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Routine data from hospital information systems can support patient recruitment for clinical studies

Martin Dugas[a], *Matthias Lange*[b], *Carsten Müller-Tidow*[c], *Paulus Kirchhof*[d] *and Hans-Ulrich Prokosch*[e]

Background Delayed patient recruitment is a common problem in clinical studies. Hospital information systems (HIS) contain data items relevant for inclusion or exclusion criteria of these studies.
Purpose We developed and assessed a system to support patient recruitment using HIS data.
Methods We developed a workflow integrated in our HIS to notify study physicians about potential trial subjects. Automatic HIS database queries based on inclusion and exclusion criteria for each clinical study are performed regularly and generate e-mail notifications via a communication server. Study physicians can verify eligibility with a specific HIS study module. The system performance was assessed with a survey addressing utility, usability, stability, change in recruitment rate, and estimated time savings.
Results During 10 months of operation, 1328 notifications were generated and 329 enrollments (25%) were documented for seven studies. Precision of alerts depends on availability of appropriate HIS items. Utility and usability were assessed as good, and stability as excellent. Users reported an increased patient recruitment rate for three studies. Three studies reported an estimated time saving of 10 min per recruited patient. The main perceived benefit was systematic identification of potentially eligible patients without time-consuming patient screening procedures in the different parts of the hospital.
Limitations Notifications about potentially eligible patients depend on HIS data quality regarding inclusion/exclusion criteria, in particular, completeness, timeliness, and validity.
Conclusions Routine HIS data can support patient recruitment for clinical studies by means of an automated notification workflow and efficient access to clinical data. *Clinical Trials* 2010; **7**: 183-189. http://ctj.sagepub.com

Introduction

Efficient patient recruitment in clinical trials is a common problem. Dilts and Sandler [1] reported on barriers to clinical trials and recruitment issues in cancer trials; out of 218 trials, 20.6% that were opened resulted in no actual accruals and 53.7% had fewer than five patients accrued. A review of 114 trials between 1994 and 2003 by the Medical Research Council and Health Technology Assessment Programmes found that less than one-third met their target recruitment within the time originally specified [2]. Various reasons were identified for this issue, such as fewer eligible

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patients than expected, staffing problems, limited funding, complexity of trial design, and length of recruitment procedure.

Problems regarding patient recruitment are not new; Charlson and Horwitz [3] analyzed trials listed in the 1979 inventory of the National Institute of Health and found that only 14 of 38 (37%) trials reached planned recruitment. In addition to missing potentially eligible patients, nonsystematic screening procedures can contribute to a reduced external validity of the study results.

In oncology and cardiology, there are a high number of simultaneously active trials. The registry of the U.S. National Cancer Institute contains more than 8000 active clinical trials [4]. In addition to the long overall development time for phase III oncology clinical trials [5], there are several studies that detail barriers once those trials are open to accrual [6,7].

Given the high patient turnover of modern hospitals in conjunction with complex inclusion and exclusion criteria of many clinical studies, patient recruitment is a challenge. There are several systems to support identification of a suitable clinical trial for a specific patient [8,9]. However, these systems are usually not integrated into routine patient care.

Because much patient information relevant for studies – such as diagnosis, age, gender, lab values – are processed electronically, it should be possible to use hospital information system (HIS) data to support patient recruitment. Recently, we reported on a system to support leukemia trials in Münster, Germany [10–12]. Based on encouraging results from this case study, we designed a study to address the following questions:

- Is a notification system for patient recruitment based on routine HIS data technically feasible for multiple studies?
- Will these notification systems be accepted in the clinical setting?
- Can implementation of these notification systems improve patient recruitment?

Methods

Automated notifications and HIS reports

For each clinical study, we designed a database query based on inclusion and exclusion criteria using available HIS data items. We applied the report generator from our HIS (ORBIS® from Agfa Healthcare) [13]. Typical HIS items for these queries are admission diagnosis (according to international classification of diseases version 10), patient age, and gender. Table 1 provides HIS items for those queries in our pilot studies. These queries are executed automatically once per day. The links to potential study patients are sent to the study physicians by a daily e-mail using a communication server (e*Gate from Sun Microsystems, Inc.). This e-mail just requests the physician to log on to the HIS and does not contain any patient names.

