Medication optimisation

Valorisation

The simultaneous use of many drugs is called polypharmacy, which is known to increase as people get older. Polypharmacy is usually defined as the concomitant use of five or more drugs. Previous research has shown that polypharmacy increases the risk of drug interactions, adverse effects, and often causes problems with patient compliance. In addition, it can lead to unnecessary hospitalisation (1-5).

A clinical decision support system (CDSS), which is a computer program designed to support healthcare professionals in clinical decision-making, has already provided a feasible solution for a basic form of medication surveillance.

Medication surveillance, one of the activities carried out by physicians and pharmacists to assure safe and beneficial use of drugs, has already been performed since several decades by using a first generation CDSS. This first generation CDSS alerts against incorrect dosages, drug-drug interactions, and contraindications (drug-disease interactions). The first generation CDSS can nowadays be combined with one of the more advanced second generation CDSSs that are able to combine information on individual patient characteristics such as diagnoses and laboratory values.

Currently, in addition to the daily (digital) medication surveillance intended to prevent incorrect dosages, drug-drug interactions, and contraindications, (manual) medication reviews of older adults are performed periodically to ensure optimal pharmacotherapy. A 'medication review' is defined as a structured evaluation of a patient's medication by a physician and a pharmacist, taking into account both the patient's medical history and laboratory values (6). In the Netherlands, the Health Care Inspectorate (IGZ) expects all residents of nursing homes and homes for the elderly to receive a medication review by a physician and a pharmacist twice a year and yearly, respectively.

Both processes, medication surveillance and medication reviews, aim for medication optimisation, which is the optimal use of medication by taking into account the benefits and safety aspects of the drugs used. This thesis has explored the possibilities of using an advanced CDSS to automate medication optimisation.

In the following paragraphs the societal relevance of the thesis will be shown in a number of highlighted messages for daily practice, each of which is subsequently explained in more detail.

> The results of this thesis confirm that a more feasible and efficient method is essential to fulfil the current IGZ-required medication reviews.

In a survey conducted among pharmacists who provide care for nursing homes and residential homes, we have demonstrated that only a part of the medication reviews required by the IGZ is actually performed with a minimum performance of 42% and a maximum of 76% with respect to the IGZ-requirements. The enormous effort needed to comply with the required medication reviews is most probably the cause of this underperformance.

We have shown that in an average pharmacy one pharmacist annually has to work full-time for 2.5 months to perform the IGZ required medication reviews. This suggests that performing all the medication reviews required by the IGZ is very time consuming and costly when performed with the currently available manual methods.

This thesis shows that automation of medication reviews may be useful. The study provides practical insight into the aspects that have to be taken into consideration and need to be optimised in order to further improve the efficiency of these reviews.

Our study indicated that automation of medication reviews can provide efficiency benefits. The idea to automate medication reviews is not new. However, our proposed approach, which does not require the manual input of individual patient data, e.g. medication and patients' characteristics, into the CDSS, followed by automated generation of drug related alerts, will most probably lead to a considerable reduction of the review time.

The first step towards the automation of medication reviews by a CDSS was to increase the efficiency of the medication surveillance of an advanced CDSS, which is pivotal in reducing alert fatigue and in being able to perform cost-efficient medication surveillance. Performing automated medication surveillance with an efficient advanced CDSS may already contribute to the optimisation of drug use, and should actually prevent suboptimal drug use that would normally only be identified through manually performed medication reviews.

The ideal advanced CDSS should optimally alert for all clinical relevant drug related problems without any false positive alerts, thereby already preventing alert fatigue. However, it might be more realistic to aim for a CDSS that alerts for all clinical relevant drug related problems of which 80% are clinically relevant.

The second step in the automation of medication reviews by a CDSS was the development of a CDSS with content that actually supports medication reviews, i.e. algorithms to identify drug related problems (DRPs). In the thesis we have described the necessary steps for the development of such a CDSS.

This thesis shows that automation of medication reviews by a comprehensive CDSS should be further improved by increasing the number of relevant algorithms that identify drug related problem. This increase in relevant algorithms is necessary to widely implement the CDSS in patient care.

The third step was to explore the value of the newly developed CDSS by comparing the performance of manual medication reviews in hospitalized geriatric patients with the DRP notifications generated by the CDSS. This comparison showed that the new CDSS

was able to support medication reviews by alerting for 10% of newly identified DRPs in relation to the DRPs previously identified in the manual medication reviews. However, in our study the overall support of the manual medication review remained limited to 28% of the total of identified DRPs, i.e. DRPs identified by the manual medication review and CDSS, thereby revealing that our new CDSS needs to be enhanced. On the other hand, the CDSS algorithms that had identified the DRPs, had a sensitivity of 73% and specificity of 99%, which is good for an advanced CDSS. Therefore, the CDSS studied is in itself already a very efficient tool to augment the first generation CDSS which was primarily used for medication surveillance. Furthermore, our study also confirmed that the categories identified are relevant for an efficient CDSS that claims to be both feasible and effective for performing automated medication reviews. Although the new CDSS should be further enhanced in order to provide optimal support for medication reviews, the DRPs that have already been identified by the CDSS, can even now be easily applied on a daily or weekly basis instead of the manual medication reviews performed once or twice per year. When the CDSS will be applied more frequently, this will allow early prevention and will increase the efficiency of medication reviews. Moreover, the already automated parts of the medication review in the CDSS have now been supported by the addition of literature references, thus allowing the healthcare provider to estimate the value of the alerts.

