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DEVELOPMENT AND VALIDATION OF A NEW TOOL TO ASSESS INPATIENT COMPLEXITY: THE PATIENT COMPLEXITY ASSESSMENT (PCA) SCORE

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ABSTRACT

Objective: We aimed to develop and validate a score to assess inpatient complexity and compare its performance with two currently used but not validated tools to estimate complexity (i.e., Charlson Comorbidity Index [CCI], patient clinical complexity level [PCCL]).

Methods: Consecutive patients discharged from the department of medicine of a tertiary care hospital were prospectively included into a derivation cohort from October 1, 2016 to February 16, 2017 (n=1,407), and a temporal validation cohort from February 17, 2017, to March 31, 2017 (n=482). The physician in charge assessed complexity. Potential predictors comprised 52 parameters from the electronic health record such as health factors and hospital care usage. We fit a logistic regression model with backward selection to develop a prediction model and derive a score. We assessed and compared performance of model and score in internal and external validation using measures of discrimination and calibration.

Results: Overall, 447 of 1,407 patients (32%) in the derivation cohort, and 116 of 482 patients (24%) in the validation cohort were identified as complex. Eleven variables independently associated with complexity were included in the score. Using a cut-off of ≥24 score points to define high-risk patients, specificity was 81% and sensitivity 57% in the validation cohort. The score's area under the receiver operating characteristic (AUROC) curve was 0.78 in both the derivation and validation cohort. In comparison, the CCI had an AUROC between 0.58 and 0.61, and the PCCL between 0.64 and 0.69, respectively.

Conclusions: We derived and internally and externally validated a score that reflects patient complexity in the hospital setting, performed better than other tools, and could help monitoring complex patients.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This is a prospective cohort study of consecutive, unselected, adult inpatients discharged from the department of medicine of a large university hospital.
- We derived and validated an easily usable score that accurately assesses patient complexity in medical inpatients that may help monitoring the proportion of complex patients.
- The reference standard used to define complexity was the physician's judgment, which per definition is partly subjective.
- The PCA score has been developed at a single tertiary hospital and may not consider a comprehensive list of important predictors.
- The PCA score includes values available only at discharge and not modifiable predictors are.

Keywords: primary care, general medicine, quality in health care, social medicine, internal medicine

INTRODUCTION

Up to one third of patients are estimated to be complex in the primary care setting, while this proportion is not well known in the hospital setting.[1-3] Complexity is not limited to multimorbidity and chronicity of disease but depends also on multiple other aspects, including psychological, social, economic and environmental factors.[1,2,4-6] Complex patients challenge the current structures, e.g., they have a higher probability of future emergency department utilization (without higher mortality rates) and show suboptimal use of the health care system.[2,7-9] Identifying complex patients is of economic, epidemiological and social importance because it may help to better allocate resources and improve health care utilization.[4,10]

The only available assessment method to identify complex inpatients is currently the physician's assessment, which limits the monitoring of patient complexity over time.[9,11,12] The Charlson Comorbidity Index (CCI), originally developed and validated to predict mortality,[13] has been assessed as a proxy for patient complexity in the primary care setting. However, agreement between the primary care physician's assessment and the CCI to identify complex patients was only modest.[1,2,4] No such assessment has been yet performed in the hospital setting.

In order to simplify and standardize the identification of complex patients, we aimed to develop and validate a new score to help identifying the most complex inpatients (Patient Complexity Assessment, PCA score) using readily available administrative and clinical data. Our hypothesis was that some data routinely collected during a hospitalization can be used as a valuable surrogate to physician's assessment. We then compared the performance of the newly developed PCA score to the CCI, and the patient clinical complexity level (PCCL) used in the Swiss DRG system to allocate reimbursement according to multimorbidity.[13,14]

METHODS

Study design and participants

This study was a prospective cohort of consecutive, unselected, adult inpatients discharged from the department of medicine of a large University hospital (Inselspital, Bern University Hospital, Bern, Switzerland) between October 1, 2016 and March 31, 2017. The only exclusion criterion was a previous study inclusion. We originally planned to consider around 35 variables in the prediction model. With an estimated proportion of complex patients of one fourth, we preset the sample size of the derivation cohort to be 1,400 (rule of thumb of 10 outcomes per variable tested).[15,16] Patients enrolled before February 16, 2017 were allocated to the derivation sample (derivation and internal validation cohort), and patients enrolled after this date were allocated to an external validation sample (temporal validation cohort). During their first admission, all patients included in the study gave their written general consent to the use of their routine data for research purposes. The study was approved by the local ethics committee (Kantonale Ethikkommission Bern, ID 2016-01319). We reported the study in accordance with the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis Or Diagnosis (TRIPOD) statement.[17]

Patient and public involvement

No patient involved.

Study outcome and predictor variables

The primary outcome was the true complexity of hospitalized patients based on the treating physician's judgement (discharging resident physician or supervising consultant if the resident physician's assessment was absent). Complex patients were defined as those using more resources, time and/or effort while hospitalized. The outcome was prospectively collected by a trained study nurse at time of patient's discharge.

The CCI is calculated by addition of score points for specific diagnoses and was originally developed to predict 10-year survival.[13,18] The PCCL was derived from the electronic health record (no complication or comorbidity: 0; light complication or comorbidity: 1; moderate complication or comorbidity: 2; severe complication or comorbidity: 3; very severe complication or comorbidity: 4) and is defined by SwissDRG.[19,20]

For all patients, information regarding International Classification of Disease (ICD) codes and other potential predictors for patient complexity were collected retrospectively through the electronic health record of the hospital. Predictor variables have been selected based on a previous survey study that asked 111 physicians about patient complexity,[21] and on a selection of readily available potential predictors. Variables that were not routinely collected were removed (i.e. variables with more than 25% missing data, such as aspartate amino transferase, C-reactive protein, and albumin at discharge). Collinearity between variables was assessed using Pearson correlation coefficients. In case of strong correlation ($r > 0.7$), only the strongest univariate predictor was kept. A final list of 52 predictors was considered in predicting complexity: baseline demographic information (age, gender, living area (rural versus urban, defined according to the Swiss Federal Statistical Office based on the patient's place of residence), marital status, institutional care before admission, nationality (Swiss vs. non-Swiss), hospital variables (urgent vs. elective admission, number of previous hospitalization in the last 12 months, patient destination [death, home, other hospital, nursing home, rehabilitation, other], stay on the intensive care unit, internal transfer), drugs (for each group of the Anatomical, Therapeutic and Chemical [ATC] classification categories) at admission and at discharge and polypharmacy (≥10 drugs, at admission and discharge), main diagnosis (cancer, chronic obstructive pulmonary disease, dementia, depression, heart failure, pneumonia, sepsis, stroke, substance abuse, syncope, malnutrition, based on the Tenth Revision of the International Statistical Classification of Diseases and Related Health Problems [ICD-10] code), number of diagnoses at discharge, CCI, laboratory values (hemoglobin, leucocyte count and thrombocyte count, serum sodium and creatinine) at admission and discharge, number of interventions and costs (normal vs. high costs, i.e., ≥ the 75th empirical percentile value) during hospitalization of blood products, drugs, imaging procedures, physiotherapy, and nursing workload.

Missing data

When missing, the second value of hemoglobin and creatinine was assumed to be identical to the first value. When missing, the second value of sodium and platelet count was considered normal. For other potential predictor variables, we assumed data to be missing at random and imputed missing data using single imputation by chained equations. To compare performance measures of the PCA with the CCI and PCCL, patients with missing values for the PCCL variable (n=3 for the derivation, n=11 for the validation dataset) were removed prior to analysis.

Statistical analysis

Multivariable logistic regression analysis with backward selection was used in the derivation set to predict complexity based on 52 potential predictor variables registered during hospitalization, removing variables with a p-value >0.1. Calibration of the final model was evaluated by constructing a calibration curve, estimating the calibration slope, calculating the difference between the mean observed proportion and mean predicted proportion of patients with high complexity (calibration-in-the-large) and the Brier score (overall measure of accuracy) in the derivation and validation set. The predictors from the final model were used to create a comprehensible score using the regression coefficient-based scoring technique.[22] Beta-coefficients were divided by the lowest coefficient and rounded up to the closest integer to generate score points, indicating increasing risk by higher scores. The discriminatory power of the score was assessed by calculating the area under the receiver operating characteristic (AUROC) curve.

The validity of performance measures was investigated by performing internal and external validation. For internal validation we used 1000 bootstrap samples, drawing samples with replacement from the derivation sample.[23] The bootstrap-corrected performance estimates were calculated by subtracting the optimism from the performance of the original model. The 95% confidence intervals (CI) for the bootstrapped performance measures were derived using the percentile method. External validation was made by estimating the same performance measures in the external validation cohort (temporal validation).

The clinical usefulness of the developed score was assessed with a decision-curve analysis investigating whether the use of the complexity score instead of the CCI alone was associated with benefit gains relative to the prediction complexity.[24]

Applying PCA, CCI and PCCL, we calculated the score of each patient and split the patient sample into a high and a low risk group. The reference point (cut-off) of each scoring system was chosen in order to make the frequency of patients in the high-risk category as close as possible to 30% (i.e. approximating the frequency of observed complex patients). To determine the accuracy of this method to predict complexity, we estimated sensitivity, specificity, and positive and negative predictive value in both the derivation and validation set for PCA and in the derivation set for CCI and PCCL.

R version 3.3.1 was used for statistical analysis.

RESULTS

A total of 1,889 patients were included in the study (figure 1). Patients enrolled before February 16, 2017 were allocated to the derivation sample (n = 1,407), patients enrolled after this date (n = 482) were allocated to the temporal validation sample. In the derivation cohort, 447 patients (31.8%) were reported as complex, and 116 (24.1%) patients in the validation cohort. The patients in the two cohorts presented with similar baseline characteristics (Table 1). The overall median age was 80 years (interquartile range 75 to 86 years).

Table 1: Baseline characteristics for all patients (derivation and validation cohort) stratified by complexity, as number and percentage or median and inter-quartile range for categorical and continuous variables, respectively.

	Overall (N=1889)	Non-complex (N=1326)	Complex (N=563)
	n (%) or median [interquartile range]		
Age			
≥ 80 years	579 (31)	442 (33)	137 (24)
70 to 79 years	437 (23)	304 (23)	133 (24)
60 to 69 years	322 (17)	211 (16)	111 (20)
< 60 years	537 (28)	363 (27)	174 (31)
Female sex	873 (46)	627 (47)	246 (44)
Living area[1]			
Urban	611 (32)	453 (34)	158 (28)
Rural	1238 (65)	848 (64)	390 (69)
Marital status			
Single	331 (17)	252 (19)	79 (14)
Couple	636 (34)	429 (32)	207 (37)
Widowed	916 (48)	641 (48)	275 (49)
Hospitalization within last 12 months	673 (36)	452 (34)	221 (39)
Medication[2]			
Antineoplastic and immunomodulating agents at admission	70 (4)	38 (3)	32 (6)
Nervous system at admission	1340 (71)	918 (69)	422 (75)
Systemic hormonal preparations, excluding sex hormones and insulins at discharge	524 (28)	318 (24)	206 (37)
High costs during hospitalization[3]			
For imaging procedures	485 (26)	255 (19)	230 (41)
For laboratory analysis	482 (25)	203 (15)	279 (50)

[1] Defined according to the Swiss Federal Statistical Office based on place of residence
[2] Group of drugs according to ATC classification
[3] Defined as costs of all imaging procedures or medication during hospital stay above 75th percentile

High nurse workload[4]	475 (25)	203 (15)	272 (48)
Charlson Comorbidity Index	2 [0; 4]	2 [0; 3]	3 [1; 5]
Principal or concomitant diagnosis at discharge			
Cancer[5]	225 (12)	136 (10)	89 (16)
COPD[6]	186 (10)	124 (9)	62 (11)
Dementia[7]	163 (9)	125 (9)	38 (7)
Depression[8]	209 (11)	140 (11)	69 (12)
Heart failure[9]	327 (17)	206 (15)	121 (21)
Pneumonia[10]	244 (13)	159 (12)	85 (15)
Sepsis[11]	229 (12)	132 (10)	97 (17)
Stroke[12]	90 (5)	65 (5)	25 (4)
Substance abuse[13]	212 (11)	129 (10)	83 (15)
Syncope[14]	81 (4)	67 (5)	14 (2)
Malnutrition[15]	265 (14)	122 (9)	143 (25)
Multimorbidity			
Low (number of diagnoses ≤ 6)	510 (27)	435 (33)	75 (13)
Middle (number of diagnoses > 6 and <14)[16]	841 (44)	603 (45)	238 (42)
High (number of diagnoses ≥ 14)	524 (28)	282 (21)	242 (43)
PCCL	3 [2; 4]	3 [1; 4]	4 [3; 4]
No complication or comorbidity	380 (20)	312 (23)	68 (12)
Light complication or comorbidity	29 (1)	21 (2)	8 (1)
Moderate complication or comorbidity	292 (15)	233 (18)	59 (10)
Severe complication or comorbidity	533 (28)	409 (31)	124 (22)
Very severe complication or comorbidity	641 (34)	345 (26)	296 (53)
Abnormal creatinine level[17]			
At admission and discharge	368 (19)	241 (18)	127 (23)
At admission only	182 (10)	106 (8)	76 (13)
At discharge only	63 (3)	34 (3)	29 (5)
Leukocytosis[18]			
At admission and discharge	77 (41)	47 (3)	30 (5)
At admission only	19 (1)	8 (<1)	11 (2)
At discharge only	13 (<1)	5 (<1)	8 (1)
Patient destination			
Death	134 (7)	91 (7)	43 (8)
Home	1178 (62)	873 (66)	305 (54)

[4] Defined as sum of hours of all nursing work (incl. sitting guard) during hospital stay above 75th percentile
[5] ICD10-codes B21, C00 through C97, Z03.1
[6] ICD10-codes J44
[7] ICD10-codes F00 through F03, F05.0, F05.1
[8] ICD10-codes F20.4, F25.1, F31.3 F31.4, F31.5, F32, F33, F41.2, F92.0
[9] ICD10-codes I50
[10] ICD10-codes A48.1, B01.2, B05.2, J10.0, J11.0, J12 through J18, J68.0, J69, J85.1, O74.0, U69.00
[11] ICD10-codes A02.1, A20.7, A22.7, A26.7, A32.7, A39.2, A39.3, A39.4, A40, A41, A42.7, B37.7
[12] ICD10-codes I63
[13] ICD10-codes F10 through F19, F53, F66.8, F66.9
[14] ICD10-codes R55
[15] ICD10-codes E40 through E46
[16] Between 25th and 75th percentile
[17] Defined as creatinine ≥100 µmol/l
[18] Defined as leukocyte count ≥20 G/l

Hospital	191 (10)	119 (9)	72 (13)
Nursing home	155 (8)	108 (8)	47 (8)
Rehabilitation	171 (9)	101 (8)	70 (12)
Others and missing	60 (3)	24 (3)	26 (5)

After backward selection, 11 of the 52 potential predictors were used to derive the PCA score **Error! Reference source not found.**). Besides diagnosis-related factors, they represented demographic characteristic, hospital variables, medication and laboratory values. Highest score points were assigned to leucocytosis (at discharge only, 16 points, and at admission and discharge, 10 points) followed by age under 60 years, high nurse workload (costs above 75th percentile for nursing expenses), and abnormal serum creatinine at discharge (≥100 µmol/l).

Table 2: PCA score weighted according to coefficients

Variable	Coefficient (95% CI)	Score points
Age		
≥ 80 years	Reference	
70 to 79 years	0.36 (0, 0.72)	3
60 to 69 years	0.5 (0.1, 0.9)	5
< 60 years	0.94 (0.56, 1.31)	9
Elective admission	0.36 (0.03, 0.69)	3
High costs during hospitalization[19]		
For imaging procedures	0.6 (0.31, 0.9)	6
For laboratory analysis	0.77 (0.46, 1.09)	7
High nurse workload[20]	0.93 (0.61, 1.26)	9
Malnutrition[21]	0.47 (0.1, 0.84)	4
Multimorbidity		
Number of diagnoses ≤ 6	Reference	
Number of diagnoses > 6 and <14[22]	0.61 (0.25, 0.96)	6
Number of diagnoses ≥ 14[23]	0.78 (0.36, 1.2)	7
Medication at admission[24]		
Antineoplastic and immunomodulating agents	0.85 (0.16, 1.54)	8
Nervous system	0.33 (0.04, 0.63)	3
Abnormal creatinine level[25]		
None	Reference	

[19] Defined as costs of all imaging procedures or medication during hospital stay above 75th percentile
[20] Defined as sum of hours of all nursing work (incl. sitting guard) during hospital stay above 75th percentile
[21] ICD10-codes E40 through E46
[22] Between 25th and 75th percentile
[23] Above 75th percentileh
[24] Group of drugs according to ATC classification
[25] Defined as serum creatinine ≥100 µmol/l

At admission only	0.23 (-0.22, 0.68)	2
At admission and discharge	0.11 (-0.22, 0.45)	1
At discharge only	0.96 (0.29, 1.63)	9
Leukocytosis[26]		
None	Reference	
At admission only	0.11 (-0.49, 0.71)	1
At admission and discharge	1.12 (-0.04, 2.29)	10
At discharge only	1.68 (0.18, 3.18)	16
Intercept	-2.93 (-3.39, -2.46)	NA

The prediction model showed a good accuracy, with a Brier score of 0.17 and 0.15 in internal and external validation, respectively. The calibration curve showed fair agreement between predicted and observed proportions of complexity in the derivation cohort and slightly lower observed proportions than predicted probabilities in the validation cohort (graphs not shown). The calibration-in-the-large coefficient of -0.51 (95% CI -0.74 to -0.27) in the validation cohort implies that the mean observed proportion was lower than the mean predicted probability. However, the calibration curve slope was satisfactory in internal and external validation (0.93 [95% CI 0.80 to 1.05] and 0.96 [95% CI 0.74 to 1.18]), respectively.

The median score was 17 points in the derivation and validation cohort (mean 18.77 and 19.03, respectively). The minimal score was 0 points in both cohorts, the maximal score reached was 54 points in the derivation cohort and 53 points in the validation cohort (theoretically maximal 81 score points). The score's area under the receiver operating characteristic (AUROC) curve was 0.77 (95% CI 0.74 to 0.79) and 0.78 (95% CI 0.74 to 0.82) in internal and external validation.

Table 3: Stratification of Observed vs. predicted complex patients applying the PCA score.

	Score points	Risk category of complexity	Patients in each category	Complex patients	Estimated risk of complexity
Derivation set	< 24	Low risk	991 (70%)	193 (19%)	19
	≥ 24	High risk	416 (30%)	254 (61%)	61
Validation set	< 24	Low risk	347 (72%)	50 (14%)	20
	≥ 24	High risk	135 (28%)	66 (49%)	62

[26] Defined as blood leukocyte count ≥20 G/l

We classified patients as low and high complexity risk (table 3) according to the selected cut-off of 24 points. The proportion of patients categorized as complex (i.e. score ≥ 24 points) was 30% and 28% in the derivation and validation dataset, respectively. Sensitivity was 57% in both the derivation and validation dataset. The specificity was 83% and 81%, respectively. Positive predictive values were 61% and 49% in the derivation and validation cohort, respectively, while negative predictive values were 81% and 86%, respectively. The discriminatory power of the PCA score was robust with an AUROC of 0.77 (95% CI 0.74 to 0.79) in internal validation (bootstrap-corrected value) and 0.78 (95% CI 0.74 to 0.82) in external validation (table 4).