Within the HIS, a specific report for each study is available, including access to the electronic patient record, enabling eligibility verification. If the patient is eligible for the study, a physician contacts the patient to obtain informed consent. By means of a custom HIS form, actual inclusion or exclusion can be documented for each patient. Figure 1 summarizes our workflow of automated notifications and HIS reports for patient recruitment. Notification workflow and HIS access were approved by the responsible data protection officer. To enable management of several studies, technical parameters for each study are organized by a study management tool that provides study title, data query for each study, and contact persons for e-mail notification.

Table 1 Hospital information system items used for automated notifications

Study number	HIS items
1	diagnosis in ('I48.11','I48.10') and department = 'CARDIOLOGY'
2	(diagnosis in ('I64') or diagnosis like 'I63.%' or diagnosis like 'G45.%' or diagnosis like 'I48.%' and diagnosis not in ('N18.0') and department = 'NEUROLOGY'
3	diagnosis like 'G35.%' and diagnosis not in ('H53.4','H54.4','H54.7','R47.0','R47.1') and department = 'NEUROLOGY'
4	diagnosis like 'M33.%' or diagnosis = 'M36.0' and department = 'DERMATOLOGY'
5	(diagnosis like 'F00.%' or diagnosis like 'F01.%' or diagnosis like 'F02.%' or diagnosis = 'F03' or diagnosis = 'F06.7', and age ≥60 and (diagnosis_text like ('%Dement%') or diagnosis_text like ('%demenz%') or diagnosis_text like ('%leichte kognitive Störung%') or diagnosis_text like ('%Alzheimer%') or diagnosis_text like ('%mild cognitive impairment%') or diagnosis_text like ('%mci%') or diagnosis_text like ('%mikroangiophatie%')) and department = 'NEUROLOGY'
6	diagnosis in ('C92.0-','C92.00','C92.01') and department = 'ONCOLOGY'
7	diagnosis in ('E05.0','E05.1','E05.2','E05.9') and department = 'NUKLEAR MEDICINE'

HIS, Hospital information system

Precision of notifications

HIS data does not contain all information regarding inclusion and exclusion criteria. For instance, in certain cancer studies, specific subtypes of the disease or special molecular analysis results are addressed, which may not be available in the routine HIS. Therefore, e-mail notification based on HIS data can generate false positive alerts. To analyze precision of notifications, we provide a custom HIS form to document for each patient inclusion or exclusion.

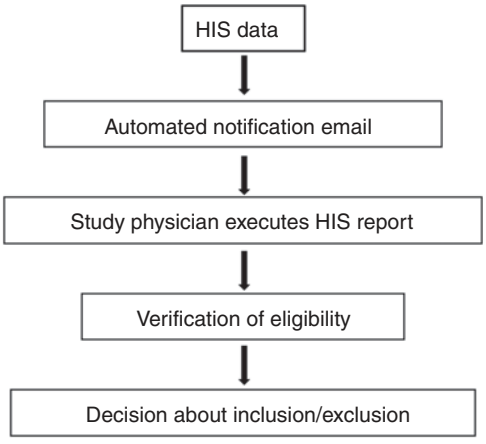

Figure 1 Summary of notification workflow for patient recruitment

User survey

We performed a user survey addressing utility, usability, stability, change in recruitment rate, and estimated time saving. Clinical users were asked to assess utility, stability, and usability of the system on a six-point scale (1 = excellent, 2 = good, 3 = satisfactory, 4 = adequate, 5 = poor, 6 = unsatisfactory). We inquired about average monthly recruitment rate before implementation of the system and relative change thereafter. In addition, we asked about an estimated time saving (minutes per recruited patient) and collected overall comments of the users. This survey form was sent electronically to the local study physician for each study.

Results

The system has been in production since May 2007. We analyzed seven studies. Until February 2008, overall 1328 notifications were generated and 329 enrollments (329 out of 1328 = 25%) were documented. Figures 2 and 3 present monthly number of notifications and enrollments for those studies with highest absolute recruitment rates. For study 1, 259 of 305 (85%) patients with notifications were enrolled in the study. In contrast, for study 6 only 52 of 429 (12%) patients were enrolled. This indicates that precision of electronic notifications

