Medication Incidents in Primary Care Medicine

A Study by the Swiss Federal Sentinel Reporting System

Sponsor und primary investigator	Markus Gnädinger, Steinach
HFV category	none, this is a project investigating preexisting completely anonymized non-genetic health related patient data
Version and date	10.0, December 18th 2014

Confidential

This protocol may not be copied or handled to others without being authorized by the project leader.

Synopsis

Sponsor and project leader (PL)	Markus Gnädinger
HFV category	none, this is a project investigating existing non-genetic health related patient data
Title	Medication Incidents in Primary Care Medicine A Study by the Swiss Federal Sentinel Reporting System
Acronym	MIPC-study
Population	Persons undergoing drug treatment in Swiss primary care medicine
Source data	Medical records in primary care or pediatric practices
Aim	To assess incidents accompanying drug therapy in primary care
Outcome	● to describe the type, frequency, seasonal and regional distribution of medication incidents ● to elucidate possible risk factors like age, gender, poly-medication, morbidity, previous hospitalization
Number of patients	500
Inclusion criteria	Any *erroneous* event (as defined by the physician) related to the medication process interfering with normal treatment course
Exclusion criteria	Lacking treatment effect, adverse drug reactions or drug-drug or drug-disease interactions, *without* detectable treatment error. Refusal of patients to refer data to the Sentinel system.
Statistics	Descriptive statistics, logistic regression.
Declaration	This project will be conducted under observation of the study protocol, the Declaration of Helsinki, and the actual Swiss Law.

Table of contents

Seite

1 List of abbreviations

IEC Independent ethical committee
PL Project leader

2 Involved persons and administration

Sponsor und and project leader:

Gnädinger Markus, Dr. med.
Birkenweg 8, 9323 Steinach
Email: markus.gnaedinger@hin.ch
Tel: #41 71 446 04 64
Fax: #41 71 446 34 11

Other persons engaged in the study direction:

Ceschi Alessandro, Dr. med.
(study direction board, knowlegde in pharmacovigilance)
Schweizerisches Toxikologisches Informationszentrum, Assoziiertes Institut der Universität Zürich, Freiestrasse 16, 8032 Zürich
Email: alessandro.ceschi@usz.ch
Tel: #41 44 251 51 51,
Fax: #41 44 252 88 33

Conen Dieter, Prof., MD,
(study direction board, president of „Patientensicherheit Schweiz“)
Bachstrasse 19, 5033 Buchs
Email: dieter.conen@bluewin.ch
Tel: #41 62 822 07 18
Fax: #41 43 244 14 81

Herzig Lilli, Dr. med.
(study direction board, French language)
IUMG, PMU, Rue du Bugnon 41,
1011 Lausanne
Email: lilli.herzig@hin.ch
Tel: #41 21 314 61 16
Fax: #41 21 314 75 90

Puhan Milo, Prof. Dr. med., MPH
(study direction board, methodology)
Institut für Soziale und Präventive Medizin,
Hirschengraben 84, 8001 Zürich
Email: milo.puhan@ifspm.uzh.ch
Tel: #41 44 634 46 11,
Fax: #41 44 634 49 86

Staehelin Alfred, Dr. med.
(study direction board, vice-president of Sentinella program commission)
Bankstrasse 20, 8400 Winterthur
Email: a.staehelin@hin.ch
Tel: #41 52 213 11 00,

Fax: #41 52 212 01 37

Zoller Marco, Dr. med.
(study direction board)
Limmattalstrasse 177, 8049 Zürich
Email: marco.zoller@hin.ch
Tel: #41 44 341 86 00,
Fax: #41 44 341 86 26

Andreas Birrer
*(Head of reporting systems „Federal Office of Public Health", **not** member of study board)*
Bundesamt für Gesundheit
Schwarztorstr. 96
3003 Bern
Email: andreas.birrer@bag.admin.ch
Tel: #41 58 46 49535
Fax: #41 58 46 38777