Table 4: Measures of performance to predict complexity

	PCA, derivation set % (95%-CI)	PCA, validation set % (95%-CI)	CCI, validation set % (95%-CI)	PCCL, validation set % (95%-CI)
Sensitivity	57 (52-61)	57 (47-66)	41 (32-50)	61 (51-70)
Specificity	83 (81-85)	81 (77-85)	75 (71-80)	75 (70-79)
Positive predictive value	61 (59-66)	49 (40-58)	34 (26-43)	42 (34-50)
Negative predictive value	81 (78-83)	86 (81-89)	80 (75-84)	86 (82-90)
Misclassification error	25 (28-23)	25 (29-21)	33 (37-29)	28 (33-24)
AUROC[27]	0.77 (0.74-0.79)[28]	0.78 (0.74-0.82)	0.62 (0.56-0.68)	0.69 (0.64-0.75)

In comparison, predictive accuracy of the CCI was lower compared to the PCA score. The AUROCs were low with 0.58 (95% CI 0.55 to 0.62) and 0.62 (95% CI 0.56 to 0.68) in the derivation and validation cohort, respectively (table 4). Sensitivity of the CCI reached 36% (95% CI 31% to 40%) and 41% (95% CI 31% to 50%) in derivation and validation cohort, respectively, while specificity was 76% (95% CI 73% to 78%) and 75% (95% CI 71% to 80%), respectively. The decision curve analysis (supplementary figure) indicates a superiority of the PCA score compared to the CCI to predict complexity.

[27] Area under receiver operating characteristic
[28] Bootstrap-corrected from internal validation

AUROCs of PCCL were between those of CCI and PCA score with 0.64 (95% CI 0.61 to 0.67) and 0.69 (95% CI 0.64 to 0.75) in the derivation and validation cohort, respectively (table 4). Sensitivity was 52% (95% CI 47% to 56%) and 61% (95% CI 51% to 70%), respectively, while specificity was 73% (95% CI 71% to 76%) and 75% (95% CI 70% to 79%).

DISCUSSION

We derived and validated the PCA score that accurately assessed patient complexity in medical inpatients. The final score of eleven independent and readily available factors, included age, hospital variables, diagnosis related aspects and laboratory variables. The PCA score showed overall good performance with a discriminatory power of 0.78 that surpasses other comorbidity-based tools such as the Charlson comorbidity index and the PCCL.

In this cohort of medical inpatients, 32% and 24% were considered “complex” by the treating physician, in the derivation and the validation cohort, respectively. This first estimate of patient complexity in the hospital setting is consistent with a previous assessment in an outpatient population where 26% of total 4,302 patients were categorized as being complex by a primary care physician.[1] Based on these data, the authors later derived a model to identify around 20% of 143,372 primary care patients as complex. Using the model and outpatient CCI or PCCL, only modest agreement between the methods was observed (37% and 40%, respectively).[2] Therefore, a tool not solely based on multimorbidity, such as the newly developed PCA score, seems to better identify complex patients.

In the present study, age was an inverse predictor of complexity. In a previous study of outpatients, mean age of complex patients was 60 years versus 48 years in non-complex patients.[1] Nonetheless, the same study reported noteworthy age-related variability: in younger patients the association of certain diagnoses (e.g. alcohol-related diseases) with complexity was stronger, and deprivation as contributor to complexity is independent of age.[1,4] In our setting, discharge planning processes for older patients may be better established (e.g. including hospital social services, decision making based on patient’s provision and discharge to geriatric rehabilitation facilities or nursing homes) compared to younger patients.[1,8,25,26] Elective admissions to a tertiary hospital may represent a cohort of rather complex patients preselected by primary care physicians and smaller hospitals (21% elective admissions in complex patients versus 14% in non-complex patients). It is also possible that these patients are only perceived as more complex by the

treating physician because patients admitted directly to the medical ward are pending initial work-up otherwise provided in the emergency department.

Patients with high costs of imaging procedures may reflect the patients with more severe diseases or more diagnosis uncertainty. Similarly, high costs for laboratory analysis may be explained by a higher need of costly or repeated measurements in more complex patients. High costs for care/nursing were predictors of complexity highlighting some concordance between the nurse workload and the medical complexity.

In our study multimorbidity is defined as a number of more than 6 diagnoses was a predictor of complexity. Comorbidity-based scores, i.e., the CCI, are commonly used to identify complex patients. Indeed, in the study of Grant et al. the proportion of multimorbid patients identified by a CCI of 2 or more was higher in complex patients, i.e., 26% of complex patients were multimorbid versus 9% of non-complex patients.[1] However, many multimorbid patients are not complex and not all complex patients are multimorbid. In our cohort (derivation and validation datasets together) 34% of polymorbid patients (CCI ≥2) were complex versus 24% in the group of CCI <2. Comparably, nearly one half of patients with a CCI of 2 or greater were classified as non-complex in the study of Grant et al.[1] Therefore, a system to identify complexity should not depend on diagnosis alone.

In the PCA score, malnutrition was a risk factor of complexity. Malnutrition in hospitalized patients is associated with more complications, increased mortality, longer hospital stays and higher costs [27,28]. Therefore, malnutrition and complexity may both reflect a cluster of severe and chronic disease as well as socioeconomic circumstances.[1]

Antineoplastic and immunomodulating medication at admission was a predictor of complexity. These drugs are used for oncologic patients, but also in patients with rheumatologic disease or after receiving organ transplants. These patients may be complex because of challenging infectious diseases, end-of-life issues and interdisciplinary care. Abnormal values of serum creatinine and leukocyte counts at discharge were predictive of complexity whether the values were normal or abnormal at admission. These patients may also requiring more interaction between specialists and may complicate the discharge process.

Personal characteristics or mental health issues and use of psychoactive medication, i.e., narcotics, selective serotonin reuptake inhibitors, benzodiazepines, smoking cessation agents and antipsychotics, have been described as characterizing complex patients, especially in younger patients.[1] This is in line with the observation that in the PCA score, use of medication affecting the nervous system at admission (including antipsychotics, mood-stabilizers, sedatives, analgesics including opioids, anticonvulsive medication and anti-dementia drugs) was a predictor of complexity. These patients may challenge the known pathways of the healthcare system, e.g. by parallel use of general internal medicine and psychiatric resources.

There are several limitations of the study. First, we used physician's assessment to define complexity, which per definition is subjective. Nonetheless, there is no better standard reference (gold standard) and the proportion of patients identified as complex was similar in previous studies.[1,2] Second, the PCA score has been developed at a single tertiary hospital and therefore may not be generalizable to other settings. Third, it is likely that our model does not consider every important predictor, but it allows deriving an easily usable tool which kept its fair sensitivity and good specificity in our external validation. Fourth, the PCA score includes values available only at discharge, which makes patient-aimed interventions during hospitalization difficult. This is however also true for alternative assessment tools, such as the CCI and the PCCL, which had a lower performance in identifying complex patients in our cohort. Fifth, the included predictors are not modifiable. For example, a patient will still be complex if receiving less imaging procedures to reduce costs.

To our knowledge, the PCA score is the first tool to identify complex medical patients in the hospital setting. It can easily be calculated and is therefore predestined to be used for population-based studies as it does not involve individual judgement of a physician. With its prospective design and inclusion of a large number of medical inpatients, this study has a strong design.

Identification of complex patients by this simple tool using electronically available data may help monitoring the proportion of complex patients in the hospital setting and comparing patient complexity level between hospitals. Thereby, the PCA score might improve the monitoring of resources distribution and coordination of care.

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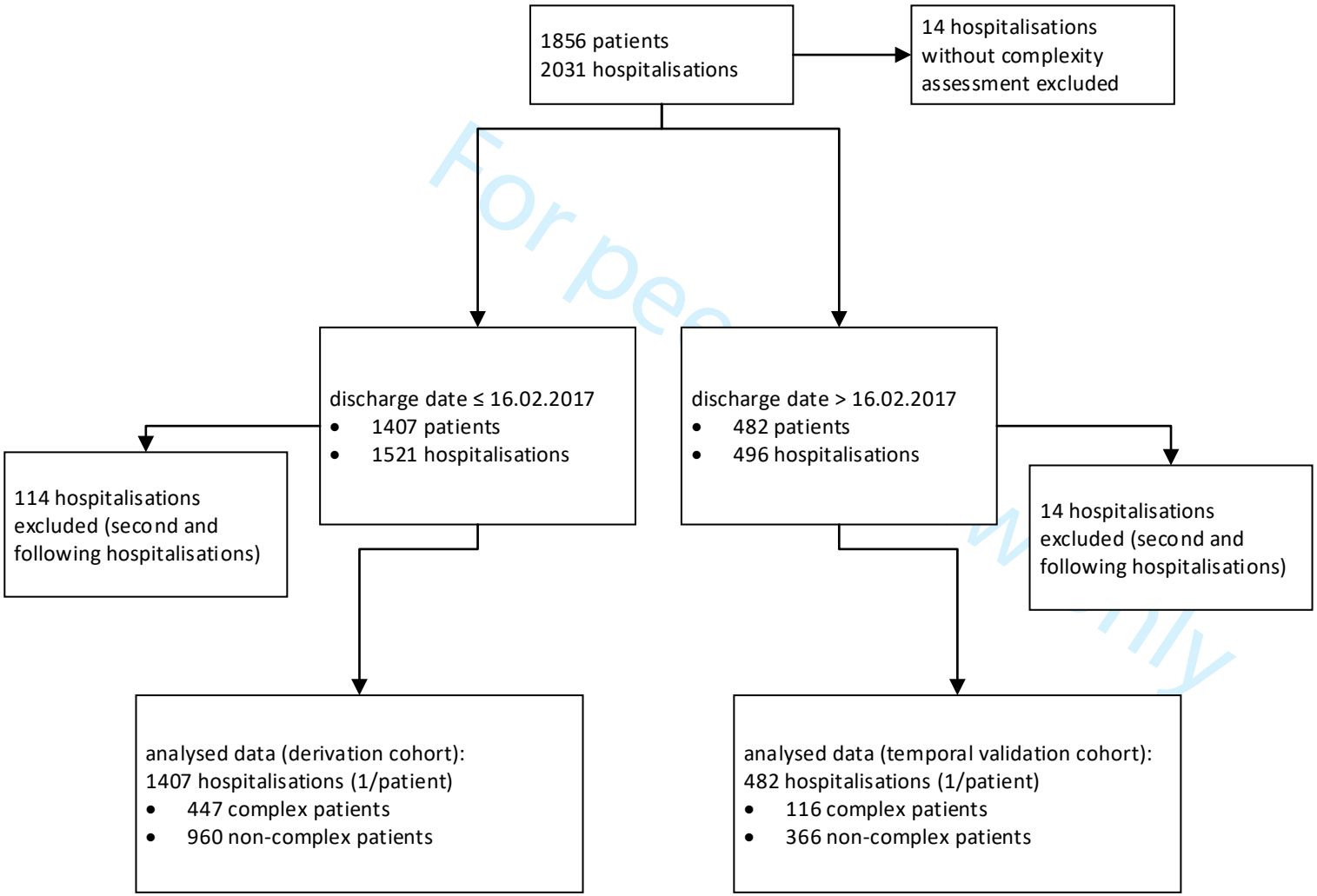
FIGURE 1 CAPTION

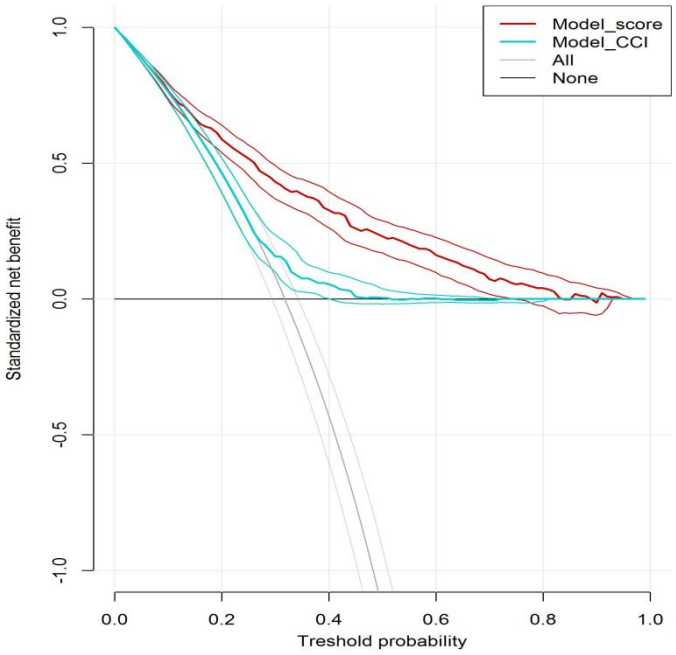
Flow chart. Derivation sample (derivation and internal validation cohort) and external validation sample (temporal validation cohort).



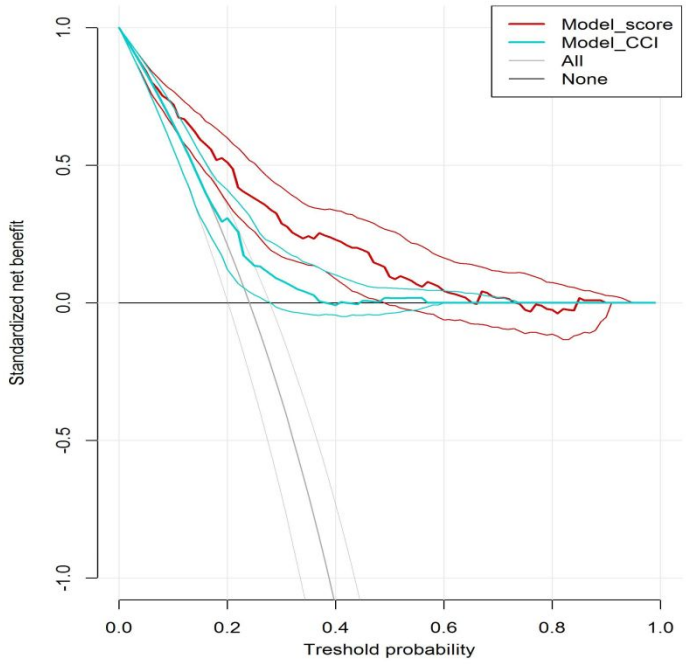
Supplementary figure: Decision curve analysis

Grey line: assume all patients are “treated” for complexity. Thin black line: assume none of the patient is “treated” for complexity (“treat none”). Blue line: prediction model based on the Charlson comorbidity index. Red line: prediction model based on the PCA score.

A) Derivation dataset



B) Validation dataset



Reporting checklist for prediction model development and validation study.

Based on the TRIPOD guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

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		Reporting Item	Page Number
Title			
	#1	Identify the study as developing and / or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract			

	#2	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	3
Introduction			
	#3a	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	5
	#3b	Specify the objectives, including whether the study describes the development or validation of the model or both.	5
Methods			
Source of data	#4a	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	6
Source of data	#4b	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	6
Participants	#5a	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	6
Participants	#5b	Describe eligibility criteria for participants.	6
Participants	#5c	Give details of treatments received, if relevant	n/a

Outcome	#6a	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	6
Outcome	#6b	Report any actions to blind assessment of the outcome to be predicted.	n/a
Predictors	#7a	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured	7
Predictors	#7b	Report any actions to blind assessment of predictors for the outcome and other predictors.	n/a
Sample size	#8	Explain how the study size was arrived at.	6
Missing data	#9	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	8-9
Statistical analysis methods	#10a	If you are developing a prediction model describe how predictors were handled in the analyses.	8-9
Statistical analysis methods	#10b	If you are developing a prediction model, specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	8-9
Statistical analysis methods	#10c	If you are validating a prediction model, describe how the predictions were calculated.	8-9
Statistical analysis methods	#10d	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	8-9

Statistical analysis methods	#10e	If you are validating a prediction model, describe any model updating (e.g., recalibration) arising from the validation, if done	8-9
Risk groups	#11	Provide details on how risk groups were created, if done.	n/a
Development vs. validation	#12	For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.	8-9
Results			
Participants	#13a	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	9 + 24
Participants	#13b	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	9 + 18
Participants	#13c	For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors and outcome).	9 + 18
Model development	#14a	If developing a model, specify the number of participants and outcome events in each analysis.	9
Model development	#14b	If developing a model, report the unadjusted association, if calculated between each candidate predictor and outcome.	9

Model specification	#15a	If developing a model, present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	9 + 21
Model specification	#15b	If developing a prediction model, explain how to the use it.	10 + 21
Model performance	#16	Report performance measures (with CIs) for the prediction model.	10, 11, 23
Model-updating	#17	If validating a model, report the results from any model updating, if done (i.e., model specification, model performance).	10-11
Discussion			
Limitations	#18	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	14
Interpretation	#19a	For validation, discuss the results with reference to performance in the development data, and any other validation data	11-14
Interpretation	#19b	Give an overall interpretation of the results, considering objectives, limitations, results from similar studies, and other relevant evidence.	11-14
Implications	#20	Discuss the potential clinical use of the model and implications for future research	14

Other information

Supplementary information	#21	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	25
Funding	#22	Give the source of funding and the role of the funders for the present study.	2

BMJ Open

Development and validation of a score to assess complexity of general internal medicine patients at hospital discharge: a prospective cohort study

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Development and validation of a score to assess complexity of general internal medicine patients at hospital discharge: a prospective cohort study

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Abstract

Objective: We aimed to develop and validate a score to assess inpatient complexity and compare its performance with two currently used but not validated tools to estimate complexity (i.e., Charlson Comorbidity Index [CCI], patient clinical complexity level [PCCL]).

Methods: Consecutive patients discharged from the department of medicine of a tertiary care hospital were prospectively included into a derivation cohort from October 1, 2016 to February 16, 2017 (n=1,407), and a temporal validation cohort from February 17, 2017, to March 31, 2017 (n=482). The physician in charge assessed complexity. Potential predictors comprised 52 parameters from the electronic health record such as health factors and hospital care usage. We fit a logistic regression model with backward selection to develop a prediction model and derive a score. We assessed and compared performance of model and score in internal and external validation using measures of discrimination and calibration.

Results: Overall, 447 of 1,407 patients (32%) in the derivation cohort, and 116 of 482 patients (24%) in the validation cohort were identified as complex. Eleven variables independently associated with complexity were included in the score. Using a cut-off of ≥24 score points to define high-risk patients, specificity was 81% and sensitivity 57% in the validation cohort. The score's area under the receiver operating characteristic (AUROC) curve was 0.78 in both the derivation and validation cohort. In comparison, the CCI had an AUROC between 0.58 and 0.61, and the PCCL between 0.64 and 0.69, respectively.

Conclusions: We derived and internally and externally validated a score that reflects patient complexity in the hospital setting, performed better than other tools, and could help monitoring complex patients.