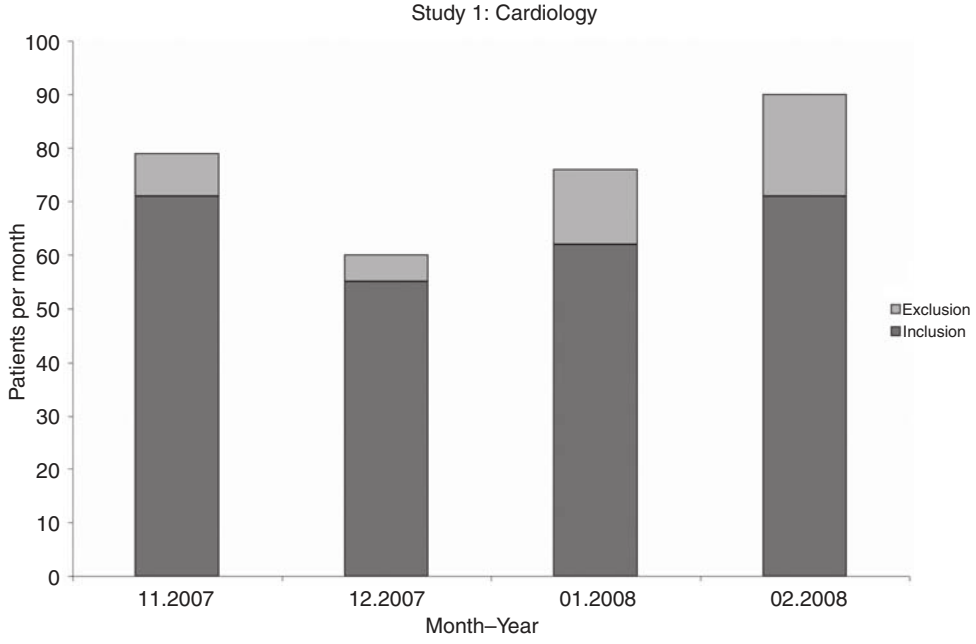

Figure 2 Number of patients per month, which were identified by the notification workflow for study 1. Overall, 259 of 305 (85%) patients with notifications could be enrolled in the study

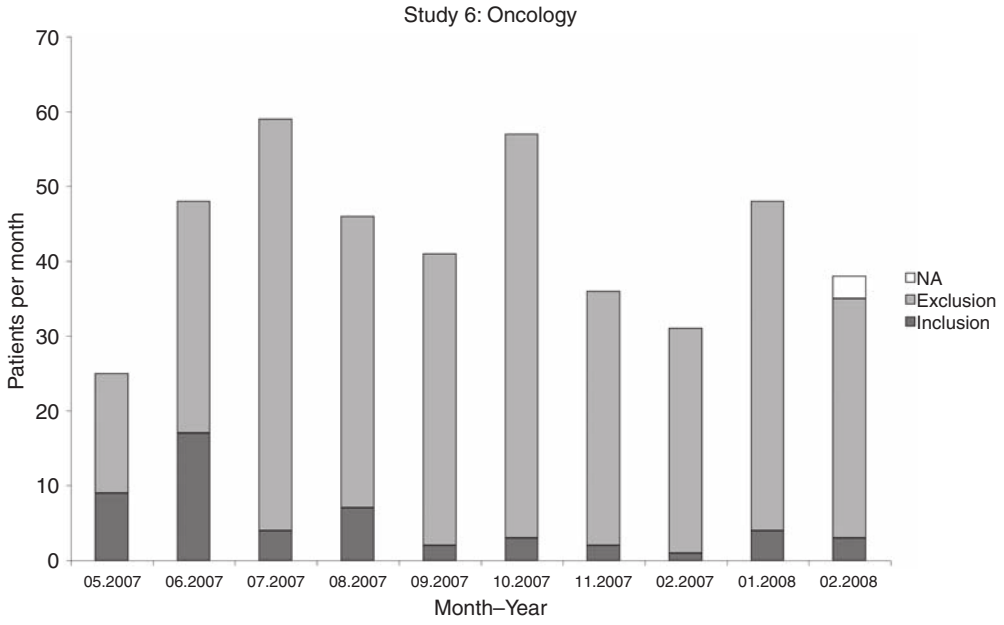

Figure 3 Number of patients per month, which were identified by the notification workflow for study 6. Overall, 52 of 429 (12%) patients with notifications could be enrolled in the study. NA: inclusion or exclusion is not documented

Table 2 Results of user survey

Study number	Study domain	Utility	Stability	Usability	Average monthly recruitment rate (baseline)	Relative change in recruitment	Estimated time saving (min/recruited patient)
1	Cardiology	2	2	3	45	+40%	5
2	Neurology	1	1	1	3.3	+40%	10
3	Neurology	1	1	1	3.3	+40%	10
4	Dermatology	3	2	2	0.2	0%	0
5	Neurology	3	1	3	1.4	0%	10
6	Oncology	1	1	1	5.2	0%	0
7	Nuclear medicine	2	2	2	NA	NA	NA