3 Introduction

Patient safety is a major concern in healthcare systems worldwide. Although most safety research has been conducted in the inpatient setting [1], evidence indicates that medical errors and adverse events pose a serious threat for patients in the primary care setting as well since most patients receive ambulatory care [2-4]. Gandhi and Lee noted that safety concerns in the outpatient setting differ from those in the hospital setting in obvious and non-obvious ways [5]. Diagnostic errors and adverse drug events have been identified as frequent safety concerns; furthermore, there is a body of literature about the safety of outpatient procedures and the consequences of coordination as well as continuity-of-care failures [6]. Hospital and outpatient care also differ in their infrastructure and in many processes, as well as their ability to detect, monitor and address safety issues. Information about frequency and outcomes of safety incidents in primary care is required to identify risks or "hot spots," to prioritize them and to take the action as needed.

Definition of terms
For the purpose of our study, we use the terminology of the International Classification for Patient Safety (World Health Organization) [7]. There, a *patient safety incident* is defined as an event or a circumstance which could have resulted or did result in unnecessary harm to a patient. Causes can be an *error*, as defined by: failure to carry out a planned action as intended or an application of an incorrect rule, or a *violation*, as defined by: deliberate deviation from an operating procedure, standard or rule, or an (external) *circumstance*, as defined by: a situation or a factor that may influence an event, agent or a person. We want to distinguish incidents from *adverse drug reactions* (ADR) which are defined as: unexpected harm resulting from a justified action where the correct medication process was followed for the context in which the event occurred, or *drug-drug* or *drug-disease interactions*. *Critical Incident Reporting System* (CIRS) confers to a voluntary anonymous database system to which Swiss family physicians or pediatricians may or may not report incidents as they occurred in their practices.

We will restrict the topic of our study to medication-related incidents. *Medication* or medicine confers to a pharmaceutical drug, officially called medicinal product, which can be loosely defined as any chemical substance — or product comprising such — intended for use in the medical diagnosis, cure, treatment, or prevention of disease [Wikipedia].

Information retrieval
Methods to collect information about adverse incidents are manifold [2,8-10]. They may be based on voluntary vs. mandatory reporting systems or audit of medical charts. Furthermore, questionnaires can be applied to patients, or pharmacists may report to registering systems. Interviews can be held with physicians or questionnaires filled out by them. Charts of deceased patients can be audited meticulously, or medico-legal cases may be analyzed. Information may be derived prospectively in an actual case by case manner or retrospectively along case-vignettes. The two methods most commonly applied are incident reporting and chart review. Both methods have in common the potential to systematically cover information on the entire range of safety events in medical offices.

Incident reporting has a long tradition in clinical risk management and is increasingly used in outpatient care [11-13]. Indeed, incident reporting has been the dominant method for study of safety incidents in primary care [14]. It is based on voluntary and usually anonymous reports of physicians and nurses and is used to describe the types and characteristics of patient safety incidents. These reports may vary considerably with respect to the information which is included, and the likelihood of "true" incidents being reported is unclear. Studies based on this method describe strong variations in the number of reports submitted [15]. Moreover, professional groups differ in their frequency of reporting; in-hospital care physicians reported preferentially severe incidents while nurses did so over the whole spectrum of impact levels [16]. O'Beirne et al concluded from a very low report rate (<1 report per person per year) that incident reporting may be a costly but not very effective way to study safety problems in primary care [17]. The same problem applies to ADR notification systems which also bare non-reporting rates of more than 90% [18]. A recent Swiss study analyzed safety in primary care [10]. This was a semi-quantitative, retrospective investigation in over 300 nurses and physicians. Seven of 23 issues corresponded to drug treatment. Frequently named were insufficient monitoring of potential side effects, missing prescriptions of required treatment, and errant medication as concerning route of administration, dosage or timing. The low and perhaps biased reporting of incidents in any system makes it difficult, say impossible to get valuable information from quantitative inferential statistics on critical incident reporting systems [19].

With *chart review*, medical records are analyzed by independent experts in order to identify adverse events and to assess potential harm and preventability in each case [20]. Such analysis requires complete and correct patient documentation to provide valid results. In many cases relevant information may be unavailable [21]. As chart review is a time-consuming approach, many resources are needed to analyze a large number of patient records at different primary care offices; furthermore this kind of analysis is mainly retrospective.