Strengths and limitations of this study

- This is a prospective cohort study of consecutive, unselected, adult inpatients discharged from the department of medicine of a large university hospital.
- We derived and validated an easily usable score that accurately assesses patient complexity in medical inpatients that may help monitoring the proportion of complex patients (Patient Complexity Assessement (PCA) score).
- The reference standard used to define complexity was the physician's judgment, which per definition is partly subjective.
- The PCA score has been developed at a single tertiary hospital and may not consider a comprehensive list of important indicators.
- The PCA score includes values available only at discharge and indicators are not modifiable.

Keywords: primary care, general medicine, quality in health care, social medicine, internal medicine

Introduction

One fourth of patients are estimated to be complex in the primary care setting, while this proportion is not well known in the hospital setting.[1-4] Generally, those patients using more resources, time and/or effort are regarded as complex patients, although no universal definition of patient complexity is available. Complexity is not limited to multimorbidity and chronicity of disease but depends also on multiple other aspects, including psychological, social, economic and environmental factors.[1,2,5-7] Complex patients challenge the current structures, e.g., they have a higher probability of future emergency department utilization (without higher mortality rates) and show suboptimal use of the health care system.[2,8-10] Identifying complex patients is of economic, epidemiological and social importance because it may help to better allocate resources and improve health care utilization.[5,11]

The only available assessment method to identify complex inpatients is currently the physician's assessment, which limits the monitoring of patient complexity over time.[10,12,13] The Charlson Comorbidity Index (CCI), originally developed and validated to predict mortality,[14] has been assessed as a proxy for patient complexity in the primary care setting. However, agreement between the primary care physician's assessment and the CCI to identify complex patients was only modest.[1,2,5] No such assessment has been yet performed in the hospital setting. The patient clinical complexity level (PCCL) is calculated for each treatment episode to indicate the effect of complications and comorbidities in a patient. The PCCL ranges from 0 (no complication or comorbidity) to 4 (very severe complication or comorbidity), according to a complex algorithm. [14,15] Identification of complex patients at discharge could help to identify those, who would profit from more intense follow-up, e.g. by general practitioners or social workers, although effectiveness of such interventions would have to be proven first.

In order to simplify and standardize the identification of complex patients, we aimed to develop and validate a new score to help identifying the most complex inpatients (Patient Complexity Assessment, PCA score) using readily available administrative and clinical data. Our hypothesis was that some data routinely collected during a hospitalization can be used as a valuable surrogate to physician's assessment. We then compared the performance of the newly developed PCA score to the CCI, and the PCCL used in the Swiss DRG system to allocate reimbursement according to multimorbidity.[14,15]

Methods

Study design and participants

This study was a prospective cohort of consecutive, unselected, adult inpatients discharged from the department of medicine of a large University hospital (Inselspital, Bern University Hospital, Bern, Switzerland) between October 1, 2016 and March 31, 2017. The only exclusion criterion was a previous study inclusion. We originally planned to consider around 35 variables in the prediction model. With an estimated proportion of complex patients of one fourth, we preset the sample size of the derivation cohort to be 1,400 (rule of thumb of 10 outcomes per variable tested).[16,17] We predefined, that if more than 1,400 patients will be included during the study period of 6 months, we would use these patients to externally validate the prediction model. Patients enrolled before February 16, 2017 were allocated to the derivation sample (derivation and internal validation cohort), and patients enrolled after this date were allocated to an external validation sample (temporal validation cohort). During their first admission, all patients included in the study gave their written general consent to the use of their routine data for research purposes. The study was approved by the local ethics committee (Kantonale Ethikkommission Bern, ID 2016-01319). We reported the study in accordance with the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis Or Diagnosis (TRIPOD) statement.[18]

Patient and public involvement

No patient involved.

Study outcome and predictor variables

The primary outcome was the predictive accuracy of the PCA against the treating physician's judgment as the gold standard to identify complex general internal medicine inpatients. Complex patients were defined as those using more resources, time and/or effort while hospitalized. The resident (or supervising consultant) was asked by a trained study nurse to assess at time of discharge the level of complexity of the entire hospital stay of her/his patient (complex or not-complex).

The CCI was originally developed to predict 10-year survival by using an algorithm based on addition of score points for specific diagnoses.[14,19] The PCCL was derived from the electronic health record (no complication or comorbidity: 0; light complication or comorbidity: 1; moderate complication or comorbidity:

2; severe complication or comorbidity: 3; very severe complication or comorbidity: 4) and is defined by SwissDRG.[20,21]

For all patients, information regarding International Classification of Disease (ICD) codes and other potential indicators for patient complexity were collected retrospectively through the electronic health record of the hospital. Candidate predictor variables have been selected based on a previous survey among general internists in the hospital setting which asked them to identify factors that contribute to patient complexity,[4] and on a selection of readily available potential predictors to have a broad spectrum of candidate predictors. Variables that were not routinely collected were removed (i.e. variables with more than 25% missing data, such as aspartate amino transferase, C-reactive protein, and albumin at discharge). Collinearity between variables was assessed using Pearson correlation coefficients. In case of strong correlation ($r > 0.7$), only the strongest univariate predictor was kept. A final list of 52 indicators was considered in denoting complexity: baseline demographic information (age, gender, living area (rural versus urban, defined according to the Swiss Federal Statistical Office based on the patient's place of residence), marital status, institutional care before admission, nationality (Swiss vs. non-Swiss), hospital variables (urgent vs. elective admission, number of previous hospitalization in the last 12 months, patient destination [death, home, other hospital, nursing home, rehabilitation, other], stay on the intensive care unit, internal transfer), drugs (for each group of the Anatomical, Therapeutic and Chemical [ATC] classification categories) at admission and at discharge and polypharmacy (≥10 drugs [22], at admission and discharge), main diagnosis (cancer, chronic obstructive pulmonary disease, dementia, depression, heart failure, pneumonia, sepsis, stroke, substance abuse, syncope, malnutrition, based on the Tenth Revision of the International Statistical Classification of Diseases and Related Health Problems [ICD-10] code), number of diagnoses at discharge, CCI, laboratory values (hemoglobin, leucocyte count and thrombocyte count, serum sodium and creatinine) at admission (first lab values at admission) and discharge (last lab values before discharge), number of interventions and costs (normal vs. high costs, i.e., ≥ the 75th empirical percentile value) during hospitalization of blood products, drugs, imaging procedures, physiotherapy, and nursing workload.

Missing data

When missing, the value of hemoglobin and creatinine at discharge was assumed to be identical to the value at admission. When missing, the value of sodium and platelet count at discharge was considered normal. For other potential indicators of complexity, we assumed data to be missing at random and imputed missing data using single imputation by chained equations. To compare performance measures of the PCA with the CCI and PCCL, patients with missing values for the PCCL variable (n=3 for the derivation, n=11 for the validation dataset) were removed prior to analysis.

Statistical analysis

Multivariable logistic regression analysis with backward selection was used in the derivation set to predict complexity based on 52 potential indicators of complexity variables registered during hospitalization, removing variables with a p-value >0.1. Calibration of the final model was evaluated by constructing a calibration curve, estimating the calibration slope, calculating the difference between the mean observed proportion and mean predicted proportion of patients with high complexity (calibration-in-the-large) and the Brier score (overall measure of accuracy) in the derivation and validation set. The predictors from the final model were used to create a comprehensible score using the regression coefficient-based scoring technique.[23] Beta-coefficients were divided by the lowest coefficient and rounded up to the closest integer to generate score points, indicating increasing risk by higher scores. The discriminatory power of the score was assessed by calculating the area under the receiver operating characteristic (AUROC) curve.

The validity of performance measures was investigated by performing internal and external validation. For internal validation we used 1000 bootstrap samples, drawing samples with replacement from the derivation sample.[24] The bootstrap-corrected performance estimates were calculated by subtracting the optimism from the performance of the original model. The 95% confidence intervals (CI) for the bootstrapped performance measures were derived using the percentile method. External validation was made by estimating the same performance measures in the external validation cohort (temporal validation).

The clinical usefulness of the developed score was assessed with a decision-curve analysis investigating whether the use of the complexity score instead of the CCI alone was associated with benefit gains relative to the prediction complexity.[25]

Applying PCA, CCI and PCCL, we calculated the score of each patient and split the patient sample into a high and a low risk group. The reference point (cut-off) of each scoring system was chosen in order to make the frequency of patients in the high-risk category as close as possible to 30% (i.e. approximating the frequency of observed complex patients). To determine the accuracy of this method to predict complexity, we estimated sensitivity, specificity, and positive and negative predictive value in both the derivation and validation set for PCA and in the derivation set for CCI and PCCL.

R version 3.3.1 was used for statistical analysis.

Results

A total of 1,889 patients were included in the study (figure 1). Patients enrolled before February 16, 2017 were allocated to the derivation sample (n = 1,407), patients enrolled after this date (n = 482) were allocated to the temporal validation sample. In the derivation cohort, 447 patients (31.8%) were reported as complex, and 116 (24.1%) patients in the validation cohort. The patients in the two cohorts presented with similar baseline characteristics (table 1 and supplementary material table S1 and S2). The overall median age was 80 years (interquartile range 75 to 86 years).

Table 1: Baseline characteristics for all patients (derivation and validation cohort) stratified by complexity, as number and percentage or median and inter-quartile range for categorical and continuous variables, respectively.

	Overall (N=1889)	**Non-complex (N=1326)**	**Complex (N=563)**
	n (%) or median [interquartile range]		
Age			
≥ 80 years	579 (31)	442 (33)	137 (24)
70 to 79 years	437 (23)	304 (23)	133 (24)
60 to 69 years	322 (17)	211 (16)	111 (20)
< 60 years	537 (28)	363 (27)	174 (31)
Missing	14 (0.7)	6 (0.5)	8 (1.4)
Gender			
Male	1002 (53)	693 (52)	309 (55)
Female	873 (46)	627 (47)	246 (44)
Missing	14 (0.7)	6 (0.5)	8 (1)

Living area[1]			
Urban	611 (32)	453 (34)	158 (28)
Rural	1238 (65)	848 (64)	390 (69)
Missing	40 (2)	25 (1)	15 (3)
Marital status			
Single	331 (17)	252 (19)	79 (14)
Couple	636 (34)	429 (32)	207 (37)
Widowed	916 (48)	641 (48)	275 (49)
Missing	6 (0.3)	4 (0.3)	2 (0.4)
Hospitalization within last 12 months	673 (36)	452 (34)	221 (39)
Medication[2]			
Antineoplastic and immunomodulating agents at admission	70 (4)	38 (3)	32 (6)
Nervous system at admission	1340 (71)	918 (69)	422 (75)
Systemic hormonal preparations, excluding sex hormones and insulins at discharge	524 (28)	318 (24)	206 (37)
High costs during hospitalization[3]			
For imaging procedures	485 (26)	255 (19)	230 (41)
For laboratory analysis	482 (25)	203 (15)	279 (50)
High nurse workload[4]	475 (25)	203 (15)	272 (48)
Charlson Comorbidity Index	2 [0; 4]	2 [0; 3]	3 [1; 5]
Principal or concomitant diagnosis at discharge			
Cancer[5]	225 (12)	136 (10)	89 (16)
COPD[6]	186 (10)	124 (9)	62 (11)
Dementia[7]	163 (9)	125 (9)	38 (7)
Depression[8]	209 (11)	140 (11)	69 (12)
Heart failure[9]	327 (17)	206 (15)	121 (21)
Pneumonia[10]	244 (13)	159 (12)	85 (15)
Sepsis[11]	229 (12)	132 (10)	97 (17)
Stroke[12]	90 (5)	65 (5)	25 (4)
Substance abuse[13]	212 (11)	129 (10)	83 (15)
Syncope[14]	81 (4)	67 (5)	14 (2)
Malnutrition[15]	265 (14)	122 (9)	143 (25)
Multimorbidity			
Low (number of diagnoses ≤ 6)	510 (27)	435 (33)	75 (13)

[1] Defined according to the Swiss Federal Statistical Office based on place of residence
[2] Group of drugs according to ATC classification
[3] Defined as costs of all imaging procedures or medication during hospital stay above 75th percentile
[4] Defined as sum of hours of all nursing work (incl. sitting guard) during hospital stay above 75th percentile
[5] ICD10-codes B21, C00 through C97, Z03.1
[6] ICD10-codes J44
[7] ICD10-codes F00 through F03, F05.0, F05.1
[8] ICD10-codes F20.4, F25.1, F31.3 F31.4, F31.5, F32, F33, F41.2, F92.0
[9] ICD10-codes I50
[10] ICD10-codes A48.1, B01.2, B05.2, J10.0, J11.0, J12 through J18, J68.0, J69, J85.1, O74.0, U69.00
[11] ICD10-codes A02.1, A20.7, A22.7, A26.7, A32.7, A39.2, A39.3, A39.4, A40, A41, A42.7, B37.7
[12] ICD10-codes I63
[13] ICD10-codes F10 through F19, F53, F66.8, F66.9
[14] ICD10-codes R55
[15] ICD10-codes E40 through E46

Middle (number of diagnoses > 6 and <14)[16]	841 (44)	603 (45)	238 (42)
High (number of diagnoses ≥ 14)	524 (28)	282 (21)	242 (43)
PCCL	3 [2; 4]	3 [1; 4]	4 [3; 4]
No complication or comorbidity	380 (20)	312 (23)	68 (12)
Light complication or comorbidity	29 (1)	21 (2)	8 (1)
Moderate complication or comorbidity	292 (15)	233 (18)	59 (10)
Severe complication or comorbidity	533 (28)	409 (31)	124 (22)
Very severe complication or comorbidity	641 (34)	345 (26)	296 (53)
Missing	14 (0.7)	6 (0.5)	8 (1.4)
Abnormal creatinine level[17]			
At admission and discharge	368 (19)	241 (18)	127 (23)
At admission only	182 (10)	106 (8)	76 (13)
At discharge only	63 (3)	34 (3)	29 (5)
Missing	364 (19)	311 (23)	53 (9)
Leukocytosis[18]			
At admission and discharge	77 (41)	47 (3)	30 (5)
At admission only	19 (1)	8 (<1)	11 (2)
At discharge only	13 (<1)	5 (<1)	8 (1)
Missing	351 (19)	306 (23)	45 (8)
Patient destination			
Death	134 (7)	91 (7)	43 (8)
Home	1178 (62)	873 (66)	305 (54)
Hospital	191 (10)	119 (9)	72 (13)
Nursing home	155 (8)	108 (8)	47 (8)
Rehabilitation	171 (9)	101 (8)	70 (12)
Others and missing	60 (3)	24 (3)	26 (5)

After backward selection, 11 of the 52 potential predictors were used to derive the PCA score (Table 2). Besides diagnosis-related factors, they represented demographic characteristic, hospital variables, medication and laboratory values. Highest score points were assigned to leukocytosis (at discharge only, 16 points, and at admission and discharge, 10 points) followed by age under 60 years, high nurse workload (costs above 75th percentile for nursing expenses), and abnormal serum creatinine at discharge (≥100 µmol/l).

Table 2: PCA score weighted according to coefficients

Variable	Coefficient (95% CI)	Score points
Age		
≥ 80 years	Reference	
70 to 79 years	0.36 (0, 0.72)	3

[16] Between 25th and 75th percentile
[17] Defined as creatinine ≥100 µmol/l
[18] Defined as leukocyte count ≥20 G/l

60 to 69 years	0.5 (0.1, 0.9)	5
< 60 years	0.94 (0.56, 1.31)	9
Elective admission	0.36 (0.03, 0.69)	3
High costs during hospitalization[19]		
For imaging procedures	0.6 (0.31, 0.9)	6
For laboratory analysis	0.77 (0.46, 1.09)	7
High nurse workload[20]	0.93 (0.61, 1.26)	9
Malnutrition[21]	0.47 (0.1, 0.84)	4
Multimorbidity		
Number of diagnoses ≤ 6	Reference	
Number of diagnoses > 6 and <14[22]	0.61 (0.25, 0.96)	6
Number of diagnoses ≥ 14[23]	0.78 (0.36, 1.2)	7
Medication at admission[24]		
Antineoplastic and immunomodulating agents	0.85 (0.16, 1.54)	8
Nervous system	0.33 (0.04, 0.63)	3
Abnormal creatinine level[25]		
None	Reference	
At admission only	0.23 (-0.22, 0.68)	2
At admission and discharge	0.11 (-0.22, 0.45)	1
At discharge only	0.96 (0.29, 1.63)	9
Leukocytosis[26]		
None	Reference	
At admission only	0.11 (-0.49, 0.71)	1
At admission and discharge	1.12 (-0.04, 2.29)	10
At discharge only	1.68 (0.18, 3.18)	16
Intercept	-2.93 (-3.39, -2.46)	NA

The prediction model showed a good accuracy, with a Brier score of 0.17 and 0.15 in internal and external validation, respectively. The calibration curve showed fair agreement between predicted and observed proportions of complexity in the derivation cohort and slightly lower observed proportions than predicted probabilities in the validation cohort (graphs not shown). The calibration-in-the-large coefficient of -0.51 (95% CI -0.74 to -0.27) in the validation cohort implies that the mean observed proportion was lower than

[19] Defined as costs of all imaging procedures or medication during hospital stay above 75th percentile
[20] Defined as sum of hours of all nursing work (incl. sitting guard) during hospital stay above 75th percentile
[21] ICD10-codes E40 through E46
[22] Between 25th and 75th percentile
[23] Above 75th percentile
[24] Group of drugs according to ATC classification
[25] Defined as serum creatinine ≥100 µmol/l
[26] Defined as blood leukocyte count ≥20 G/l

the mean predicted probability. However, the calibration curve slope was satisfactory in internal and external validation (0.93 [95% CI 0.80 to 1.05] and 0.96 [95% CI 0.74 to 1.18]), respectively.

The median score was 17 points in the derivation and validation cohort (mean 18.77 and 19.03, respectively). The minimal score was 0 points in both cohorts, the maximal score reached was 54 points in the derivation cohort and 53 points in the validation cohort (theoretically maximal 81 score points). The score's area under the receiver operating characteristic (AUROC) curve was 0.77 (95% CI 0.74 to 0.79) and 0.78 (95% CI 0.74 to 0.82) in internal and external validation.

Table 3: Stratification of Observed vs. predicted complex patients applying the PCA score.

	Score points	Risk category of complexity	Patients in each category	Complex patients	Estimated risk of complexity
Derivation set	< 24	Low risk	991 (70%)	193 (19%)	19
	≥ 24	High risk	416 (30%)	254 (61%)	61
Validation set	< 24	Low risk	347 (72%)	50 (14%)	20
	≥ 24	High risk	135 (28%)	66 (49%)	62

We classified patients as low and high complexity risk (table 3) according to the selected cut-off of 24 points (approximating the frequency of observed complex patients of 30%). The proportion of patients categorized as complex (i.e. score ≥ 24 points) was 30% and 28% in the derivation and validation dataset, respectively. Sensitivity was 57% in both the derivation and validation dataset. The specificity was 83% and 81%, respectively. Positive predictive values were 61% and 49% in the derivation and validation cohort, respectively, while negative predictive values were 81% and 86%, respectively. The discriminatory power of the PCA score was robust with an AUROC of 0.77 (95% CI 0.74 to 0.79) in internal validation (bootstrap-corrected value) and 0.78 (95% CI 0.74 to 0.82) in external validation (table 4 and supplementary figure S2).

