Dizziness in older patients in general practice: away from diagnostic nihilism

Dros, J.

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Chapter 8

Functional prognosis of dizziness in older primary care patients: a prospective cohort study

Jacquelien Dros
Otto R. Maarsingh
Leo Beem
Henriëtte E. van der Horst
Gerben ter Riet
François G. Schellevis
Henk C.P.M. van Weert

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ABSTRACT

Objectives
To investigate the six months functional prognosis of dizziness in older primary care patients, to identify key predictors for dizziness-related impairment, and to construct a score to assist risk prediction.

Design
Prospective cohort study with six months follow-up.

Setting
Twenty-four primary care practices in the Netherlands.

Participants
417 consecutive older patients (mean age 78.5, range 65-95, 74% female) presenting with dizziness in primary care.

Measurements
We performed tests, including patient history, and physical and additional examination, previously selected by an international expert panel and based on an earlier systematic review. Our main outcome measure was the six-months dizziness-related impairment score measured with the Dizziness Handicap Inventory.

Results
Follow-up was complete for 92% of patients. Although 61% of patients experienced less impairment at six months, 130 patients (34%) showed persistent dizziness-related impairment. Factors most predictive of dizziness-related impairment at six months were onset of dizziness at least six months before inclusion, standing still as dizziness provoking circumstance, trouble with walking and/or (almost) falling (associated symptom), poly-pharmacy, absence of diabetes, presence of anxiety and/or depressive disorder, and impaired functional mobility. A score was constructed using these predictors to estimate the functional prognosis of dizziness at six months.

Conclusion
A score based on the presence of easily obtainable clinical information facilitates identification of older primary care patients with poor functional prognosis of their dizziness without exactly knowing the cause(s) of their dizziness. Clinical management might be most effective treating those factors that can be influenced, like poly-pharmacy, anxiety and depression, and functional mobility.

INTRODUCTION

Dizziness is a common symptom, especially in older patients. Annual consultation rates for dizziness in primary care increase from 8% for patients over 65 years of age to 18% for the oldest elderly (85+).[1;2] Moreover, two-third of older patients presenting with dizziness experience chronic dizziness, with complaints persisting or recurring for more than six months.[3-5] Not only is dizziness in the elderly common, it also tends to be multicausal, resulting from defects in different organ systems simultaneously.[6] Patients without a diagnosis make up 20-40% of all patients presenting with dizziness in primary care.[7-9] Even if specific diseases are revealed, these cannot always be treated effectively.[10]

In fact, dizziness can be a great burden for older patients, resulting in serious impairment in daily functioning, falls, social isolation, and eventually nursing home admission.[5;10;11] Despite the need to gain more insight into the prognosis of dizziness, few prospective studies have investigated the course of dizziness and dizziness-related impairment in primary care patients, and none of these provided information on older patients.[12-14] This study aimed to determine the functional prognosis of dizziness in older primary care patients after 6 months of follow-up. In addition, our aim was to identify predictors for persisting impairment due to dizziness and to construct a risk score for use in primary care, using information collected in clinical practice.

METHODS

Study design and participants

This study is part of the DIEP-study (Dizziness In Elderly Patients); details of patient population and data collection have been published previously.[15;16] Briefly, in a prospective observational cohort study of consecutive patients of 65 years and older presenting with dizziness in primary care, 417 patients from 45 general practitioners (GPs) in 24 Dutch practices were followed up for six months.

As dizziness in the elderly mostly reflects a multifactorial problem and symptoms are often non-specific, our definition of dizziness included a giddy or rotational sensation, a feeling of imbalance, light-headedness, and/or a sensation of impending faint, as reported by consulting patients. Criteria for exclusion were inability to speak Dutch or English, significant cognitive impairment, a corrected visual acuity of less than 3/60 for the best eye, inability to communicate verbally, and wheelchair dependency. Participants completed questionnaires at inclusion and six months after the index consultation. The study was approved by the medical ethics committees of the two academic medical centers involved. All patients provided written informed consent.

