Kantonsspital Baden
Apotheke

Forschungsprojekt nationaler Tragweite 2017: Zwischenbericht 2020

Detection and prevention of delirium triggered by adverse drug events

1. Introduction:

Adverse drug events (ADEs) are frequent complications experienced during hospitalization, especially in the geriatric population. ADEs are still considered to be heavily underreported while half are classified as pADEs (preventable ADEs). Thus, the prediction of ADEs becomes more important every day to identify patient at high risk and alert the physician or a multidisciplinary care team to perform specific interventions.
A common ADE in elderly hospitalized patients is delirium having a huge impact on health outcomes, hospitalization length of stay, and health care costs. One of the many risk factors are drugs, especially anticholinergic (ACH) medications. Owing to multiple indications, prescription of these drugs increases with hospitalization. The most common method for determining the ACH burden in a person is an expert based list of medications with ACH properties, the so-called ACH scales. These scales assign a number from 1 (=low) to 3 (=high) to a specific substance according to its ACH properties. In a small study conducted in the intensive care unit (ICU) of our hospital, we observed that patients with delirium had a higher ACH burden compared to those without. As this drug-drug interaction was often unnoticed by interaction check programs, delirium may remain unrecognized. Hence, the ability to predict patients at high risk would enhance proper screening and be a potential source of prevention.

2. Aim:

a. To predict delirium and identify risk factors in different population groups
b. To prevent delirium by automatically calculating anticholinergic burden of drug therapy, displaying alerts in the electronic patient record (EPR) and automatically directing daily lists of orders with candidate medications to experts for review

3. Objectives:

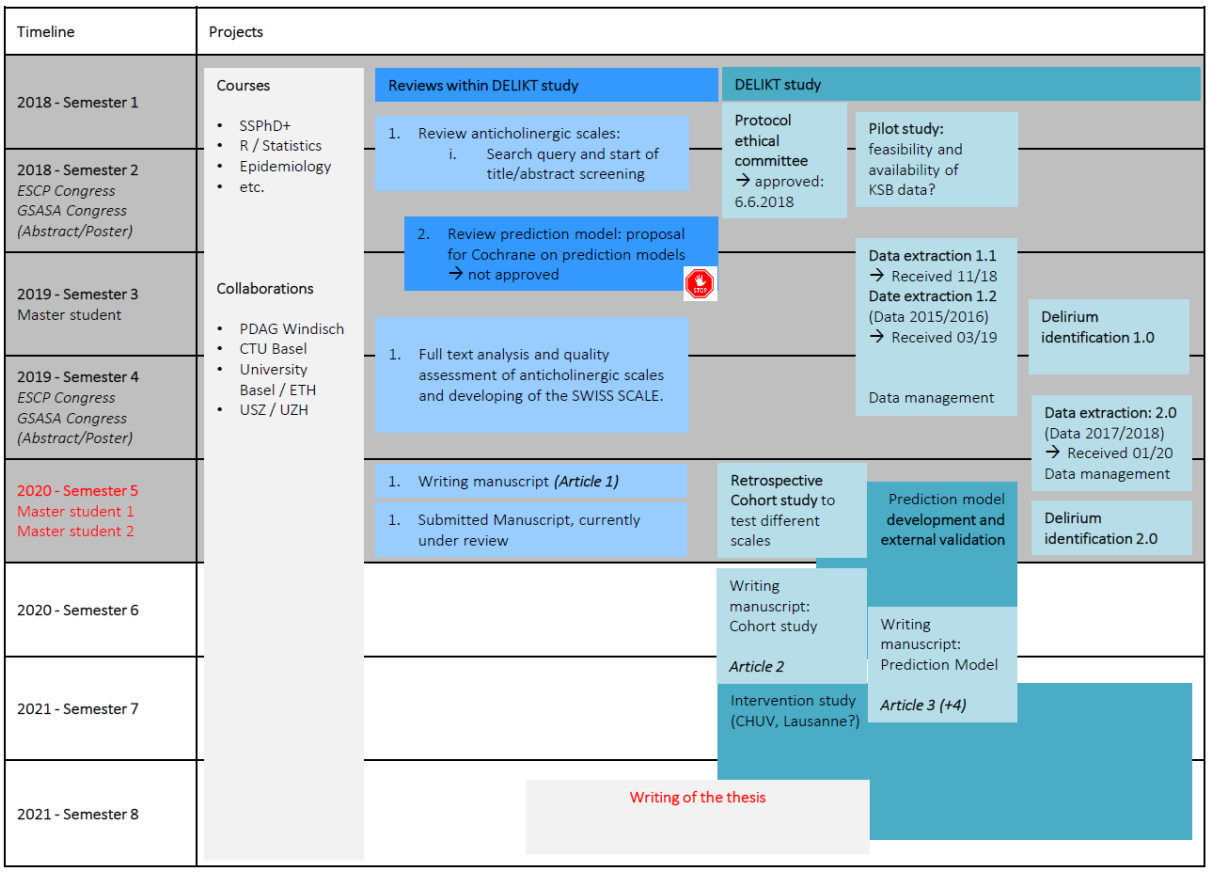
a. To identify the best anticholinergic burden scales to develop the Swiss ACH burden scale (SABS)
b. To establish the association between delirium and the SABS
c. To develop and validate a prediction model to identify patient at high risk for delirium including the SABS
d. To decrease the incidence of delirium by implementing the prediction tool in the hospital's CPOE

4. Changes:

The PhD thesis has been extended by one year until end of 2021.