Table 4: Measures of performance to predict complexity

	PCA, derivation set % (95%-CI)	PCA, validation set % (95%-CI)	CCI, validation set % (95%-CI)	PCCL, validation set % (95%-CI)
Sensitivity	57 (52-61)	57 (47-66)	41 (32-50)	61 (51-70)
Specificity	83 (81-85)	81 (77-85)	75 (71-80)	75 (70-79)
Positive predictive value	61 (59-66)	49 (40-58)	34 (26-43)	42 (34-50)
Negative predictive value	81 (78-83)	86 (81-89)	80 (75-84)	86 (82-90)

Misclassification error	25 (28-23)	25 (29-21)	33 (37-29)	28 (33-24)
AUROC[27]	0.77 (0.74-0.79)[28]	0.78 (0.74-0.82)	0.62 (0.56-0.68)	0.69 (0.64-0.75)

In comparison, predictive accuracy of the CCI was lower compared to the PCA score. The AUROCs were low with 0.58 (95% CI 0.55 to 0.62) and 0.62 (95% CI 0.56 to 0.68) in the derivation and validation cohort, respectively (table 4). Sensitivity of the CCI reached 36% (95% CI 31% to 40%) and 41% (95% CI 31% to 50%) in derivation and validation cohort, respectively, while specificity was 76% (95% CI 73% to 78%) and 75% (95% CI 71% to 80%), respectively. The decision curve analysis (supplementary figure S1) indicates a superiority of the PCA score compared to the CCI to predict complexity.

AUROCs of PCCL were between those of CCI and PCA score with 0.64 (95% CI 0.61 to 0.67) and 0.69 (95% CI 0.64 to 0.75) in the derivation and validation cohort, respectively (table 4). Sensitivity was 52% (95% CI 47% to 56%) and 61% (95% CI 51% to 70%), respectively, while specificity was 73% (95% CI 71% to 76%) and 75% (95% CI 70% to 79%).

Discussion

We derived and validated the PCA score that accurately assessed patient complexity in medical inpatients. The final score of eleven independent and readily available factors, included age, hospital variables, diagnosis related aspects and laboratory variables. The PCA score showed overall good performance with a discriminatory power of 0.78 that surpasses other comorbidity-based tools such as the Charlson comorbidity index and the PCCL.

In this cohort of medical inpatients, 32% and 24% were considered “complex” by the treating physician, in the derivation and the validation cohort, respectively. This first estimate of patient complexity in the hospital setting is consistent with a previous assessment in an outpatient population where 26% of total 4,302 patients were categorized as being complex by a primary care physician.[1] Based on these data, the authors later derived a model to identify around 20% of 143,372 primary care patients as complex.

[27] Area under receiver operating characteristic
[28] Bootstrap-corrected from internal validation

Using the model and outpatient CCI or PCCL, only modest agreement between the methods was observed (37% and 40%, respectively).[2] Therefore, a tool not solely based on multimorbidity, such as the newly developed PCA score, seems to better identify complex patients.

In the present study, age was an inverse indicator of complexity. In a previous study of outpatients, mean age of complex patients was 60 years versus 48 years in non-complex patients.[1] Nonetheless, the same study reported noteworthy age-related variability: in younger patients the association of certain diagnoses (e.g. alcohol-related diseases) with complexity was stronger, and deprivation as contributor to complexity is independent of age.[1,5] In our setting, discharge planning processes for older patients may be better established (e.g. including hospital social services, decision making based on patient's provision and possibility for indiscriminate discharge to geriatric rehabilitation facilities or nursing homes) compared to younger patients.[1,9,26,27] Treating physicians may therefore perceive the discharge planning process of some younger patients as difficult and categorize these patients as complex. Furthermore, young non-complex patients may more often be treated as outpatients or by specialist's clinics instead of our tertiary care general internal medicine ward. Elective admissions to a tertiary hospital may represent a cohort of rather complex patients preselected by primary care physicians and smaller hospitals (21% elective admissions in complex patients versus 14% in non-complex patients). It is also possible that these patients are only perceived as more complex by the treating physician because patients admitted directly to the medical ward are pending initial work-up otherwise provided in the emergency department.

Patients with high costs of imaging procedures may reflect the patients with more severe diseases or more diagnosis uncertainty. Similarly, high costs for laboratory analysis may be explained by a higher need of costly or repeated measurements in more complex patients. High costs for care/nursing were indicators of complexity highlighting some concordance between the nurse workload and the medical complexity.

In our study multimorbidity (defined as a number of more than 6 diagnoses) was an indicator of complexity. Comorbidity-based scores, i.e., the CCI, are commonly used to identify complex patients. Indeed, in the study of Grant et al. the proportion of multimorbid patients identified by a CCI of 2 or more was higher in complex patients, i.e., 26% of complex patients were multimorbid versus 9% of non-complex patients.[1] However, many multimorbid patients are not complex and not all complex patients are

multimorbid. In our cohort (derivation and validation datasets together) 34% of polymorbid patients (CCI ≥2) were complex versus 24% in the group of CCI <2. Comparably, nearly one half of patients with a CCI of 2 or greater were classified as non-complex in the study of Grant et al.[1] Therefore, a system to identify complexity should not depend on diagnosis alone.

In the PCA score, malnutrition was a risk factor of complexity. Malnutrition in hospitalized patients is associated with more complications, increased mortality, longer hospital stays and higher costs [28,29]. Therefore, malnutrition and complexity may both reflect a cluster of severe and chronic disease as well as socioeconomic circumstances.[1]

Antineoplastic and immunomodulating medication at admission was an indicator of complexity. These drugs are used for oncologic patients, but also in patients with rheumatologic disease or after receiving organ transplants. These patients may be complex because of challenging infectious diseases, end-of-life issues and interdisciplinary care. Abnormal values of serum creatinine and leukocyte counts at discharge were denoting complexity whether the values were normal or abnormal at admission. These patients may also requiring more interaction between specialists and may complicate the discharge process.

Personal characteristics or mental health issues and use of psychoactive medication, i.e., narcotics, selective serotonin reuptake inhibitors, benzodiazepines, smoking cessation agents and antipsychotics, have been described as characterizing complex patients, especially in younger patients.[1] This is in line with the observation that in the PCA score, use of medication affecting the nervous system at admission (including antipsychotics, mood-stabilizers, sedatives, analgesics including opioids, anticonvulsive medication and anti-dementia drugs) was an indicator of complexity. These patients may challenge the known pathways of the healthcare system, e.g. by parallel use of general internal medicine and psychiatric resources.

There are several limitations of the study. First, we used physician's assessment to define complexity, which per definition is subjective. Nonetheless, there is no better standard reference (gold standard) and the proportion of patients identified as complex was similar in previous studies.[1,2] Second, the PCA score has been developed at a single tertiary hospital in Switzerland and therefore may not be generalizable to other settings, e.g. other health care systems. However, costs and nursing workload are not measured as absolute values but as those above the 75th percentile, making it transferable to other

settings. Also, some patients may appear as complex in one setting, while they will be judged as non-complex in other settings (e.g. primary care vs. university hospital), nevertheless the proportion of complex patients in out setting was similar to the one in primary care.[1] Third, it is likely that our model does not consider every important indicator, but it allows deriving an easily usable tool which kept its fair sensitivity and good specificity in our external validation. Fourth, the PCA score includes values available only at discharge, which makes patient-aimed interventions during hospitalization difficult. This is however also true for alternative assessment tools, such as the CCI and the PCCL, which had a lower performance in identifying complex patients in our cohort. Fifth, imputation of missing data may have changed the outcome of the study. However, potential predictors with more than 25% missing data were excluded. Sixth, most of the included indicators are not modifiable. For example, a patient will still be complex if receiving less imaging procedures to reduce costs.

To our knowledge, the PCA score is the first tool to identify complex medical patients in the hospital setting. It can easily be calculated and is therefore predestined to be used for population-based studies as it does not involve individual judgement of a physician. With its prospective design and inclusion of a large number of medical inpatients, this study has a strong design.

Identification of complex patients by this simple tool using electronically available data may help monitoring the proportion of complex patients in the hospital setting and comparing patient complexity level between hospitals. Thereby, the PCA score might improve the monitoring of resources distribution and coordination of care, e.g. by flagging complex patients to general practitioners or social workers for closer follow-up or low-threshold service.

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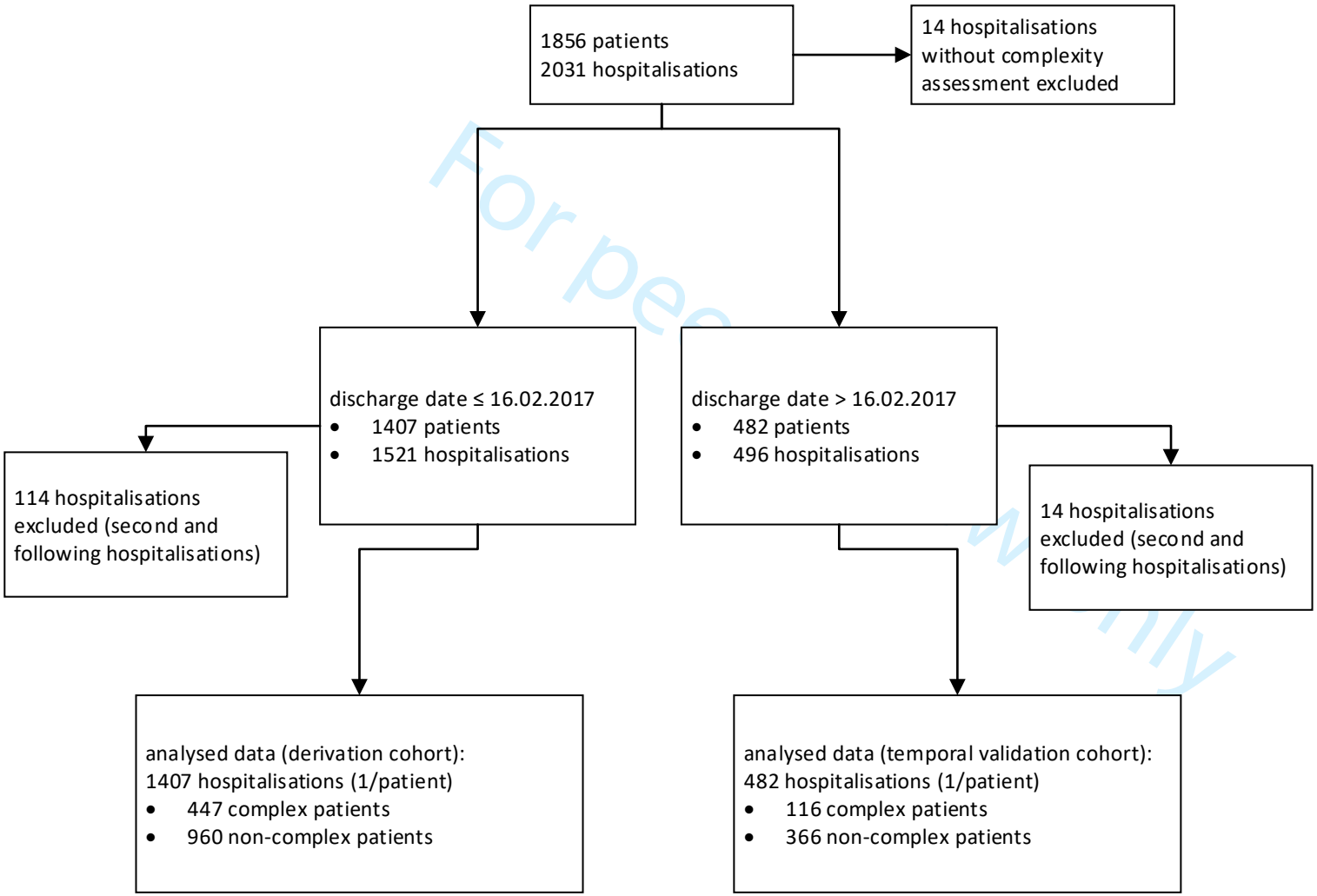
Figure 1 caption

Flow chart. Derivation sample (derivation and internal validation cohort) and external validation sample (temporal validation cohort).



Supplementary Material

Table S1: Baseline characteristics for derivation cohort stratified by complexity.

	Overall (N=1889)	Non-complex (N=1326)	Complex (N=563)
	n (%) or median [interquartile range]		
Age			
≥ 80 years	447 (32)	337 (35)	110 (25)
70 to 79 years	327 (23)	218 (23)	109 (24)
60 to 69 years	239 (17)	152 (16)	87 (19)
< 60 years	391 (28)	251 (26)	140 (31)
Missing	3 (0.2)	2 (0.2)	1 (0.2)
Gender			
Male	748 (53)	494 (51)	254 (57)
Female	656 (47)	464 (48)	192 (43)
Missing	3 (0.2)	2 (0.2)	1 (0.2)
Living area[1]			
Urban	460 (33)	335 (35)	125 (28)
Rural	923 (66)	606 (63)	317 (71)
Missing	24 (2)	19 (2)	5 (1)
Marital status			
Single	477 (34)	306 (32)	171 (38)
Couple	673 (48)	458 (48)	215 (48)
Widowed	252 (18)	193 (20)	59 (13)
Missing	5 (0.4)	3 (0.3)	2 (0.4)
Hospitalization within last 12 months	480 (34)	317 (33)	163 (36)
Medication[2]			
Antineoplastic and immunomodulating agents at admission	43 (3)	20 (2)	23 (5)
Nervous system at admission	1001 (71)	666 (69)	335 (75)
Systemic hormonal preparations, excluding sex hormones and insulins at discharge	253 (18)	163 (17)	90 (20)
High costs during hospitalization[3]			
For imaging procedures	367 (26)	179 (19)	188 (42)
For laboratory analysis	365 (26)	147 (15)	218 (49)
High nurse workload[4]	358 (25)	146 (15)	212 (47)
Charlson Comorbidity Index	2 [0; 4]	2 [0; 3]	2.5 [1; 5]
Principal or concomitant diagnosis at discharge			
Cancer[5]	175 (12)	104 (11)	71 (16)
COPD[6]	139 (10)	91 (9)	48 (11)
Dementia[7]	120 (8)	89 (9)	31 (7)
Depression[8]	148 (10)	94 (10)	54 (12)
Heart failure[9]	235 (17)	143 (15)	92 (21)

[1] Defined according to the Swiss Federal Statistical Office based on place of residence
[2] Group of drugs according to ATC classification
[3] Defined as costs of all imaging procedures or medication during hospital stay above 75th percentile
[4] Defined as sum of hours of all nursing work (incl. sitting guard) during hospital stay above 75th percentile
[5] ICD10-codes B21, C00 through C97, Z03.1
[6] ICD10-codes J44
[7] ICD10-codes F00 through F03, F05.0, F05.1
[8] ICD10-codes F20.4, F25.1, F31.3 F31.4, F31.5, F32, F33, F41.2, F92.0
[9] ICD10-codes I50

Pneumonia[10]	186 (13)	115 (12)	71 (16)
Sepsis[11]	162 (11)	88 (9)	74 (17)
Stroke[12]	72 (5)	50 (5)	22 (5)
Substance abuse[13]	154 (11)	90 (9)	64 (14)
Syncope[14]	68 (5)	55 (6)	13 (3)
Malnutrition[15]	190 (13)	82 (8)	108 (24)
Multimorbidity			
Low (number of diagnoses ≤ 6)	387 (27)	322 (33)	65 (14)
Middle (number of diagnoses > 6 and <14)[16]	642 (46)	443 (46)	199 (44)
High (number of diagnoses ≥ 14)	375 (27)	193 (20)	182 (41)
PCCL			
No complication or comorbidity	297 (21)	239 (25)	58 (13)
Light complication or comorbidity	22 (2)	15 (2)	7 (2)
Moderate complication or comorbidity	211 (15)	161 (17)	50 (11)
Severe complication or comorbidity	390 (28)	289 (30)	101 (23)
Very severe complication or comorbidity	484 (34)	254 (26)	230 (51)
Missing	3 (0.2)	2 (0.2)	1 (0.2)
Abnormal creatinine level[17]			
At admission and discharge	278 (20)	181 (19)	97 (22)
At admission only	128 (9)	72 (7)	56 (12)
At discharge only	50 (4)	24 (2)	26 (6)
Missing	275 (19)	229 (24)	46 (10)
Leukocytosis[18]			
At admission and discharge	15 (1)	6 (0.6)	9 (2)
At admission only	60 (4)	35 (4)	25 (6)
At discharge only	11 (0.8)	3 (0.3)	8 (2)
Missing	260 (18)	223 (23)	37 (8)
Patient destination			
Death	105 (7)	73 (8)	32 (7)
Home	875 (62)	621 (65)	254 (57)
Hospital	141 (10)	85 (9)	56 (12)
Nursing home	109 (8)	79 (8)	30 (7)
Rehabilitation	138 (10)	79 (8)	59 (13)
Others and missing	39 (3)	23 (2)	16 (4)

Table S2: Baseline characteristics for all patients in the validation cohort stratified by complexity.