Outcome: dizziness-related impairment

Outcome was defined as dizziness-related impairment, assessed with the validated Dutch version of the Dizziness Handicap Inventory (DHI).[17;18] The DHI is a self-report questionnaire designed to quantify the impact of dizziness originating in the vestibular system,[17] but has frequently been used for patients with dizziness of any cause.[19-23] The DHI is the most commonly used and accepted questionnaire to quantify the impact of dizziness and has been translated in many languages.[18;23-29] The questionnaire contains 25 items covering functional, emotional and physical subscales. “Yes” scores 4 points, “sometimes” 2 points and “no” 0 points. DHI-scores range from 0 to 100, higher scores indicate greater perceived disability, and a DHI-score of 30 has been used as cut-off point for substantial impairment.[23;30] We therefore defined an unfavourable outcome a DHI-score of >30 at 6 months.

Potential predictors of dizziness-related impairment

In a 3-round Delphi procedure 16 international experts, representing dizziness-relevant medical specialties, selected 21 tests as potentially contributing to the diagnostic process in older patients presenting with dizziness to a general practitioner (GP). The tests included four elements of patient history, eleven on physical examination, and six additional diagnostic tests.[15] In addition to these tests we collected data on demographic variables and measured functional mobility using the validated timed up-and-go test.[31]

In the baseline dataset 0.2% of the data were missing. To minimize bias we imputed these missing data using the iterative chained equations method (ICE) in STATA/SE 10.0 (StataCorp, College Station, TX, USA). The details of this procedure have been published previously.[6]

From these tests and measurements resulted a total of 87 variables of which we selected 33 candidate predictors concerning demographic and lifestyle factors, characteristics of dizziness, data on relevant diagnoses and drugs, the DHI-score at baseline, and information about relevant conditions or tests (e.g. orthostatic hypotension, functional mobility, Dix-Hallpike test).[32] This clinical selection process was based on: (1) plausibility of relation with the impact of dizziness, (2) prevalence in the study population between 10% and 90%, and (3) Spearman correlation coefficient between these candidate predictors between -0.50 and 0.50.

Statistical analysis

We described the distribution of DHI-scores at baseline and at 6 months follow-up, and the differences in DHI-scores between baseline and follow-up. We dichotomized the DHI-score at six months at the predefined cut-off, with > 30 as “high” and ≤ 30 as “low”.

Loss to follow-up and imputation

We explored the predictability of loss to follow-up with all-possible-subset and stepwise logistic regression techniques. Next we imputed missing data at follow-up with the regression method in SPSS 18, using the DHI-score at baseline and the 32 other variables. To minimize bias, five datasets with imputed scores were created and these datasets were combined into one large dataset.

Identification of predictors for impairment due to dizziness at six months

First we calculated bivariate Pearson correlations of the DHI-score at 6 months and all 33 candidate predictors to assess predictive performance of each variable separately. Next, backward logistic regression was applied to investigate the predictability of the dichotomous DHI-scores at 6 months, once with and once without the DHI-score at baseline added to this set. For stability reasons, backward regression was conducted in each of 1500 bootstrap samples from the combined imputed dataset. The selection criterion ("p-remove") was set at 0.05. The model without the DHI-score at baseline is described.

Construction of the final risk prediction model and score

From the models selected in the bootstrap samples, variables were retained for a final model if they were selected in at least 67% of the 1500 bootstrap samples. The parameters of this model were then estimated in the five imputation samples and Rubin's rules[33;34] were applied to obtain pooled estimates and their standard errors. From these, odds ratios and their confidence intervals were calculated. We also calculated the average regression weights for each variable over all (1500) bootstrap samples (B_m)[35] and the regression weights of the (7) variables selected in the final model (B_s). For comparison reasons, we both calculated weighted sum scores (based on the above mentioned B_s), and simple sum scores (based on simply counting the number of predictors that are present in a particular patient).

Finally, the calibration of the final model was evaluated by comparing the observed and estimated outcome probabilities for all values of the simple sum score. The fit was evaluated using the Hosmer-Lemeshow Goodness-of-Fit test and the ability of the simple sum score model to identify patients with an unfavourable course of dizziness was estimated using the area under the Receiver Operating Characteristic (ROC) curve (AUC).