To apply a supplemental method to gaining additional insight into safety hot spots in primary care, we aim at assessing medication errors by using the Swiss National *Sentinel Network*. Founded in 1986, it was mainly designed to survey transmissible diseases. Later on, it also assessed other health problems of public interest. Approx. 150 family physicians and pediatricians report to the system. It generates daily to weekly current data. Covering the whole geographic and linguistic regions of our country, this study should last a whole year period.

Sandars et al. described a frequency of 5 – 80 medical errors per 100'000 consultations in primary care patients [2]. Incidents as defined above may also result from circumstantial factors (without an error) and therefore occur somewhat more frequently. In order to not to overburden the participating physicians with our study, we decided to limit our focus to medication incidents. These make up between 9 to 42 % of all registered incidents [2,9,22-24], and of them approx. 70% may be prescription errors [25]. In contrast to the study by Sandars et al, pilot study performed in 21 physicians during July to October 2013 showed a rate of approx. one medication incident per two months and per physician [unpublished data], while the former calculated a rate of about one in two years.

Concerning predisposing factors, Avery et al found a propensity for becoming victim of medication errors with young (<15) or elderly (>64) age [26]. The latter was confirmed by Salanitro et al [27]. Two studies by Fields et al reported morbidity as promoting errors [27,28]. All studies listed poly-medication as a key factor [26-30]. Better knowledge of factors associated with medication errors would be helpful to implement preventive measures and therefore reduce frequency of avoidable incidents in the future.

4 Aims of the project

To assess incidents accompanying drug therapy in primary care.

5 Design

This is a project to re-use existing non-encrypted non-genetic health-related medical record data. The data will be collected from January 1st to December 31th 2015.

5.1 Outcomes

● to describe the type, frequency, seasonal and regional distribution of medication incidents
● to elucidate possible risk factors like age, gender, poly-medication, morbidity, previous hospitalization.

6 Population

Any person undergoing drug treatment in Swiss primary care medicine. This includes children, mentally retarded, and very old people. We suppose that in this vulnerable patient group treatment error frequencies could be higher and that interface problems of communication could be increased.

6.1 Inclusion criteria

- Any *erroneous* event (as defined by the physician) related to the medication process interfering with normal treatment course.

Age and gender: any.

6.2 Exclusion criteria

- Lacking treatment effect, adverse drug reactions or drug-drug or drug-disease interactions *without* detectable treatment error.
- Refusal of patients to refer data to the Sentinel system.

7 Patient's information and consent

We are collecting health-related patient data and submitting them in an anonymized form to the Sentinel system. We are not demanding explicit consent from them, but explicit refusals to participate are respected. Eventual information of the patients has to be recorded in the patient history.

8 Data handling

This study re-uses clinical record data without generating new information. Whenever an item cannot be answered, "missing" is entered to the data file.

For our study, there are principally three data sources. Firstly, incident-related patient data are reported. They are generated by the caring process – no data but the ones needed for treatment will be collected. Secondly, we collect denominator data from patients visiting the practices but without undergoing a medication incident. Thirdly, we earn information from the physicians describing their practices and their reasoning about prevention of further incidents.

The patient data are reported either by a paper/pencil version or by an online questionnaire. The paper version is sent in a closed envelope to the Sentinella administration, which mails it further to the PL. Only the PL has access to incident-related patient data. As for the denominator data: they are collected by the Sentinella administration and thereafter shared with the PL. The physician-related data will be handled likewise as the incident-related patient's ones.

The Sentinella administration figures as an intermediary. The PL does not know the identity of the physician, while the Sentinella administration has no clinical information about the incident-related patient data. While the physician-related information is coded by their Sentinella-identification number, the incident-related data is anonymous.

We have the additional possibility to get denominator data from Interpharma, providing us with medicament selling rates by indication groups on demand. This may help to compare incident rates by indication groups with others (e.g. non-steroidal anti-inflammatory drugs vs. serotonin reuptake inhibitors).