Nevertheless, the limitations of the newly developed CDSS, i.e. undetected DRPs and irrelevant alerts, should be solved so that the number of relevant DRPs identified by the CDSS can be further increased. In addition, in our study we have characterized DRPs that are not easily automated and implemented into a CDSS, i.e. algorithms that initiate deprescribing. These DRPs, and the other described limitations, offer a roadmap of important issues that should be investigated further to improve the CDSS even more. When eventually it will be possible to automate medication reviews to a maximum, this will create the possibility to spend more time on the non-automated parts of the medication review process, such as the consultations between physician, pharmacist, and patient.

This thesis has revealed that a CDSS may also be used in the detection of patients prone to develop a delirium.

Finally, the use of a CDSS in the prediction of a sub-acute disease was also explored in this thesis. In 18 European countries 182 billion US dollars is spent yearly on care for delirium patients alone, while 30-40% of the delirium cases might have been prevented and delirium diagnoses are often missed (7). Delirium occurs frequently in hospitalised older adults, and is associated with increased morbidity and mortality.

Our study revealed that a CDSS can indeed be used to automatically predict a delirium. Despite the absence of important electronically available risk factors, the devel-

oped prediction model showed to be already worthwhile with only the electronically available delirium risk factors. The absence of important risk factors uncovered the limitations of the currently available information in electronic health records. In general there is a lack of recorded documentation of relevant patient information in electronic health records (8). If this patient information, including relevant risk factors, would be available for automation, then the predictive quality of the developed delirium model developed during our study would increase even more.

Furthermore, automated presentation of patients at risk for delirium would be very beneficial since it does not seem realistic to assume that every physician has similar expertise on high impact diseases such as delirium. Automated prediction models do not have to be limited to delirium, but can also be used more widely for other prediction algorithms such as the risk of falling or the risk of neonatal sepsis. In the case of an increased risk of falling, additional preventive measures could be initiated in time or medication causing the fall risk could be minimised. In the case of the early alerting for neonatal sepsis by automated prediction, this has already been shown to decrease mortality (9, 10).

This type of applicability of a CDSS may be very useful in the future to improve patient care and patient safety, although more research is needed to fully appreciate advanced CDSSs for the use in the automated prediction of delirium and other relevant diseases or care problems.

REFERENCES

1. Maher RL, Hanlon J, Hajjar ER. Clinical consequences of polypharmacy in elderly. Expert Opin Drug Saf. 2014;13(1):57-65.
2. Gandhi TK, Weingart SN, Borus J, Seger AC, Peterson J, Burdick E et al. Adverse drug events in ambulatory care. N Engl J Med. 2003;348(16):1556-64.
3. Tsai KT, Chen JH, Wen CJ, Kuo HK, Lu IS, Chiu LS et al. Medication adherence among geriatric outpatients prescribed multiple medications. Am J Geriatr Pharmacother. 2012;10(1):61-8.
4. Field TS, Gurwitz JH, Avorn J, McCormick D, Jain S, Eckler M et al. Risk factors for adverse drug events among nursing home residents. Arch Intern Med. 2001;161(13):1629-34.
5. Nobili A, Pasina L, Tettamanti M, Lucca U, Riva E, Marzona I et al. Potentially severe drug interactions in elderly outpatients: results of an observational study of an administrative prescription database. J Clin Pharm Ther. 2009;34(4):377-86.
6. Zermansky A, Petty D, Raynor T, Lowe C, Freemantle N. Clinical medication review by a pharmacist of patients on repeat prescriptions in general practice: a randomised controlled trial. Health Technol Assess. 2002;6(20):86.
7. Inouye SK, Westendorp RG, Saczynski JS. Delirium in elderly people. Lancet. 2014;383(9920):911-22.
8. Hope C, Estrada N, Weir C, Teng CC, Damal K, Sauer BC. Documentation of delirium in the VA electronic health record. BMC Res Notes. 2014;7:208.
9. Fairchild KD. Predictive monitoring for early detection of sepsis in neonatal ICU patients. Curr Opin Pediatr. 2013;25(2):172-9.
10. Deschamps T, Le Goff CG, Berrut G, Cornu C, Mignardot J-B. A decision model to predict the risk of the first fall onset. Exp Gerontol. 2016;81:51-5.