5. Steps and planning:

Duration: 4 years (2018-2021)



6. Status July 2020:

End of 2019 a new data set of patients hospitalised in 2017/2018has been extracted from KISIM, our ERP.
A first publication with the title "Quality of anticholinergic burden scales and their impact on clinical outcomes – a systematic review" has been submitted – after 3 rejections – to the Eur J Clin Pharm. It is still under review (abstract see appendix 1).
Giulia Gallucci has finished her master thesis in Mai. She developed and validated several prediction models for delirium in hospitalized older patients, see abstract in appendix 2.
A second master thesis is ongoing. The aim is to show an association between the anticholinergic burden and delirium via a retrospective cohort study using the data set 2015/2016 as for the previous master thesis developing the prediction model. In addition, we compared all 19 identified anticholinergic burden scales identified in the systematic review. Results will be presented at the end of July.

As there is another project planned in the KSB aiming to prevent delirium the implementation of the algorithm has been postponed to next year. Currently we work together with the other project leaders planning a joint study. There also plans to organize a multicentre interventions study together with the CHUV, Lausanne, next year.

Baden, den 14.7.2020

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Appendix 1 (Abstract Systematic Review)

"Quality of anticholinergic burden scales and their impact on clinical outcomes – a systematic review"

Abstract

Purpose: Older people are at risk of anticholinergic side effects due to changes affecting drug elimination and higher sensitivity to drug's side effects. Anticholinergic burden scales (ABS) were developed to quantify the anticholinergic drug burden (ADB). We aim to identify all published ABS, to systematically compare them and to evaluate their associations with clinical outcomes.

Methods: We conducted a literature search in MEDLINE and EMBASE to identify all published ABS and a Web of Science citation (WoS) analysis to track validation studies implying clinical outcomes. Quality of the ABS was assessed using an adapted AGREE II tool. For the validation studies we used the Newcastle-Ottawa Scale and the Cochrane tool Rob2.0. The validation studies were categorized into six evidence levels on the propositions of the Oxford center for Evidence-based Medicine with respect to their quality. At least two independent researchers performed screening and quality assessments.

Results: Out of 1297 records we identified 19 ABS and 104 validations studies. All ABS were recommended for use despite quality differences. The Anticholinergic Cognitive Burden (ACB) scale and the German Anticholinergic Burden Scale (GABS) achieved the highest percentage in quality. Though most ABS are validated, we lack validation studies for newer scales and only two studies compared eight ABS simultaneously. The four most investigated clinical outcomes delirium, cognition, mortality and falls showed contradicting results.

Conclusion: There is need for good quality validation studies comparing multiple scales to define the best scale and to conduct a meta-analysis for the assessment of their clinical impact.

Appendix 2 (Master thesis Giulia Gallucci, University of Basel)

"Derivation and validation of a multivariable prediction model for delirium in hospitalized patients aged 65 and older"

Abstract

Background: Delirium is frequent and underdiagnosed in hospital settings, resulting in increased mortality and sanitary costs. Anticholinergic drugs are classified as inappropriate medications for the geriatric population, and they may contribute to the development of delirium. Prediction models including risk factors such as anticholinergic drugs could be used to prevent delirium.

Aim: The objective of this study was to develop and validate a multivariable and ward-independent model which daily predicts delirium in older inpatients.

Methods: We retrospectively analyzed two datasets: the derivation and the validation datasets, recorded between 2015 and 2016, respectively 2017 and 2018. These included patients aged 65 years or older, which were hospitalized at least 48 hours, and which did not spend more than 24 hours on the ICU. We excluded patient cases with delirium on admission and with delirium due to substances abuse. Furthermore, we identified the exact date of delirium diagnosis following a previously written protocol. We used a logistic regression method on the derivation dataset to select predictive variables among the candidate variables available on the electronic recording system of our hospital. Subsequently, we developed different prediction models considering on one side continuous variables and on the other variable categorization. We used five machine learning methods: logistic regression, naïve Bayes, random forest, decision tree and deep learning. We internally and externally validated fifteen prediction models and compared both their predictive ability and their performance measures, in order to find the best performing prediction model.

Results: The validation dataset included 13'713 patient cases, of which 491 developed delirium during the hospitalization. The areas under the receiver operating curves ranged from 0.500 to 0.798. The prediction models developed using a random reduced dataset performed better than the others due to a highly imbalanced dataset. We did not find substantial difference in the prediction between models considering categorical and continuous variables. The method which outperformed among all developed models was naïve Bayes. Moreover, decreasing the threshold we achieved improvement in the sensitivities of our models. We identified limitations in data collection methods, variables selection and model development.

Conclusion: Although the developed models resulted in relatively high areas under the receiver operating curves, their sensitivity was lower than 50%. Further improvements in variables selection and model development are necessary before the implementation of the prediction model in a clinical setting. The enhancements in the predictive ability will allow a more precise identification of patients with high-risk for delirium, which will benefit from an earlier start of preventive measures.