic regression models based on a relatively large (n=169) data set of the FARAO cohort, a project concerning fall-risk assessment in older adults, with independent variables obtained either from questionnaires, from daily-life accelerometry, or from a combination of both.

However, Shany and colleagues(19) pointed out that current studies of sensor-based fall risk estimation were overly optimistic due to small sample sizes, flawed modelling and validation methods, (e.g. inherent problems with overly cross-validation techniques, lack of external validation). In addition, Nouredanesh and colleagues (20) have shown that there are many inconsistencies in studies of free-living fall prediction, such as the terminology (e.g., definition of gait quality and fall/fallers), hyperparameters (locomotion windows, description index of gait quality, duration of daily-life data and sampling frequency), and data processing approaches (e.g. the cut-off thresholds to define ambulatory walking bouts). More importantly, they also indicated that none of these prediction models have been externally validated, so the repeatability and generalizability cannot be guaranteed, which hinders the establishment and implementation of a unified fall prediction model for community-dwelling older adults.

In this study, we aimed to assess the external validity of the FARAO fall prediction models (1) by using an external cohort of community-dwelling older adults. Moreover, as the ambulatory assessments specifically quantify the amount and quality of daily-life gait, we also focused on walk-falls only. In addition, we calibrated the FARAO prediction models. Finally, we evaluated models based on the optimal model parameters of the new cohort and compared the odds ratio for individual variables between original and new cohorts.

2. Materials and Methods

2.1 Participants

The data in this study were available from the "Veilig in beweging blijven" (VIBE), which translates to "Safely remaining active" cohort. Participants were included if they had a Mini-Mental State Examination (MMSE) score ≥ 19 (21) and were able to walk 20 meters, if necessary with a walking aid, without dizziness or perceiving chest pain or pressure, and were able to understand the Dutch language. The protocol was approved by the ethics committee of the faculty of Behavioural and Movement Sciences of the Vrije Universiteit Amsterdam (VCWE-2016-129). Among 441 persons who expressed interest, 283 were eligible to participate and agreed to 12 months follow-up on falls. All participants provided signed informed consent before participation.

2.2 Questionnaire related to fall risk

Descriptive characteristics such as age, weight, height, the use of a walking aid and 6-month fall history were obtained from all participants. In addition, participants independently filled out validated questionnaires and tests on fall-risk factors, i.e. cognitive function (Mini Mental State Examination; MMSE), concern about falling (16-item fall efficacy scale; FES-I (22)), LASA fall-risk profile (Longitudinal Aging Study Amsterdam) (23) and Geriatric Depression Scale (GDS-15 (24)). The LASA fall-risk profile comprised questions concerning dizziness, independence in daily life, having pets, alcohol consumption, education duration and required the measurement of hand grip strength, which was quantified using a handgrip dynamometer (TKK 5401, Takei Scientific Instruments, Tokyo, Japan). The GDS-15 is an effective scale for depressive symptoms in older populations, where 5 negative items and 10 positive items indicate symptoms of depression (25). GDS forms missing ≤20% of items were imputed according to (26). Scores of 0-4 are considered normal, depending on age, education, and complaints; 5-8 indicate mild depression; 9-11 indicate moderate depression; and 12-15 indicate severe depression. Since the GDS-30 was used in the original model, we had to convert our GDS-15 scores to GDS-30 scores. We did so by using a regression equation, in which GDS-15 scores are converted to GDS-30 scores: GDS-30 scores = 1.95*GDS-15 scores + 1.57 (27).

2.3 Assessment and analyses of daily-life gait characteristics

Conforming to the FARAO cohort study (1), participants were instructed to wear a tri-axial accelerometer (DynaPort MoveMonitor, McRoberts, The Hague, the Netherlands) at home for 7 consecutive days, except during aquatic activities such as showering. The sensor was worn on the trunk at the level of L5 using an elastic belt, whose three axes of orientation corresponded to vertical (VT), anterior-posterior (AP) and medial-lateral (ML), ranged from −6g to +6g, with sampling frequency around 100 Hz. We omitted the first 6 hours of the measurements from analysis, to discard any possible artefacts caused by transportation from the research team to the participants' home. To have a valid measure of the amount of daily activity, the accelerometer had to be worn for more than twelve hours each day (28). At the same time, the minimum valid days for daily physical activities are 2 days except for lying for which it is 3 days (28), so the worn time of the sensors should not be < 2 days to get valid accelerometer assessment in our study. For identification of periods of non-wearing, locomotion, sitting, lying, shuffling, and standing, we used the manufacturer's validated algorithms (29). We calculated the total duration of lying, and the number of strides, averaged over valid days, to obtain reliable, and valid indicators of the amount of daily activity.