RESULTS

From July 2006 to January 2008, 417 consecutive older patients presenting with dizziness in primary care were enrolled (table 1). As expected, did most patients not present one clear-cut type of dizziness, but presented with two or more subtypes of dizziness.[6] Follow-up data were available for 385 patients (92.3%) at six months (Appendix table 1). Reasons for loss to follow-up were death (17 patients, 4.1%), refusal to participate (10 patients, 2.4%), and unknown destination (5 patients,1.2%). Patients with and without follow-up did not differ in baseline characteristics (Appendix table 1). Sensitivity analysis did not identify significant differences in results with and without the 32 subjects lost to follow-up. Furthermore, the fact that the DHI-score at baseline, which was by far the best predictor for the DHI-score at 6 months follow-up (appendix table 2), did not play a role in predicting mortality, suggested that loss to follow-up due to mortality (53%) was not related to the outcome, and thus imputation was allowed. Accordingly, we imputed the outcome variable for the 8% incomplete cases.

Table 1. Baseline characteristics of 417 dizzy older patients in primary care

Variable	No. (%) of patients
Sex, female	307 (74)
Age in years, mean (range)	78.5 (65-95)
Medical history	
Cardiovascular disease	205 (49)
Hypertension	239 (57)
Diabetes	78 (19)
Neurologic disease	145 (35)
Psychiatric disease	142 (34)
Onset of dizziness	
<6 months	128 (31)
≥6 months	289 (69)
Dizziness subtype*	
Disequilibrium	360 (86)
Presyncope	302 (72)
Vertigo	259 (62)
Atypical	146 (42)
Number of dizziness subtypes per patient	
1	62 (15)
2	115 (28)
3	152 (36)
4	88 (21)

*Adds up to more than 100%, because most patients described more than one subtype.

Dizziness Handicap Inventory scores

At baseline the median DHI-score was 34 and the interquartile range 22 to 50; at six months the median DHI-score was 24, the interquartile range 8 to 44, and 56 patients (15%) had score 0 (figure 1).

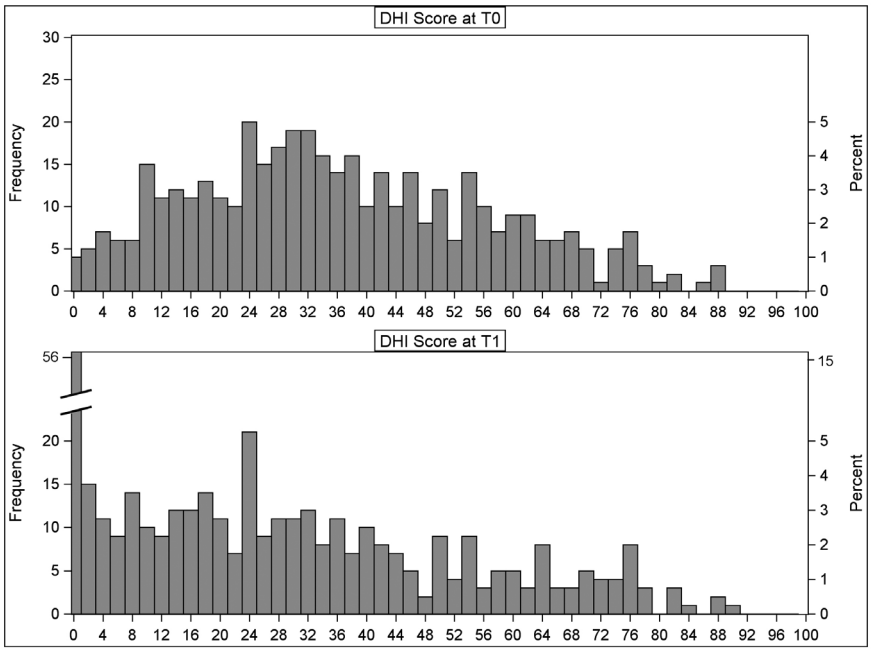

Figure 1. DHI-scores at baseline and at 6 months follow-up

In addition, 130 patients (34%) showed persistent dizziness-related impairment, with DHI-scores >30 both at baseline and at 6 months.

