CHAPTER 4

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VALIDATING AND IMPROVING ACG'S FUTURE HOSPITALIZATION AND HIGH-COST PREDICTION MODELS FOR DUTCH PRIMARY CARE

Shelley-Ann M Girwar, Marta Fiocco, Stephen P Sutch, Mattijs E Numans, Marc A Bruijnzeels

Submitted

Abstract

Introduction

The rise in healthcare costs, caused by older and more complex patient populations, requires Population Health Management approaches including risk stratification. With risk stratification, patients are assigned individual risk scores based on medical records. These patient stratifications focus on future high costs and expensive care utilization such as hospitalization, for which different models exist. With this study, we validated the accuracy of risk prediction scores for future hospitalization and high healthcare costs, calculated by the ACG's risk stratification models, using Dutch primary care health data registries. In addition, we aimed to adjust the US-based predictive models for Dutch primary care.

Methods

The statistical validity of the existing models was assessed. In addition, the underlying prediction models were trained on 95,262 patients' data from de Zoetermeer region and externally validated on data of 48,780 patients from Zeist, Nijkerk and Urk. Information on age, sex, number of GP visits, International Classification of Primary Care coded information on the diagnosis and Anatomical Therapeutic Chemical Classification coded information on the prescribed medications, were incorporated in the model. C-statistics were used to validate the discriminatory ability of the models. Calibrating ability was assessed by visual inspection of calibration plots.

Results

Adjustment of the hospitalization model based on Dutch data improved C-statistics from 0.69 to 0.75, whereas adjustment of the high-cost model improved C-statistics from 0.78 to 0.85, indicating good discrimination of the models. The models also showed good calibration.

Conclusion

In conclusion, the local adjustment of the ACG prediction models, show great potential for use in Dutch primary care, in terms of prediction of future hospitalization and high costs.

Introduction

Multimorbidity is increasingly being recognized as the norm rather than the exception, since patient populations are becoming older and more complex, and patient information is becoming more complete. The increased complexity leads to increased healthcare utilization. In particular, there is a rise in expensive care such as hospital and emergency care, which has a major effect on healthcare costs. To manage these rising health costs, approaches that focus on complete patients' health profiles are needed. Population Health Management is focusing on the coordination of care delivery across specified sub-populations to improve the population's health and care utilization (1, 2). In addition, analysis of routine health registry data is increasingly being used to provide a basis for proactive care interventions, attempting to lower healthcare costs by reducing expensive and avoidable care such as hospital admissions. Risk stratification, the assignment of individual risk scores to patients based on registered health profiles, has proven to be an effective tool in the provision of proactive care. A study by Freund *et al* successfully selected high risk patients for care management programs, using risk stratification (3). Another study has shown that efficient care management approaches using risk stratification have led to reduced hospitalization rates (4).

A wide variety of risk stratification tools exist, with risk predictions for various health and health utilization outcomes, such as the risk for future hospitalization, high healthcare costs, emergency care utilization and even mortality. One of the most frequently used risk stratification tools in primary care is the Johns Hopkins Adjusted Clinical Groups (ACG) system (5), with proven efficacy for prediction of not only health outcomes such as morbidity, but also of different types of future healthcare utilization, such as hospitalization and emergency department visits, and future health costs (6).

Most risk stratification tools predominantly use hospital data, with and without primary care data. However, patient's privacy protection in Europe is complicating the linkage of different health data sources. Performing risk stratification based on primary care routine registry data, extracted from only one source in which essential information from most other relevant sources is present, is a way to overcome the privacy challenge. Evidence of the efficacy and accuracy of risk stratification approaches based on primary care data, is still insufficient in the Netherlands. With this study, we aimed to validate the accuracy of the ACG's risk prediction scores for future hospitalization and high healthcare costs, using Dutch primary care health data registries as input data, and to adjust the US based predictive models for Dutch primary care.

Methods

Design

This study had three aims: 1) assessment of two existing prediction models within the ACG tool, which are based on US data, 2) adjustment of the prediction algorithms towards Dutch primary care data and 3) assessment of the adjusted prediction models.

Assessment of ACG's fixed prediction models (based on US data)

The ACG system, developed by the Johns Hopkins University, includes many different risk prediction models. With this study, two of those existing prediction models were assessed: 1) the 'hospitalization model', estimating probabilities for becoming hospitalized at least once in the following 12 months and 2) the 'high cost model', estimating probabilities for being in the top 5% of the population with the highest healthcare costs in the following 12 months.

