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eSource-Enabled vs. Traditional Clinical Trial Data Collection Methods: A Site-Level Economic Analysis

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Abstract. Directly extracting data from site electronic health records for updating clinical trial databases (eSource) can reduce site data collection times and errors. We conducted a study to determine clinical trial characteristics that make eSource vs. traditional data collection methods more and less economically attractive. The number of patients a site enrolls, the number of study data elements, study coordinator data collection times, and the percent of study data elements that can be extracted via eSource software all impact eSource economic attractiveness. However, these factors may not impact all clinical trial designs in the same way.

Keywords. economic analysis, clinical trial, data collection, eSource, HL7 FHIR

1. Introduction

The complexity of clinical trial protocols continues to increase and is associated with higher clinical trial total and per patient costs [1]. Site-related costs account for 70% of late phase clinical trial total costs [2]. While remote monitoring has been shown to reduce site management costs by reducing the number of on-site monitoring visits [3], there has been less success in reducing costs associated with site personnel workload. Directly extracting data from site electronic health records (EHRs) for updating clinical trial databases (eSource software) has been shown to reduce site data collection time and errors [4,5]. However, previous studies did not consider the costs of the informatics infrastructure needed for sites participating in eSource-enabled clinical trials.

Decision analytic methods are used to simulate complex decisions by combining disparate data sources [6,7]. These tools are particularly useful where there is uncertainty regarding key decision parameters. We conducted a study to determine which clinical trial characteristics make eSource-enabled versus traditional data collection methods more and less economically attractive for clinical trial sites.

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2. Methods

Model Design: We developed a decision analytic model to compare per patient total data collection costs for eSource-enabled vs. traditional data collection methods at clinical trial sites. Our base case model uses characteristics of the TRANSFORM-HF clinical trial [8]. Briefly, TRANSFORM-HF is a 6000 patient, 50-site pragmatic clinical trial to evaluate the use of two loop diuretic medications in patients hospitalized for new or worsening heart failure. Sites in this trial are responsible for collecting information related to the patient's enrolling hospitalization and a centralized call center conducts follow-up patient interviews.

Decision Model Structure: The decision analytic model used here was constructed to evaluate two data collection strategies: eSource-enabled and traditional (i.e., manual data abstraction from medical records by humans). During the patient's enrolling hospitalization, three types of data collection occur: (1) a study coordinator collects and enters hospitalization data, (2) the study coordinator resolves queries regarding those data, and (3) an on-site monitor verifies selected cases against the source data. Queries are divided into those that can be resolved while the study coordinator is still in the patient's EHR and those subsequent queries that require the study coordinator to reopen the patient's record in the EHR. The study's model includes four types of measurement data: (1) clinical trial site characteristics, (2) study personnel costs and productivity, (3) eSource costs and productivity, and (4) study outcomes.

Clinical Trial Characteristics: Our model includes six clinical trial site characteristics: (1) number of patients enrolled, (2) number of data elements collected for the study database, (3) percent of study data elements that are FHIR accessible (can be accessed via eSource software using the HL7 Fast Healthcare Interoperability Resources (FHIR) standard) [9], (4) number of queries generated, (5) number of onsite monitoring visits and (6) number of cases reviewed per monitoring visit (Table 1). The TRANSFORM-HF study design assumes that each site will randomize 120 patients on average during a 24-month enrollment period.

Garza et al. identified 155 unique TRANSFORM-HF data elements of which 82 (52.9%) could be mapped to the US Common Core and would be accessible using HL7 FHIR [9]. In a review of 14 protocols for which study data were managed by our institution, queries were generated for 1.5% of study data elements. Based upon operational experience with multicenter studies coordinated by our institution, approximately, 67% of these queries would be resolved during initial data entry while the site coordinator was in the patient's medical record and 33% would be resolved after initial data entry was completed, requiring the patient's medical record to be reopened and reexamined. We assumed a risk-based monitoring strategy where each site would have one monitoring visit, 30% of sites would have a second visit and 10% of sites would have a third visit (average 1.4 visits per site). We also assumed monitors would verify source documents for 5 patients per visit (average of 7 cases for all visits).

Table 1. TRANSFORM-HF Clinical Trial Characteristics

Variable	Estimate	Range Tested (+/- 50%)	Data Source
Patients randomized	120	60 to 180	Protocol (Ref 8)
Study data elements	155	78 to 232	Garza (Ref 9)
FHIR accessible rate (%)	52.9%	27% to 79%	Garza (Ref 9)

Study Personnel Costs and Productivity: We used keystroke level modeling to estimate the number of data elements a study coordinator would collect and enter per hour for (1) initial data entry, (2) query resolution during initial data entry while in the patient's medical record and (3) query resolution after initial data entry requiring the medical record to be reopened and reexamined (Table 2). Keystroke level modeling estimates the length of time an expert will take to accomplish an interactive computer system task without errors [10,11]. We then estimated the number of data elements site personnel would map and confirm to FHIR resources per hour as well as the hourly costs for study site and monitoring personnel. Although site monitors typically are paid by study sponsors (and are not included in site personnel costs), we included monitoring costs to obtain estimates of all data collection costs incurred at clinical trial sites. Hourly costs were estimated by inflating annual salary costs by a 35% fringe benefit rate and 50% indirect costs. Based upon our experience, we assumed personnel could allocate a maximum of 30 hours per week to specific projects.