8.1 Questionnaire development

Because questionnaires suitable for continuous reporting and adapted to our local conditions do not exist, we had to develop new ones. The construction of the questionnaires included questions on the social and clinical state of the patients, on the type of incident, and on possible causative factors. Therefore based on literature [10] we performed a pilot study from July until September 2013 to test the questionnaires in a sample of primary care physicians or pediatricians in two language sets (German and French) in the three different language regions of Switzerland (German 11, French 7, and Italian 3) for eight weeks. Validation of the questionnaires was not imperative, since we did not measure hidden constructs (like "depression") by our questions, and information was mainly needed about influencing our target variable, i.e. the type and frequency of incidents.

8.2 Data to be collected

Physician-related data:
A (initial questionnaire): Sentinella number, number of physicians and number of Sentinella-reporting physicians working in the practice, working hours per week, drug distribution system, electronic drug prescription, availability of X-ray, ECG, ultrasound, interaction controlling system, electronic medical history or quality certificate, team sessions, quality circle participation, special education/interests, caring for a patient institution, other activities. The following variables will be

delivered by Sentinella administration: gender, age, specialization, localization (urbanity, language region).
B (terminal questionnaire): proportion of non-reporting.

Patient-related data:
A (incident questionnaire, only pre-existing data from medical records): year of birth, gender, relationship to the patient, dwelling, social problems, dementia or mental retardation, psychiatric problems, use of psychotropic drugs, linguistic problems, smoking, substance abuse, visual blurring, hearing loss, gait disturbance, renal insufficiency, liver cirrhosis/insufficiency, previous hospitalization, foreign care, number of chronically administered active drugs, number of diagnoses for chronic disease, scale value of "Thurgau Morbidity Index (TMI)" [31], description of incident, who noticed the incident, what was wrong, name of drug, other drugs eventually used, endangering of patient, damaging amount, organ system, duration, recovery, treatment, possible causal triggers, interface problems, information of the patient about the incident and his reaction, consequences of the incident, responsibility, possibility to anticipate the incident, whether a similar incident was yet notified within the study, general proposals.
B (denominator, 14 days per year detailed analysis of physician-to-patient contacts): previous hospitalization, foreign care, number of active drugs, number of diagnoses, TMI, year of birth, gender.
C (denominator, 365 days per year): daily physician-to-patient contacts.

8.3 Data encrypting

Only the Sentinella administration knows the names and addresses of the physicians. Only the physicians know the identity of the patients. The PL has no access to either information.

8.4 Limitations

For the detection of possible underreporting, we included an item to our final questionnaire. From the weekly reporting forms, we can estimate the amount of missing incident reporting forms. We collect information only from physicians (because only they report to the Sentinel system) not from nurses, so some selective reporting towards more severe cases may occur. Notably, there was only a minimal overlap between physician-driven reporting on the one hand and in-deep chart review on the other [8]. The bias by non- or selective reporting or non-detection of an error and others make it difficult to retrieve any other than qualitative and descriptive information from our study data [19]; these aspects would have to be analyzed in a future qualitative study.

8.5 Time schedule

The pilot study took place in July until September 2013. The study protocol and the key findings of the pilot study shall be submitted to publication in winter 2014/5. The main study shall take place during the year 2015. Evaluation of the study data and writing of the publication will be performed during 2016.

9 Statistics

9.1 Expected number of cases

Based on our pilot trial (unpublished data) we expect one drug-related incident to happen every two months per physician. In the Sentinella system at this moment there are 165 physicians actively reporting. When assuming they are working 10 months per year, this would result in 660 incidents. We have to downsize this number so some extent because not all physicians work 100%, there will be some non-reporting or non-detecting of incidents, and some of the physicians are pediatricians, generating a much lower rate of incidents. So we expect a number of approx. 500 cases in our study.

9.2 Statistical methods

For analysis of our data, we will use descriptive statistics. Where denominator data are available, we will apply logistic regression.

10 Independent ethical committee (IEC)

The ethical committee of Canton Zurich decided that our study did not need formal approval, because the data are anonymous (KEK-ZH 2014-0400). The study was recorded to www.ClinicalTrials.gov NCT02295371, as well as to our national study registry (www.kofam.ch; SNCTP000001207).