The mean change in DHI-scores between baseline and at 6 months was 7.5 (SD 19.2) (figure 2).

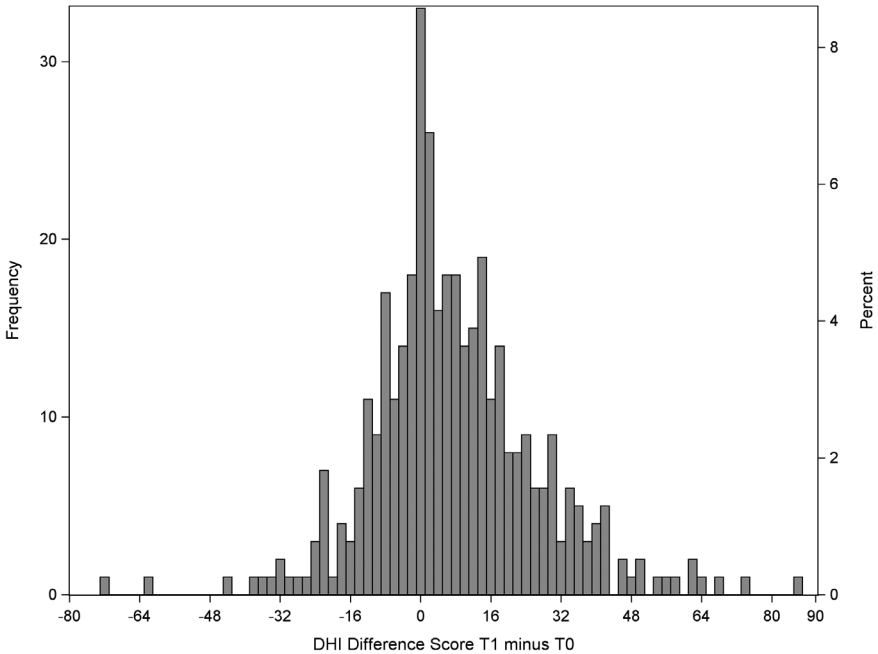

Figure 2. Differences in DHI-scores between baseline and at 6 months

According to findings of Tamber et al.[23], the cut-off point of a clinically meaningful change in DHI between baseline and at six months was set at ±12. At follow-up, 116 patients (30%) experienced more dizziness-related impairment, of which 46 (12%) had a clinically relevant increase (Δ DHI-score ≥ 12); 236 patients (61%) experienced less impairment, of which 136 (35%) had a clinically relevant decrease (Δ DHI-score ≥ -12).

Predictors of dizziness-related impairment

DHI-score at baseline was omitted from the final model, because the DHI is nor a clinical instrument, neither does it deliver suggestions for clinical interventions. Besides, in using the DHI both as candidate predictor (DHI-score at baseline) and as outcome (DHI-score at 6 months) it became the best predictor and overruled other relevant predictors. Finally, predictors retained in the final logistic model were: (1) onset of dizziness (6 months ago or more at baseline), (2) dizziness provoked by standing still, (3) trouble with walking and/or (almost) falling (associated symptom), (4) poly-pharmacy (≥ 5 drugs), (5) no diabetes, (6) anxiety and/or depressive disorder, and (7) (impaired) functional mobility measured with the timed up-and-go test (table 2).

Table 2. Predictors of moderate-severe dizziness-related impairment in older primary care patients

	Prev, %	B_m	B_s*	p-value (B_s)	OR (95%CI) pooled* (n=417)
Chronic dizziness (≥6 months)	69	1.14	1.04	0.0002	2.83 (1.57-5.10)
Standing still (provoking circumstance)	24	0.76	0.74	0.0068	2.09 (1.20-3.65)
Trouble with walking and/or (almost) falling (associated symptom)	50	0.88	0.83	0.0011	2.30 (1.38-3.84)
Poly-pharmacy (≥5 drugs)	42	0.82	0.93	0.0003	2.53 (1.51-4.23)
No diabetes	81	0.93	0.97	0.0011	2.64 (1.38-5.07)
Anxiety and/or depressive disorder	22	0.94	0.99	0.0036	2.69 (1.49-4.84)
Impaired functional mobility	60	0.76	0.82	0.0013	2.28 (1.39-3.75)
Constant			-3.72		