[10] ICD10-codes A48.1, B01.2, B05.2, J10.0, J11.0, J12 through J18, J68.0, J69, J85.1, O74.0, U69.00
[11] ICD10-codes A02.1, A20.7, A22.7, A26.7, A32.7, A39.2, A39.3, A39.4, A40, A41, A42.7, B37.7
[12] ICD10-codes I63
[13] ICD10-codes F10 through F19, F53, F66.8, F66.9
[14] ICD10-codes R55
[15] ICD10-codes E40 through E46
[16] Between 25th and 75th percentile
[17] Defined as creatinine ≥100 µmol/l
[18] Defined as leukocyte count ≥20 G/l

	Overall (N=1889)	Non-complex (N=1326)	Complex (N=563)
	n (%) or median [interquartile range]		
Age			
≥ 80 years	132 (27)	105 (29)	27 (23)
70 to 79 years	110 (23)	86 (23)	24 (21)
60 to 69 years	83 (17)	59 (16)	24 (21)
< 60 years	146 (30)	112 (31)	34 (29)
Missing	11 (2)	4 (1)	7 (6)
Gender			
Male	254 (53)	199 (54)	55 (47)
Female	217 (45)	163 (44)	54 (47)
Missing	11 (2)	4 (1)	7 (6)
Living area[1]			
Urban	151 (31)	118 (32)	33 (28)
Rural	315 (65)	242 (66)	73 (63)
Missing	16 (3)	6 (2)	10 (9)
Marital status			
Single	159 (33)	123 (34)	36 (31)
Couple	243 (50)	183 (50)	60 (52)
Widowed	79 (16)	59 (16)	20 (17)
Missing	1 (0.2)	1 (0.3)	0 (0)
Hospitalization within last 12 months	193 (40)	135 (37)	58 (50)
Medication[2]			
Antineoplastic and immunomodulating agents at admission	27 (6)	18 (5)	9 (8)
Nervous system at admission	339 (70)	252 (69)	87 (75)
Systemic hormonal preparations, excluding sex hormones and insulins at discharge	105 (22)	73 (20)	32 (28)
High costs during hospitalization[3]			
For imaging procedures	118 (24)	76 (21)	42 (36)
For laboratory analysis	117 (24)	56 (15)	61 (53)
High nurse workload[4]	117 (24)	57 (15.6)	60 (52)
Charlson Comorbidity Index	2 [0; 4]	2.00 [0; 3]	3 [1; 5]
Principal or concomitant diagnosis at discharge			
Cancer[5]	50 (10)	50 (10)	50 (10)
COPD[6]	32 (9)	32 (8)	32 (9)
Dementia[7]	18 (15)	18 (15)	18 (15)
Depression[8]	47 (10)	47 (10)	47 (10)
Heart failure[9]	33 (9)	33 (9)	33 (9)
Pneumonia[10]	14 (12)	14 (12)	14 (12)
Sepsis[11]	43 (9)	43 (9)	43 (9)

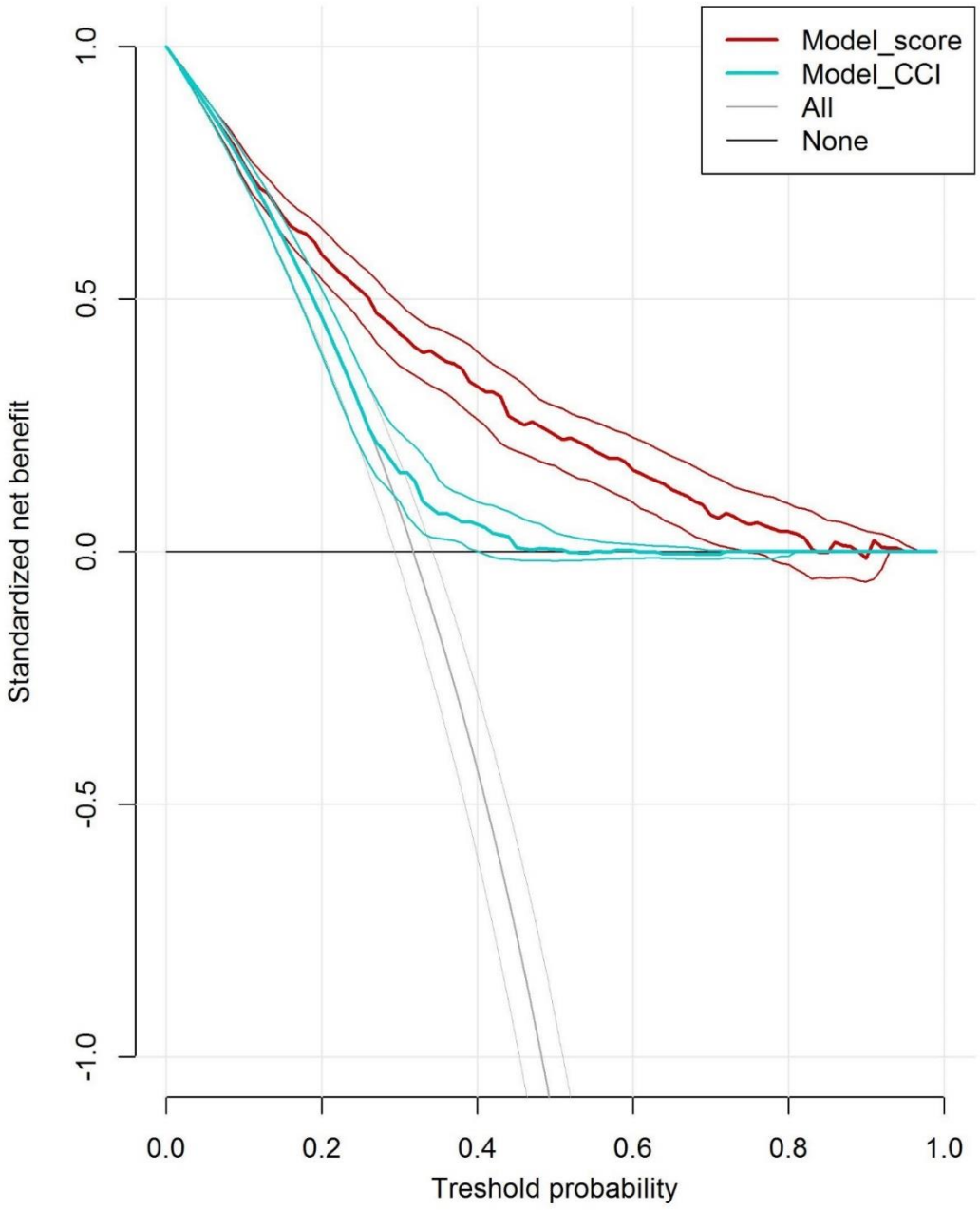
[1] Defined according to the Swiss Federal Statistical Office based on place of residence
[2] Group of drugs according to ATC classification
[3] Defined as costs of all imaging procedures or medication during hospital stay above 75th percentile
[4] Defined as sum of hours of all nursing work (incl. sitting guard) during hospital stay above 75th percentile
[5] ICD10-codes B21, C00 through C97, Z03.1
[6] ICD10-codes J44
[7] ICD10-codes F00 through F03, F05.0, F05.1
[8] ICD10-codes F20.4, F25.1, F31.3 F31.4, F31.5, F32, F33, F41.2, F92.0
[9] ICD10-codes I50
[10] ICD10-codes A48.1, B01.2, B05.2, J10.0, J11.0, J12 through J18, J68.0, J69, J85.1, O74.0, U69.00
[11] ICD10-codes A02.1, A20.7, A22.7, A26.7, A32.7, A39.2, A39.3, A39.4, A40, A41, A42.7, B37.7

Stroke[12]	36 (10)	36 (9)	36 (10)
Substance abuse[13]	7 (6)	7 (6)	7 (6)
Syncope[14]	61 (13)	61 (13)	61 (13)
Malnutrition[15]	46 (13)	46 (13)	46 (13)
Multimorbidity			
Low (number of diagnoses ≤ 6)	123 (25)	113 (31)	10 (9)
Middle (number of diagnoses > 6 and <14)[16]	199 (41)	160 (44)	39 (34)
High (number of diagnoses ≥ 14)	149 (31)	89 (24)	60 (52)
PCCL			
No complication or comorbidity	83 (1)	73 (20)	10 (9)
Light complication or comorbidity	7 (1)	6 (2)	1 (0.9)
Moderate complication or comorbidity	81 (17)	72 (20)	9 (8)
Severe complication or comorbidity	143 (30)	120 (33)	23 (20)
Very severe complication or comorbidity	157 (33)	91 (24)	66 (57)
Missing	11 (2)	4 (1)	7 (6)
Abnormal creatinine level[17]			
At admission and discharge	90 (19)	60 (16)	30 (26)
At admission only	54 (11)	34 (9)	20 (17)
At discharge only	13 (2.7)	10 (3)	3 (3)
Missing	89 (18)	82 (22)	7 (6)
Leukocytosis[18]			
At admission and discharge	4 (0.8)	2 (0)	2 (2)
At admission only	17 (3)	12 (3)	5 (4)
At discharge only	2 (0.4)	2 (0.5)	0 (0)
Missing	91 (19)	83 (23)	8 (7)
Patient destination			
Death	134 (7)	91 (7)	43 (8)
Home	1178 (62)	873 (66)	305 (54)
Hospital	191 (10)	119 (9)	72 (13)
Nursing home	155 (8)	108 (8)	47 (8)
Rehabilitation	171 (9)	101 (8)	70 (12)
Others and missing	60 (3)	34 (3)	26 (5)

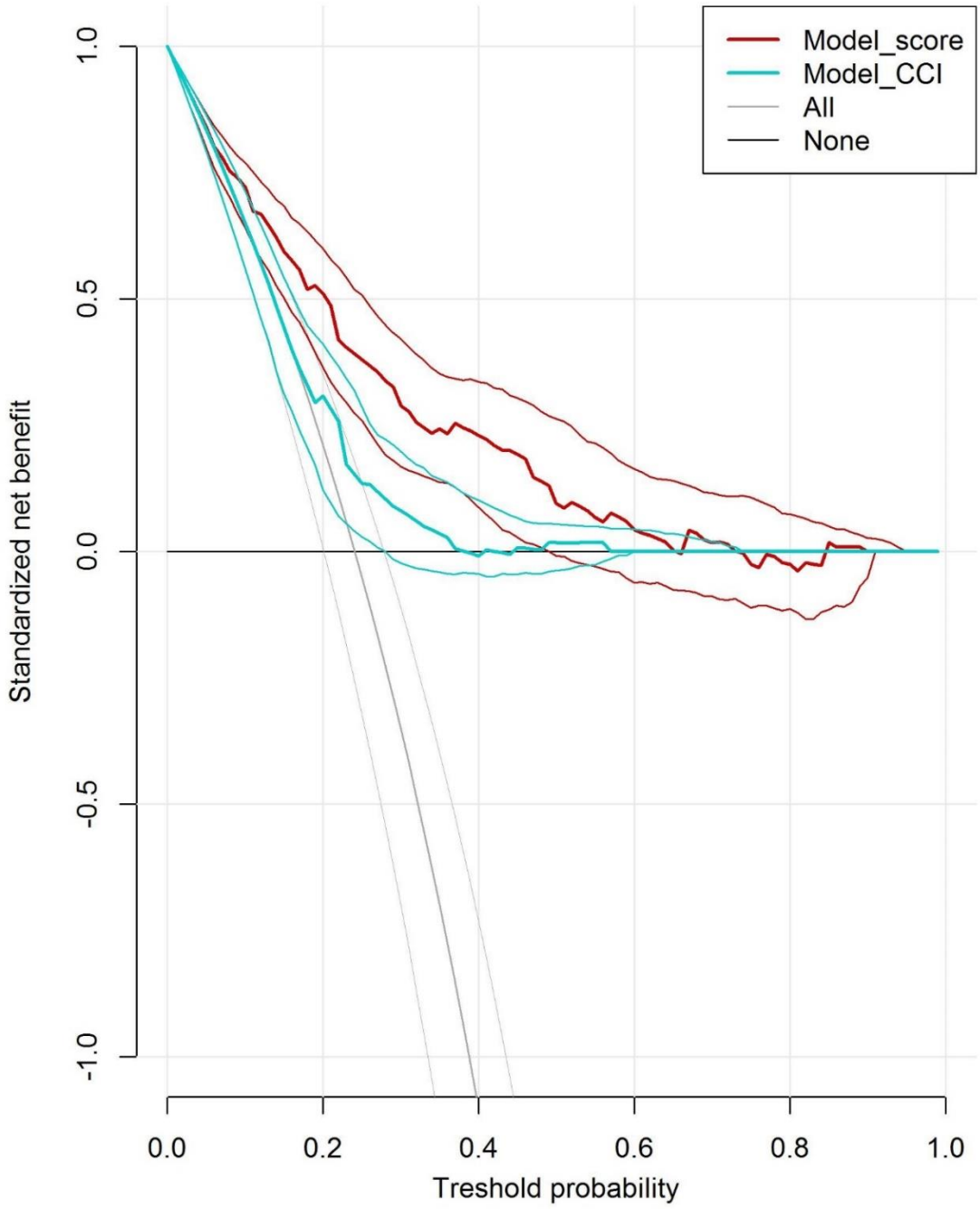
[12] ICD10-codes I63
[13] ICD10-codes F10 through F19, F53, F66.8, F66.9
[14] ICD10-codes R55
[15] ICD10-codes E40 through E46
[16] Between 25th and 75th percentile
[17] Defined as creatinine ≥100 µmol/l
[18] Defined as leukocyte count ≥20 G/l

Supplementary figure S1. Decision curve analysis. A, derivation dataset. B, validation dataset. CCI, Charlson comorbidity index.

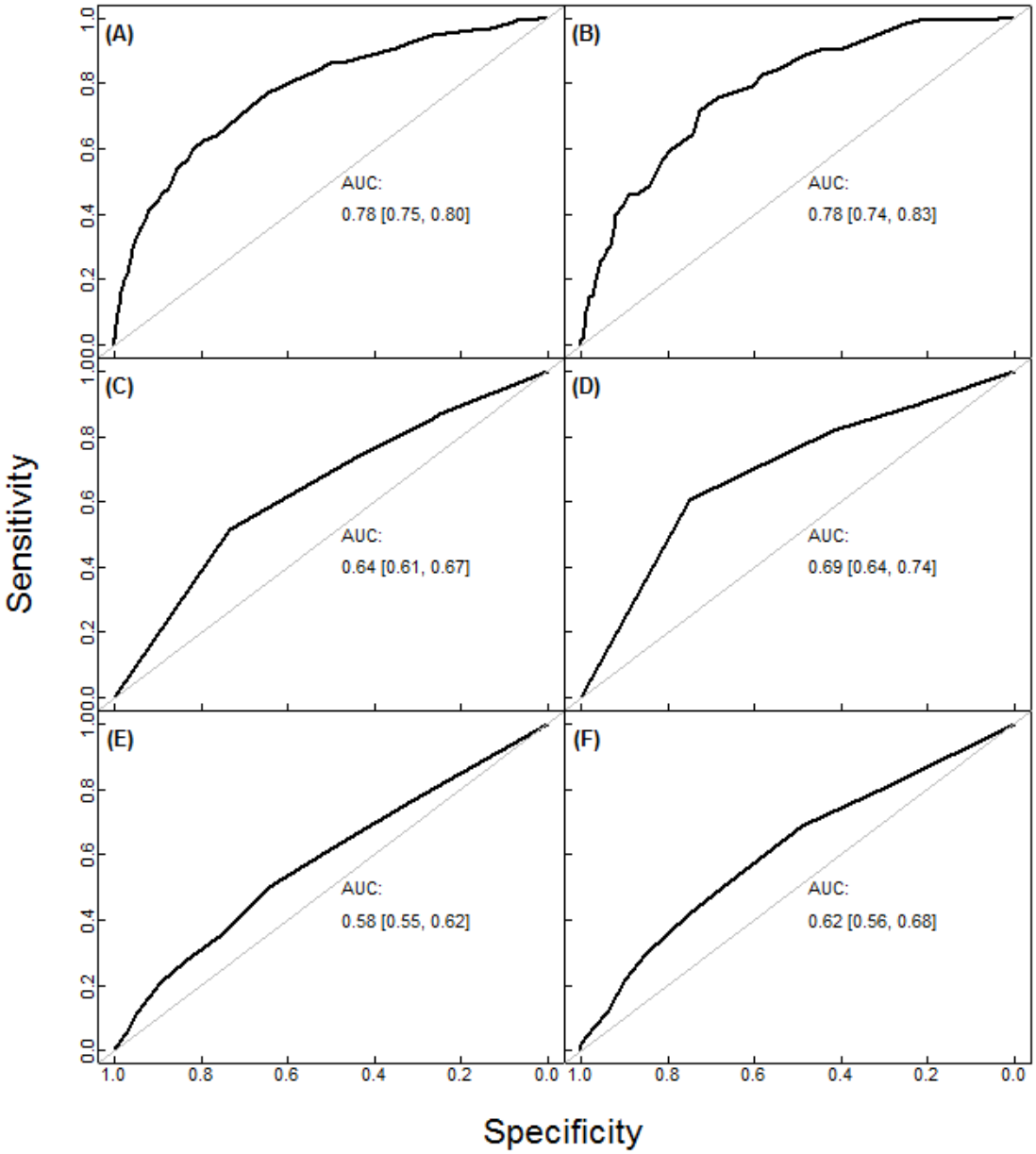
A)



B)



Supplementary figure S2. A, PCA score, derivation dataset. B, PCA score, validation dataset. C, PCCL, derivation dataset. D, PCCL, validation dataset. E, CCI, derivation dataset. F, CCI, validation dataset.



Reporting checklist for prediction model development and validation study.

Based on the TRIPOD guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

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In your methods section, say that you used the TRIPODreporting guidelines, and cite them as:

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		Reporting Item	Page Number
Title			
	#1	Identify the study as developing and / or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract			

	#2	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	3
Introduction			
	#3a	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	5
	#3b	Specify the objectives, including whether the study describes the development or validation of the model or both.	5
Methods			
Source of data	#4a	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	6
Source of data	#4b	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	6
Participants	#5a	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	6
Participants	#5b	Describe eligibility criteria for participants.	6
Participants	#5c	Give details of treatments received, if relevant	n/a

Outcome	#6a	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	6
Outcome	#6b	Report any actions to blind assessment of the outcome to be predicted.	n/a
Predictors	#7a	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured	7
Predictors	#7b	Report any actions to blind assessment of predictors for the outcome and other predictors.	n/a
Sample size	#8	Explain how the study size was arrived at.	6
Missing data	#9	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	8-9
Statistical analysis methods	#10a	If you are developing a prediction model describe how predictors were handled in the analyses.	8-9
Statistical analysis methods	#10b	If you are developing a prediction model, specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	8-9
Statistical analysis methods	#10c	If you are validating a prediction model, describe how the predictions were calculated.	8-9
Statistical analysis methods	#10d	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	8-9

Statistical analysis methods	#10e	If you are validating a prediction model, describe any model updating (e.g., recalibration) arising from the validation, if done	8-9
Risk groups	#11	Provide details on how risk groups were created, if done.	n/a
Development vs. validation	#12	For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.	8-9
Results			
Participants	#13a	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	9 + 24
Participants	#13b	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	9 + 18
Participants	#13c	For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors and outcome).	9 + 18
Model development	#14a	If developing a model, specify the number of participants and outcome events in each analysis.	9
Model development	#14b	If developing a model, report the unadjusted association, if calculated between each candidate predictor and outcome.	9

Model specification	#15a	If developing a model, present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	9 + 21
Model specification	#15b	If developing a prediction model, explain how to the use it.	10 + 21
Model performance	#16	Report performance measures (with CIs) for the prediction model.	10, 11, 23
Model-updating	#17	If validating a model, report the results from any model updating, if done (i.e., model specification, model performance).	10-11
Discussion			
Limitations	#18	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	14
Interpretation	#19a	For validation, discuss the results with reference to performance in the development data, and any other validation data	11-14
Interpretation	#19b	Give an overall interpretation of the results, considering objectives, limitations, results from similar studies, and other relevant evidence.	11-14
Implications	#20	Discuss the potential clinical use of the model and implications for future research	14

Other information

Supplementary information	#21	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	25
Funding	#22	Give the source of funding and the role of the funders for the present study.	2

BMJ Open

Development and validation of a score to assess complexity of general internal medicine patients at hospital discharge: a prospective cohort study

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Development and validation of a score to assess complexity of general internal medicine patients at hospital discharge: a prospective cohort study

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Patient consent for publication: Not required.

Data availability: Data are available upon reasonable request.

Abstract

Objective: We aimed to develop and validate a score to assess inpatient complexity and compare its performance with two currently used but not validated tools to estimate complexity (i.e., Charlson Comorbidity Index [CCI], patient clinical complexity level [PCCL]).

Methods: Consecutive patients discharged from the department of medicine of a tertiary care hospital were prospectively included into a derivation cohort from October 1, 2016 to February 16, 2017 (n=1,407), and a temporal validation cohort from February 17, 2017, to March 31, 2017 (n=482). The physician in charge assessed complexity. Potential predictors comprised 52 parameters from the electronic health record such as health factors and hospital care usage. We fit a logistic regression model with backward selection to develop a prediction model and derive a score. We assessed and compared performance of model and score in internal and external validation using measures of discrimination and calibration.