11 Collection of health related patient data without explicit consent

11.1 Why an informed consent cannot be achieved

In our pilot study, there has been a rate of approx. 50% non-declaration to the victim patients of an incident. If we would demand an informed consent to retrieve these data, a substantial proportion of physicians would probably decide not to report an incident, leading to biased results.

11.2 Weighing up research interest against patient confidentiality

The circumstances of medication incidents may be more compromising to physicians or other health-professionals than to the patients. So it is understandable, that physicians do not like to confess an error that has yet been corrected – presenting no more danger the patients – and so unnecessary undermining the trustful relationship with them. Our study will also explore the reasons why not to communicate and the reactions among patients after confession of an error to them.

11.3 List of persons with access to the data

As mentioned above, the only one with direct access to un-aggregated patient data is the PL.

11.4 Other measures to preserve confidentiality

The fact that an intermediary is providing data exchange will enhance confidentiality. Furthermore for the online questionnaires, we will not collect IP-addresses.

12 Confidentiality of data

The collection, transfer, storage and analysis of personal data within this project are carried out in accordance with applicable Swiss data protection regulations.

The data will be entered in our online questionnaire (SurveyMonkey) either directly by the physicians, or the PL will enter the paper/pencil data to the online questionnaire. From the questionnaire database an SPSS file will be created for analysis. All data will be preserved for 10 years after the last database entry. No one but the PL has data access.

13 Publication

The study protocol is aimed to be published together with the pilot study data in winter 2014/5. The data of the main study will be published in international peer-reviewed journals.

14 Signatures

The persons signing accept the content of this project and confirm this statement with their signature.

Sponsor und principal investigator

I hereby confirm that this project protocol

- was reviewed by using the moral, ethical and scientific principles of clincal research and has been approved by me. I certify that the data will be handled and used in accordance with national data protection regulations.