The ACG models are existing models, based on years of research with US data. We applied these two ACG models to retrospective Dutch primary care data, available in general practitioners' (GPs) electronic medical records. Subsequently, we assessed model performances, using observed outcomes extracted from historic medical specialty data.

Adjustment of the models, based on Dutch primary care data

In addition to the application and assessment of the fixed prediction models of the ACG tool, we aimed to adjust the two prediction models to the Dutch situation. Therefore, we produced logistic regression models for hospitalization and high-cost with the same predictors used by the ACG, using retrospective data from a Dutch primary care population, and adjusted the coefficients of those predictors.

Assessment of the adjusted models

To assess the performance of both the hospitalization and the high-cost model, we investigated the discriminating and calibrating ability. The discriminating ability relates to how well a prediction model can distinguish those with the outcome from those without, while the calibrating ability relates to the agreement between observed and predicted values (7). The assessment was performed by externally validating the models with retrospective data from a second Dutch primary care population.

Data and study population

For this study, we used data from GP enlisted patient populations in the Netherlands. We used extractions of the GPs' electronic medical records as input data for the applied prediction models, and secondary care (hospital) data for the observed outcomes of the models.

Assessment of ACG's existing prediction models

To assess the ACG's existing prediction models, the models were applied to historic primary care data from 95,262 primary care patients within the Zoetermeer region in the Netherlands. Data from January to December 2014, were extracted from participating GPs' electronic health records and were used as input data for the prediction model. Information on age, sex, number of GP visits, International Classification of Primary Care version 1 (ICPC-1) coded information on the diagnosis and Anatomical Therapeutic Chemical Classification (ATC) coded information on the prescribed medications, were incorporated in the model. We translated ICPC-1 codes, used in Dutch primary care, to the international ICPC-2 codes, required as input for the ACG System. As ICPC-1 codes are sometimes more specific than ICPC-2 codes, we have translated some ICPC-1 codes to International Classification of Diseases 10th revision (ICD-10) codes, a coding system that can also be recognized by the ACG System, rather than to ICPC-2 codes. Translation was based on ICPC-1 and ICPC-2 differences described by Wonca International Classification Committee (8) with additional expert opinions. (supplementary table 1)

The outcome variables for the prediction models were extracted from medical specialty care records, available as microdata from Statistics Netherlands, the Dutch Central Bureau for Statistics. Outcomes extracted from Statistics Netherlands' microdata included information on hospitalization and reimbursed healthcare costs from January to December 2015. In the Netherlands, healthcare costs are reimbursed by health insurers based on mandatory basic health insurance law and only the costs covered by the basic health insurance are included as healthcare costs for this study.

As GP data from 2014 were used, patients were included when registered with one of the participating GP practices for the complete year of 2014, but only when linkage with the Statistics Netherlands database was possible (91.7% of the patients).

Data from the GP's electronic health registries was linked to medical specialty data by encryption of both datasets. To each individual a unique Record Identification Number (RIN) was assigned, based on birth date, gender, and complete postal code. The RINs were the used to link the GP data to the Statistics Netherlands' microdata.

Adjustment of the models, based on Dutch primary care data

For the adjustment of the two US based prediction models, the same data and study population were used as described in previous paragraphs.

Assessment of the adjusted models

To assess the adjusted prediction models, a second study population was used. The study population of 48,780 patients from Zeist, Nijkerk and Urk was used to externally validate the prediction models. Similar retrospective primary and secondary care data were used as described previously.

Statistical Analysis

Firstly, the similarity between the two study populations was assessed. Continuous variables have been tested with t-tests. In case of violation of the normality assumption, a non-parametric test was used. For the categorical variables, chi-squared test was used.

Assessment of ACG's existing prediction models

The ACG System US based hospitalization and high costs models were assessed on model performance. Predicted values, generated by the ACG were compared to the observed outcomes (described in the next section 'Adjustment of the models') by calculation of C-statistics. C-statistics below 0.6 were taken to indicate poor model performance, C-statistics between 0.6 and 0.7 to indicate sufficient model performance and C-statistics above 0.7 indicate good model performance (9).

