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Medication incidents in primary care medicine: protocol of a study by the Swiss Federal Sentinel Reporting System

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ABSTRACT

Background/rationale: Patient safety is a major concern in healthcare systems worldwide. Although most safety research has been conducted in the inpatient setting, evidence indicates that medical errors and adverse events are a threat to patients in the primary care setting as well. Since information about the frequency and outcomes of safety incidents in primary care is required, the goals of this study are to describe the type, frequency, seasonal and regional distribution of medication incidents in primary care in Switzerland and to elucidate possible risk factors for medication incidents.

Methods and analysis: Study design and setting: We will conduct a prospective surveillance study to identify cases of medication incidents among primary care patients in Switzerland over the course of the year 2015. *Participants*: Patients undergoing drug treatment by 167 general practitioners or paediatricians reporting to the Swiss Federal Sentinel Reporting System. *Inclusion criteria*: Any *erroneous* event, as defined by the physician, related to the medication process and interfering with normal treatment course. *Exclusion criteria*: Lack of treatment effect, adverse drug reactions or drug–drug or drug–disease interactions *without* detectable treatment error. *Primary outcome*: Medication incidents. *Risk factors*: Age, gender, polymedication, morbidity, care dependency, hospitalisation. *Statistical Analysis*: Descriptive statistics to assess type, frequency, seasonal and regional distribution of medication incidents and logistic regression to assess their association with potential risk factors. *Estimated sample size*: 500 medication incidents. *Limitations:* We will take into account under-reporting and selective reporting among others as potential sources of bias or imprecision when interpreting the results.

Ethics and dissemination: No formal request was necessary because of fully anonymised data. The results will be published in a peer-reviewed journal.

Trial registration number: NCT0229537.

Strengths and limitations of this study

- First Swiss prospective and systematic collection of incident data in primary care.
- Covering three linguistic regions and two distribution systems.
- Bias from selective and under-reporting or non-detection.

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[5] noted that safety concerns in the outpatient setting differ from those in the hospital setting in obvious and non-obvious ways. Medication-related incidents are also important in primary care, but are perhaps not as well documented as in secondary care. A study by Gandhi and Lee[6] in primary care showed that 25% of 661 ambulatory care patients with at least one prescription had such an incident, of which 13% were classified as serious and 39% as preventable or ameliorable. In a study by Pirmohamed *et al* in the UK, medication-related incidents caused about 6.8% of all hospitalisations[7] and in Switzerland, these incidents are responsible for about 7.2% of hospitalisations.[8] Diagnostic errors[9] 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.[10] Hospital and outpatient care also differ in their infrastructure and in many processes, as well as in their ability to detect, monitor and address safety issues. Information about the frequency and outcomes of safety incidents in primary care is required to identify risks or 'hot spots', to prioritise them and to take action as needed.

Definition of terms

For the purpose of our study, we use the terminology of the International Classification for Patient Safety (WHO).[11] Here, 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. There are several possible causes. (1) An *error*, defined as: failure to carry out a planned action as intended or an application of an incorrect rule; (2) A *violation*, defined as: deliberate deviation from an operating procedure, standard or rule; (3) An (external) *circumstance*, defined as: a situation or factor that may influence an event, agent or 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. The same applies to *drug–drug* or *drug–disease interactions* (DDI). *Critical Incident Reporting System* (CIRS) refers to a voluntary anonymous database system to which Swiss family physicians or paediatricians may report incidents as those occurred in their practices.

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

Information retrieval

Methods to collect information about adverse incidents are manifold.[2 11–14] In the literature, different ways to collect adverse incident information are described: voluntary versus mandatory reporting systems, patient questionnaires, or pharmacists reporting to registries. Interviews can be held with physicians or questionnaires can be filled out by them. Charts of deceased patients can be audited meticulously or medicolegal cases may be analysed. Information may be derived prospectively in an actual case by case manner or retrospectively along case vignettes. The two methods most commonly used are incident reporting and chart review. Both methods have the potential to systematically cover information on the entire range of safety events in medical offices in common.

