Study Protocol

External validation of EPIC's Risk of Unplanned Readmission model, the LACE+ index and SQLape® as predictors of unplanned hospital readmissions: A monocentric, retrospective, diagnostic cohort study in Switzerland

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CONTENT

ABSTRACT

Introduction: Readmissions after an acute care hospitalization are relatively common, costly to the health care system, and are associated with significant burden for patients. As one way to reduce costs and simultaneously improve quality of care, hospital readmissions receive increasing interest from policy makers. It is only relatively recently that strategies were developed with the specific aim of reducing unplanned readmissions by applying prediction models. EPIC's Risk of Unplanned Readmission model, developed in 2015 for the U.S. acute care hospital setting, promises superior calibration and discriminatory abilities. However, its routine application in the Swiss hospital setting requires external validation first. Therefore, the main objective of this study is to externally validate the EPIC's Risk of Unplanned Readmission model, LACE+ index and SQLape® model as predictors of unplanned hospital readmissions.

Methods: For this reason, a monocentric, retrospective, diagnostic cohort study will be conducted. The study will include inpatients, who were hospitalized between the 1st of January 2018 and the 31st of December 2019 in the Lucerne Cantonal hospital in Switzerland. Cases will be inpatients that experienced an unplanned (all-cause) readmission within 18 or 30 days after the index discharge. The control group will consist of individuals who had no unscheduled readmission.

For external validation, discrimination of the scores under investigation will be assessed by calculating the area under the receiver operating characteristics curves (AUC). For calibration, the Hosmer-Lemeshow goodness-of-fit test will be graphically illustrated by plotting the predicted outcomes by decile against the observations. Other performance measures to be estimated will include the Brier Score, Net Reclassification Improvement (NRI) and the Net Benefit (NB).

All patient data will be retrieved from electronic clinical data bases.

Discussion

This is a presentation of the study protocol only. Results and discussion will be published after completion of this study.

Others

The study protocol was approved by the Ethics Committee Northwest- and Central Switzerland (ID:2019-01861) and will be registered on ClinicalTrials.gov.

INTRODUCTION

Readmissions after an acute care hospitalization are relatively common, costly to the health care system and are associated with significant burden for patients (1-5). A readmission increases the risk of dependence and functional or psychosocial decline [5]. Moreover, a readmission increases the risk of decompensation of other comorbid conditions, thus increasing the frailty of elderly patients [6].

The belief that readmission rates are a valid indicator to assess quality of care has led to their inclusion in hospital quality surveillance (6, 7). In September 2018, the Swiss National Association for Quality Development in Hospitals and Clinics (ANQ) reported its most recent findings. Accordingly, based on 2016 figures, the number of Swiss hospitals that reported more readmissions, as expected according to their patient mix, has more than doubled. In total, 47 out of 145 hospitals reported rates (observed/expected) outside the norm, i.e. significantly higher than 1 (8). This increase (+3.3%) in observed unplanned readmissions has been ongoing since 2011 and is proving to be statistically significant (9).

In the last few years, the observed increase in costs has been posing major challenges for the healthcare system. Healthcare costs in Switzerland have risen by a good third within the last decade (10). As one way to reduce costs and simultaneously improve quality of care, hospital readmissions receive increasing interest from policy makers. It is only relatively recently that policies were developed with the specific aim of reducing readmissions. In Switzerland, the readmission policy involves financial penalties, i.e., that patient records of the first admission and the relevant readmission are merged into a single case, if certain criteria are met. Consequently, hospitals receive only one DRG-based payment for both admissions (11). In result, and despite the fact that some readmissions cannot be avoided and the proportion of potentially avoidable readmissions (PARAs) remains debatable, health care organizations invest considerable resources into efforts to reduce hospital readmissions (12-14).

To most efficiently reduce readmissions, hospitals need to target effective discharge and post-discharge interventions at those who need them the most. One of the more recent strategies is the application of prediction models. As systematic reviews have shown, there are many models aimed at identifying those at greater risk of readmission (15, 16). The majority includes readily available predictors such as demographic and administrative data, comorbidities, laboratory, and medications (15). Among these models, the EPIC's Risk of Unplanned Readmission model, developed in 2015 for the U.S. acute care hospital setting, promises superior calibration and discriminatory abilities. The model was developed by EPIC Systems corporation based on data from 26 EPIC community member hospitals, including more than 275'000 inpatient hospital admission encounters to determine a patient's risk of unplanned readmission within 30 days of being discharged from an index admission.

