

# Development of an Electronic Health Record-based Clinical Trial Alert System to Enhance Recruitment at the Point of Care

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## ABSTRACT

*Clinical trials are essential to the progress of medical science. Physician participation in trial recruitment is vital, but most do not participate. Few approaches to improve physician participation in trial recruitment have been described or proven successful. Previously described approaches have largely relied on locally developed technology or been designed for use in specialized settings, thereby limiting their generalizability.*

*We describe the design, operation and initial testing of a new Clinical Trial Alert (CTA) system built upon the existing capabilities of a commercial EHR in use across a large academic healthcare system. Given the trend toward implementation of similarly capable EHRs in institutions engaged in clinical research, this approach should be widely applicable and may represent a solution to the common problem of inadequate clinical trial recruitment. Further study of this system is ongoing.*

## BACKGROUND

Clinical trials are critical to the advancement of medical science and to the research missions of academic health centers and research funding agencies [1]. The growing rate of biomedical discoveries, their potential to benefit humanity, and their associated high costs make the need for conducting clinical trials all the more pressing and the difficulties inherent in doing so even more frustrating [2].

Inadequate recruitment of patients represents a major impediment to successful clinical trial conduct, with only a small fraction of potentially eligible subjects being considered for enrollment. Data regarding the factors that impact clinical trial recruitment suggest that physician participation is essential to the success of most recruitment efforts. Not only do physicians play a vital role by identifying potentially eligible subjects, but patients are much more likely to participate in a trial if a physician has actively suggested it to them [3].

Unfortunately, the identification and recruitment of eligible patients during the course of busy clinical practice can be difficult. In order to successfully recruit patients, physicians must remember which trials are active, recall the trial's details in order to determine patient eligibility, and take time to perform

additional recruitment activities. Doing all of this while also providing the individual patient with comprehensive care during a short clinic visit can be difficult, at best. New patient privacy regulations add yet another obstacle to overcome in finding solutions to the problem of slow and insufficient trial recruitment [4].

Consequently, relatively few clinicians, mostly those in university settings, do most of the recruiting for clinical trials [3, 5, 6]. In addition to frustrating progress, these factors can introduce bias to the trial and prevent some patients from receiving potentially beneficial state-of-the-art therapy. Even in fields like oncology where clinical trial enrollment is considered the optimal management approach for many patients, only about 3% of patients enroll in clinical trials [5, 7].

Previous studies have identified various reasons why physicians fail to recruit patients for trials. These include physician discomfort explaining the study protocol to patients, the perception of too much paperwork, and not practicing in a university setting [3, 6].

In addition to physician factors, there are patient-related factors that predict whether a patient will choose to participate in a trial. One study found that patients who took time to consider their decision were more than three times as likely to participate and those who felt actively involved in making the decision were more than eight times as likely to participate [3]. A recent Harris poll also assessed the reasons why patients choose to participate in trials. Over a quarter of clinical trial enrollees surveyed mentioned that their doctor's recommendation was a key factor in their decision to participate. Moreover, while only 16% of all respondents indicated ever having been asked to participate in a clinical trial, 63% of those asked to participate had done so, further emphasizing the importance of being asked [8].

In recent years, several computerized approaches have been developed in attempts to improve trial recruitment, mostly by manually matching patients to trials or trials to patients [9-13]. While valuable contributions and undoubtedly useful in certain settings, few of these efforts have focused on increasing physician participation in trial recruitment or have been reported to significantly improve trial accrual.

Approaches that automate subject identification by making use of clinical data repositories have recently demonstrated some success. Butte, Weiner, and colleagues made use of a locally developed automated paging system to alert a trial's coordinator when a potentially eligible patient's data were entered into a database upon presentation to an emergency department [14, 15]. While elegantly designed and effective at increasing referrals for certain trials in that particular setting, increased enrollments were not demonstrated and it is unclear whether this methodology would work outside of an emergency department in its current form. Moreover, the approach would likely not comply with current privacy regulations without some modification. In another study, Afrin and colleagues used paging and email systems linked to a healthcare system's laboratory database to identify patients who might be eligible for an ongoing trial and notify their physicians [16]. While successful at signaling the patient's physician most of the time, and while the notification of the patient's physician rather than the study coordinator complied with privacy regulations, most physicians did not follow-up on the alerts and the impact on referral and enrollment rates was small. Although the reasons for this were unclear, the fact that the alert occurred outside the context of the patient encounter and relied on the physician initiating contact with the patient after the visit may have contributed to the limited success observed.

Whatever their limitations, these approaches demonstrate the promise of using clinical data repositories for the secondary purpose of identifying patients eligible for clinical trials. Indeed, this is not a new idea. In the 1990s, Musen, Carlson, and colleagues developed and tested their T-Helper system designed to help community-based AIDS/HIV practitioners manage patients and comply with clinical trial protocols. Their investigations revealed that many patients eligible for ongoing trials were missed [17, 18]. In their 1995 manuscript, Carlson and colleagues concluded that, "The true value of a computer-based eligibility screening system such as ours will thus be recognized only when such systems are linked to integrated, computer-based medical-record systems." [18]

Comprehensive EHR systems are increasingly being implemented across health systems today [19]. Such systems now offer built-in capabilities like computerized provider order entry (CPOE) and clinical decision support systems (CDSS) that have been demonstrated to influence clinician behavior for the benefit of patient safety and healthcare quality [20].