With dichotomous DHI-scores as dependent variable, wherein scores 0-30 (mild impact of dizziness) = 0, and scores 31-100 (moderate + severe impact of dizziness) = 1. Stepwise backward logistic regression analysis, bootstrap 1500x, α=0.05. Only variables selected in ≥1000 of the 1500 bootstrap samples were retained for the final model and presented as predictors in this table. Prev: prevalence in the study population; B_m: average regression weight over all bootstrap samples; B_s: regression weight in selected model; OR: Odds Ratio; CI: Confidence Interval. *Averaged from or pooled across 5 imputed databases.

The model with simple sum scores performed as well as the model with weighted sum scores, indicating that by using the simple sum score little information is lost. Therefore, and because this is easier to use, only the model with the simple sum scores is presented. The Hosmer-Lemeshow test (p = 0.10) confirmed the significant match of observed and expected simple sum scores and as such the predictive power of the final model. The AUC of the final model is 0.80 (95% CI = 0.75 to 0.84), and the ROC-curve shows the ability of the simple sum score model to identify patients with an unfavourable course of dizziness, especially for sum scores of 4 and higher (figure 3).

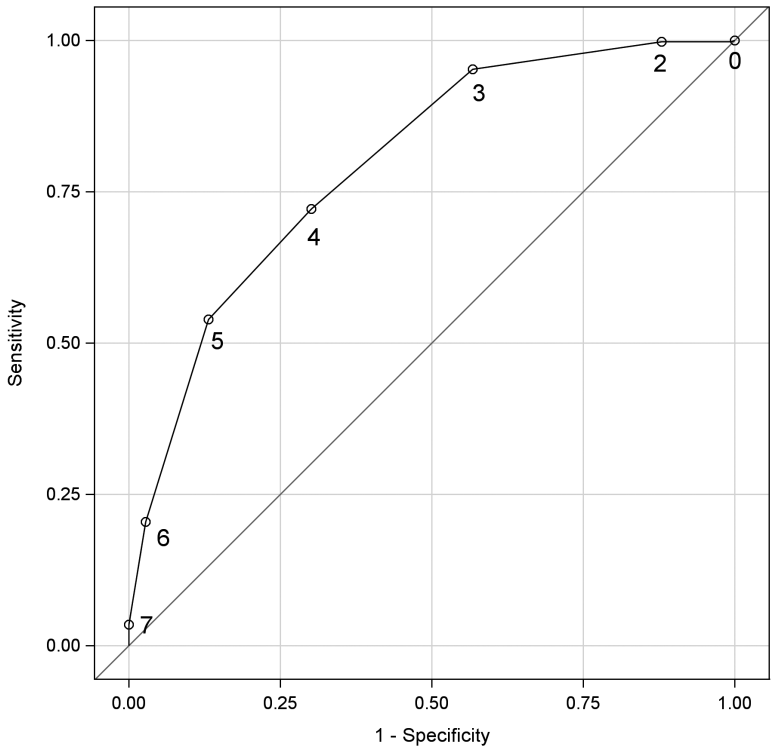

Figure 3. ROC curve of the final prognostic model with seven predictors related to an unfavourable course of dizziness in older primary care patients

Area Under the Curve (AUC) is 0.80 (CI 0.75-0.84). The ROC curve shows all* values of the sum score and their corresponding sensitivity and (1-)specificity. A simple sum score of 3 corresponds with a predicted probability of 0.28, a score of 4 with 0.49, a score of 5 with 0.70, and a score of 6 with 0.85 of a poor functional prognosis of dizziness. *Except for sum score 1 (see Appendix figure).

DISCUSSION

Summary of main findings

In this study of the 6 month functional prognosis of dizziness in older primary care patients, nearly two out of three experienced less impairment, only one in ten had a substantial increase in impairment, and four out of ten experienced impairment at 6 months. Seven factors predicted an unfavourable course: chronic dizziness (onset at baseline at least six months ago); standing still as a dizziness provoking circumstance; trouble with walking and/or (almost) falling as associated symptom; poly-pharmacy; absence of diabetes; having an anxiety and/or depressive disorder; and impaired functional mobility. These all refer to easily obtainable clinical information and with this instrument clinicians

can identify patients with the poorest functional prognosis. A clinician can choose an acceptable cut-off score, depending on his/her desire to be sensitive or specific.