RATIONALE & OBJECTIVES

Prediction models require internal and external validation. Whereas internal validations means testing the model in the population used to develop it, external validation means applying the model with its predictors and assigned weights, as estimated from the development study, to a new population; measuring the predictor and outcome values; and quantifying the model's predictive performance (calibration and discrimination).

Even though EPIC's Risk of Unplanned Readmission model was developed for the acute care hospital setting, variations in demographic features, disease prevalence and differences in test conditions (e.g. defining criteria of relevant readmissions, time frame of measurement) entail external validation prior to routine application in the Swiss acute care hospital setting.

For this reason, the main objective of this study is to externally validate EPIC's Risk of Unplanned Readmission model as i) a predictor of all-cause unplanned hospital readmissions within 30 days, ii) a predictor of unplanned readmissions within 18 days according to SwissDRG's specification, and to compare the model with the LACE+ index and the SQLape® readmission algorithm.

METHODS

Study design & study sites

This monocentric, retrospective, diagnostic cohort study will include all inpatients from the Lucerne Cantonal Hospital, which is the largest provider of basic and highly specialized healthcare services in Central Switzerland. This study is designed not to meet the criteria for research involving human subjects. The Ethics Committee Northwest- and Central Switzerland (EKNZ) will be informed and asked for an ethics waiver.

Participants

All inpatients, aged one year or older (max. 100 years), who were hospitalized either between the 1st of January 2018 and the 31st of December 2018, or between the 23rd of September and the 31st of December 2019 will be included. Cases will be inpatients that experienced (i) an unplanned readmission within 18 days according to SwissDRG's specifications; (ii) an unplanned all-cause readmission within 30 days after the index discharge. The control group will consist of individuals who had no unplanned readmission within the relevant days after the index discharge.

Exclusion criteria will be (a) admission/transfer from another psychiatric, rehabilitative or acute care ward from the same institution, (b) discharge destination other than the patient's home or (c) transfer to another acute care hospital, both being considered as treatment continuation; (d) foreign residence, (e) deceased before discharge, (f) discharged on admission day, (g) refusal of general consent, and (h) unknown patient residence or discharge destination.

For individuals with multiple readmissions during the study period, only the first readmission will be included into the analysis.

Predictors

The following paragraph provides a description of the predictive models to be evaluated. A distinct definition of the variables included is available from the corresponding author upon reasonable request. In advance, it needs to be mentioned, that the EPIC's Risk of Unplanned Readmission and the SQLape® Readmission Risk model are commercially distributed products. Implicitly, due to copyright issues, not all information about the predictors required to replicate this validation study were allowed to be disclosed in sufficient detail/at all. Replicating this study requires licensing.

EPIC's Risk of Unplanned Readmission model: The EPIC's Risk of Unplanned Readmission model is a logistic regression model that predicts the risk of all-cause unplanned readmissions within 30 days of the index hospital discharge. An all-cause unplanned readmission was defined according to the Centers for Medicare & Medicaid Services (CMS) Planned Readmission algorithm (version 2.1) (17).

The data set used for the development of the model included more than 275'000 hospital inpatient encounters from 26 different hospitals. Three of these hospitals were large academic medical centers (1000+ beds each), while the others were either smaller regional hospitals or community hospitals. All included sites were chosen from very distinct geographic regions in the US to ensure a population as diverse as possible. A selection by specialties/medical disciplines was not applied; all ages; any payer; and encounters for which patients leave the hospital against medical advice were included.

After feature selection, using a least absolute shrinkage and selection operator (LASSO) penalty, the final model consisted of 27 predictive parameters.

The internal and external validation of the model showed acceptable discrimination at predicting all-cause unplanned readmission within 30 days post discharge with an area under the receiver operating characteristic curve (AUC of the ROC curve) ranging from 0.69 to 0.74.

LACE+: The LACE+ risk index is a point score derived from a logistic regression model, which was developed to predict the risk of 30-day post-discharge death or urgent readmission (18). It was developed and internally validated based on a large, randomly selected, population-based sample from Ontario, Canada in 2012. The development sample excluded patients who underwent same-day surgeries, psychiatric and obstetric admissions.