Adjustment of the models

To adjust the two prediction models to the Dutch primary care data, we used the underlying logistic regressions for hospitalization and high healthcare costs. We estimated the logistic regressions using the first primary care population to find new coefficients for the predictors, resulting in adjusted prediction models.

Dependent variables

The dependent variable for the first model was hospitalization in the second year. Hospitalization in the second year was defined as being at least on hospital admission in the period between January and December 2015 based on Statistic Netherlands microdata.

The dependent variable for the second prediction model was high healthcare costs in the next year. High healthcare costs in the next year was defined as being in the top 5% of highest healthcare costs within the population in the period between January and December 2015, again based on Statistic Netherlands microdata.

Independent variables

Independent variables concern all variables of the ACG's hospitalization and high costs models, which were available in our Dutch data. Next to patients' characteristics such as age, sex and GP care utilization, independent variables included specific diagnoses, types of diagnosis, burden of care categories and mutually exclusive multimorbidity categories, which are based on complete diagnosis and medication profiles of individual patients.

Assessment of the adjusted models

C-statistics were calculated to assess model performance regarding discrimination. First, C-statistics were calculated for the prediction model estimated in the first population, resulting in coefficients adjustments of the fixed AGC models. C-statistics for those adjusted prediction models were compared to those of the existing US-based ACG models. The adjusted models show improvement when C-statistics are higher than those of the US-based ACG models.

Second, the adjusted prediction models were externally validated in a second study population. Both discrimination and calibration were estimated. Calibration was assessed by dividing the validation dataset population into deciles based on ascending predicted values for the different outcomes. For each group the mean observed and expected values were plotted in a calibration plot. Models with a 45-degree angle plot (mean observed value equals mean expected value) are considered perfectly calibrated. Models below this reference line are overestimating, whereas models above it are underestimating.

Privacy

Primary care patients were informed about the use of their data for research purposes. Patients were given the opportunity to opt out.

Patient data were encrypted by Statistics Netherlands under strict rules to secure individuals´ privacy. Linkage and analyses of the data was performed within the secured environment of Statistics Netherlands.

Results

Population Characteristics

In table 1 the differences for various characteristics between the two study populations are shown. The two populations are comparable with respect to the percentage of females within the population, the mean number of GP visits in 2014 and the percentage of people hospitalized in 2015. The mean age shows a difference of one year between the two populations.

Table 1: Population characteristics; differences between the populations (Zoetermeer versus Nijkerk + Urk + Zeist).

	Total population	**Zoetermeer (n= 95, 262)**	**Nijkerk, Urk, Zeist (n= 48, 780)**
Mean age in years (SD)	39.5 (22.2)	39.9 (22.0)	38.8 (22.8)
Sex (% females)	50.9	51.4	50.0
Number of GP visits < 2 (n; %) >= 2 (n; %)	 66, 643; 46,3% 77, 399; 53,7%	 41, 480; 43.5% 53, 782; 56.5%	 16, 834; 34.5% 31, 946; 65.5%
Hospitalized in 2015 (%)	9.9	10.1	9.4
Median costs in 2015	€ 479,99	€ 531,18	€ 393,35

Statistical Assessment

Assessment of ACG’s existing prediction models (based on US data)

To assess the performance of the existing ACG models, which are based on US data, we calculated C-statistics. The C-statistic for the ACG hospitalization model was

0.69, suggesting a modest performance of the model. With a C-statistic of 0.78, the discriminating ability of the high-cost model can be classified as good.