Comparison with other research

This is the first prognostic study on the course and related impairment of dizziness in older primary care patients. In line with our study, the three earlier studies on the prognosis of dizziness in primary care reported a mainly favourable prognosis after 3 to18 months.[12-14]

More complicated is the comparison between prognostic factors in our study and those identified in the above mentioned studies. First, there are differences in both age and sampling procedures in the populations studied. Furthermore, there was no uniform set of predictors, the studies used different approaches to building a prognostic model, and, due to differences in sample size (117 (Bailey), 98 (Kroenke), 247 (Nazareth), and 417 (present study)), they had different statistical power to detect prognostic associations. Nonetheless, significant findings are consistent. For example, all four studies reported adverse prognostic factors to include anxiety and, in agreement with our study, Bailey et al. and Kroenke et al. reported impaired mobility as an adverse prognostic factor. Finally, Bailey et al. found that long duration of dizziness (longer than 1 year) was an adverse prognostic factor, as in our study (longer than 6 months).

We found two other predictors for persistent dizziness impact, namely poly-pharmacy and the absence of diabetes, neither of which have been previously reported. Given the often described relationship between dizziness and drugs[10;11;36-40] it is not surprising we identified poly-pharmacy as a predictor for persistent impact of dizziness. The finding that diabetes is not predicting a poor outcome is not obvious. An explanation might be that patients with diabetes, compared with patients without diabetes, more often consult their PCP (as in the Netherlands almost all patients with diabetes are in a chronic care program) and therefore have ample opportunity to present symptoms. The result of this might be that these patients present relatively less disabling problems. Furthermore, predictors for an unfavourable course of dizziness found in the psychiatric and mobility domain merit comment. The relation between anxiety/depression and the severity and prognosis of dizziness might be circular: dizziness provokes anxiety and depression and anxiety or depression (and some pharmacological treatments) may provoke dizziness. In our opinion the exact causative relation is less important. The fact that psychiatric illness (or the pharmacological treatment of these illnesses) independently predicts a worse prognosis of dizziness makes an evaluation of possible comorbid psychiatric illness in older patients essential, as is an evaluation of medication. Next, two of the three predictors in the mobility domain (trouble with walking and impaired functional mobility) might be interrelated, although both are identified as independent predictors to a worse prognosis. In that sense it might be

expected that interventions like exercise and physical therapy positively influence both factors. The third mobility predictor, standing still as a dizziness provoking circumstance, might indicate disturbances in the autonomous nerve system, as can often be found in older adults, especially e.g. when using medication for cardiovascular disorders.

Strengths and limitations

An important strength of our study is the comprehensive assessment of candidate predictors by choosing variables from a broad spectrum of the diagnostic process, including demographic data, history, physical examination and diagnostic tests. Nonetheless, some potential predictors may have been missed. For example, we did not include self-rated health, or dependency in instrumental activities of daily living (IADL).[12;13] Our dataset was almost complete and our sampling procedure ensured the inclusion of consecutive patients to avoid selection bias. In contrast with earlier studies we focussed on older patients and finally, a sample size of initially 417 patients and 385 at follow-up enabled robust analyses.

It is interesting to note that three of the six diagnostic factors associated with a high dizziness-related impairment in our former cross-sectional study[32] are similar to the seven prognostic factors found in this study: onset of dizziness six months ago or more; presence of anxiety and/or depressive disorder; and impaired functional mobility. This indicates that the same clinical information used to identify those patients who suffer most from their dizziness at present, can also be used to identify those who will suffer most in the future. In other words, those patients with the highest impact of their dizziness now will be the patients with the poorest dizziness prognosis.

Although the cut-off score of 30 and higher to mark substantial impact of dizziness is frequently used, it has only been validated once in a study on the Norwegian DHI (DHI-N, AUC of 0.89).[23] In addition, Tamber et al. were the first to determine the responsiveness of the DHI. The optimal threshold value for detecting change was found to be a difference in DHI-scores of ±12, and although of great importance and the best available, this has not yet been validated.