Table 2. Personnel Characteristics

Variable	Estimate		Source
TRANSFORM-HF			
Site coordinator data collection rate	134 data elements per hour		Keystroke level model
Number of queries resolved			
While in patient's medical record	134 data elements per hour		Keystroke level model
No longer in patient's medical record	106 data elements per hour		Keystroke level model
FHIR Mapping			
Data element mapping	10 data elements per hour		Observation
Data element mapping time	15.5 hours		Computation
Data element confirmation	30 data elements per hour		Estimation
Data element confirmation time	5.2 hours		Computation
Personnel Costs	Annual	Hourly	
Site principal investigator	$200,000	$260	UAMS
Site study coordinator	$80,000	$104	UAMS
Information technologist	$65,000	$84	UAMS
Information security officer	$100,000	$130	UAMS
Site monitor	$80,000	$104	UAMS

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eSource Costs and Productivity: eSource software implementation costs have fixed and variable components. The fixed costs are incurred to set-up a trial and the variable costs are incurred per study data element. Fixed costs include (1) study materials presented to site team members and (2) site eSource security review/approval, setting up the EHR research record, connectivity testing and eSource user training. Variable costs include the time to map study data elements to site EHR FHIR resources and to confirm those mappings. For study material presentation and review, we estimated the site principal investigator, site study coordinator, an information technologist and the site security officer each would require 5 hours (20 total hours, $2890 cost). For eSource security, we estimated the site coordinator would require 7 hours, the information technologist 4 hours, and the security officer 4 hours (15 total hours, $1584). Lastly, we estimated the site coordinator and information technologist would require 15.5 hours each to map the TRANSFORM-HF data elements (n=155) to EHR FHIR resources, and the site coordinator would require an additional 5.2 hours to confirm these mappings (36.2 total hours, $4474 cost) (Table 2).

Study Outcomes and Analyses: The primary study outcome is total per patient data collection costs for each strategy (eSource-enabled and traditional). Secondary outcomes include the major components of total costs and study coordinator costs. The study's model estimates primary and secondary outcomes and sensitivity analyses. For each data collection strategy, we consider the lower cost strategy to be preferred. Sensitivity analyses investigated the impact of 50% increases and decreases in clinical trial characteristics upon per patient data collection costs. These analyses also identified threshold values for clinical trial characteristics that make eSource-enabled the preferred data collection strategy vs. traditional data collection.

3. Results

Cost Outcomes: The study's model estimated TRANSFORM-HF per patient total data collection cost was $10 lower for eSource-enabled versus traditional methods ($119 vs. $129) (Table 3). Coordinator costs were $68 lower ($61 vs. $129) while the per-patient cost for eSource software implementation was $58 higher. Thus, for a site that could enroll 120 patients over the 24-month accrual period, investing in eSource infrastructure would be marginally economically attractive. Coordinator cost savings included $64 for initial data collection, $1 query resolution, and $4 onsite monitoring.

Table 3. TRANSFORM-HF Cost Outcomes

	Data Collection Method		
Cost Outcome	**eSource-Enabled**	**Traditional**	**Difference**
Total Costs	$119	$129	($10)
Coordinator component	$61	$129	($68)
eSource component	$58	$0	$58
Coordinator Costs			
Initial data collection	$57	$120	($64)
Query resolution	$1	$2	($1)
Site monitoring	$3	$7	($4)

Sensitivity Analyses: The benefit of eSource-enabled vs. traditional data collection in TRANSFORM-HF clearly was influenced by clinical trial characteristics (Table 4). With a small number of patients, a small study database (number of data elements), a lower FHIR accessible rate (percent study data elements accessible via eSource software), and a higher site coordinator data entry rate, the use of eSource vs. traditional data collection would not be cost saving. However, at higher values for these parameters, the use of eSource software becomes much more economically attractive.

Table 4. TRANSFORM-HF Sensitivity Analysis

Variable	Less 50%	Strategy Cost Difference	Plus 50%	Strategy Cost Difference	Break Even Value	Total Strategy Cost
Number of patients	60	$45	180	($28)	102	$130
Study data elements	78	$14	232	($33)	123	$102
FHIR accessible rate	27%	$35	79%	($55)	47%	$130
Data elements / hour	67	($74)	201	$12	158	$111

4. Discussion and Conclusion

Our results demonstrate that eSource-enabled vs. traditional data collection methods can be cost saving for the typical TRANSFORM-HF clinical trial site. Our decision analytic model estimated a $68 per patient reduction in site coordinator data collection costs and a $58 per patient increase in eSource-related costs. However, these results vary greatly depending upon the number of patients a site enrolls, the number of study data elements and the percent of those data elements that are accessible via HL7 FHIR.

Our study was confined to the economics of sites contemplating the use of eSource software. This work contrasts with the EHR4CR cost-benefit analysis that took the pharmaceutical company perspective [12]. We believe the site perspective is both important and under-investigated. If the use of eSource is not economically attractive for sites, adoption of this technology is unlikely unless clinical trial sponsors include additional study start-up compensation.

If eSource-enabled clinical trials are to become a reality, clinical trial coordinating centers and sites will need to have personnel with the requisite skill sets to implement and manage eSource software. Our model omitted potential eSource benefits such as greater data quality and shorter clinical trial durations. Nonetheless, we believe we have started an important dialogue that could lead to greater recognition of the value of eSource-enabled data collection as we learn more about the ways in which clinical trial design factors drive the economics of eSource-enhanced data collection.

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