Incident reporting has a long tradition in clinical risk management and is increasingly used in outpatient care.[15–18] Indeed, incident reporting has been the dominant method for the study of safety incidents in primary care.[19] 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 large variations in the number of reports submitted.[20] Moreover, professional groups differ in their frequency of reporting; in-hospital care physicians reported preferentially severe incidents, while nurses cover the whole spectrum of impact levels.[20] Selective reporting by physicians may have multifactorial causes such as lack of time, thinking that an ADR which is already known is not worth mentioning, or concerns about data confidentiality. Non-reporting may be as frequent as 94%.[21 22] 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".[23] A recent Swiss study analysed safety issues in primary care.[12] This was a semiquantitative, retrospective investigation involving over 300 nurses and physicians. Seven of 23 issues were related to drug treatment. Frequently named issues were insufficient monitoring of potential side effects, missing prescriptions of required treatment, and errant medication relating to the route of administration, dosage or timing. The low and perhaps, selective reporting of incidents in any system makes it difficult or virtually impossible to collect valuable quantitative information from CIRS.[24]

In *chart review*, medical records are analysed by independent experts in order to identify adverse events, and to assess potential harm and preventability in each case.[25] Such analysis requires complete and correct patient documentation to provide valid results. In many cases relevant information may be unavailable.[25] As chart review is a time-consuming approach, many resources are needed to analyse a large number of patient records at different primary care offices; furthermore, this kind of analysis is usually retrospective.

Sandars and Esmail[2] described a frequency of 5–80 medical errors per 100 000 consultations in primary care patients. Incidents, as defined above, may also result from circumstantial factors (without any errors) and therefore, occur somewhat more frequently. In order to not overburden the participating physicians with our study, we decided to limit our focus to medication incidents. These make up between 9% and 42% of all registered incidents[2 9 26–28] and of these, approximately 70% may be prescription errors.[29] In contrast to the study by Sandars and Esmail, our pilot study found a rate of approximately one medication incident per 2 months and per physician (see online supplementary appendix 1), while the former reported a rate of about one in 2 years.

Concerning predisposing factors, Avery *et al*[30] found a propensity for becoming a victim of medication errors with the young (<15 years) or elderly (>64 years) ages. The latter was confirmed by Salanitro *et al*.[31] Two studies by Field *et al*[32 33] reported morbidity as promoting errors. All studies listed polymedication as a key factor.[30–34] Better knowledge of factors associated with medication errors would be helpful to implement preventive measures and therefore, reduce the frequency of avoidable incidents in the future.

The Swiss National Sentinel Reporting Network (http://www.sentinella.ch)

To apply a supplementary method to gaining insight into safety hot spots in primary care, we aim to assess

medication errors by using the Swiss National *Sentinel Reporting Network*. Founded in 1986, it was mainly designed to survey transmissible diseases. Later, it also assessed other health problems of public interest. In 2015, besides our project, the areas covered are: surveillance of mumps, whooping cough, flu or *Borrelia,* pneumonia and middle ear infections, tick bites, vaccinations against measles or whooping cough, and alcohol use among adolescents. One hundred and forty general internal medicines and 27 paediatric practices report to the system, 109 of them in the German, 44 in the French, and 14 in the Italian part of Switzerland. It generates daily to weekly current data and covers the entire geographic and linguistic regions of our country.

METHOD

Aims of the project

To describe the type, frequency, seasonal and regional distribution of medication incidents in primary care in Switzerland and to elucidate possible risk factors such as age, gender, polymedication, morbidity, and previous hospitalisation.

Study design

We will conduct a prospective surveillance study to identify cases of medication incidents among primary care patients over the course of 1 year.

Population

Any person undergoing drug treatment in general internal or paediatric practices participating in the Sentinella network. The latter covers a representative sample of patients in primary care for Switzerland (see above). These patients include children, individuals with mental retardation or the elderly—all of whom might be at increased risk for medication errors.

Inclusion criteria

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

Exclusion criteria

- Lacking treatment effect, ADR, or drug–drug interaction or DDI *without* detectable treatment error.
- Refusal of patients to refer data to the Sentinel system.

Questionnaire development

As we could not identify questionnaires suitable for continuous reporting and adaptable to our local conditions, we had to develop new ones. We tested these in an 8-week pilot study (see online supplementary appendix 1).