Each study completed one questionnaire. Utility, stability, and usability were assessed on a six-point scale (1 = excellent, 6 = unsatisfactory). Average monthly recruitment rate for each study before implementation of the system is provided. Three studies reported an increase in recruitment since implementation of the system. Study 7 did apply the system from the beginning of the study; therefore, there is no comparison to previous values.

can vary substantially, depending on inclusion and exclusion criteria of each individual study and available HIS items. Study 1 is a cardiology registry with very general inclusion criteria; study 6 is a cancer clinical trial. The following HIS items were used for this analysis: admission diagnosis (coded as ICD-10), both individual values or lists of inclusion/exclusion diagnoses, diagnosis comment, patient age, admission date, and name of clinic.

We sent an electronic user survey form to the local study physician for each of seven studies and collected answers from all participants (Table 2). Overall utility, usability, and stability were rated positively, with no ratings less than satisfactory, and most in the good to excellent range. Users reported an increased patient recruitment rate of 40% for three studies and none for the others. Three studies reported an estimated time saving of 10 min per recruited patient, one reported a savings of 5 min and two reported no change.

User comments were generally positive (e.g., 'good system, we want to use it in future studies'). A first test version of the program was criticized because several clicks were necessary to navigate between patient list and individual patient records. We updated this mechanism to improve usability. It was mentioned that the system had limitations regarding outpatients because diagnosis codes are

not documented electronically for outpatients in our setting. The main perceived benefit was systematic identification of potentially eligible patients without time-consuming patient screening procedures in the different parts of the hospital.

Discussion

Patient recruitment continues to be an important issue in clinical research. A Cochrane review [14] analyzed strategies to improve recruitment to research studies and identified 15 trials. Monetary incentives, an additional questionnaire at invitation and treatment information on the consent form demonstrated benefit. An electronic workflow to improve patient recruitment was not addressed in this review. Ohmann and Kuchinke [15] reviewed several factors with relevance for the recruitment process, such as psychological, organizational, legal, and technical elements. He states, 'The critical point ... is to be aware of a suitable clinical trial at the point of care'. Thadani *et al*. [16] reported recently about improved efficiency in clinical trial recruitment using electronic screening.

We conducted a PubMed query (MeSH terms 'patient selection' and 'hospital information systems', manual review of search results) and found relatively few reports of clinical trial alert systems, mainly in the outpatient setting. Embi *et al*. [17,18] describes a system for a diabetes mellitus trial in an outpatient setting, which resulted in an increase of patient enrollment from 2.9 to 6.0 per month and was well accepted. Butte *et al*. [19] describes a real-time alerting system to improve recruitment for a hypoglycemia study. Weiner *et al*. [20] analyzed a real-time alerting system in the emergency department and reports improved study investigator notification (56% vs 84% of eligible patients). Ahmad *et al*. [21] also describes a prototype for patient study enrollment in emergency medicine. Afrin *et al*. [22] applied mass screening of lab values for a lupus nephritis trial but with limited effect on enrollment – 7 million lab values were screened, 70 potential patients identified, but only 3 were enrolled. Séroussi and Bouaud [23] reported a 50% increase of patient enrollment to a breast cancer trial using computer-based eligibility screening with OncoDoc, a decision support system for breast cancer therapy.

Based on previous work and a case study in our setting [10,24], we implemented a notification system for seven studies – integrated in our routine HIS – and analyzed data from 10 months of operation. Consistent with systems for individual studies, this notification approach proved to be technically feasible and users rated technical stability as good or excellent. We did not perform an in-depth evaluation of usability and utility of the system, but results from our user survey indicate good clinical acceptance.

A key differentiator of our approach is the use of coded diagnosis information to improve precision of alerts, which is currently available for inpatients in our setting. Starting from the year 2010, outpatients will also be coded using ICD-10 in Germany. Depending on detailed inclusion and exclusion criteria as well as availability of HIS items, precision of study notifications can vary substantially – we found 85% in study 1, 12% in study 6. Interestingly, study 6 did not report an increase in patient recruitment or a time saving in contrast to study 1. Therefore, our approach seems to be effective only for a subset of clinical studies, that is, addressing patients where sufficient HIS items are available to generate precise alerts.