Steinach, 18.12.14 **Dr. med. Markus Gnädinger**

place, date	signature

15 References

1. **Manias E:** Detection of medication-related problems in hospital practice: a review. Br J Clin Pharmacol 2012; 76 (1): 7-20.
2. **Sandars J, Esmail A.** The frequency and nature of medical error in primary care: understanding the diversity across studies. *Fam Pract.* 2003;20(3):231-236.
3. **Thomsen LA, Winterstein AG, Søndergaard B, Haugbølle LS, Melander A.** Systematic review of the incidence and characteristics of preventable adverse drug events in ambulatory care. *Ann Pharmacother.* 2007;41(9):1411-1426.
4. **Miller GC, Britth HC, Valenti L.** Adverse drug events in general practice patients in Australia. *Med J Aust.* 2006;184(7):321-324.
5. **Gandhi TK, Lee TH.** Patient safety beyond the hospital. *N Engl J Med.* 2010;363(11):1001-1003.
6. **Fröhlich T, Zorina O, Fontana AO, et al:** Evaluation of medication safety in the discharge medication of 509 surgical inpatients using electronic prescription support software and an extended operational interaction classification. Eur J Clin Pharmacol. 2011; 67 (12): 1273-82.
7. **Runciman W, Hibbert P, Thomson R, et al:** Towards an international classification for patient safety: key concepts and terms. Int J Qual Health Care 2009; 21 (1): 18-26.
8. **Wetzels R, Wolters R, van Weel C, Wensing M:** Mix of methods is needed to identify adverse events in general practice: A prospective observational study. BMC Fam Pract 2008; 9:35.
9. **Gaal S, Harman C, Giesen P; et al:** Complaints against family physicians submitted to disciplinary tribunals in the Netherlands: lessons for patient safety. Ann Fam Med 2011; 9 (6): 522-7.
10. **Gehring K, Schwappach DLB, Battaglia M, et al.** Frequency of and harm associated with primary care safety incidents. Am J Manag Care. 2012;18(9):e323-e337.
11. **Rubin G, George A, Chinn DJ, Richardson C.** Errors in general practice: development of an error classification and pilot study of a method for detecting errors. *Qual Saf Health Care.* 2003;12(6):443-447.
12. **Elder NC, Vonder Meulen M, Cassedy A.** The identification of medical errors by family physicians during outpatient visits. *Ann Fam Med.* 2004;2(2):125-129.
13. **Makeham MA, Kidd MR, Saltman DC, et al.** The Threats to Australian Patient Safety (TAPS) study: incidence of reported errors in general practice. *Med J Aust.* 2006;185(2):95-98.
14. **Makeham MA, Dovey S, Runciman WB, Larizgoitia I.** *Methods and Measures used in Primary Care Patient Safety Research*. Geneva, Switzerland: World Health Organization; 2008.
15. **Makeham MA, Dovey SM, County M, Kidd MR.** An international taxonomy for errors in general practice: a pilot study. *Med J Aust.* 2002; 177(2):68-72.
16. **Rowin EJ, Lucier D, Pauker SG, Kumar S, Chen J, Salem DN.** Does error and adverse event reporting by physicians and nurses differ? *Jt Comm J Qual Patient Saf.* 2008;34(9):537-545.
17. **O'Beirne M, Sterling PD, Zwicker K, Hebert P, Norton PG.** Safety incidents in family medicine. *BMJ Qual Saf.* 2011;20(12):1005-1010.
18. **Gnädinger M, Mellinghoff HU.** The out-of-focus bias in drug surveillance. Eur J Clin Pharmacol, 2012, DOI 10.1007/s00228-012-1371-x
19. **Pham JC, Girard T, Pronovost PJ:** What to do with healthcare incident reporting systems? J Publ Health Res 2013; 2: e27.
20. **Gandhi TK, Weingart SN, Borus J, et al.** Adverse drug events in ambulatory care. *N Engl J Med.* 2003;348(16):1556-1564.
21. **Stange KC, Zyzanski SJ, Smith TF, et al.** How valid are medical records and patient questionnaires for physician profiling and health services research? A comparison with direct observation of patient visits. *Med Care.* 1998;36(6):851-867.
22. **Gaal S, Verstappen W, Wolters R et al:** Prevalence and consequences of patient safety incidents in general practice in the Netherland: a retrospective medical record review study. Implementation Sci 2011; 6: 37.

23. **Wetzels R, Wolters R, van Weel C, Wensing M:** Harm caused by adverse events in primary care: a clinical observational study. J Eval Clin Pract 2009; 15: 323-7.
24. **Khoo EM, Lee WK, Saraks S et al:** Medical errors in primaray care clinics – a cross sectional study. BMC Fam Pract 2012; 13: 127.
25. **Kuo GM, Phillips RL, Graham D et al:** Medication errors reported by US family physicians and their office staff. Qual Saf Health Care 2008; 17: 286-90.
26. **Avery AJ, Maisoon G, Barber N et al:** The prevalence and nature of prescribing and monitoring errors in English general practice: a retrospective case note review. Br J Gen Pract 2013; e534-53.
27. **Salanitro AH, Osborn CY, Schnipper JL et al:** Effect of patient- and medication-related factors on inpatient medication reconciliation errors. J Gen Intern Med 2012; 27 (8): 924-32.
28. **Field TS, Gurwitz JH, Harrold LR et al:** Risk factors for Adverse drug events among older adults in the ambulatory setting. J Am Geriatr Soc 2004; 52: 1349-54.
29. **Field TS, Mazor KM, Briesacher B et al:** Adverse drug events resulting from patient errors in older adults. J Am Geriatr Soc 2007; 55: 271-6.
30. **Mira JJ, Orozco-Beltran D, Perez-Jover V et al:** Physician patient communication failure facilitates medication errors in older polymedicated patients with multiple comorbidities. Fam Pract 2013; 30: 56-63.
31. **Fischer JE, Peltenburg M, Kühne R et al:** Der TMI auf dem Prüfstand: Güte und Probleme der Kostenvorhersage anhand einfach kodierbarer Patientenmorbidität. SAEZ 2077; 88 (26): 1156-65.