The accelerometer data analyses were performed in Matlab R2019a (Mathworks, Natwick, MA), using the

Gait Analysis toolbox [https://github.com/VU-HMS/Gait-Analysis.git]. Prior to estimation of gait
characteristics, data from each locomotion episode was realigned with the vertical axis, which was
estimated from the direction of the mean acceleration signal (30), and anteroposterior and mediolateral
directions, which were estimated by optimizing the left–right symmetry (31). Locomotion episodes were
then split into epochs of 10 seconds to avoid possible sample size-related bias in outcome measures (32).
Median gait characteristics were calculated over epochs of each gait episode, identical to the data length
requirements of characteristics determined, i.e., logarithmic divergence rate AP (33), range VT, index of
harmonicity ML (34) and sample entropy VT (35). The mean over all episodes in a week for these measures
were calculated as outcome measure (18) .

2.4 Outcome: Falls and walk-falls

Although participants were monitored prospectively for falls over a 12-month period following the baseline
assessment by means of a fall diary and monthly telephone contact, we only focused on the first 6 months
of follow-up for consistency with the original models. However, to explore if extended follow-up periods
resulted in better model performance, we also analyzed data obtained from the 1-year fall history and 1-
year prospective fall recordings; these results are reported in the supplementary materials. A fall was
defined as an unintentional change in position resulting in coming to rest at a lower level or on the ground
(36). Participants were classified as being a faller based on the number of prospectively monitored falls (≥1)
they experienced over the 6-month period. Participants who did not record their fall diary for the complete
6 months but experienced at least one fall within the recorded follow-up period were also classified as
fallers.

When a fall happened, the activities and circumstances were also recorded, including walking, climbing the
stair, riding a bicycle, showering, etc. Because the models were based on gait parameters, we also
investigated how all models performed for people that fell specifically during walking. Participants were
classified as walk-fallers if they had one record of a fall during walking.

2.5 Statistical analysis

Statistical analysis was performed in Matlab R2021a (MathWorks, Natick, MA) and R (R core team, Vienne).
Unpaired T-tests were used for comparisons between fallers and non-fallers, and between walking fallers
and non-fallers, separately. All continuous parameters in models were transformed to z-scores prior to
analyses to facilitate interpretations.

The FARAO prediction models were all originally based on stepwise forward logistic regression analyses,
among which, model 1 included as independent variables 6-months history of falls and GDS-30, model 2
contained accelerometry-based daily life gait quantity and quality characteristics, and model 3 combined
variables from both model 1 and model 2.

To validate predictive models on our VIBE cohort data, with either all falls or walking falls as outcome, we
first calculated model performance for our VIBE cohort when we used the FARAO model coefficients,
original cut-offs (0.279, 0.352 and 0.396) and the mean/SDs of the FARAO cohort to calculate the z-score.

Next, we checked if recalibration (37) of the original models would improve model performance. To this
aim, the agreement between the predicted probability of the models and observed binary outcomes was
evaluated using a logistic regression, using predicted probability based on external cohort as independent

variable and faller status as dependent variable, see equation 1

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$$Actual\ values = \frac{1}{1+e^{-(\beta_0 + \beta_1 * predicted\ probablity)}}$$
(1).

Where the slope (β_1) evaluates the spread of estimated risks and the intercept (β_0) is an assessment of
calibration-in-the-large. Slope = 1 and intercept = 0 means perfect model calibration (37). If these
recalibrated models perform well, it suggests a simple scaling of the model would be enough to use the
model in other populations.

Then models with coefficients and cut-offs optimal to our VIBE dataset were evaluated to see whether
performance could be improved, considering potential differences in the sample measured. Finally,
univariate logistic regression was performed to identify the association between model variables and
prospective falls, and these resulting odds ratio were compared with those from the FARAO cohort (1).

3. Results

3.1 Descriptive Characteristics

283 participants filled in questionnaires and wore an accelerometer for one week at baseline, but 5
participants' acceleration data could not be read. Among the remaining 278 participants, 15 participants
were excluded due to missing more than 20% of the GDS items (n=3, 1 person missed 5 items and 2 persons
missed 15 items), incomplete records within 6 months and no record of falls (n=3), accelerometer
assessment duration of less than 2 days (n=3), ≤ 50 episodes of overall measurement time (n=6). Figure 1
presents a flowchart of the included fallers and non-fallers.