There are reports that recruitment of outpatients in routine consultation is not practical because it is too time consuming, even when computer alerts are available [25]. Seyfried *et al*. [26] used a specific search engine (electronic medical record search engine (EMERSE)) and found significant time savings for eligibility verification compared to manual chart review. In contrast to our approach, EMERSE provides free-text search capabilities on patient records but does not send automated alerts to physicians.

Another important feature of our approach is HIS integration, that is, access to lists of potential study patients with direct links to their electronic patient records. There are several reports on early prototypes regarding electronic patient recruitment without HIS integration [23,27–29]. Integration into the routine workflow has several major advantages, for instance, direct access to patient records can support eligibility verification. Efficiency of HIS-based reminders has been shown in a recent study regarding postoperative nausea and vomiting prevention [30]. In some trial protocols, particularly when therapeutic decisions must be made quickly, rapid patient identification is needed to identify eligible patients before start of therapy.

Data privacy regulations are covered by standard HIS access controls and protocols, so there is no need for additional authentication systems. This concept was approved by the responsible data protection officer. In the US, the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule took effect in 2003, which requires health care providers to implement policies safeguarding all protected health information, that is, individually identifiable patient data. Therefore, researchers who are not directly involved in the care of a patient can no longer recruit that patient

directly [31]. There are reports that patient recruitment and follow-up declined significantly after implementation of HIPAA [32,33]. HIS-based patient recruitment needs to be designed carefully to comply with HIPAA requirements, but it seems to be feasible [17,18].

In our setting, the study physician is directly involved in patient care. Our notification workflow also supports quality management because it assures that a local expert for a specific disease is involved into diagnostic and treatment decisions as soon as a suitable patient is being documented in the HIS. Clinical acceptance is facilitated because clinical users are familiar with HIS and redundant data entry is avoided. When informed consent is obtained, additional orders can be placed in the HIS order entry system according to each study protocol.

In our setting, three studies reported an increase in patient recruitment. Three studies reported an estimated time saving of 10 min per recruited patient by direct access to electronic records, which also indicates a potential for increased efficiency. We have no information that other factors – like staffing changes, training, new strategies, or varying patient load – explained these changes. If a study is well organized and has sufficient resources, conventional patient recruitment can work very well [34] and the potential for improvement by electronic alert systems is small. Unfortunately, consistent with the literature [2,3,14,15] and in the context of economic pressure on the health care system, this is not always the case and electronic tools can help to make patient recruitment more efficient. More research is needed to assess the quantitative effect of electronic notifications on patient recruitment in a wider array of settings and study types.

Our approach can be applied to various types of studies, such as observational studies, registries, and controlled clinical trials. It may be beneficial for studies with high patient numbers (improved workflow) as well as studies of rare diseases (increased awareness). The technical infrastructure can be reused for several studies at the same site; therefore, it is best suited for tertiary care referral centers with many active studies. From our perspective, it would be advantageous if HIS vendors would add this functionality to their products to make it available for a large community of clinical researchers. Broad availability of this technology would also provide the infrastructure to evaluate the effect on patient recruitment in other settings.

There are several limitations of our approach. Notifications about potentially eligible patients depend on HIS data quality regarding inclusion/exclusion criteria, in particular completeness, timeliness, and validity. HIS software products and related data structures can vary substantially between different hospitals; therefore, more research is warranted regarding technical efforts in a multicenter setting. Time savings regarding patient recruitment should be verified in other settings, preferably with objective time measurements instead of self-reporting.

Documentation for clinical trials needs to be compliant with regulatory requirements, such as Good Clinical Practice [35]. In particular, there is a need to validate electronic documentation systems for these trials, which led to development of trial documentation systems separate from routine HIS. A single source of data for research and patient care is still a vision, but first feasibility studies were conducted [36–38]. Our approach utilizes routine HIS data – captured for administrative and clinical purposes – to support patient recruitment. Even if not all items needed for inclusion and exclusion are available in the routine HIS, basic information like diagnosis and age appear to be sufficient for an automated screening tool. Additional research in medical informatics on efficient data management is needed to get more complete data for all aspects of clinical research, but more electronic support of patient recruitment is an important first step toward meeting accrual targets.

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Prof. Dr Martin Dugas designed the concept and wrote the manuscript. Dr Matthias Lange designed the software. Prof. Dr Carsten Müller-Tidow, Prof. Dr Paulus Kirchhof, and Prof. Dr Hans-Ulrich Prokosch reviewed the concept and the manuscript.

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