Backward feature selection was performed (with a significance level of $\alpha = 0.05$) and resulted in 11 significant covariates. The final point score ranges from -15 to 114, a score greater than 90 is considered with a high risk for unplanned readmission or death within 30 days after discharge. The internal validation of the 11-item index, excluding the Canada specific case-mix group (CMG) score,

showed reasonable discrimination with an AUC of the ROC curve of 0.743 for all-cause unplanned readmission, but poor calibration (H – L statistic 58.93, $p < 0.0001$).

SQLape®: The SQLape® readmission risk model (Striving for Quality Level and analyzing of patient expenditures), a computerized validated algorithm, was developed in 2002, in Switzerland (6). The SQLape® prediction model predicts unforeseen hospital readmission within 30 days after hospital discharge. The development sample consisted of 131'809 inpatient stays from 49 Swiss acute care hospitals, of which 12 hospitals were located in the French speaking part of Switzerland.

Healthy newborns, residents outside of Switzerland and elective surgical patients that could usually be performed as day surgery were excluded. After backward elimination was performed, the Poisson regression model consisted of six variables/SQLape variable groups. Of the beforementioned 131'809 inpatient stays, 66'069 were used for internal validation. The discrimination was measured by the Harrell's C statistic, which is also referred to as the estimated area under the Receiver Operating Characteristics (ROC) curve (AUC). A value of 0.72 showed reasonable discriminative ability.

Outcome(s)

The predicted outcome of all prediction models will be compared with the observed outcome. Both outcomes will be assessed retrospectively. The primary outcome will be the all-cause unplanned readmission to the same hospital within 30 days after the index hospital discharge. An unplanned readmission will be defined as an urgent readmission, i.e. not scheduled in advance and requires treatment within 12 hours.

The secondary outcome, as defined by the SwissDRG, will be the unplanned readmission to the same hospital, that resulted in a case merging (19). According to SwissDRG, patient records of the index admission and the n^{th} readmission are merged into a single case if they fall into the same major diagnostic category (MDC), occurred within 18 days after the index/preceding hospital discharge date, and are not excluded from the case merging rule.

Sample size

Sample size calculations resulted in a aspired sample size of at least 1000 participants (500 cases and 500 controls) for each site. The proposed sample size is based upon precision. 500 cases and 500 controls will ensure that the half-width of a 95% confidence interval for sensitivity and specificity (using frequencies of predicted vs. actual outcome) does not exceed 5%; even for a point estimate of 50%, leading to the widest possible confidence interval, the half-width is supposed to remain slightly below 4.5%. This can be considered to be an appropriate target precision for the purpose of this study.

Data collection

Demographic and administrative data, medications, orders, International Classification of Disease (ICD) diagnosis codes, and biological data will be extracted in an anonymized manner from electronic patient records. Data covering the initial period will be retrieved from several different Information Systems (e.g. Dorner Lab. System, NEXUS/Medfolio etc.). Because of the introduction of a new Clinical Information System (CIS) in 2019, data covering the latter period of interest (23rd of September to 31st of December 2019) will be retrieved separately, i.e., from the new Clinical Information System from EPIC Systems corporation.

Missing data

Missing data required to compute the prediction models will be handled as following: Missing biological data (hemoglobin, sodium, calcium etc.) will be coded as normal values. Missing comorbidity and medication data will be considered as absence of the condition and no active medication, respectively. Missing order data (imaging, restraining, electrocardiogram) will be considered as an intervention not ordered. Lastly, missing records of utilization of health care resources (e.g. ED visits, scheduled future admissions etc.) will be considered as non-utilization.

Missing demographic or administrative data to describe patient's characteristics will result in the patient's exclusion from the analysis.

Statistical analysis

The EPIC's Risk of Unplanned Readmission model predictions and LACE+ scores will be calculated as the inverse of $1+e^{-(intercept+\beta^1 * x^1+\cdots+\beta^K * x^K)}$, where β will be the regression coefficient of each covariate (x), and K will be the total number of covariates. SQLape® readmission predictions will be automatically calculated by the plugin provided by the author.