Results: Overall, 447 of 1,407 patients (32%) in the derivation cohort, and 116 of 482 patients (24%) in the validation cohort were identified as complex. Eleven variables independently associated with complexity were included in the score. Using a cut-off of ≥24 score points to define high-risk patients, specificity was 81% and sensitivity 57% in the validation cohort. The score's area under the receiver operating characteristic (AUROC) curve was 0.78 in both the derivation and validation cohort. In comparison, the CCI had an AUROC between 0.58 and 0.61, and the PCCL between 0.64 and 0.69, respectively.

Conclusions: We derived and internally and externally validated a score that reflects patient complexity in the hospital setting, performed better than other tools, and could help monitoring complex patients.

Strengths and limitations of this study

- This is a prospective cohort study of consecutive, unselected, adult inpatients discharged from the department of medicine of a large university hospital.
- We derived and validated an easily usable score that accurately assesses patient complexity in medical inpatients that may help monitoring the proportion of complex patients (Patient Complexity Assessement (PCA) score).
- The reference standard used to define complexity was the physician's judgment, which per definition is partly subjective.
- The PCA score has been developed at a single tertiary hospital and may not consider a comprehensive list of important indicators.
- The PCA score includes values available only at discharge and indicators are not modifiable.

Keywords: primary care, general medicine, quality in health care, social medicine, internal medicine

Introduction

One fourth of patients are estimated to be complex in the primary care setting, while this proportion is not well known in the hospital setting.[1-4] Generally, those patients using more resources, time and/or effort are regarded as complex patients, although no universal definition of patient complexity is available. Complexity is not limited to multimorbidity and chronicity of disease but depends also on multiple other aspects, including psychological, social, economic and environmental factors.[1,2,5-7] Complex patients challenge the current structures, e.g., they have a higher probability of future emergency department utilization (without higher mortality rates) and show suboptimal use of the health care system.[2,8-10] Identifying complex patients is of economic, epidemiological and social importance because it may help to better allocate resources and improve health care utilization.[5,11]

The only available assessment method to identify complex inpatients is currently the physician's assessment, which limits the monitoring of patient complexity over time.[10,12,13] The Charlson Comorbidity Index (CCI), originally developed and validated to predict mortality,[14] has been assessed as a proxy for patient complexity in the primary care setting. However, agreement between the primary care physician's assessment and the CCI to identify complex patients was only modest.[1,2,5] No such assessment has been yet performed in the hospital setting. The patient clinical complexity level (PCCL) is calculated for each treatment episode to indicate the effect of complications and comorbidities in a patient. The PCCL ranges from 0 (no complication or comorbidity) to 4 (very severe complication or comorbidity), according to a complex algorithm. [14,15] Identification of complex patients at discharge could help to identify those, who would profit from more intense follow-up, e.g. by general practitioners or social workers, although effectiveness of such interventions would have to be proven first.

In order to simplify and standardize the identification of complex patients, we aimed to develop and validate a new score to help identifying the most complex inpatients (Patient Complexity Assessment, PCA score) using readily available administrative and clinical data. Our hypothesis was that some data routinely collected during a hospitalization can be used as a valuable surrogate to physician's assessment. We then compared the performance of the newly developed PCA score to the CCI, and the PCCL used in the Swiss DRG system to allocate reimbursement according to multimorbidity.[14,15]

Methods

Study design and participants

This study was a prospective cohort of consecutive, unselected, adult inpatients discharged from the department of medicine of a large University hospital (Inselspital, Bern University Hospital, Bern, Switzerland) between October 1, 2016 and March 31, 2017. The only exclusion criterion was a previous study inclusion. We originally planned to consider around 35 variables in the prediction model. With an estimated proportion of complex patients of one fourth, we preset the sample size of the derivation cohort to be 1,400 (rule of thumb of 10 outcomes per variable tested).[16,17] We predefined, that if more than 1,400 patients will be included during the study period of 6 months, we would use these patients to externally validate the prediction model. Patients enrolled before February 16, 2017 were allocated to the derivation sample (derivation and internal validation cohort), and patients enrolled after this date were allocated to an external validation sample (temporal validation cohort). During their first admission, all patients included in the study gave their written general consent to the use of their routine data for research purposes. The study was approved by the local ethics committee (Kantonale Ethikkommission Bern, ID 2016-01319). We reported the study in accordance with the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis Or Diagnosis (TRIPOD) statement.[18]

Patient and public involvement

No patient involved.

Study outcome and predictor variables

The primary outcome was the predictive accuracy of the PCA against the treating physician's judgment as the gold standard to identify complex general internal medicine inpatients. Complex patients were defined as those using more resources, time and/or effort while hospitalized. The resident (or supervising consultant) was asked by a trained study nurse to assess at time of discharge the level of complexity of the entire hospital stay of her/his patient without providing any specific scoring system (complex or not-complex).

The CCI was originally developed to predict 10-year survival by using an algorithm based on addition of score points for specific diagnoses.[14,19] The PCCL was derived from the electronic health record (no complication or comorbidity: 0; light complication or comorbidity: 1; moderate complication or comorbidity:

2; severe complication or comorbidity: 3; very severe complication or comorbidity: 4) and is defined by SwissDRG.[20,21]

For all patients, information regarding International Classification of Disease (ICD) codes and other potential indicators for patient complexity were collected retrospectively through the electronic health record of the hospital. Candidate predictor variables have been selected based on a previous survey among general internists in the hospital setting which asked them to identify factors that contribute to patient complexity,[4] and on a selection of readily available potential predictors to have a broad spectrum of candidate predictors. Variables that were not routinely collected were removed (i.e. variables with more than 25% missing data, such as aspartate amino transferase, C-reactive protein, and albumin at discharge). Collinearity between variables was assessed using Pearson correlation coefficients. In case of strong correlation ($r > 0.7$), only the strongest univariate predictor was kept. A final list of 52 indicators was considered in denoting complexity: baseline demographic information (age, gender, living area (rural versus urban, defined according to the Swiss Federal Statistical Office based on the patient's place of residence), marital status, institutional care before admission, nationality (Swiss vs. non-Swiss), hospital variables (urgent vs. elective admission, number of previous hospitalization in the last 12 months, patient destination [death, home, other hospital, nursing home, rehabilitation, other], stay on the intensive care unit, internal transfer), drugs (for each group of the Anatomical, Therapeutic and Chemical [ATC] classification categories) at admission and at discharge and polypharmacy (≥10 drugs [22], at admission and discharge), main diagnosis (cancer, chronic obstructive pulmonary disease, dementia, depression, heart failure, pneumonia, sepsis, stroke, substance abuse, syncope, malnutrition, based on the Tenth Revision of the International Statistical Classification of Diseases and Related Health Problems [ICD-10] code), number of diagnoses at discharge, CCI, laboratory values (hemoglobin, leucocyte count and thrombocyte count, serum sodium and creatinine) at admission (first lab values at admission) and discharge (last lab values before discharge), number of interventions and costs (normal vs. high costs, i.e., ≥ the 75th empirical percentile value) during hospitalization of blood products, drugs, imaging procedures, physiotherapy, and nursing workload.

Missing data

When missing, the value of hemoglobin and creatinine at discharge was assumed to be identical to the value at admission. When missing, the value of sodium and platelet count at discharge was considered normal. For other potential indicators of complexity, we assumed data to be missing at random and imputed missing data using single imputation by chained equations. To compare performance measures of the PCA with the CCI and PCCL, patients with missing values for the PCCL variable (n=3 for the derivation, n=11 for the validation dataset) were removed prior to analysis.

Statistical analysis

Multivariable logistic regression analysis with backward selection was used in the derivation set to predict complexity based on 52 potential indicators of complexity variables registered during hospitalization, removing variables with a p-value >0.1. Calibration of the final model was evaluated by constructing a calibration curve, estimating the calibration slope, calculating the difference between the mean observed proportion and mean predicted proportion of patients with high complexity (calibration-in-the-large) and the Brier score (overall measure of accuracy) in the derivation and validation set. The predictors from the final model were used to create a comprehensible score using the regression coefficient-based scoring technique.[23] Beta-coefficients were divided by the lowest coefficient and rounded up to the closest integer to generate score points, indicating increasing risk by higher scores. The discriminatory power of the score was assessed by calculating the area under the receiver operating characteristic (AUROC) curve.

The validity of performance measures was investigated by performing internal and external validation. For internal validation we used 1000 bootstrap samples, drawing samples with replacement from the derivation sample.[24] The bootstrap-corrected performance estimates were calculated by subtracting the optimism from the performance of the original model. The 95% confidence intervals (CI) for the bootstrapped performance measures were derived using the percentile method. External validation was made by estimating the same performance measures in the external validation cohort (temporal validation).

The clinical usefulness of the developed score was assessed with a decision-curve analysis investigating whether the use of the complexity score instead of the CCI alone was associated with benefit gains relative to the prediction complexity.[25]

Applying PCA, CCI and PCCL, we calculated the score of each patient and split the patient sample into a high and a low risk group. The reference point (cut-off) of each scoring system was chosen in order to make the frequency of patients in the high-risk category as close as possible to 30% (i.e. approximating the frequency of observed complex patients). To determine the accuracy of this method to predict complexity, we estimated sensitivity, specificity, and positive and negative predictive value in both the derivation and validation set for PCA and in the derivation set for CCI and PCCL.

R version 3.3.1 was used for statistical analysis.

Results

A total of 1,889 patients were included in the study (figure 1). Patients enrolled before February 16, 2017 were allocated to the derivation sample (n = 1,407), patients enrolled after this date (n = 482) were allocated to the temporal validation sample. In the derivation cohort, 447 patients (31.8%) were clinically judged as complex, and 116 (24.1%) patients in the validation cohort. The patients in the two cohorts presented with similar baseline characteristics (table 1 and supplementary material table S1 and S2). The overall median age was 80 years (interquartile range 75 to 86 years).

Table 1: Baseline characteristics for all patients (derivation and validation cohort) stratified by complexity, as number and percentage or median and inter-quartile range for categorical and continuous variables, respectively.

	Overall (N=1889)	Non-complex (N=1326)	Complex (N=563)
	n (%) or median [interquartile range]		
Age			
≥ 80 years	579 (31)	442 (33)	137 (24)
70 to 79 years	437 (23)	304 (23)	133 (24)
60 to 69 years	322 (17)	211 (16)	111 (20)
< 60 years	537 (28)	363 (27)	174 (31)
Missing	14 (0.7)	6 (0.5)	8 (1.4)
Gender			
Male	1002 (53)	693 (52)	309 (55)
Female	873 (46)	627 (47)	246 (44)
Missing	14 (0.7)	6 (0.5)	8 (1)

Living area[1]			
Urban	611 (32)	453 (34)	158 (28)
Rural	1238 (65)	848 (64)	390 (69)
Missing	40 (2)	25 (1)	15 (3)
Marital status			
Single	331 (17)	252 (19)	79 (14)
Couple	636 (34)	429 (32)	207 (37)
Widowed	916 (48)	641 (48)	275 (49)
Missing	6 (0.3)	4 (0.3)	2 (0.4)
Hospitalization within last 12 months	673 (36)	452 (34)	221 (39)
Medication[2]			
Antineoplastic and immunomodulating agents at admission	70 (4)	38 (3)	32 (6)
Nervous system at admission	1340 (71)	918 (69)	422 (75)
Systemic hormonal preparations, excluding sex hormones and insulins at discharge	524 (28)	318 (24)	206 (37)
High costs during hospitalization[3]			
For imaging procedures	485 (26)	255 (19)	230 (41)
For laboratory analysis	482 (25)	203 (15)	279 (50)
High nurse workload[4]	475 (25)	203 (15)	272 (48)
Charlson Comorbidity Index	2 [0; 4]	2 [0; 3]	3 [1; 5]
Principal or concomitant diagnosis at discharge			
Cancer[5]	225 (12)	136 (10)	89 (16)
COPD[6]	186 (10)	124 (9)	62 (11)
Dementia[7]	163 (9)	125 (9)	38 (7)
Depression[8]	209 (11)	140 (11)	69 (12)
Heart failure[9]	327 (17)	206 (15)	121 (21)
Pneumonia[10]	244 (13)	159 (12)	85 (15)
Sepsis[11]	229 (12)	132 (10)	97 (17)
Stroke[12]	90 (5)	65 (5)	25 (4)
Substance abuse[13]	212 (11)	129 (10)	83 (15)
Syncope[14]	81 (4)	67 (5)	14 (2)
Malnutrition[15]	265 (14)	122 (9)	143 (25)
Multimorbidity			
Low (number of diagnoses ≤ 6)	510 (27)	435 (33)	75 (13)

[1] Defined according to the Swiss Federal Statistical Office based on place of residence
[2] Group of drugs according to ATC classification
[3] Defined as costs of all imaging procedures or medication during hospital stay above 75th percentile
[4] Defined as sum of hours of all nursing work (incl. sitting guard) during hospital stay above 75th percentile
[5] ICD10-codes B21, C00 through C97, Z03.1
[6] ICD10-codes J44
[7] ICD10-codes F00 through F03, F05.0, F05.1
[8] ICD10-codes F20.4, F25.1, F31.3 F31.4, F31.5, F32, F33, F41.2, F92.0
[9] ICD10-codes I50
[10] ICD10-codes A48.1, B01.2, B05.2, J10.0, J11.0, J12 through J18, J68.0, J69, J85.1, O74.0, U69.00
[11] ICD10-codes A02.1, A20.7, A22.7, A26.7, A32.7, A39.2, A39.3, A39.4, A40, A41, A42.7, B37.7
[12] ICD10-codes I63
[13] ICD10-codes F10 through F19, F53, F66.8, F66.9
[14] ICD10-codes R55
[15] ICD10-codes E40 through E46

Middle (number of diagnoses > 6 and <14)[16]	841 (44)	603 (45)	238 (42)
High (number of diagnoses ≥ 14)	524 (28)	282 (21)	242 (43)
PCCL	3 [2; 4]	3 [1; 4]	4 [3; 4]
No complication or comorbidity	380 (20)	312 (23)	68 (12)
Light complication or comorbidity	29 (1)	21 (2)	8 (1)
Moderate complication or comorbidity	292 (15)	233 (18)	59 (10)
Severe complication or comorbidity	533 (28)	409 (31)	124 (22)
Very severe complication or comorbidity	641 (34)	345 (26)	296 (53)
Missing	14 (0.7)	6 (0.5)	8 (1.4)
Abnormal creatinine level[17]			
At admission and discharge	368 (19)	241 (18)	127 (23)
At admission only	182 (10)	106 (8)	76 (13)
At discharge only	63 (3)	34 (3)	29 (5)
Missing	364 (19)	311 (23)	53 (9)
Leukocytosis[18]			
At admission and discharge	77 (41)	47 (3)	30 (5)
At admission only	19 (1)	8 (<1)	11 (2)
At discharge only	13 (<1)	5 (<1)	8 (1)
Missing	351 (19)	306 (23)	45 (8)
Patient destination			
Death	134 (7)	91 (7)	43 (8)
Home	1178 (62)	873 (66)	305 (54)
Hospital	191 (10)	119 (9)	72 (13)
Nursing home	155 (8)	108 (8)	47 (8)
Rehabilitation	171 (9)	101 (8)	70 (12)
Others and missing	60 (3)	24 (3)	26 (5)

After backward selection, 11 of the 52 potential predictors were used to derive the PCA score (Table 2). Besides diagnosis-related factors, they represented demographic characteristic, hospital variables, medication and laboratory values. Highest score points were assigned to leukocytosis (at discharge only, 16 points, and at admission and discharge, 10 points) followed by age under 60 years, high nurse workload (costs above 75th percentile for nursing expenses), and abnormal serum creatinine at discharge (≥100 µmol/l).

Table 2: PCA score weighted according to coefficients

Variable	Coefficient (95% CI)	Score points
Age		
≥ 80 years	Reference	
70 to 79 years	0.36 (0, 0.72)	3

[16] Between 25th and 75th percentile
[17] Defined as creatinine ≥100 µmol/l
[18] Defined as leukocyte count ≥20 G/l

60 to 69 years	0.5 (0.1, 0.9)	5
< 60 years	0.94 (0.56, 1.31)	9
Elective admission	0.36 (0.03, 0.69)	3
High costs during hospitalization[19]		
For imaging procedures	0.6 (0.31, 0.9)	6
For laboratory analysis	0.77 (0.46, 1.09)	7
High nurse workload[20]	0.93 (0.61, 1.26)	9
Malnutrition[21]	0.47 (0.1, 0.84)	4
Multimorbidity		
Number of diagnoses ≤ 6	Reference	
Number of diagnoses > 6 and <14[22]	0.61 (0.25, 0.96)	6
Number of diagnoses ≥ 14[23]	0.78 (0.36, 1.2)	7
Medication at admission[24]		
Antineoplastic and immunomodulating agents	0.85 (0.16, 1.54)	8
Nervous system	0.33 (0.04, 0.63)	3
Abnormal creatinine level[25]		
None	Reference	
At admission only	0.23 (-0.22, 0.68)	2
At admission and discharge	0.11 (-0.22, 0.45)	1
At discharge only	0.96 (0.29, 1.63)	9
Leukocytosis[26]		
None	Reference	
At admission only	0.11 (-0.49, 0.71)	1
At admission and discharge	1.12 (-0.04, 2.29)	10
At discharge only	1.68 (0.18, 3.18)	16
Intercept	-2.93 (-3.39, -2.46)	NA

The prediction model showed a good accuracy, with a Brier score of 0.17 and 0.15 in internal and external validation, respectively. The calibration curve showed fair agreement between predicted and observed proportions of complexity in the derivation cohort and slightly lower observed proportions than predicted probabilities in the validation cohort (graphs not shown). The calibration-in-the-large coefficient of -0.51 (95% CI -0.74 to -0.27) in the validation cohort implies that the mean observed proportion was lower than

[19] Defined as costs of all imaging procedures or medication during hospital stay above 75th percentile
[20] Defined as sum of hours of all nursing work (incl. sitting guard) during hospital stay above 75th percentile
[21] ICD10-codes E40 through E46
[22] Between 25th and 75th percentile
[23] Above 75th percentile
[24] Group of drugs according to ATC classification
[25] Defined as serum creatinine ≥100 µmol/l
[26] Defined as blood leukocyte count ≥20 G/l

the mean predicted probability. However, the calibration curve slope was satisfactory in internal and external validation (0.93 [95% CI 0.80 to 1.05] and 0.96 [95% CI 0.74 to 1.18]), respectively.

The median score was 17 points in the derivation and validation cohort (mean 18.77 and 19.03, respectively). The minimal score was 0 points in both cohorts, the maximal score reached was 54 points in the derivation cohort and 53 points in the validation cohort (theoretically maximal 81 score points). The score's area under the receiver operating characteristic (AUROC) curve was 0.77 (95% CI 0.74 to 0.79) and 0.78 (95% CI 0.74 to 0.82) in internal and external validation.

Table 3: Stratification of Observed vs. predicted complex patients applying the PCA score.