Figure 1. Flowchart of participants included for analyses. Fall records were considered incomplete when

one or more months of fall records were missing.

Descriptive characteristics of the participants are summarized in Table 1. Of the 263 participants, 39.9%
(n=105) experienced one or more falls during follow-up, 19% (n=50) had fallen during walking. In addition,
37.6% of all participants, 43.8% of all fallers, 50% of walk-fallers and 33.5% of non-fallers had a fall history
in the past 6 months. The average number of prospective and past falls, GDS scores, FES-I and LASA fall risk
profile (score) were significantly different between fallers and non-fallers, and between walk-fallers and
non-fallers. Furthermore, walk-fallers had significantly lower hand grip strength, and poorer independence
in life, compared to non-fallers.

Figure 2(A) shows the main activities when a fall happened, including walking (39%), riding a bicycle (13%),
movement transfer (12%), going up or down the stairs (12%), doing sports (6%), standing and sitting (in
static positions) (4%), and other activities (15%). Among these, hiking was classified as a sport in this study.
Working in the garden, wearing clothes, etc. were classified as "Other". Furthermore, main causes of falls
during walking were shown in Figure 2(B), which were trip/stumble (34%), balance loss (31%), slip (17%),
physiological discomfort (8%), being distracted (2%) and other (8%). Trip/stumble often happened on
uneven roads or roads with obstacles, and balance loss was more likely to occur when there was sudden
disturbance, opposite walking height to the expected. Falling due to slips usually occurred in the bathroom
or on a slippery floor. In addition, physiological discomfort included ankle sprain, sudden dizziness, drops
in blood pressure, eye injury and weakened muscle strength, etc. Falling caused by distraction included
chatting, looking at map, or doing other tasks when walking. Lastly, some unknown, poorly classified
reasons were divided into "Other".

Table 1. Descriptive characteristics (Mean (SD)) of the participants

Characteristics	All participants	All fallers	Walk-fallers	Non-fallers
Number	263	105	50	158
Age (years)	71.8 (5.7)	71.9 (5.4)	71.9 (6.2)	71.8 (5.9)
Gender (%female)	68.1 (179)	68.6 (72)	72 (36)	67.7 (107)
Weight (kg)	74.1 (13.5)	72.6 (12.9)	70.6 (12.4)	75.1 (13.8)
Height (cm)	169.1 (8.5)	168.6 (9.1)	166.4 (8.2)	169.5 (8.1)
Number of Falls in follow-up 6 months	0.6 (1.02)	1.6 (1.04) [A]	2.0 (1.3) [B]	0 [A, B]
At least one fall in follow-up 6 months (%/n)	39.9 (105)	100 (105)	100 (50)	0
Two or more falls in follow-up 6 months (%/n)	14.5 (38)	36.2 (38)	56 (28)	0
Number of Falls in past 6 months	0.7 (1.4)	1 (1.9) [A]	1.4 (2.5) [B]	0.5 (0.8) [A, B]
At least one fall in past 6 months (%/n)	37.6 (99)	43.8 (46)	50 (25)	33.5 (53)
Two or more falls in past 6 months (%/n)	13.7 (36)	20 (21)	30 (15)	9.5 (15)
Hand grip strength (kg)	58.8 (16.6)	57.5 (17.5)	53.6 (17.5) [b]	59.7 (15.9) [b]
Geriatric depression score 30, GDS (score)	4.4 (4.3)	5.5 (5.3) [A]	6.5 (6.3) [B]	3.7 (3.3) [A, B]
Fall efficacy scale, FES-I(score)	20.5 (5.1)	21.4 (6.5) [a]	21.5 (6) [b]	19.9 (3.9) [a, b]
Cognitive function (MMSE score)	28.2 (1.6)	28.3 (1.6)	28.5 (1.7)	28.2 (1.6)
LASA fall risk profile (score)	3.4 (3.3)	4.4 (3.8) [A]	5.4 (4.5) [B]	2.8 (2.8) [A, B]
Inability of using transport(%/n)[1]	0.4 (1)	1 (1)	0 (0)	0 (0)
Living independently (%/n)	99.2 (261)	98.1 (103)	96 (48) [b]	100 (158) [b]
Use of a walking aid (%/n)	6.8 (18)	8.6 (9)	10 (5)	5.7 (9)

200   ***Note:*** [1]Either public or own transport. [A] significant difference between all fallers and non-fallers with p<0.01; [a] significant difference
201   between all fallers and non-fallers with p<0.05; [B] significant difference between walking fallers and non-fallers with p<0.01; [b]
202   significant difference between walking fallers and non-fallers with p<0.05.