Adjustment of the models, based on Dutch primary care data

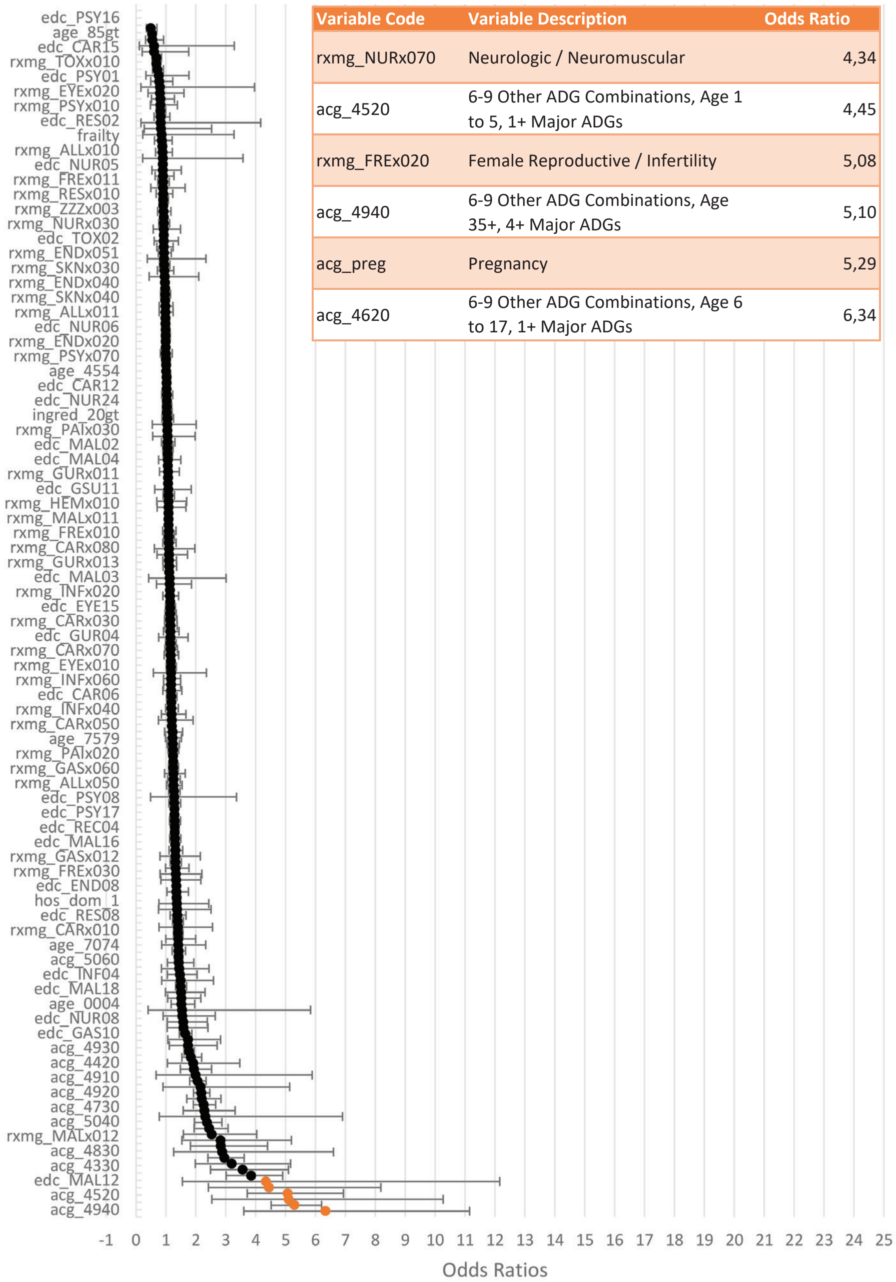
To adjust the models to the Dutch primary care setting, we first estimated and then validated the logistic regression models, producing new prediction models. Figures 1 and 2 show the odds ratios along with the 95% confidence interval for the variables included in respectively the hospitalization and high cost prediction models, arranged from lowest (top) to highest (bottom). For the hospitalization model the ACG categories for children under 18 years old with six to nine diagnoses types, amongst which at least one was assigned as a major diagnosis and the ACG category for adults above 34, years old, with six to nine diagnoses types, amongst which at least four were assigned as major diagnoses, along with neurological/neuromuscular problems, female infertility and pregnancy are the variables with the highest odds ratios (>4).

With odds ratios above five, ACG categories for children under 18 years old with four to nine diagnoses, with or without major diagnoses, along with conditions such as female infertility, acute major viral infections, malignancies with high impact and Multiple Sclerosis, all contribute highly to the high-cost model. In addition, pregnancy, systemic inflammation with high impact, muscle spasms, chromosomal anomalies, chronic kidney disease and the ACG category for males between 18 and 34 years old with six to nine diagnoses, amongst which two or more major ones, also contribute highly to the model with odds ratios above four.