In the Sentinella study, the Italian speaking physicians had to decide whether to report in German or French. For the main study, we developed only two language sets of questionnaires, since these had to be filled in only by physicians, not by patients. We deemed assessment of construct validity of the questionnaires not imperative, since we did not measure hidden constructs (like 'depression') by our questions and information was mainly needed about influencing our target variable, that is, the type and frequency of incidents.

Data to be collected

The data to be collected in our study are summarised in boxes 1 (physician related) and 2 (patient related/incident related); for the latter, only pre-existing data from medical records will be collected. Furthermore, we collected denominator data as depicted in box 3.

Time schedule

The pilot study took place from July until September 2013. The final questionnaires in both languages and their English translation are available at http://www.medication-incidents.ch. The main study takes place from January until December 2015. Evaluation of the study data and writing of the publication will be performed in 2016.

Statistics

Expected number of cases

On the basis of our pilot trial (see online supplementary appendix), we expect at least one drug-related incident to be reported every 2 months per physician. In the Sentinella system, there are currently 167 physicians actively reporting, among them are 27 paediatricians.

Box 1 Physician-related data

Initial questionnaire
Sentinella identification number
Gender*
Age*
Specialisation (general practitioner or paediatrician)*
Number of physicians in practice, and among them those reporting to Sentinella*
Working hours per week*
Drug distribution system (by pharmacist or by physician)
Drug prescription system (electronic, machine written, hand-written)
Electronic drug–drug interaction (DDI) system
Availability of X-ray, ECG, ultrasound
Medical history (electronic or paper based)
Quality certificate
Team sessions
Physician's participation in quality circle
Localisation (urbanity, language region)*
Special education/interests
Caring for institutions
Final questionnaire
Proportion of non-reporting incidents during the study

The data are collected from each physician reporting to the Sentinella system. The questionnaire and the coding plan are available at http://www.medication-incidents.ch.
*These data is delivered by Sentinella administration. All other data will be collected by use of questionnaires.

Box 2 Patient-related data

Patient-related/incident-related items
Week of reporting
Year of birth
Gender
Physician-to-patient relationship
Dwelling situation
Social problems
Dementia or learning disabilities
Psychiatric problems
Use of psychotropic drugs
Linguistic problems
Smoking or substance abuse
Visual blurring or hearing loss
Gait disturbance
Renal insufficiency
Liver cirrhosis/insufficiency
Previous hospitalisation (12 months)
Care dependency
Number of chronically administered active drugs*
Number of diagnoses for chronic disease
Scale value of 'Thurgau Morbidity Index' (TMI)[35]
Description of incident
Who noticed the incident
What went wrong
Name of drug
Other drugs used possibly related to the incident
Endangering of patient
Amount of damage
Organ system involved
Duration
Recovery
Treatment/surveillance
Causal triggers
Interface problems
Information to the patient about the incident and his reaction
Consequences of the incident
Responsibility
Possibility to anticipate the incident
Whether a similar incident was previously notified within the study
General proposals
Physician-related items
Sentinella identification number

The data are collected for each incident. The *basic reporting* of a medication incident is collected weekly. It includes the Sentinella identification number, the gender of the patients and their year of birth. The questionnaire and the coding plan are available at http://www.medication-incidents.ch.
*Each regularly prescribed or administered pharmacological specialty counts per active substance contained, according to the latest available medication list. All therapies regularly taken during at least 1 month are considered. Drugs that are prescribed for shorter periods (eg, antibiotics for a week) are not included. Regularly administered eye drops, inhalations, nasal sprays count if a general systemic effect is intentional (eg, calcitonin nasal spray) or must be taken into account (eg, timolol eye drops). Also transcutaneous, subcutaneous or vaginal hormone-releasing systems, and preparations administered by the specialist (eg, gynecologist: birth control pills) should be recorded. Herbal drugs count—regardless of the number of plants—as one medication. Homeopathic drugs, cell salts, etc, are not counted. Multivitamins count if they are taken due to a medical indication (eg, short bowel syndrome), but not when the administration was adopted as 'roborant'; multivitamins are considered *one* drug. Also therapies at the hospital administered such as oncology are counted. Whether the patient also applies the drug (compliance) is irrelevant to the study, the important thing is that it is so prescribed. Prescribed medications to relieve on requirement which do not need to be taken daily, or self-medication is not recorded.