Figure 2. Main activities of all falls (A) and causes of walk-falls (B)

3.2 Validation of predicting all falls and walk-falls based on existing models

By using optimal cut-offs (0.279, 0.352 and 0.396), coefficients and mean (SD) (for z-score) from the original cohort, we obtained model performance of the three prediction models based on only questionnaires, only accelerometry, and combined questionnaires and accelerometry. Table 2 shows the results of each prediction model, with either all falls or walk-falls as outcome (Model performance for 12 months based on FARAO cohort can be seen in Supplementary Table 1). Model 1, with only questionnaires, performed best for predicting all falls and walk-falls, with AUC (area under the curve) of 0.62 and 0.68, respectively. Model 3 and model 2 were less effective than model 1, although model 3 was slightly better than model2, with AUC 0.56 and 0.59 for model3, 0.50 and 0.49 for model 2. However, the precision and sensitivity in both groups were low, which meant the ability of predicting a fall was low for all models.

Table 2. Model performance based on models from FARAO cohort

Performance	All falls			Walk-falls		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
Accuracy	0.58	0.50	0.62	0.63	0.53	0.75
Precision	0.48	0.37	0.56	0.34	0.20	0.49
Sensitivity	0.50	0.36	0.22	0.58	0.32	0.34
Specificity	0.64	0.59	0.89	0.64	0.59	0.89
AUC	0.62	0.50	0.56	0.68	0.49	0.59

3.3 Model recalibration

Calibration slope and intercepts are shown in Table 5. Intercepts of all models in both groups were negative, and the slope of model 2 was <1, contrary to model 1 and model 3, which had slopes >1. The performance of the calibrated models is shown in Table 6. The AUC of all calibrated models ranged from 0.51-0.62. The sensitivity of calibrated model 2 was best with 0.92, better then calibrated model 1 (0.53) and model 3 (0.28).

Table 5. Calibration slope and intercept

Coefficient	All falls			Walk-falls		
	Model1	Model2	Model3	Model1	Model2	Model3
intercept	-1.06 (0.24) **	-0.58 (0.40)	-0.83 (0.20) **	-2.18(0.31) **	-1.16(0.50) *	-1.83(0.27) **
slope	2.24 (0.68) **	0.55 (1.23)	1.40 (0.51) **	3.26(0.79) **	0.06(1.54)	2.09(0.62) **

Table 6. Calibration FARAO Model performance

Performance	All falls			Walk-falls		
	Calibration Model1	Calibration Model2	Calibration Model3	Calibration Model1	Calibration Model2	Calibration Model3
Optimal cut-offs	0.36	0.38	0.45	0.23	0.24	0.29
Accuracy	0.59	0.46	0.63	0.71	0.40	0.75
Precision	0.49	0.42	0.59	0.42	0.21	0.47
Sensitivity	0.53	0.92	0.28	0.50	0.56	0.36
Specificity	0.63	0.15	0.87	0.78	0.35	0.87
AUC	0.62	0.52	0.58	0.68	0.51	0.62

3.4 Validation of predicting all falls and walk-falls based on the external validation dataset

The optimal cut-offs of the external validation VIBE cohort, which balanced the high sensitivity (true positive rate) and the low false positive rate (1-specificity), were 0.38, 0.40 and 0.37 in all models for predicting all falls, and 0.20, 0.23 and 0.20 for predicting walk-falls. Based on these optimal cut-offs, and the coefficients of this validation cohort, the model performances are shown in Table 3 and Figure 3. Specificity and sensitivity were still moderate for these models (ranging from 0.59-0.66). Model3 performed best in both groups (AUC=0.65 and 0.73, respectively), and then model 1 and model 2.