Given the recognized importance of physician participation in recruitment efforts, the recognized

reasons why physicians tend not to refer patients for clinical trials, and the known usefulness of computer-generated alerting systems when applied at the point of care, it follows that incorporating a clinical trial alerting system into the process of clinical care could enhance recruitment.

Despite the work done to date, no system has been proven to significantly increase physicians' participation in trial recruitment or enrollments. Moreover, reported approaches have largely relied on locally developed software or been applied to specialized settings [14, 16, 21]. According to our review of the literature, the capabilities of a widely used, production EHR have not been repurposed to address the common problem of inadequate trial recruitment by physicians.

### **SYSTEM DESIGN AND IMPLEMENTATION**

We developed our Clinical Trial Alert (CTA) system by using the CDSS and communications capabilities of the commercial EHR (EpicCare, Epic Systems, Madison, WI) in use at the Cleveland Clinic. IRB approval was obtained for our tests involving human subjects.

As with many such systems, our EHR's CDSS can present a reminder to a user and facilitate documentation and order entry within the context of the reminder through appropriately customized order forms. The CDSS can be configured using Boolean logic across several parameters: patient age or gender; a medication (generic or brand name) or medication class; a diagnosis (ICD9 code); one or more lab test results (value and change in value); and procedures or orders. It can further be targeted to particular provider 'types' as defined in the system (e.g. staff physician, resident physician, nurse, etc), only during designated encounter 'types' (e.g. an office visit, as opposed to a telephone encounter), and in some clinical practice locations but not others. At this time, without further customization, the CDSS cannot be configured to target an individual provider.

As users interact with the EHR, certain actions initiate the CDSS process to assess whether configured criteria are met in the EHR and trigger an alert if they are. User-EHR interactions that can initiate this process include: opening the order entry screen; entering a new medication, order, or diagnosis; or viewing a result.

To create our CTA system, we configured our EHR's CDSS to trigger an alert if a patient is likely eligible for an ongoing clinical trial, rather than for a more typical clinical purpose such as prompting a clinician to order a test or medication. As part of our process, we configured the CTA to trigger only during clinical encounters for several reasons. By prompting physician action at the point of care, we

hope to capitalize on the recognized benefit of having the physician recruit the patient. This also provides the opportunity to have the physician assess whether the patient is a good candidate for the trial based on general knowledge about the patient, thereby enhancing the accuracy of the process. Because the patient is present at the moment of the alert, no additional effort is required to contact the patient, hopefully improving the chance that a physician will respond. Finally, this allows the physician to easily obtain a patient's permission for the trial coordinator to conduct a thorough chart review.

Should a physician elect to proceed rather than dismiss the alert when presented with a CTA, a customized CTA order form appears (Figure 1). This form serves to remind the physician of the clinical trial precisely when she is encountering a potentially eligible patient. Instructions included on this screen prompt the physician to assess a few additional eligibility criteria not consistently retrievable from the EHR and to assess the patient's willingness to participate in the trial.

**Figure 1: Clinical Trial Order Form**

To further facilitate physician participation, we have not requested that they perform any more than minimal screening nor have we required them to obtain signed informed consent from the patient. Instead, these activities are left to the clinical trial's coordinator should the patient and physician choose to refer the patient for trial consideration. The CTA also facilitates the documentation and the referral process by providing the physician with three checkbox options that can be processed.

Based on the physician's assessment of the patient and discussion regarding the patient's interest in the trial, the physician can click the appropriate box to process the associated CTA order. Options include: (1) Yes, patient meets criteria and is interested (referral order); (2) No, patient does not

meet criteria at this time (not eligible); (3) No, patient meets criteria, but is not interested (not interested). We created distinct orders for each option. By "accepting" the order form, the selected order is processed, entered into the patient's record, and serves as documentation of the patient's willingness to allow chart review by the clinical trial's coordinator.

To facilitate communication between the physician and the study coordinator regarding patient eligibility, we considered several options for transmitting a message based upon the entry of a referral order in the patient's EHR. Ultimately, we decided to make use of the EHR's order transmittal process, which allows us to route a message to a pool of EHR workstations. Whenever a user logs into her EHR account using a workstation in the "pool", a message appears in her account "In-Basket" for review. For our purpose, we created a pool consisting of a single workstation located in the clinical trial coordinator's office and used only by her. Thus, whenever a referral order is entered into the system, it immediately generates a message to her workstation. The message is a copy of the referral order that permits the coordinator to review the associated patient's chart for eligibility determination. Because all information is sent within the secure EHR environment between personnel with a legitimate reason and patient authorization to view the information, this approach does not compromise the patient's privacy.