When assuming that they work 10 months per year, this would result in 660 reported incidents. We, hence, have to decrease this number to some extent because not all physicians work 100%, there will be some non-reporting or non-detection of incidents, and paediatricians report lower rate of incidents (according to the results of our

Box 3 Denominator data

Fortnight analysis (only once in study, from 7 to 20 March 2015)
Previous hospitalisation (during the preceding year)
Care dependency
Number of active drugs chronically administered
Number of chronic diagnoses
Scale value of 'Thurgau Morbidity Index' (TMI)[35]
Year of birth*
Gender*
Multiple consultation (within the 14-day period)
Sentinella identification number
Daily analysis
Physician-to-patient contacts
Sentinella identification number

The data are collected from each patient consulting the practice during the year 2015, irrespective of the presence of an incident. *Year of birth and gender will be collected during another 14-day period in fall but without the other items. The questionnaire and the coding plan are available at http://www.medication-incidents.ch. Definition of medication count: see box 2.

pilot study). So we expect approximately 500 incidents in our study.

Statistical methods

For the analysis of our data, we will use descriptive statistics in order to describe the type, frequency, seasonal and regional distribution of medication incidents. We will use logistic regression to assess the association of medication incidents with potential risk factors. We will use SPSS.

Independent ethical committee

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

STROBE statement: Where applicable, our publication will follow the general STROBE guidelines (http://www.equator-network.org/).

RESULTS FROM A PILOT STUDY

From the existing literature,[12] we included questions on the social and clinical state of the patients, on the type of incident, and on possible causative factors, and tested these in a pilot study, from July until September 2013, with a sample of general physicians or paediatricians; these were in two language sets (German and French) for the three different language regions of Switzerland (German 11, French 7, Italian 3) for 8 weeks. Fifty-one cases were recorded, leading to an incident rate of 0.4 (median, IQR 0.4) per family physician, and week or 4 (5) per family physician and 1000 patient contacts. Virtually no incidents were observed by paediatricians (details of this study are presented in online supplementary appendix 1).

DISCUSSION

Strength and limitations

Our study is the first prospective and systematic collection of incident data in Swiss primary care. The well-motivated reporting physicians, the duration of 12 months and the coverage of the three main linguistic regions as well as of two drug distribution systems will deliver new and relevant insights.

Not all cases may be reported; there may be some selective reporting of cases of higher clinical importance, and some cases may not be reported due to lack of time or legal considerations. Some cases may not be detected by the physicians. Some non-prescription treatments may be missed if they are not causally linked to the incident. The sample size may be too small for inferential statistics. The 14-day denominator period may not be representative for the patient collective over the whole year. The definition of inclusion criteria may be interpreted varyingly by the physicians. Qualitative information may be missed in this study and has perhaps to be further addressed in qualitative research. The low and perhaps selective reporting of incidents in any system makes it difficult or virtually impossible to collect valuable quantitative information from CIRS.[24]

CONCLUSION

Data on safety issues in ambulatory primary care patients is scarce and this is also true for Switzerland. The retrospective qualitative study by Gehring *et al*[12] and the study by Livio *et al*[8] on hospitalisations makes it reasonably clear that things are in no way better than that in UK[7] or USA,[6] where 6.5% of all hospitalisations and 4.0% of all hospital care days as well as 1 in 667 hospital deaths are caused by medication incidents. Since up to 72% of these appear to be preventable or ameliorable, it seems worthwhile to focus on these so as to further elucidate risk factors.

The data of our study should allow for describing the type, frequency, seasonal and regional distribution of medication incidents in Swiss primary care practices and for helping to identify risk factors. The definition of 'hot spots' could sensitise the physicians to focus on dangerous situations and help them to redefine their standing operational procedures (SOPs).