Implications for clinical practice and future research

In this study we identified predictors indicating which older patients will suffer most from their dizziness after six months without knowing the precise cause(s) of their dizziness. Given the relatively benign prognosis of chronic dizziness and with this relatively simple risk prediction model, clinicians should focus on impairment reduction strategies in older patients at greatest risk of a poor functional prognosis of dizziness. In line with Tinetti's[10] recommendations, our findings suggest that clinical management might be most effective when treating those factors that can be influenced, like anxiety and depression, polypharmacy, and functional mobility. Future research is needed to determine whether these interventions are effective in reducing dizziness-related impairment.

APPENDIX

Table 1. Baseline characteristics of 417 dizzy older patients in primary care with and without completed follow-up

Variable	Follow-up incomplete (n = 32) %	Follow-up complete (n = 385) %	P value*
Sex, female	59	75	0.06
Age in years, mean (range)	77.9 (65-90)	78.5 (65-95)	0.66
Living situation			
Alone	59	61	0.85
In residential home	9	16	0.31
Ethnic background			
Dutch native	72	83	
Western immigrant	19	6	0.02**
Non-western immigrant	9	11	
Level of education			
Elementary school	38	28	
High school	47	60	0.33
College/university	16	12	
Medical history			
Cardiovascular disease	66	48	0.05
Hypertension	50	58	0.40
Diabetes	25	18	0.34
Neurologic disease	31	35	0.66
Psychiatric disease	25	35	0.26
Onset of dizziness			
<6 months	25	31	0.47
≥6 months	75	69	

* For differences in proportions or means between patient with and without complete follow-up data.
** 2 of 6 cells had expected counts less than 5.

Table 2. Association of all candidate predictors with dizziness-related impairment in older primary care patients at six months follow-up

	Logistic Model (dichotomous DHI-scores)*			
	P_{1500}	B_m	OR† (95%CI)	B_s
Demographic				
Age	.17	0.01	1.3 (1.1-1.5)§	
Sex	.00	0.00	1.4 (0.9-2.2)	
Ethnicity	.00	0.00	0.6 (0.2-1.4)	
Living in residential home	.03	0.02	2.3 (1.3-3.9)	
Lifestyle factors				
Smoking	.00	.00	1.1 (0.6-2.0)	
Excessive alcohol intake	.22	.25	1.3 (0.6-3.0)	
Dizziness characteristics				
Onset	**1.00**	**1.14**	**3.6 (2.1-5.9)**	**1.08**
Frequency	.64	.41	2.0 (1.3-3.1)	
Duration	.07	-.04	1.7 (1.1-2.5)	
Subtype description of dizziness				
Light-headedness/presyncope	.01	.00	1.4 (0.9-2.3)	
Spinning sensation/vertigo	.00	.00	1.0 (0.7-1.6)	
Unsteadiness/disequilibrium	.00	.00	3.1 (1.5-6.3)	
Not classifiable dizziness	.00	.00	1.5 (1.0-2.3)	
Provoking circumstances				
Standing still	**.82**	**.62**	**3.3 (2.0-5.3)**	**.77**
Exercise	.01	-.01	1.0 (0.6-1.5)	
Changes in head position	.01	.01	2.2 (1.2-3.8)	
Getting up from lying or sitting	.07	.05	1.9 (1.2-3.0)	
Associated symptoms				
Presyncopal symptoms (without panic disorder)	.00	.00	1.3 (0.9-2.0)	
Trouble with walking and/or (almost) falling	**1.00**	**.88**	**3.4 (2.2-5.3)**	**.83**
Relevant diseases and drugs				
No Cardiovascular disease	.04	.03	1.3 (0.7- 2.3)	
No Diabetes	**.95**	**.89**	**1.6 (0.9-2.7)**	**1.10**
Hearing problems	.00	.00	1.9 (1.2-3.1)	
Anxiety and/or depressive disorder	**.97**	**.91**	**3.9 (2.3-6.6)**	**.88**
Poly-pharmacy	**.96**	**.79**	**2.4 (1.6-3.6)**	**.93**
Use of sedative drugs	.51	.34	2.6 (1.7- 4.1)	