Assessment of the adjusted models

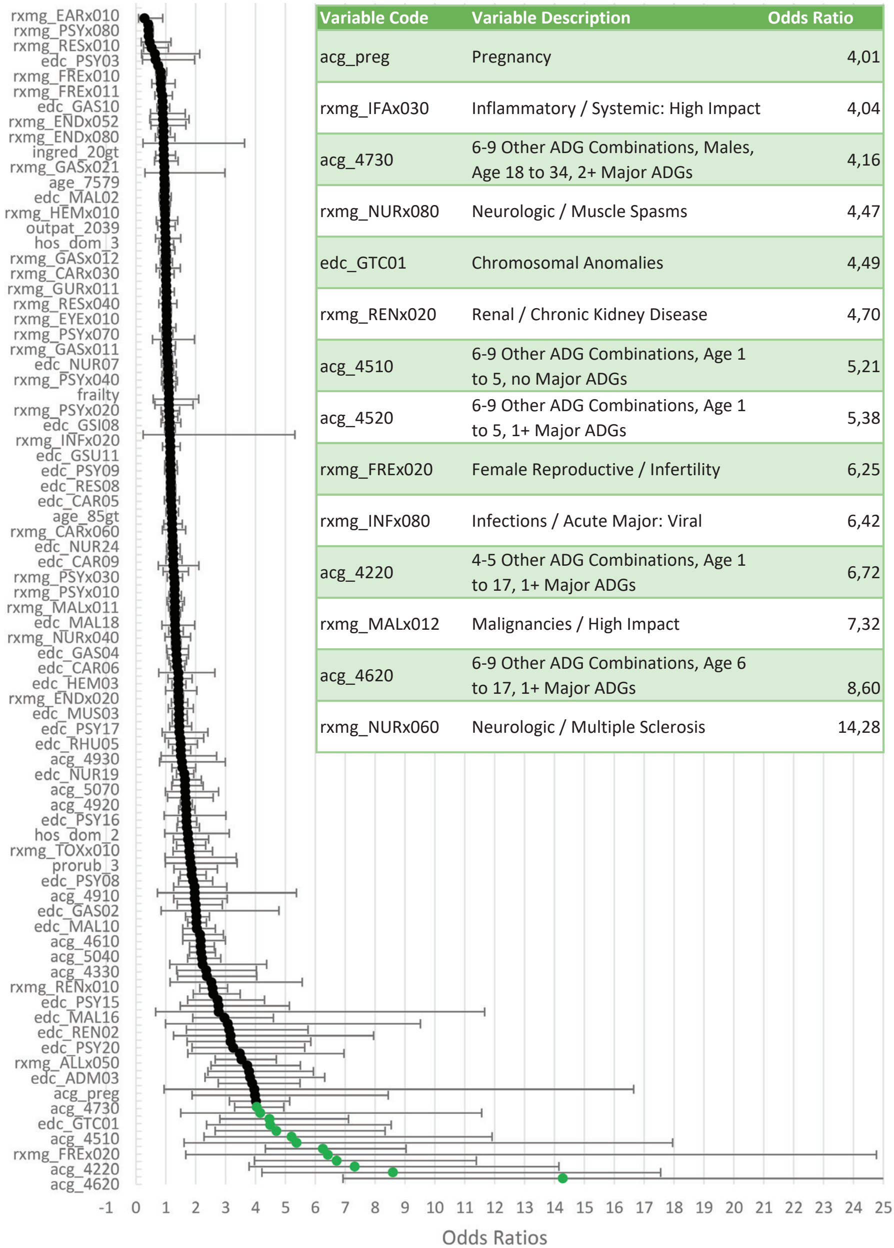
Discriminatory ability

To assess the discriminatory ability of the adjusted models, we compared the C-statistics estimated for the model based on the Dutch data, to those for the US-based models. Table 2 shows fairly high C-statistics for the US hospitalization and high-cost models (0.69 (CI 0.68, 0.70) and 0.78 (CI 0.77, 0.79)). In addition, the Dutch models both show improvements of discriminatory ability with C-statistics raising to 0.75 (CI 0.74, 0.75) for the hospitalization model and 0.85 (CI 0.84, 0.85) for the high-cost one. C-statistics for both Dutch adjusted models were similar for training and validating datasets, suggesting a similar discriminating performance of the adjusted models in an external study population.