To assess the performance, the traditional statistical approach is to quantify how close predictions are to the actual outcome. As overall performance measure, composing of discrimination and calibration, the Brier score will be calculated. Assessed separately, the discriminative ability will be measured using the Harrell's C-statistic, which, for binary outcomes, is identical to the area under the Receiver Operating Characteristic (ROC) curve (AUC). For calibration, the Hosmer-Lemeshow goodness-of-fit test will be graphically illustrated by plotting the predicted outcomes by decile against the observations. Furthermore, other performance measures to be estimated will include the Net Reclassification Improvement (NRI) and the Net Benefit (NB). All statistical analyses will be performed in R.

Risk groups

Risk groups will be established based on the recommendations by the developers of EPIC's Risk of Unplanned Readmission model, i.e., to use the organization's current readmission rate as baseline

risk and group as follows: "no risk = 0 – baseline", "low risk = baseline – 2 x baseline", "medium risk = 2 x baseline – 3 x baseline", "high risk = > 3 x baseline".

Development vs. validation

The differences in this validation study compared to the development studies are briefly summarized below:

EPIC's Risk of Unplanned Readmission	**Setting:** U.S. multi-centric study, including more than 275'000 adult inpatients from 26 different hospitals; the national readmission rate equals 10%-15% (20, 21) **Eligibility criteria:** No relevant differences **Outcome:** The primary outcome was the unplanned readmission within 30 days of the index hospital discharge, defined according to the Centers for Medicare & Medicaid Services (CMS) Planned Readmission algorithm **Predictors:** ICD-10 codes vary slightly by country - diagnosis grouper will need modification; medication vendors and medicinal products can vary from country to country – ATC groups will need modification; less frequent ED use compared to the US – hence, the predictor might have a smaller effect (22, 23)
LACE+	**Setting:** Multi-centric, Canadian study including medical and surgical adult inpatients who had been discharged to the community from an Ontario hospital; the study involved 500'000 randomly selected patients; the Canadian national readmission rate equals 9%-10% **Eligibility criteria:** All medical and surgical patients, excluding discharges to rehabilitation and long-term care facilities, patients who underwent same-day surgeries, psychiatric and obstetric and patients who were ineligible for health care coverage in Ontario. **Outcome:** The primary outcome was death or urgent readmission within 30 days of hospital discharge, the secondary outcome was only urgent readmission within 30 days of hospital discharge; variations in regard to the excluded procedures and diagnoses can be expected; the development sample covered, to some extent, external readmissions, i.e. patients being readmitted to another hospital – not considering external readmissions in the validation study can lead to over- or underestimation **Predictors:** The original study included the predictor variable case-mix group (CMG) to capture important acute diagnoses and procedures performed during the index admission. Because the CMG score cannot be calculated for hospitals outside Canada the authors conducted a secondary analysis to determine the performance of the LACE+ index without the CMG score for the potential use in other countries. The performance was only slightly worse (AUC): 30-day death or urgent readmission resulted in 0.759 instead of 0.771, 30-day urgent readmission – 0.743 instead of 0.753; 30-day death – 0.860 instead of 0.883; ICD-10 codes vary slightly by country - diagnosis grouper will need modification; less frequent ED use compared to Canada – the predictor might have a smaller effect (23, 24)
SQLape®	**Setting:** No relevant differences **Eligibility criteria:** No relevant differences **Outcome:** The development study outcome was potentially avoidable readmissions within 30 days – compared to the outcome of this validation study, variations in regard to the excluded procedures and diagnoses can be expected **Predictors:** No relevant differences

Reporting

The study will follow the criteria from the transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD) Initiative (25).

Limitations

Due to copyright issues, it will not be possible to describe the EPIC and SQLape® model in sufficient detail that would allow other researchers to replicate this study without licensing. Furthermore, this study will conduct its performance evaluation based on the assumption that if a specific parameter is not documented, it's true value is considered as uneventful. Compared to a prospective study design, where each required data input would be available as either positive or negative value, this study design is less powerful. Lastly, only readmissions to the same hospital will be considered, this can result in over-/underestimation of performance.

Other information

Supplementary information

Appendix A – RRM Study Prediction Model Variables (can be requested from the corresponding author)

Funding

This study will be conducted without specific funding.

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