Table 2, *continued*

	Logistic Model (dichotomous DHI-scores)*			
	P_{1500}	B_m	OR† (95%CI)	B_s
Information relevant conditions or tests				
Often unexplained complaints	.32	.27	2.5 (1.4-4.4)	
Orthostatic hypotension	.01	.00	1.1 (0.7-1.8)	
Functional mobility	**.70**	**.53**	**3.7 (2.3-5.8)**	**.84**
Impairment of hip/knee/ankle joints	.33	.20	2.4 (1.6-3.7)	
Neurological impairment feet	.11	.07	1.8 (1.2-2.8)	
Dix-Hallpike test	.00	.00	1.1 (0.6-2.1)	
Visual acuity	.12	.08	1.8 (1.2-2.9)	
DHI-score at baseline	1.00		1.4 (1.3-1.5)§	

Stepwise backward linear and logistic regression analysis, bootstrap 1500x, α=0.05. P_{1500}: proportion selected in all bootstrap samples; B_m: average regression weight over all bootstrap samples; OR: Odds Ratio; CI: Confidence Interval; B_s: regression weight in selected model.
*Dichotomous DHI-scores: scores 0-30 (mild impact of dizziness) = 0, scores 31-100 (moderate and severe impact of dizziness) = 1. §OR is estimated per 5 years or 5 points increase or decrease. †Univariate analysis. Proportions are rounded to two decimals, regression weights to one decimal. Variables selected in ≥1000 of the 1500 bootstrap samples were retained for the final models and highlighted in bold (predictors).

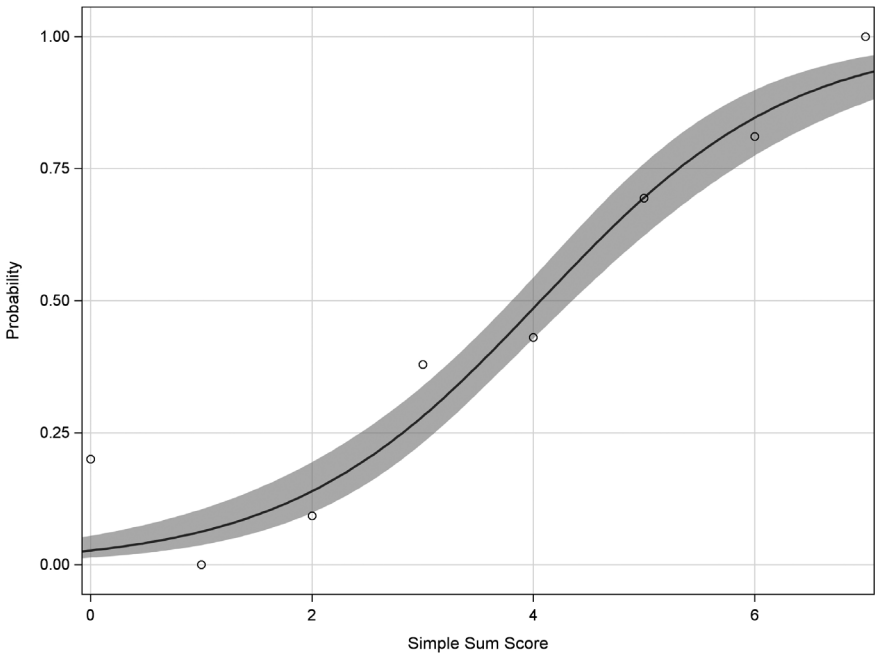

Figure Observed and predicted probabilities of an unfavourable course of dizziness for all values of the simple sum score (0 to 7) of prognostic factors

o: proportion of observed moderate-severe dizziness impact corresponding with a particular sum score

—: proportion of patients with moderate-severe dizziness impact as predicted by the model; the grey band represents the 95% confidence interval. A simple sum score of ≥ 4 means a probability of ≥ 0.49 of an unfavourable course of dizziness in an older patient. Notice that sum score 1 was not observed in this study population.

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