Variable Code	Variable Description	Odds Ratio
rxmg_NURx070	Neurologic / Neuromuscular	4,34
acg_4520	6-9 Other ADG Combinations, Age 1 to 5, 1+ Major ADGs	4,45
rxmg_FREx020	Female Reproductive / Infertility	5,08
acg_4940	6-9 Other ADG Combinations, Age 35+, 4+ Major ADGs	5,10
acg_preg	Pregnancy	5,29
acg_4620	6-9 Other ADG Combinations, Age 6 to 17, 1+ Major ADGs	6,34

Figure 1: On the left: S-curve of the odds ratios including confidence intervals for the variables included in the hospitalization model, arranged from highest (bottom) to lowest (top); on the right: table zoomed in on the odds ratio's above four.



Variable Code	Variable Description	Odds Ratio
acg_preg	Pregnancy	4,01
rxmg_IFAx030	Inflammatory / Systemic: High Impact	4,04
acg_4730	6-9 Other ADG Combinations, Males, Age 18 to 34, 2+ Major ADGs	4,16
rxmg_NURx080	Neurologic / Muscle Spasms	4,47
edc_GTC01	Chromosomal Anomalies	4,49
rxmg_RENx020	Renal / Chronic Kidney Disease	4,70
acg_4510	6-9 Other ADG Combinations, Age 1 to 5, no Major ADGs	5,21
acg_4520	6-9 Other ADG Combinations, Age 1 to 5, 1+ Major ADGs	5,38
rxmg_FREx020	Female Reproductive / Infertility	6,25
rxmg_INFx080	Infections / Acute Major: Viral	6,42
acg_4220	4-5 Other ADG Combinations, Age 1 to 17, 1+ Major ADGs	6,72
rxmg_MALx012	Malignancies / High Impact	7,32
acg_4620	6-9 Other ADG Combinations, Age 6 to 17, 1+ Major ADGs	8,60
rxmg_NURx060	Neurologic / Multiple Sclerosis	14,28

Figure 2: On the left: S-curve of the odds ratios including confidence intervals for the variables included in the high cost model, arranged from highest (bottom) to lowest (top); on the right: table zoomed in on the odds ratio's above four.

Table 2: C-statistics for hospitalization and high healthcare costs (top 5% highest healthcare costs) models: fixed US model versus adjusted model based on Dutch data.

	Hospitalization Model *C-statistics (95% CI interval)*	**High Cost Model** *C-statistics (95% CI interval)*
US-based model (training dataset)	0.689 (0.683, 0.695)	0.779 (0.772, 0.786)
US-based model (validation dataset)	0.704 (0.695, 0.712)	0.793 (0.784, 0.803)
Dutch Model (training dataset)	0.748 (0.743, 0.753)	0.844 (0.838, 0.850)
Dutch Model (validation dataset)	0.756 (0.748, 0.763)	0.857 (0.849, 0.865)

Calibrating ability

The calibration plots of both the adjusted hospitalization model (figure 3) and the high-cost model (figure 4) are located near the 45 degree reference line, indicating that the calibrating ability of both models is good: the persons with higher predicted values indeed have a higher chance of being hospitalized or generating higher healthcare costs.

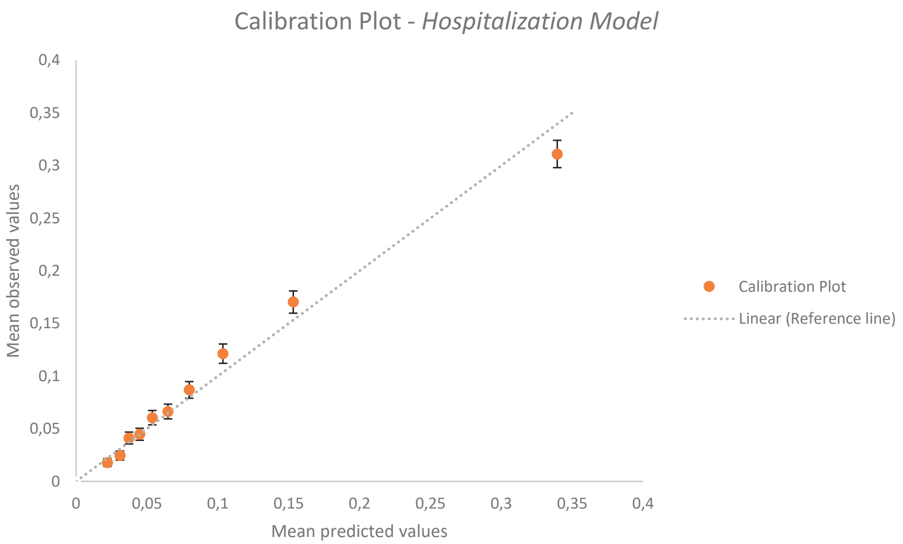


Figure 3: Calibration plot hospitalization model (external validation)