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Contributors MG lead the study, did the pilot study (questionnaire development, data entering and processing), wrote all documents, made all the contacts with the Sentinella administration, ethics committee and others, programmed the electronic questionnaires, will enter the hand-written questionnaires into the database, will do the data processing and will write the publication after data collection. LH is French speaking and will help others to understand the French-printed questionnaires. MP was responsible for sound methodology. AS conceived the idea for the study. All the authors have seen all the study documents and contributed intellectually to this publication. All the authors have contributed to the revision of the draft of this publication, and approved the submitted version of this publication.

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Medication Incidents in Primary Care Medicine

Protocol of a Study by the Swiss Federal Sentinel Reporting System

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Appendix 1. Results of the pilot study

Summary

From July to September 2013 in 18 Swiss family and pediatric practices, a pilot trial on medication incidents took place. 51 notifications were recorded, leading to an incident rate of 0.4 (0.4) (median, interquartile range) per family physician and week or 4 (5) per family physician and 1'000 patient contacts. Virtually no incidents were observed in pediatricians.

Aims of the pilot study

- to test the questionnaires (logistical feasibility, understandability of questions, correctness and consistency of responses)

- to limit the inclusion criteria to obtain complete information without too much redundancy with other notification systems such as the Critical Incident Reporting System (CIRS) or spontaneous reporting of ADRs (pharmacovigilance).

Study design

Prospective, explorative observational questionnaire study with a case-control design

Methods

Questionnaires and Physicians

Because questionnaires suitable for continuous reporting and adapted to our local conditions do not exist, we had to develop new ones. Therefore, based on existing literature, the study directors tested a pre-pilot version in their own praxis. The questionnaires included items on the social and clinical state of the index patients, on the kind of incident, and on possible causative factors. Before using them in a main study of the national Sentinel system, we performed a pilot study to test the questionnaires in a sample of primary care physicians or pediatricians, in each of the German, French or Italian speaking parts of Switzerland for a period of six to eight weeks. All medication-related incidents were recorded and the daily patient-to-physician contacts were counted. To identify factors correlated to specific incidents, the physicians had to collect information for each case also from a *control* patient, matched on age and sex. The initial version of the questionnaire was in German; thereafter it was translated into French. The Italian-speaking physicians could select either version. The patient information sheets were translated into Italian, too.

Inclusion criteria (Physicians)

Willingness to report 6 to 8 weeks of work from July to September 2013.

Exclusion criteria (Physicians)

Participation in the Federal Sentinel reporting system.

Inclusion criteria (Incidents)

Any unexpected event (as defined by the physician) related to the medication process which interfered with the normal course of treatment.

Exclusion criteria (Incidents)

An expected (but unavoidable) ADR, or drug-drug interaction (DDI).

Ethics

This pilot study protocol was submitted to the ethics board of the Canton Zurich, which decided that formal approval was not necessary. An informed consent form had to be signed by the patients. If patients declined participation in the study, reporting was still conducted, but without their personal data; the same applied to minor incidents when the physician was reluctant to confront the patient with information that she or he judged to be irrelevant or could cause a possible loss of confidence. Notification of incidents without informed consent is important for detection of a possible “ethical bias”.

Support

The pilot study was supported by the Bangeter-Rhyner Foundation, Basel.

Data concealing / Statistics

For the purpose of patient tracking, gender and full birth day data were indispensable. In the final dataset, the day and month from the birth information was deleted. Data are presented as median (interquartile range) or frequencies unless stated otherwise. The data sheets were sent to MG, who recorded them on an Excel spreadsheet. Descriptive statistics were performed by using SPSS. No other person had access to the raw data.

Study registration

No registration was conducted.

Results

The study took place from July to September 2013.

From the 24 physicians who were initially willing to participate our pilot trial, 6 dropped out (lack of time, did not understand the sense of the project), leading to a set of 18 to be analyzed. Their characteristics and those of their practices are summarized in Table A1. The median age of all patients was 51 (20) years for family doctors and 7 (interquartile range could not to be calculated) for pediatricians. Two of the family physicians declared that they were in care of a nursing home for the elderly, and two of the pediatricians were responsible for children's homes. Most physicians reported a rate of zero of missed notifications during the study period, but two (who admitted having missed 10% or 80% of incidents) declared not to have notified any. Four of the physicians were surprised by the frequency of the incidents, 11 were not (3 missing); 3 were surprised by the type, 11 were not (4 missing). The total time expenditure for the pilot participation was declared to be 3 (2) hours. For the planned main trial, 9 of the participants would have preferred a university institute to send in their notifications, 1 the Federal Health Agency, and the others were indifferent.