	Score points	Risk category of complexity	Patients in each category	Complex patients	Estimated risk of complexity
Derivation set	< 24	Low risk	991 (70%)	193 (19%)	19
	≥ 24	High risk	416 (30%)	254 (61%)	61
Validation set	< 24	Low risk	347 (72%)	50 (14%)	20
	≥ 24	High risk	135 (28%)	66 (49%)	62

We classified patients as low and high complexity risk (table 3) according to the selected cut-off of 24 points (approximating the frequency of observed complex patients of 30%). The proportion of patients categorized as complex (i.e. score ≥ 24 points) was 30% and 28% in the derivation and validation dataset, respectively. Sensitivity was 57% in both the derivation and validation dataset. The specificity was 83% and 81%, respectively. Positive predictive values were 61% and 49% in the derivation and validation cohort, respectively, while negative predictive values were 81% and 86%, respectively. The discriminatory power of the PCA score was robust with an AUROC of 0.77 (95% CI 0.74 to 0.79) in internal validation (bootstrap-corrected value) and 0.78 (95% CI 0.74 to 0.82) in external validation (table 4 and supplementary figure S2).

Table 4: Measures of performance to predict complexity

	PCA, derivation set % (95%-CI)	PCA, validation set % (95%-CI)	CCI, validation set % (95%-CI)	PCCL, validation set % (95%-CI)
Sensitivity	57 (52-61)	57 (47-66)	41 (32-50)	61 (51-70)
Specificity	83 (81-85)	81 (77-85)	75 (71-80)	75 (70-79)
Positive predictive value	61 (59-66)	49 (40-58)	34 (26-43)	42 (34-50)
Negative predictive value	81 (78-83)	86 (81-89)	80 (75-84)	86 (82-90)

Misclassification error	25 (28-23)	25 (29-21)	33 (37-29)	28 (33-24)
AUROC[27]	0.77 (0.74-0.79)[28]	0.78 (0.74-0.82)	0.62 (0.56-0.68)	0.69 (0.64-0.75)

In comparison, predictive accuracy of the CCI was lower compared to the PCA score. The AUROCs were low with 0.58 (95% CI 0.55 to 0.62) and 0.62 (95% CI 0.56 to 0.68) in the derivation and validation cohort, respectively (table 4). Sensitivity of the CCI reached 36% (95% CI 31% to 40%) and 41% (95% CI 31% to 50%) in derivation and validation cohort, respectively, while specificity was 76% (95% CI 73% to 78%) and 75% (95% CI 71% to 80%), respectively. The decision curve analysis (supplementary figure S1) indicates a superiority of the PCA score compared to the CCI to predict complexity.

AUROCs of PCCL were between those of CCI and PCA score with 0.64 (95% CI 0.61 to 0.67) and 0.69 (95% CI 0.64 to 0.75) in the derivation and validation cohort, respectively (table 4). Sensitivity was 52% (95% CI 47% to 56%) and 61% (95% CI 51% to 70%), respectively, while specificity was 73% (95% CI 71% to 76%) and 75% (95% CI 70% to 79%).

Discussion

We derived and validated the PCA score that accurately assessed patient complexity in medical inpatients. The final score of eleven independent and readily available factors, included age, hospital variables, diagnosis related aspects and laboratory variables. The PCA score showed overall good performance with a discriminatory power of 0.78 that surpasses other comorbidity-based tools such as the Charlson comorbidity index and the PCCL.

In this cohort of medical inpatients, 32% and 24% were considered “complex” by the treating physician, in the derivation and the validation cohort, respectively. This first estimate of patient complexity in the hospital setting is consistent with a previous assessment in an outpatient population where 26% of total 4,302 patients were categorized as being complex by a primary care physician.[1] Based on these data, the authors later derived a model to identify around 20% of 143,372 primary care patients as complex.

[27] Area under receiver operating characteristic
[28] Bootstrap-corrected from internal validation

Using the model and outpatient CCI or PCCL, only modest agreement between the methods was observed (37% and 40%, respectively).[2] Therefore, a tool not solely based on multimorbidity, such as the newly developed PCA score, seems to better identify complex patients.

In the present study, age was an inverse indicator of complexity. In a previous study of outpatients, mean age of complex patients was 60 years versus 48 years in non-complex patients.[1] Nonetheless, the same study reported noteworthy age-related variability: in younger patients the association of certain diagnoses (e.g. alcohol-related diseases) with complexity was stronger, and deprivation as contributor to complexity is independent of age.[1,5] In our setting, discharge planning processes for older patients may be better established (e.g. including hospital social services, decision making based on patient's provision and possibility for indiscriminate discharge to geriatric rehabilitation facilities or nursing homes) compared to younger patients.[1,9,26,27] Treating physicians may therefore perceive the discharge planning process of some younger patients as difficult and categorize these patients as complex. Furthermore, young non-complex patients may more often be treated as outpatients or by specialist's clinics instead of our tertiary care general internal medicine ward. Elective admissions to a tertiary hospital may represent a cohort of rather complex patients preselected by primary care physicians and smaller hospitals (21% elective admissions in complex patients versus 14% in non-complex patients). The inverse relationship between age and complexity, and the relationship between elective admissions and complexity may therefore represent structural incentives to hospitalize complex younger patients which overburden outpatient care. It is also possible that these patients are only perceived as more complex by the treating physician because patients admitted directly to the medical ward are pending initial work-up otherwise provided in the emergency department.

Patients with high costs of imaging procedures may reflect the patients with more severe diseases or more diagnosis uncertainty. Similarly, high costs for laboratory analysis may be explained by a higher need of costly or repeated measurements in more complex patients. High costs for care/nursing were indicators of complexity highlighting some concordance between the nurse workload and the medical complexity.

In our study multimorbidity (defined as a number of more than 6 diagnoses) was an indicator of complexity. Comorbidity-based scores, i.e., the CCI, are commonly used to identify complex patients.

Indeed, in the study of Grant et al. the proportion of multimorbid patients identified by a CCI of 2 or more was higher in complex patients, i.e., 26% of complex patients were multimorbid versus 9% of non-complex patients.[1] However, many multimorbid patients are not complex and not all complex patients are multimorbid. In our cohort (derivation and validation datasets together) 34% of polymorbid patients (CCI ≥2) were complex versus 24% in the group of CCI <2. Comparably, nearly one half of patients with a CCI of 2 or greater were classified as non-complex in the study of Grant et al.[1] Therefore, a system to identify complexity should not depend on diagnosis alone.

In the PCA score, malnutrition was a risk factor of complexity. Malnutrition in hospitalized patients is associated with more complications, increased mortality, longer hospital stays and higher costs [28,29]. Therefore, malnutrition and complexity may both reflect a cluster of severe and chronic disease as well as socioeconomic circumstances.[1]

Antineoplastic and immunomodulating medication at admission was an indicator of complexity. These drugs are used for oncologic patients, but also in patients with rheumatologic disease or after receiving organ transplants. These patients may be complex because of challenging infectious diseases, end-of-life issues and interdisciplinary care. Abnormal values of serum creatinine and leukocyte counts at discharge were denoting complexity whether the values were normal or abnormal at admission. These patients may also requiring more interaction between specialists and may complicate the discharge process.

Personal characteristics or mental health issues and use of psychoactive medication, i.e., narcotics, selective serotonin reuptake inhibitors, benzodiazepines, smoking cessation agents and antipsychotics, have been described as characterizing complex patients, especially in younger patients.[1] This is in line with the observation that in the PCA score, use of medication affecting the nervous system at admission (including antipsychotics, mood-stabilizers, sedatives, analgesics including opioids, anticonvulsive medication and anti-dementia drugs) was an indicator of complexity. These patients may challenge the known pathways of the healthcare system, e.g. by parallel use of general internal medicine and psychiatric resources.

There are several limitations of the study. First, we used physician's assessment to define complexity, which per definition is subjective. Nonetheless, there is no better standard reference (gold standard) and the proportion of patients identified as complex was similar in previous studies.[1,2] Second, the PCA

score has been developed at a single tertiary hospital in Switzerland and therefore may not be generalizable to other settings, e.g. other health care systems. However, costs and nursing workload are not measured as absolute values but as those above the 75th percentile, making it transferable to other settings. Also, some patients may appear as complex in one setting, while they will be judged as non-complex in other settings (e.g. primary care vs. university hospital), nevertheless the proportion of complex patients in out setting was similar to the one in primary care.[1] Therefore, in other health systems the final indicators may vary, which might be considered when validating the PCA score. Third, it is likely that our model does not consider every important indicator, but it allows deriving an easily usable tool which kept its fair sensitivity and good specificity in our external validation. Fourth, the PCA score includes values available only at discharge, which makes patient-aimed interventions during hospitalization difficult. This is however also true for alternative assessment tools, such as the CCI and the PCCL, which had a lower performance in identifying complex patients in our cohort. Fifth, imputation of missing data may have changed the outcome of the study. However, potential predictors with more than 25% missing data were excluded. Sixth, most of the included indicators are not modifiable. For example, a patient will still be complex if receiving less imaging procedures to reduce costs.

To our knowledge, the PCA score is the first tool to identify complex medical patients in the hospital setting. It can easily be calculated and is therefore predestined to be used for population-based studies as it does not involve individual judgement of a physician. With its prospective design and inclusion of a large number of medical inpatients, this study has a strong design.

Identification of complex patients by this simple tool using electronically available data may help monitoring the proportion of complex patients in the hospital setting and comparing patient complexity level between hospitals. Thereby, the PCA score might improve the monitoring of resources distribution and coordination of care, e.g. by flagging complex patients to general practitioners or social workers for closer follow-up or low-threshold service.

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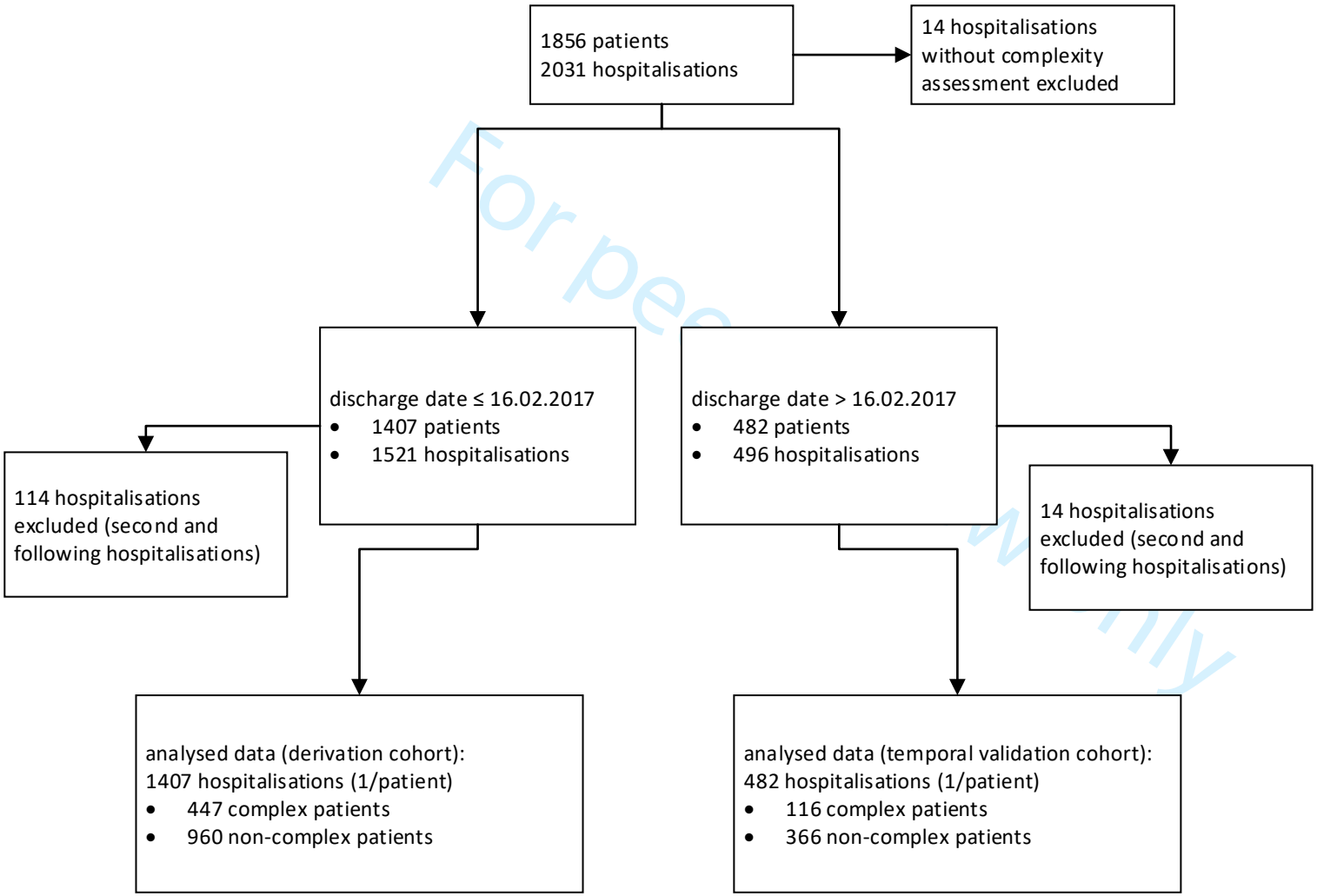
Figure 1 caption

Flow chart. Derivation sample (derivation and internal validation cohort) and external validation sample (temporal validation cohort).



Supplementary Material

Table S1: Baseline characteristics for derivation cohort stratified by complexity.

	Overall (N=1889)	Non-complex (N=1326)	Complex (N=563)
	n (%) or median [interquartile range]		
Age			
≥ 80 years	447 (32)	337 (35)	110 (25)
70 to 79 years	327 (23)	218 (23)	109 (24)
60 to 69 years	239 (17)	152 (16)	87 (19)
< 60 years	391 (28)	251 (26)	140 (31)
Missing	3 (0.2)	2 (0.2)	1 (0.2)
Gender			
Male	748 (53)	494 (51)	254 (57)
Female	656 (47)	464 (48)	192 (43)
Missing	3 (0.2)	2 (0.2)	1 (0.2)
Living area[1]			
Urban	460 (33)	335 (35)	125 (28)
Rural	923 (66)	606 (63)	317 (71)
Missing	24 (2)	19 (2)	5 (1)
Marital status			
Single	477 (34)	306 (32)	171 (38)
Couple	673 (48)	458 (48)	215 (48)
Widowed	252 (18)	193 (20)	59 (13)
Missing	5 (0.4)	3 (0.3)	2 (0.4)
Hospitalization within last 12 months	480 (34)	317 (33)	163 (36)
Medication[2]			
Antineoplastic and immunomodulating agents at admission	43 (3)	20 (2)	23 (5)
Nervous system at admission	1001 (71)	666 (69)	335 (75)
Systemic hormonal preparations, excluding sex hormones and insulins at discharge	253 (18)	163 (17)	90 (20)
High costs during hospitalization[3]			
For imaging procedures	367 (26)	179 (19)	188 (42)
For laboratory analysis	365 (26)	147 (15)	218 (49)
High nurse workload[4]	358 (25)	146 (15)	212 (47)
Charlson Comorbidity Index	2 [0; 4]	2 [0; 3]	2.5 [1; 5]
Principal or concomitant diagnosis at discharge			
Cancer[5]	175 (12)	104 (11)	71 (16)
COPD[6]	139 (10)	91 (9)	48 (11)
Dementia[7]	120 (8)	89 (9)	31 (7)
Depression[8]	148 (10)	94 (10)	54 (12)
Heart failure[9]	235 (17)	143 (15)	92 (21)

[1] Defined according to the Swiss Federal Statistical Office based on place of residence
[2] Group of drugs according to ATC classification
[3] Defined as costs of all imaging procedures or medication during hospital stay above 75th percentile
[4] Defined as sum of hours of all nursing work (incl. sitting guard) during hospital stay above 75th percentile
[5] ICD10-codes B21, C00 through C97, Z03.1
[6] ICD10-codes J44
[7] ICD10-codes F00 through F03, F05.0, F05.1
[8] ICD10-codes F20.4, F25.1, F31.3 F31.4, F31.5, F32, F33, F41.2, F92.0
[9] ICD10-codes I50

Pneumonia[10]	186 (13)	115 (12)	71 (16)
Sepsis[11]	162 (11)	88 (9)	74 (17)
Stroke[12]	72 (5)	50 (5)	22 (5)
Substance abuse[13]	154 (11)	90 (9)	64 (14)
Syncope[14]	68 (5)	55 (6)	13 (3)
Malnutrition[15]	190 (13)	82 (8)	108 (24)
Multimorbidity			
Low (number of diagnoses ≤ 6)	387 (27)	322 (33)	65 (14)
Middle (number of diagnoses > 6 and <14)[16]	642 (46)	443 (46)	199 (44)
High (number of diagnoses ≥ 14)	375 (27)	193 (20)	182 (41)
PCCL			
No complication or comorbidity	297 (21)	239 (25)	58 (13)
Light complication or comorbidity	22 (2)	15 (2)	7 (2)
Moderate complication or comorbidity	211 (15)	161 (17)	50 (11)
Severe complication or comorbidity	390 (28)	289 (30)	101 (23)
Very severe complication or comorbidity	484 (34)	254 (26)	230 (51)
Missing	3 (0.2)	2 (0.2)	1 (0.2)
Abnormal creatinine level[17]			
At admission and discharge	278 (20)	181 (19)	97 (22)
At admission only	128 (9)	72 (7)	56 (12)
At discharge only	50 (4)	24 (2)	26 (6)
Missing	275 (19)	229 (24)	46 (10)
Leukocytosis[18]			
At admission and discharge	15 (1)	6 (0.6)	9 (2)
At admission only	60 (4)	35 (4)	25 (6)
At discharge only	11 (0.8)	3 (0.3)	8 (2)
Missing	260 (18)	223 (23)	37 (8)
Patient destination			
Death	105 (7)	73 (8)	32 (7)
Home	875 (62)	621 (65)	254 (57)
Hospital	141 (10)	85 (9)	56 (12)
Nursing home	109 (8)	79 (8)	30 (7)
Rehabilitation	138 (10)	79 (8)	59 (13)
Others and missing	39 (3)	23 (2)	16 (4)

Table S2: Baseline characteristics for all patients in the validation cohort stratified by complexity.