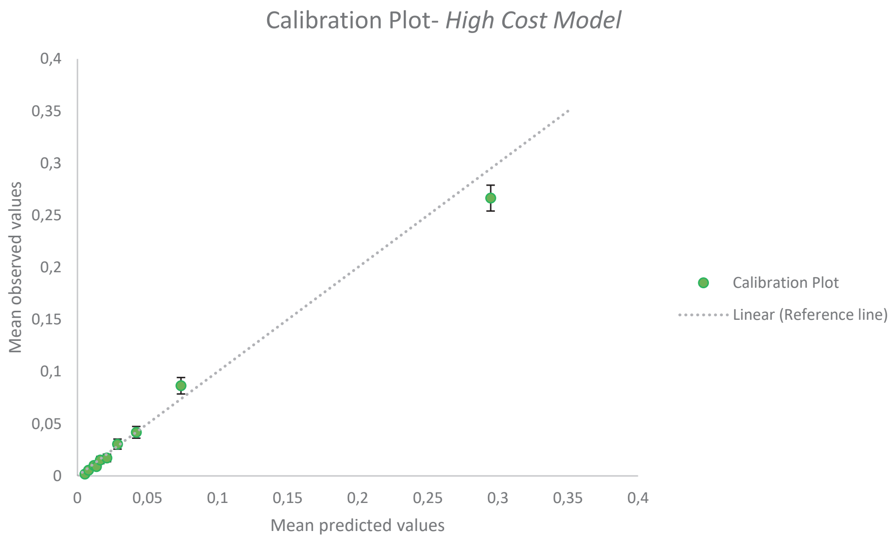


Figure 4: Calibration plot high healthcare costs / top 5% highest healthcare costs model (external validation)

Discussion

With this study we have identified promising risk stratification tools to be used in Dutch primary care. With the ACG tool applied on Dutch primary care data, model performances for the US based models are 0.69 for the hospitalization model and 0.78 for the high-cost model. The ACG has already been proven to be an efficient risk stratification tool in different countries with C-statistics between 0.73 and 0.82 for hospitalization risk and C-statistics of 0.76 for prediction of high healthcare costs (10, 11, 12). This study suggests that the ACG's can also be used properly in the Netherlands, especially after adjustment of the model towards Dutch data. Adjustment of the hospitalization model based on Dutch data improved C-statistics to 0.75, upgrading the model's performance. The high-cost model produced C-statistics of 0.85 after adjustment, which is regarded as 'very good'. Next to good discriminatory ability, the models also showed good calibrating ability: the models can discriminate well between low- and high-risk individuals and the predicted values are in line with the observed ones. The models show excellent potential for predicting high risk individuals within a Dutch primary care population.

Good prediction models to identify future risk of hospitalization or high costs, can be of great value for planning and organizing effective healthcare provision. Applying such models in primary care, enables identification of high-risk patients at an early stage, potentially resulting in pro-active care and proper allocation of resources. As resources are getting scarce in most European countries, including the Netherlands, approaches focusing on effective and efficient resource allocation are highly valuable.

Different studies have already shown the success of selecting appropriate patients for specific interventions such as care management programs with the use of efficient risk stratification tools (3). Subsequently, the effect of tailor-made approaches based on patients' individual risks has proven its value in reducing hospitalization and high healthcare costs (4). Population Health Management approaches like those have the capacity to keep healthcare costs under control.

This study has shown the high potential of the ACG's adjusted risk models. However, this study only focused on the ACG's hospitalization and high costs model. The many other risk models that are included in the ACG and other similar tools, all need to be validated in the Netherlands before being used in practice. However, with the validation of the hospitalization and high costs models, we expect that the other ACG models will also perform well.