Table 3. Model performance based on the external validation VIBE cohort

Performance	All falls			Walk-falls		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
Optimal cut-offs	0.38	0.40	0.37	0.20	0.23	0.20

Accuracy	0.62	0.53	0.57	0.66	0.54	0.6
Precision	0.53	0.43	0.47	0.38	0.27	0.33
Sensitivity	0.56	0.53	0.58	0.66	0.54	0.62
Specificity	0.66	0.53	0.56	0.66	0.54	0.59
AUC	0.63	0.53	0.65	0.69	0.56	0.73

Figure 3. Receiver operating curves (ROC) for the three fall prediction models of all falls **(A)** and walk-falls **(B)**

for coefficients optimized on the VIBE-cohort data

3.5 Odds ratio comparison

To better understand differences in model performance between the original models and models fitted on our external dataset, the comparison of descriptive statistics and odds ratio of measures for the original FARAO cohort (1) and our external VIBE cohort are presented in Table 4. Prevalence of fall history prior to 6 months in VIBE cohort was 37.6%, which was slightly higher than 35.5% in the FARAO cohort. GDS and LASA score were associated with prospective falls both in VIBE cohort and FARAO cohort. Number of strides walked in our cohort were higher than in the FARAO cohort. Gait characteristics were very similar, except range VT, which was smaller in the VIBE cohort than in the FARAO cohort. Furthermore, only one measure in the VIBE cohort showed a significant association with follow-up falls, which was index of harmonicity ML, while in FARAO cohort, all selected gait characteristics showed significant associations with falls.

Table 4. Mean (SD) and odds ratios (OR) for VIBE cohort (n=263) and FARAO cohort (n=169) (1)

Measures	Prevalence or Mean (SD) for VIBE cohort	Prospective Falls OR (95% CI)	Prevalence or Mean (SD) for FARAO cohort	Prospective Falls OR (95% CI)

Demographic information				
Age (years)	71.8 (5.7)	NA	75.4 (6.8)	NA
Gender (% female)	68.1 (179)	NA	52.1	NA
Weight (kg)	74.1 (13.5)	NA	74.1 (14.2)	NA
Height (cm)	169.1 (8.5)	NA	170.8 (8.9)	NA
Cognitive function (MMSE score)	28.2 (1.6)	NA	27.7 (2.2)	NA
Living independently (%)	99.2	NA	88.1	NA
Questionnaires				
6-months history of falls	37.6%	1.6 (1.2-2.2) [**]	35.5%	3.1 (1.6–6.1) [**]
Hand grip strength (kg)	58.8 (16.6)	0.9 (0.7-1.1)	58.4 (20.5)	0.97 (0.7–1.4)
Geriatric depression score, GDS-30	4.4 (4.3)	1.5 (1.2-2.0) [**]	4.6 (4.2)	1.6 (1.1–2.2) [**]
Fall efficacy scale, FES-I(score)	20.5 (5.1)	1.3 (1.1-1.7) [*]	20.8 (4.4)	1.1 (1.0–1.1) [*]
Cognitive function (MMSE score)	28.2 (1.6)	1.1 (0.9-1.4)	27.7 (2.2)	0.9 (0.7-1.2)
LASA fall-risk profile (score)	3.4 (3.3)	1.7 (1.3-2.2) [**]	5.5 (4.7)	1.6 (1.1–2.2) [**]
Inability to use public transportation	0.4%	NA [***]	7.1%	2.8 (0.8–9.5)
Living independently	99.2%	NA [***]	91.1%	0.8 (0.4-1.8)
Use of walking aid	6.8%	1.6 (0.6-4.1)	17.2%	1.4 (0.6–3.2)
Daily activities (per day)				
Number of strides (N)	4023 (2053)	1.1 (0.8-1.4)	3060 (1527)	0.9 (0.7–1.3)
Duration of lying (h)	9.2 (4.1)	1.0 (0.8-1.3)	10 (2.1)	0.9 (0.7-1.2)
Gait characteristics				
Logarithmic divergence rate AP (/stride)	1.5 (0.3)	0.9 (0.7-1.2)	1.9 (0.3)	1.7 (1.2–2.4) [**]
Range VT (m/s^2)	9.1 (1.9)	0.9 (0.7-1.1)	11.8 (5.6)	0.4 (0.2–0.8) [**]
Index of harmonicity ML	0.4 (0.2)	1.3 (1.0-1.7) [*]	0.5 (0.2)	1.2 (0.9-1.6)
Sample entropy VT	0.2 (0.03)	0.9 (0.7-1.1)	0.2 (0.05)	1.5 (1.1-2.3) [**]

250 **Notes:** AP = anteroposterior direction; ML = mediolateral direction; VT = vertical direction; N/A = not applicable; Continuous
251 parameters are z-transformed. *p < 0.05, **p < 0.01. ***No solution (Infinity).

4. Discussion

We validated the predictive ability of three FARAO fall prediction models based on questionnaires,
accelerometry of daily life gait, and both, for our external data from the VIBE cohort of community-dwelling
older adults. We found that the external validity of the models developed based on the FARAO cohort was
limited for predicting all falls as well as when focusing on walking falls. Subsequently, we explored why this
may have been so.