During the pilot, the median number of patient contacts per physician was 686 (320); resulting in 93 (37) per week and physician for family physicians, and 87 (45) for pediatricians. For family physicians, the median number of incidents per week was 0.4 (0.4), and per 1'000 contacts 4 (5), while for pediatricians they were virtually zero.

Fifty-one detailed notification sheets were sent to the study director. Concerning the patient data, 26 were male, 20 female, in 4 cases the gender was not reported, and in 1 case the reporting did not apply to a specific patient. The median age was 67 (23) years. Informed consent was achieved in 22 patients, while in 19 patients, the physician did not ask; in 2 cases the patient refused to participate, in 3 cases the physician could not ask the patient because of dementia, in 4 cases this information was missing, and in 1 case there was no relation to a specific patient to be asked.

In 46% of the cases, the incident was observed by the reporting physician or the staff in his practice, in 36% by the patient or his family, in 8% by the pharmacist, in 6% by the community nurse or the institution they were living in, in 2% by another physician (1 missing information). Types of incidents are listed in Table A2. In 69% of the notifications, one or more organ systems were involved; they are listed in Table A3; 31% were without any damage. The causes of the incidents as defined by the physicians are listed in Table A4; in 31% there was no distinct cause (e.g. unexpected ADR). In reaction to the incident, 24% of the physicians changed standard operating procedures (SOPs) within his practice, in 6% of the cases he made an arrangement with others, in 2% of the cases he wrote a Swissmedic ADR notification ("yellow leaflet"), in 2% a CIRS notification was made, in 32% other reactions were mentioned, and in 34% there wasn't any

reaction to the incident at all (multiple answers, 5 missing information). In 1 case the physician declared that he had a similar incident within the study period, while in the other 44 this was not the case. The notification without a specific patient concerned the interruption of cholecalciferol ampoules production by Streuli Co.

Concerning the drugs involved in the incidents, there were 9 naming of anti-hypertensives, 7 anticoagulants, 5 anti-diabetics, 5 antibiotics (2x amoxicillin, 1x amoicillin+clavulanic acid, 2x clarithromycin, 1x co-trimoxozole), 5 antidepressants, 3 neuroleptics, 3 analgesics, 2 statins, 2 vaccines, 1 antiepileptic (lamotrigin), 1 benzodiazepine, and 17 other groups.

Within the 3 cases of alleged DDI, there were 3 naming of antibiotics, 2 anti-hypertensives, 2 antidepressants, 2 non-steroidal anti-inflammatory drugs, and 7 other groups.

Within the 18 cases with an ADR, 1 Swissmedic-ADR leaflet was filled (visual hallucinations after valaciclovir). Within the 24 other cases, mostly related to an error, one CIRS notification was made (hypoglycemia in an insulin-treated diabetic after application of amoxicilline+clavulanic acid and clarithromycine).

Harm by the incident was declared to be: no harm at all 32%, mild 26%, moderate 26%, severe 16% (6 times question did not apply, and 2 missing information). Within the 25 cases with harm, the duration was: “days” 68%, “weeks” 20%, “longer” 4%, and “not yet defined” 8% (3 times missing information). Recovery was described as complete 93%, and not yet defined 8%. Treatment was none 58%, ambulatory 31%, hospital care 11%.

To discern predisposing factors to become victim of an incident, we also collected information from control patients. Table A5 compares the patient data with them.

Many physicians were not able to report the mean age of their patients, and many of them could not estimate the percentage of prescribed medications as compared to the ones directly delivered to the patients. Many respondents had difficulties understanding our concept of drug applications, meant to be the number of distinct medications times the number of their daily applications (e.g.: medication A 1 – 0 – 0, and medication B 1- 0 – 1 are *three* applications). Several physicians stated that they didn’t understand the distinction between foreseen but accepted risk vs. unexpected ADR or DDI.

