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Title: Drug-induced allergies: detection and prevention through electronic coding systems and development of alerting tools in a tertiary care hospital

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Drug allergy is a frequent adverse drug reaction (ADR) that endangers patients' safety leading to hospitalisation and death. Allergic drug reactions are preventable when the patient's drug allergy history is known. Ignoring this history is among the most frequent prescribing errors. Most drug allergy-induced errors are categorised as likely preventable with electronic prescribing systems. These prescribing systems require proper coding of allergies to be easily integrated into their knowledge bases.

The aim of this study was to evaluate the value of ICD-10 codes as triggers for allergy alerts in an electronic prescribing system, and allocate different drugs and drug groups to the related ICD-10 codes. Secondly, to determine the pattern of drug prescribing in adult patients with a drug allergy history, assess the appropriateness of prescribing quality in those patients, and assess the quality of electronic coding and the relationship between prescribing errors and the location of allergy documentation in the chart. Finally develop and pilot a CDSS with a drug allergy module and test its functionality.

In the first project, ICD-10 codes coding for a history of drug-induced allergy were assessed (Z88.0-Z88.9) and the corresponding Anatomical Therapeutic Chemical (ATC) classification codes of all drugs belonging to the same group of compounds were allocated to each of these codes. Then the hospital information system (HIS) was searched for all patients with a (Z88.0-Z88.9) code admitted during the year 2007 to the University Hospital of Heidelberg. Actual prescriptions to patients with drug allergy codes were then evaluated for the presence of drugs likely causing allergic reactions upon (re)exposure. The assessment of ICD-10 codes revealed that drugs grouped under some Z88 code have a significant potential of causing

allergies and/or cross-allergies in patients allergic to one member of those groups. In the patient data analysis only 178 patients out of 54420 admissions in the year 2007 had 200 different (Z88) coded drug-induced allergies in their charts. Evaluation of their prescriptions revealed three patients allergic to penicillin to be prescribed a drug likely causing an allergic reaction.

In the second project, in addition to the previously assessed ICD-10 codes, more codes coding for manifest drug allergies were included and assessed. Then a random sample of 265 in-patients was drawn from all admissions to our University Hospital in 2007. The charts were individually screened for actual and past diagnoses or ICD-10 codes alluding to drug allergies. All prescriptions to patients with drug allergies were evaluated for the presence of drugs likely causing allergic reactions upon (re)exposure. In the analysed sample 56 patients (28%) of the total cohort had an allergy either documented or coded in their charts. Out of the 56 patients with documented drug allergies twelve (21%; 95%-CI: 12-34.4%) were prescribed twenty-three times an allergy-inducing drug either as the same culprit drug (N=12, 52%) (95%-CI: 31-73%) or as a cross-reacting compound (N=11, 46 %) (95%-CI: 26-69 %). There was no difference in the risk of prescribing drugs that potentially cause allergic reactions to patients with drug allergies whether the allergy information was documented in the paper medical records or electronically.

In the third project, a drug allergy knowledge base was constructed containing the important allergenic drugs and inactive ingredients, cross-allergies between them, and also ICD-10 codes related to drug-induced allergies. All data was collected and stored to be implemented in the hospital-wide available drug information system *AiDKlinik*. An algorithm was developed structuring the functional and logical steps of the sequence of the decisions to be taken in an advanced allergy alerting tool. A graphical user interface (GUI) was designed to act as an input for patient allergy information and display for alerts. After the developed tool was manually tested to ensure the functionality of the module before and after integration in the intended setting, the allergy module was run through a database containing data of all patients admitted in the year 2007 and having an electronic prescription in *AiDKlinik*. This resulted in a set of patient logging data that was stored in a database. These logging data were analysed to determine the prevalence of allergy alerts in a representative patient population of our University Hospital. The resulting output (alerts) was analysed and evaluated for appropriateness. In the patient data analysis 206 patients had one risk factor of allergic drug reactions as ICD-10 codes and a total of 126 alerts were generated. 165 patients had a Z88 code specifying prevalent drug allergies. Only two cases (penicillin allergic patients Z88.0)

were prescribed a penicillin. In two further cases with penicillin allergy potentially drugs triggering cross-allergies were detected. In 26 % (95%-CI: 20.4-32.8%) of the cases having any of the risk factors, an inappropriate drug was prescribed to the patient.

This study has shown that inpatients in our hospital having ICD-10 codes relating to drug allergies are less prevalent than those reported in earlier studies. Suggesting that documentation and coding of allergic events in our setting is incomplete. Another major finding of this study is that ICD-10 codes for drug allergies are ambiguous and the usefulness of the ICD-10 classification to identify patients at risk is therefore limited. It also revealed a remarkable number of inpatients with documented allergies receiving potentially allergy-causing drugs. Additionally, prescribing the same or cross-reacting drug(s) happened frequently, indicating how important physicians' education or alerting in this regard can be. All this has stressed the necessity of implementing an electronic tool for drug allergies that advises physicians during the prescribing process against prescribing the same or any cross-reacting substance. The retrospective evaluation of the developed allergy tool using a real patient database confirmed that inappropriate prescribing to patients with known allergies or at risk of developing them occurs in hospitals.

This study has successfully achieved to code allergies not coded otherwise (e.g. using ICD-10 code) through the developed tool's entry platform. Additionally, it successfully designed and constructed an electronic tool that can alert physicians of patients with a potential of developing drug allergies and/or intolerances using highly specific alerts that do not interrupt the physicians' work flow.