Selection of the referral order option also appends information to the "after-visit-instructions" printed for patients at the close of each clinic visit. This includes basic clinical trial information, a statement that the patient should expect to be contacted by the study coordinator within 2 weeks regarding potential eligibility for the trial, a statement that the patient is under no obligation to proceed, and the coordinator's contact information.

A referral order also serves as an exclusion criterion for subsequent triggering of the CTA, preventing unnecessary alerts for a given patient during future visits. Because a patient's eligibility criteria or interest might change, we have opted to allow subsequent CTA triggering if other order options are selected.

To create our CTA prototype, we identified an active clinical trial of patients with type 2 diabetes mellitus. Based on that trial's eligibility criteria, we configured the CTA to trigger if the following are true: age>40, Hemoglobin A1c≥7.5%, and ICD-9 diagnoses of Type 2 diabetes mellitus (ICD9 250.xx). For system testing, we designated that the CTA trigger only for physician providers at a particular general internal medicine clinic. We also configured

the CTA to generate an alert only once per encounter in order to minimize the intrusiveness of the alerts.

### **CTA SYSTEM TESTING**

Following initial development of our CTA prototype, we first evaluated its functionality in the EHR's test environment. We started by identifying existing EHR test patient accounts and modifying them as needed so that three test patients' charts contained data necessary to trigger a CTA and three others did not meet the designated criteria.

We then tested the system under the range of circumstances expected to be present across the institution in order to assess whether the CTA operated appropriately. These tests demonstrated that the CTA functioned exactly as intended, triggering only for those patients whose EHR data met criteria and only for the designated provider type performing activities for the designated encounter types in the appropriate clinical locations.

During our testing, we also confirmed that messages to the trial coordinator's workstation appropriately appeared upon processing of a CTA referral order, but not after processing of other orders. After-visit summaries containing the CTA instructions also printed appropriately whenever a referral order was entered but not when non-referral orders or no orders were processed.

To further evaluate the system's functionality and usability, we recruited three physician volunteers who were frequent users of the EpicCare EHR system and engaged them in three mock-clinic visits. During each, they were asked to start an EHR-based clinical encounter with a test patient account whose EHR data would trigger a CTA. One of our investigators (PJE) played the role of the test patient, timed the physicians' CTA processing activities, and solicited feedback from the physician about their CTA experience. All physician test subjects followed the CTA process as intended, engaged the test patient in discussion as instructed by the CTA, and processed the appropriate order based on an assessment of the patients' eligibility criteria and level of interest. Completion of the CTA process took each physician volunteer subject less than 60 seconds to complete. Their feedback resulted only in minor changes to the wording of the CTA.

Our CTA was assigned a unique identifier to allow us to track when it was triggered. CTA orders were also assigned unique identifiers and were captured in our EHR. All data elements were tagged with user identifiers and timestamps and were extracted into our clinical data repository (Oracle database server, Oracle Corporation, Redwood Shores, California). We demonstrated our ability to successfully query this database for all instances of

CTA triggering and for orders (referral; not eligible; not interested) placed during our tests, as well as data regarding the practice setting in which each CTA response was generated. This monitoring capability was put to use in the recently concluded CTA intervention study, the findings of which are currently in press [22].

### **DISCUSSION**

We developed our Clinical Trial Alert (CTA) system by utilizing the resources of our institution's fully implemented, commercial EHR. Our goal was to design a system to efficiently alert physicians of their patients' potential eligibility for a trial, prompt brief but active patient recruitment by the physician, minimize the physician's workload, and do all of this in a manner compliant with current privacy regulations. Our testing indicates that the system functions as intended.

The CTA approach addresses many of the recognized obstacles to physician participation in recruitment efforts by alerting at the point of care, facilitating recruitment-related documentation and communication tasks, and shifting much of the work of eligibility determination to a trial's coordinator. In addition, the system is designed to capitalize on some of the factors previously shown to enhance patient participation in trials. This combination of factors may help the CTA system succeed where previous approaches have fallen short.

By creating the CTA using the built-in capabilities of a widely used commercial EHR, this approach may be applicable in other settings. Furthermore, given that the EHR capabilities used to create our CTA are similar to those found in many other EHRs, we expect that this approach may prove generalizable and serve as a model for CTA development in other systems.

Recently, there have been calls to leverage the power of EHRs for the benefit of clinical trials [23]. This report adds to the limited literature in this area by describing the potential utility of EHRs to enhance physician participation in trial recruitment using commonly available resources. Should the CTA approach prove effective in future studies, it could represent a useful adjunct to current recruitment strategies that often fail to achieve their goals.

### **CONCLUSIONS**

A commercial EHR can easily be extended to provide point-of-care alerts about a patient's potential eligibility for a clinical trial and to facilitate the recruitment process in a manner compliant with current privacy regulations. By addressing several factors recognized to impact trial recruitment, the CTA system may lead to improved physician

participation and trial recruitment rates. Given that the CTA's functionality is built upon tools and resources common to many EHRs, it is likely that this approach can be applied in other settings. If proven effective when applied across healthcare systems, CTA use could offer a solution to the common problem of slow and insufficient clinical trial recruitment by a limited number of physicians. Further study of the CTA's usability and efficacy is ongoing.

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