Discussion

In a group of 18 family physicians or pediatricians, for 138 weeks of work and among 12’451 patient-to-physicians contacts, our pilot study resulted in 51 medication incidents.

Concerning problems to get informed consent, many physicians stated that it was oftentimes only later that an incident was detected, so it was perceived that the time and energy needed to contact the patient was a waste of time. To inform him or her about a minor incident which was readily corrected by the physician and without consequences, could in the worst case disturb the relationship to and confidence in their doctor. After discussing this issue with the responsible persons of the Federal Health Agency (Brigitte Meier, Martin Götz) it was clear that some form of general consent to collect anonymized data would be sufficient for most epidemiological research, especially for the main study of our project as planned by 2015, so that we would not have to get individual consent from the patients. This is important for our project because it would require some kind of confession to declare an error to the patient, prompting the physician into non-reporting and thus leading to massive bias of up to 50% of the incidents.

Ethical concerns beside, it seems difficult enough to get unbiased information about errors. In our study, out of 18 ADR, only one led to drug authority (Swissmedic) notification! Out of 26 other medication incidents or errors, only one was subject to notification to the CIRS system. Our pilot study clearly documents a substantial rate of underreporting to these systems. Hence we presume that the population of our study physicians was exceptionally motivated about the topic, so that the average physician doing there every day’s work would perform worse leading to an even larger proportion of non-reporting.

As declared by comments of two of the pediatricians in the study, they seldom use drug treatments (out of specialized centers) and if so, only for a short duration; this may explain the low number of incidents reported in our study.

In our pilot, the two major single reasons for error were lack of alertness (of doctor and practice staff) and lack of cooperation from patients and their relatives. The former may be dealt with by clear SOPs – adapting them was the most often cited consequence of an incident – and the latter may be helped by improving communication skills. One single case stated that the patient was misled by the package leaflet of his medication. It was the case of zaleplon, a somniferous out of trade. Although rare, such cases should be reason enough to contact the manufacturer.

Most cases were without or with only minor harm, although 18 times a moderate to severe damage was reported. All were resolved without permanent consequences to patients. There were cases of theoretical incompatibility mostly with DDI, detected by electronic control systems. No harm by DDI however was recorded in our data.

A main aim of our pilot was to test the comprehension of questionnaires. Several physicians had problems with reporting the number of daily drug applications; this may be overcome by giving them detailed examples. Some participants could not indicate the mean age of their patients; in the Sentinel system, the problem of knowing the age of their patients is solved by 2x2 weeks of detailed consultation analysis, so in this respect, the difficulties of answering this item will not be of importance for the main study.

We included many items on patient risk factors in our questionnaire to discern factors that presumably predispose having an incident. To evaluate their importance, we collected information from *control cases* of the same age and sex. Although most physicians had no difficulties to define a control patient, this issue is troublesome and time consuming. If predisposing factors should be analyzed, the information from control cases is indispensable. For our main study, we decided to collect denominator information from the detailed analysis of patient-to-physician contacts and to skip the case-control method.

As for the inclusion criteria: the participant physicians judged it to be cumbersome to discern whether the risk of an ADR or DDI was to be (theoretically) foreseen but accepted vs. unexpected. For the main trial opened inclusion criteria to any ADR or DDI irrespectively from being presumed or not, provided that an error element has been involved in its evolution.

Conclusions

The prospective and systematic reporting by the physicians of the Swiss National Sentinel Reporting System by 2015 seems to be a feasible way to collect information on medication-related incidents in primary care.

Table A1. Physicians participating in the pilot study among language regions.