When comparing the population characteristics between the two cohorts, we found that participants in
both studies had a normal (i.e., low) degree of depressive symptoms (25). The prevalence of falls in our
study was higher to original study (39.9% and 34.9%, respectively), with 14.5% participants having two or
more falls in the follow-up 6 months. In addition, both cohorts had the same definition of a faller in past
and follow-up 6 months when the number of falls was ≥1, respectively. Studies suggested that only one fall
may be an ambiguous fall, with no apparent cause (20), and people who were 'once only fallers' were
characteristically more closely related to non-fallers than 'recurrent fallers'(38) or injury-prone fallers. For
example, one study indicated that the annual incidence of falls for community residents over 70 years of
age may be 49% (39), and another study found the median annual fall prevalence rates was 33.4% for older
people over 50 years (3).

Since participants in the VIBE cohort reported more falls than participants in the FARAO study by Van
Schooten et al., we expected that there was a difference in the method of monitoring falls that led to a
wider range of falls being reported in the VIBE cohort, including relatively more falls that are not related to
walking activities. We divided the causes of the falls into 7 categories and walking accounted for 39% of all
falls, similar to other studies (40-42). However, it was not known if falls in the original study had a similar
distribution of causes. Hence the different proportion of falls during walking may affected the results, but
the models also did not work well for the walking fallers. In post-hoc analysis, results did not change when
we used a 12 month follow up (refer to supplementary table 2 and table 3). In conclusion, there may have
been differences in the classification of fallers that had an effect on the outcomes of the models. However,
we are unable to check for those unknown, factors.

After using the model parameters from FARAO cohort to classify fallers and non-fallers, we got moderated
accuracy, limited precision and sensitivity for all models in two groups. Therefore, we explored the optimal
coefficients and optimal cut-offs for the VIBE cohort and found model 3 performed best for both all falls
and walk-falls. The AUC of all models improved a little, but the precision and sensitivity remained moderate.
This indicates that if the model was run with external data, the coefficients and cut-offs based on external
data would give better results. More importantly, the model which combined the gait quality characteristics
and questionnaires was better than either one alone. Thus, while the same variable may yield a reasonable
fall prediction model, it appears that coefficients and cut-offs may be rather specific to a given population
(43).

To further study the predictors in the models, odds ratios of individual variables were compared with the
initial FARAO cohort. Studies have shown that fall history, depressive symptoms, LASA fall-risk profile, fear
of falling, and poor executive function (as assessed by TMT-A) were associated with prospective falls (23,
44, 45). Significant odds ratios of these measures in the original study confirmed this (van Schooten et al.
2015a). More importantly, these measures from the VIBE cohort also had significant odds ratios. However,
of the gait quality characteristics, only index of harmonicity ML had significant odds ratios in VIBE cohort,
while other gait quality measures have been shown to be related to future falls in FARAO cohort. Specifically,
lower harmonic ratio, reflecting lower gait symmetry, was shown to be related to falls by (46); higher
logarithmic rate of divergence, reflecting lower local stability, was associated with future falls, according to
previous findings (16, 47, 48). As outlined above, this was most likely not due to our definition of "fallers"
but could potentially be related to differences in the samples in terms of depression and cognitive abilities.

For model calibration, Negative values of the calibration intercept suggest over-estimation, whereas
positive values suggest underestimation. Calibration slopes < 1 suggests that estimated risks are too
extreme, i.e., too high for patients who are at high risk and too low for patients who are at low risk. A
slope>1 suggests the opposite, i.e., that risk estimates are too moderate. Therefore, all three models over-
estimated and the estimated risk of model 2 and 3, which included gait characteristics, were too extreme.

In conclusion, prediction of fall risk in our VIBE cohort based on the FARAO models was not as effective as
models in FARAO cohort (1) suggesting that these models have limited external validity. Despite several
earlier reports indicating the importance of daily life gait measures for predicting falls, such measures alone
were of limited value in our cohort. Moreover, the fact that optimal coefficients and cut-off were different
for our cohort, as well as the fact that we found almost no significant ORs for the gait parameters included
in the model, suggests that this kind of fall prediction models are highly specific to the cohort studied.
Nonetheless, even with these optimal coefficients and cut-offs, model performance was still poor, which
highlights the need for large representative cohorts, preferably with an external validation cohort.

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