Secondly, to strengthen the models even more, the clinical validity of the predictors in the models, needs to be reassessed for a Dutch setting. A strong statistical association with a predictor and the outcome does not necessarily establish the clinical meaning of the predictor. Focus should be put on the association of the model predictors with avoidable hospitalization and high costs. Involvement of health professionals in this process is important.

In addition, as promising as the application of a risk stratification tool is, the strength of a prediction model only reaches as far as the quality of the health registries. The more primary care physicians realize the strengths of a registry of good quality, the better routinely collected data can be used for risk stratification approaches. Creating awareness amongst physicians is the first step in successful application of risk stratification tools. Not only will awareness amongst healthcare professionals lead to better registration, but it is also important for an efficient practical use of risk stratification approaches in healthcare. To create awareness amongst professionals, more evidence is needed of the effectiveness of risk stratification models. Intervention studies in which patients are selected for specific interventions with the use of risk stratification models, will contribute to this.

In conclusion, the Dutch healthcare system might truly benefit from the use of risk stratification models, especially when applied in an early stage of care provision such as primary care. The ACG system provides a solid basis to measure multimorbidity and local adjustments of the ACG's models improve results.

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Supplementary material

Supplementary table 1: ICPC-1 translation to codes recognized by the ACG

ICPC-1 (Dutch version)	Description ICPC-1 code	ICPC-2 (international version)	Code used in models	Code Type used in models
A04.01	Chronisch vermoeidheidssyndroom	A04	F480	ICD-10
A09.01	Nachtzweten	A09	R619	ICD-10
A09.02	Gelokaliseerd overmatig zweten	A09	R619	ICD-10
A17.00		A17	R688	ICD-10
A29.01	Hart- en vaatziekten in familie-anamnese	A29	Z824	ICD-10
A29.02	Mammacarcinoom in familie-anamnese	A21	Z803	ICD-10
A29.03	Ovariumcarcinoom in familie-anamnese	-	Z804	ICD-10
A29.04	Coloncarcinoom in familie-anamnese	A21	Z800	ICD-10
A29.05	Diabetes in familie-anamnese	-	Z833	ICD-10
A29.06	Hypercholesterolemie in familie-anamnese	-	Z834	ICD-10
A76.01	Exanthema subitum/zesde ziekte	A76	B082	ICD-10
A76.02	Erythema infectiosum/vijfde ziekte	A76	B083	ICD-10
A76.03	Hand-voet-mondziekte	A76	B084	ICD-10
A78.05	Borreliose/Lyme	A78	A692	ICD-10
A87.01	Leven met stoma	A87	Z934	ICD-10
A87.02	Status na transplantatie	A87	Z949	ICD-10
A88.01	Perniones	A88	T68	ICD-10
A88.02	Zonnesteek	A88	T670	ICD-10
A88.03	Reisziekte	A88	T753	ICD-10
A89.01	Aanwezigheid pacemaker/interne defibrillator	A89	Z950	ICD-10
A90.01	Syndroom van Down	A90	Q909	ICD-10
A91.05	Gestoorde glucosetolerantie	-	R730	ICD-10
A91.06	Subklinische hypothyreoïdie	-	E02	ICD-10
A91.07	Subklinische hyperthyreoïdie	-	E059	ICD-10
A96.01	Natuurlijke dood	A96	R99	ICD-10
A96.02	Onnatuurlijke dood	A96	R99	ICD-10
A97.02	Kinderwens	-	A97	ICPC-2
A99.01	Dragerschap met risico voor eigen persoon	-	Z229	ICD-10
A99.02	Dragerschap met risico voor nageslacht/omgeving	-	Z229	ICD-10
B72.02	Non-Hodgkin lymfoom	B72	C819	ICD-10
B81.01	Foliumzuurdeficiëntie-anemie 4	B81	D529	ICD-10
B81.02	Vitamine B12-deficiëntie-anemie	B81	D519	ICD-10
K49.01	Cardiovasculair risicomanagement (CVRM)	K49	Z13.6	ICD-11
L49.01	Valpreventie/ fractuurpreventie	L49	R268	ICD-10
T90.01	Diabetes mellitus type 1	T89	E109	ICD-10
T90.02	Diabetes mellitus type 2	T90	E119	ICD-10

ICPC-1=International Classification of Primary Care version 1, used in Dutch primary care; ICPC-2= International Classification of Primary Care version 2, internationally used; ICD-10 = International Classification of Diseases 10th revision