Linguistic region	German (9) spoken	French (6) or Italian (3) spoken
Gender		
- male	7	7
- female	2	2
Specialty		
- general internal	6	8
- pediatrician	3	1
Age	53 (21)	49 (19)
Number of physicians in practice	3x1, 3x2, 2x4, 1xM	2x1, 4x2, 1x3, 1x4, 1x7
- of them reporting to the pilot	7X1, 2x2	7x1, 2x2
Medical graduation year	1987 (23)	1986 (19)
Working hours per week,	50 (15)	50 (17)
of them in practice, %	90 (20)	80 (20)
Medication delivery by pharmacist as compared to direct delivery, %	0, 8, 70, 80, 90, 96, 3xM	30, 4x100, 4xM
Localization of practice,		
- urban	5	2
- small town	1	5
- rural	3	2
Electronic interaction control system, %	33	33
Practice certification, %	22	22
Staff meetings,		
- at least monthly, %	56	33
- less frequent, %	44	56
- none, %	0	11
Quality circle participation,		
- at least monthly, %	78	67
- less frequent, %	11	33
- none, %	11	0
Weeks of reporting to the study	7 (1)	8 (1)

Patient-to-physician contacts per week	97 (56)	92 (29)
Number of incidents reported	3 (4)	2 (5)

Values denote median (interquartile range), M=missing value.

Table A2. Types of incident (n=51), multiple entries.

	Namings	Percent
Dose too high	10	19.6%
Dose too low	4	7.8%
Application too long	2	3.9%
Wrong route of application	1	2.0%
Wrong medication	5	9.8%
Necessary medication not applied	6	11.8%
Unexpected drug-drug interaction	4	7.8%
Unexpected adverse drug reaction	21	41.2%
Administration of expired or defective medication	1	2.0%
Medication not reimbursed by insurer	1	2.0%
Other type of incident	10	19.6%
Total	**65**	**127.5%**

Table A3. Organ system involved (n=35), multiple entries.

	Namings	Percent
Cardiovascular	6	17.1%
Central nervous system	13	37.1%
Gastro-intestinal /	5	14.3%
liver	0	0.0%
Kidney	1	2.4%
Skin	7	20.0%
Other	13	37.1%
Total	**45**	**128.6%**

Table A4. Causes of the incident (n=35), multiple entries.

	Namings	Percent
Failure of communication		
within practice	2	5.7%
with hospital	3	8.6%
with institution	2	5.7%
with community nurse	1	2.9%
with pharmacist	5	14.3%
with others	2	5.7%
Generic substitution	2	5.7%
Multiple prescriptions	2	5.7%
Lack of alertness within practice	11	31.4%
Lack of documentation	6	17.1%
Insufficient patient instruction	4	11.4%
Lack of cooperation of the patient or of his relatives	7	20.0%
Misleading package leaflet	1	2.9%
Misleading information from the Internet	1	2.9%
Administrative problems	1	2.9%
Distributor-related problems	2	5.7%
Insufficient maintenance	1	2.9%
Other types	6	17.1%
Total	**59**	**168.6%**

Table A5. Frequencies of circumstances presumed to influence the propensity to incidents*.

Item	N	Cases %	Controls %
Relationship with patient	31		
- "own" patient		94	78
- replacement of family physician		6	19
- institution's doctor		0	3
Dwelling	26		
- with family or partner		73	61
- alone		19	27
- in an institution		8	12
Social problems	28		
- none		68	68
- mild		14	14
- moderate to severe		18	18
Psychiatric illness or dementia	28		
- none		93	85
- mild		0	11
- moderate to severe		7	4
Treatment with psychotropic drugs (multiple entries)	27		
- *none*		59	78
- *antidepressants*		36	18
- *neuroleptics*		4	0
- *benzodiazepines*		7	11
- *opiates*		7	4
Linguistic problems	28		
- none		89	86
- mild		11	14
Addictions	27		

- none - alcohol - drugs		92 4 4	74 22 4
Smoking - no - yes	25	 76 24	 76 24
Vision problems or hearing loss (uncorrected or uncorrectable) - none - vision impaired - hearing loss - both	28	 89 4 7 0	 78 11 7 4
Mobility impairment - none - mild - moderate to severe	28	 89 7 4	 82 11 7
Who prepares the medication - him-/herself - relatives - community nurse - institution - other (or does not apply)	25	 76 8 4 8 4	 64 20 4 12 0
Number of daily medications (median, interquartile range) - number of distinct compounds - number of active substances - number of applications	 26 26 20	 4 (5) 5 (5) 6 (10)	 4 (5) 4 (5) 6 (5)

* No significant differences by testing with McNemar’s chi square test.