	Overall (N=1889)	**Non-complex (N=1326)**	**Complex (N=563)**
	n (%) or median [interquartile range]		
Age			
≥ 80 years	132 (27)	105 (29)	27 (23)

[10] ICD10-codes A48.1, B01.2, B05.2, J10.0, J11.0, J12 through J18, J68.0, J69, J85.1, O74.0, U69.00
[11] ICD10-codes A02.1, A20.7, A22.7, A26.7, A32.7, A39.2, A39.3, A39.4, A40, A41, A42.7, B37.7
[12] ICD10-codes I63
[13] ICD10-codes F10 through F19, F53, F66.8, F66.9
[14] ICD10-codes R55
[15] ICD10-codes E40 through E46
[16] Between 25th and 75th percentile
[17] Defined as creatinine ≥100 µmol/l
[18] Defined as leukocyte count ≥20 G/l

70 to 79 years	110 (23)	86 (23)	24 (21)
60 to 69 years	83 (17)	59 (16)	24 (21)
< 60 years	146 (30)	112 (31)	34 (29)
Missing	11 (2)	4 (1)	7 (6)
Gender			
Male	254 (53)	199 (54)	55 (47)
Female	217 (45)	163 (44)	54 (47)
Missing	11 (2)	4 (1)	7 (6)
Living area[1]			
Urban	151 (31)	118 (32)	33 (28)
Rural	315 (65)	242 (66)	73 (63)
Missing	16 (3)	6 (2)	10 (9)
Marital status			
Single	159 (33)	123 (34)	36 (31)
Couple	243 (50)	183 (50)	60 (52)
Widowed	79 (16)	59 (16)	20 (17)
Missing	1 (0.2)	1 (0.3)	0 (0)
Hospitalization within last 12 months	193 (40)	135 (37)	58 (50)
Medication[2]			
Antineoplastic and immunomodulating agents at admission	27 (6)	18 (5)	9 (8)
Nervous system at admission	339 (70)	252 (69)	87 (75)
Systemic hormonal preparations, excluding sex hormones and insulins at discharge	105 (22)	73 (20)	32 (28)
High costs during hospitalization[3]			
For imaging procedures	118 (24)	76 (21)	42 (36)
For laboratory analysis	117 (24)	56 (15)	61 (53)
High nurse workload[4]	117 (24)	57 (15.6)	60 (52)
Charlson Comorbidity Index	2 [0; 4]	2.00 [0; 3]	3 [1; 5]
Principal or concomitant diagnosis at discharge			
Cancer[5]	50 (10)	50 (10)	50 (10)
COPD[6]	32 (9)	32 (8)	32 (9)
Dementia[7]	18 (15)	18 (15)	18 (15)
Depression[8]	47 (10)	47 (10)	47 (10)
Heart failure[9]	33 (9)	33 (9)	33 (9)
Pneumonia[10]	14 (12)	14 (12)	14 (12)
Sepsis[11]	43 (9)	43 (9)	43 (9)
Stroke[12]	36 (10)	36 (9)	36 (10)
Substance abuse[13]	7 (6)	7 (6)	7 (6)
Syncope[14]	61 (13)	61 (13)	61 (13)

[1] Defined according to the Swiss Federal Statistical Office based on place of residence
[2] Group of drugs according to ATC classification
[3] Defined as costs of all imaging procedures or medication during hospital stay above 75th percentile
[4] Defined as sum of hours of all nursing work (incl. sitting guard) during hospital stay above 75th percentile
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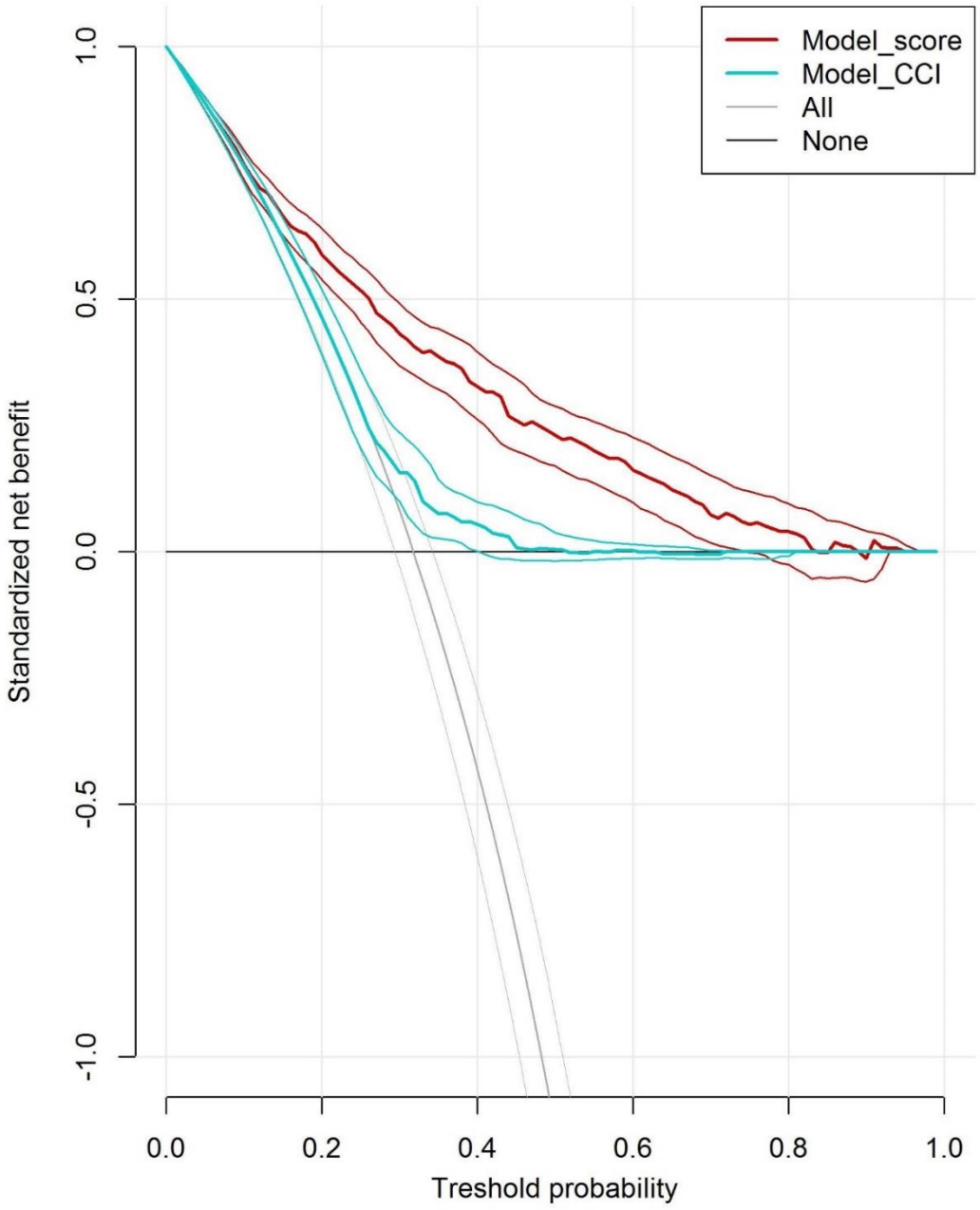
[11] ICD10-codes A02.1, A20.7, A22.7, A26.7, A32.7, A39.2, A39.3, A39.4, A40, A41, A42.7, B37.7
[12] ICD10-codes I63
[13] ICD10-codes F10 through F19, F53, F66.8, F66.9
[14] ICD10-codes R55

Malnutrition[15]	46 (13)	46 (13)	46 (13)
Multimorbidity			
Low (number of diagnoses ≤ 6)	123 (25)	113 (31)	10 (9)
Middle (number of diagnoses > 6 and <14)[16]	199 (41)	160 (44)	39 (34)
High (number of diagnoses ≥ 14)	149 (31)	89 (24)	60 (52)
PCCL			
No complication or comorbidity	83 (1)	73 (20)	10 (9)
Light complication or comorbidity	7 (1)	6 (2)	1 (0.9)
Moderate complication or comorbidity	81 (17)	72 (20)	9 (8)
Severe complication or comorbidity	143 (30)	120 (33)	23 (20)
Very severe complication or comorbidity	157 (33)	91 (24)	66 (57)
Missing	11 (2)	4 (1)	7 (6)
Abnormal creatinine level[17]			
At admission and discharge	90 (19)	60 (16)	30 (26)
At admission only	54 (11)	34 (9)	20 (17)
At discharge only	13 (2.7)	10 (3)	3 (3)
Missing	89 (18)	82 (22)	7 (6)
Leukocytosis[18]			
At admission and discharge	4 (0.8)	2 (0)	2 (2)
At admission only	17 (3)	12 (3)	5 (4)
At discharge only	2 (0.4)	2 (0.5)	0 (0)
Missing	91 (19)	83 (23)	8 (7)
Patient destination			
Death	134 (7)	91 (7)	43 (8)
Home	1178 (62)	873 (66)	305 (54)
Hospital	191 (10)	119 (9)	72 (13)
Nursing home	155 (8)	108 (8)	47 (8)
Rehabilitation	171 (9)	101 (8)	70 (12)
Others and missing	60 (3)	34 (3)	26 (5)

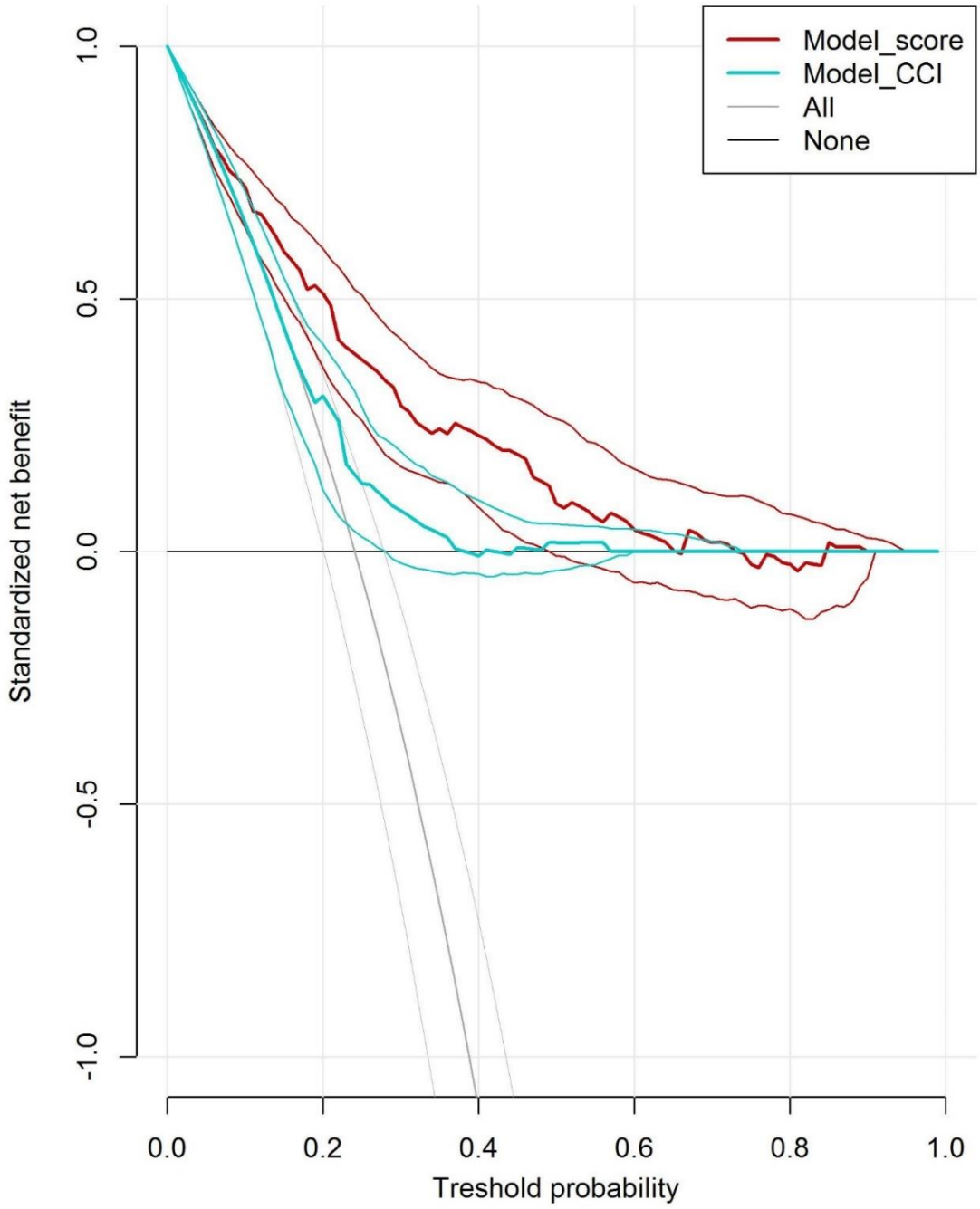
[15] ICD10-codes E40 through E46
[16] Between 25th and 75th percentile
[17] Defined as creatinine ≥100 µmol/l
[18] Defined as leukocyte count ≥20 G/l

Supplementary figure S1. Decision curve analysis. A, derivation dataset. B, validation dataset. CCI, Charlson comorbidity index.

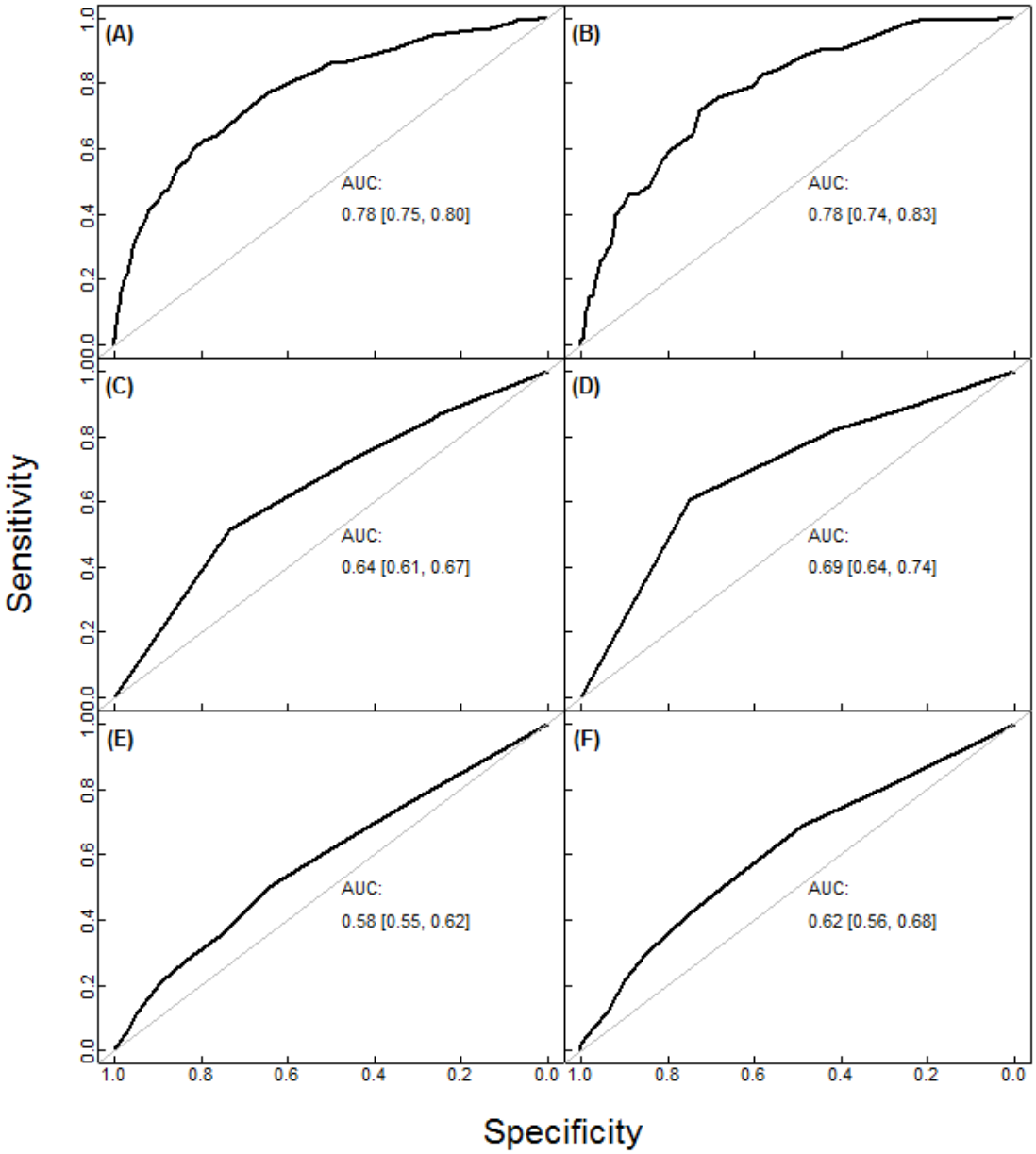
A)



B)



Supplementary figure S2. A, PCA score, derivation dataset. B, PCA score, validation dataset. C, PCCL, derivation dataset. D, PCCL, validation dataset. E, CCI, derivation dataset. F, CCI, validation dataset.



Reporting checklist for prediction model development and validation study.

Based on the TRIPOD guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the TRIPODreporting guidelines, and cite them as:

Collins GS, Reitsma JB, Altman DG, Moons KG. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): The TRIPOD statement.

		Reporting Item	Page Number
Title			
	#1	Identify the study as developing and / or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract			

	#2	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	3
Introduction			
	#3a	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	5
	#3b	Specify the objectives, including whether the study describes the development or validation of the model or both.	5
Methods			
Source of data	#4a	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	6
Source of data	#4b	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	6
Participants	#5a	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	6
Participants	#5b	Describe eligibility criteria for participants.	6
Participants	#5c	Give details of treatments received, if relevant	n/a

Outcome	#6a	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	6
Outcome	#6b	Report any actions to blind assessment of the outcome to be predicted.	n/a
Predictors	#7a	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured	7
Predictors	#7b	Report any actions to blind assessment of predictors for the outcome and other predictors.	n/a
Sample size	#8	Explain how the study size was arrived at.	6
Missing data	#9	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	8-9
Statistical analysis methods	#10a	If you are developing a prediction model describe how predictors were handled in the analyses.	8-9
Statistical analysis methods	#10b	If you are developing a prediction model, specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	8-9
Statistical analysis methods	#10c	If you are validating a prediction model, describe how the predictions were calculated.	8-9
Statistical analysis methods	#10d	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	8-9

Statistical analysis methods	#10e	If you are validating a prediction model, describe any model updating (e.g., recalibration) arising from the validation, if done	8-9
Risk groups	#11	Provide details on how risk groups were created, if done.	n/a
Development vs. validation	#12	For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.	8-9
Results			
Participants	#13a	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	9 + 24
Participants	#13b	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	9 + 18
Participants	#13c	For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors and outcome).	9 + 18
Model development	#14a	If developing a model, specify the number of participants and outcome events in each analysis.	9
Model development	#14b	If developing a model, report the unadjusted association, if calculated between each candidate predictor and outcome.	9

Model specification	#15a	If developing a model, present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	9 + 21
Model specification	#15b	If developing a prediction model, explain how to the use it.	10 + 21
Model performance	#16	Report performance measures (with CIs) for the prediction model.	10, 11, 23
Model-updating	#17	If validating a model, report the results from any model updating, if done (i.e., model specification, model performance).	10-11
Discussion			
Limitations	#18	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	14
Interpretation	#19a	For validation, discuss the results with reference to performance in the development data, and any other validation data	11-14
Interpretation	#19b	Give an overall interpretation of the results, considering objectives, limitations, results from similar studies, and other relevant evidence.	11-14
Implications	#20	Discuss the potential clinical use of the model and implications for future research	14

Other information

Supplementary information	#21	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	25
Funding	#22	Give the source of funding and the role of the funders for the present study.	2