

# **Prevalence and nature of adverse drug events and the potential for their prevention – Population-based studies among adults**

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**Katja M Hakkarainen**

Fakultetsopponent:

Professor Richard I Cook

Skolan för teknik och hälsa, Kungliga tekniska högskolan, Huddinge

This thesis is based on the following studies, referred to in text by their Roman numerals.

- I. Hakkarainen KM, Alström D, Hägg S, Carlsten A, Gyllensten H. Modelling drug-related morbidity in Sweden using an expert panel of physicians. *Eur J Clin Pharmacol* 2012;68(9):1309-1319
- II. Hakkarainen KM, Andersson Sundell K, Petzold M, Hägg S. Prevalence and perceived preventability of self-reported adverse drug events – A population-based survey of 7099 adults. *PLoS ONE* 2013;8(9):e73166
- III. Hakkarainen KM, Gyllensten H, Jönsson AK, Andersson Sundell K, Petzold M, Hägg S. Prevalence, nature and potential preventability of adverse drug events – A population-based medical record study of 4970 adults. *Br J Clin Pharmacol* 2013 [Epub ahead of print] doi: 10.1111/bcp.12314
- IV. Hakkarainen KM, Hedna K, Petzold M, Hägg S. Percentage of patients with preventable adverse drug reactions and preventability of adverse drug reactions – A meta-analysis. *PLoS ONE* 2012;7(3):e33236

Appendix Paper:

Hakkarainen KM, Andersson Sundell K, Petzold M, Hägg S. Methods for assessing the preventability of adverse drug events: A systematic review. *Drug Saf* 2012;35(2):105-126

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**UNIVERSITY OF GOTHENBURG**

# Prevalence and nature of adverse drug events and the potential for their prevention – Population-based studies among adults

Katja M Hakkarainen

Department of Public Health and Community Medicine, Institute of Medicine,  
Sahlgrenska Academy at University of Gothenburg, Sweden

## ABSTRACT

**Background:** Adverse drug events (ADEs) are common and often preventable in hospitals, but few studies have investigated ADEs in outpatient care and none addressed this issue in the general population.

**Aim:** The aim of the thesis is to estimate the prevalence of ADEs in the general population, to investigate the nature of ADEs, including categories of ADEs, and to evaluate the potential for preventing ADEs.

**Methods:** An expert panel of Swedish physicians in 2010 (n=19), a population-based survey to Swedish adults in 2010 (n=7099), medical records of adult residents of a county council in Sweden in 2008 (n=4970), and citations of bibliographic databases until 2010 (n=5770) were used as data sources, in addition to regional and national registers. ADEs were categorised into adverse drug reactions (ADRs), drug intoxications from overdose, drug dependence and abuse, sub-therapeutic effects of drug therapy (STEs), and morbidities due to drug-related untreated indications. The physicians estimated the proportions of their current patients with ADEs and preventable ADEs. The survey respondents reported experienced ADEs and their perceived preventability of ADRs and STEs. From the medical records, ADEs and their preventability were assessed manually by pharmacists and physicians, in a stepwise manner. A meta-analysis and a systematic literature review were conducted to summarise previous literature on preventable ADRs and methods to assess the preventability of ADEs.

**Results:** Swedish physicians estimated that half of their current outpatients and inpatients experienced ADEs. The one-month prevalence of self-reported ADEs in the adult general public was 19%, and the three-month prevalence of ADEs from medical records 12%. In the survey and medical record studies, ADRs and STEs constituted most ADEs and were equally prevalent. ADEs were frequently associated with nervous system and cardiovascular drugs, but the associated drugs, affected organs and seriousness varied by ADE category. The physicians estimated 24-31% of all ADEs preventable, while 39% of ADEs in the medical records were judged preventable. Of the ADE categories, a larger proportion of STEs than ADRs was perceived preventable by the survey respondents or judged preventable from the medical records. Based on the medical records, 56% of serious ADEs and 55% of serious ADRs were preventable, more than for non-serious ADEs and ADRs. Also based on the meta-analysis, half of ADRs among hospitalised and emergency patients were preventable. By large the associated drugs and affected organs for preventable ADEs were similar to all ADEs. Methods for assessing the preventability of ADEs were diverse, with unknown validity and scattered reliability.

**Conclusions:** The burden of ADEs in the adult general population, across care settings, demonstrates that ADEs are a considerable public health concern in the entire health system. The heterogeneous nature and varying potential preventability of the ADE categories indicate that categorising ADEs enhances the understanding of their nature and preventability. The diverse and limited methods for assessing the preventability of ADEs, however, enforce improving the assessment. Nonetheless, the high frequency of potentially preventable ADEs from commonly used drugs reinforces large-scale efforts to redesign safer, higher quality healthcare systems to adequately tackle the problem.

**Keywords:** adverse drug event, prevalence, preventability, medication error, patient safety, pharmacoepidemiology