



The Children's Hospital

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University
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Health
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Center



Denver,
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Integrating Electronic Health Records and Clinical Trials

An Examination of Pragmatic Issues

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Some Relevant Statistics



Only 7% of eligible patients enroll in a clinical trial

- n Only 3% of eligible cancer patients enroll

86% of all trials fail to enroll on time

- n 85%-95% study days beyond original study timetable are due to not recruiting subjects on time.

Women, minorities, children and special populations are under-represented

Only 3% board-certified physicians participate in clinical trials

- n The number of clinical investigators dropped 11% between 2001 and 2003
- n Half of all first-time PIs never conduct another FDA clinical trial

Some Relevant Statistics



Only 3% board-certified physicians participate in clinical trials

- n The number of clinical investigators dropped 11% between 2001 and 2003
- n Half of all first-time PIs never conduct another FDA clinical trial

Clinical trials capacity is not meeting demand

- n # trials / year increasing
- n # patients / trial increasing
- n duration of trials increasing

What is the question?



How can electronic health record systems (EHRs) accelerate prospective clinical trials?

- n What are the disconnects between the theoretical concepts and practical reality?

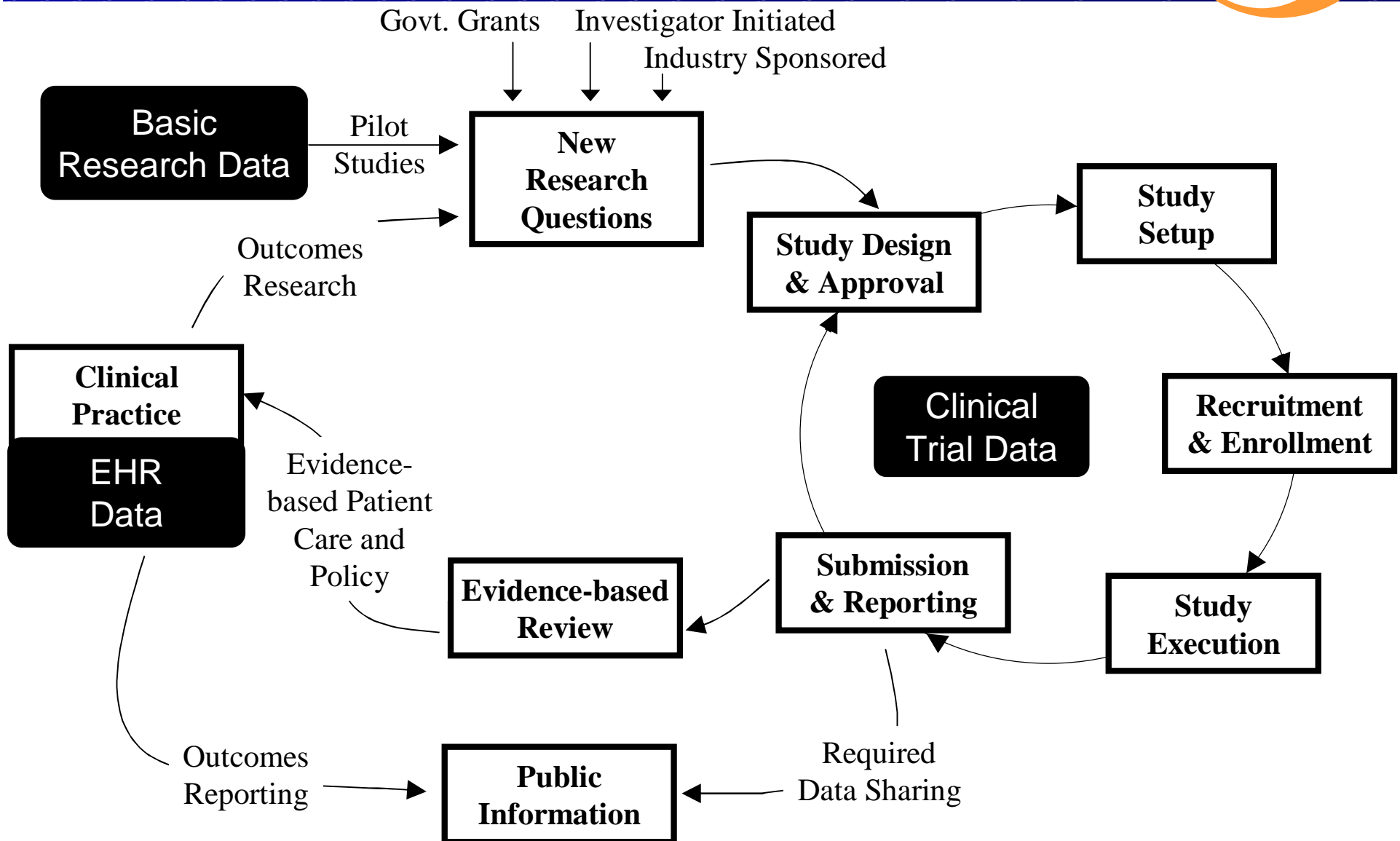
Bottom Line Messages



Regulatory issues are confusing,
conflicting, and controversial

The TCH “standard” ambulatory EMR
contains 30%-50% of CRF elements
from 3 randomly selected pediatric
GCRC protocols

A Lifecycle View of Clinical Research



How EHR's could accelerate Clinical Trials (Front-end)



| Trial Step | EHR potential role |
|------------------|---|
| Study set-up | <ul style="list-style-type: none">§ Query EHR database to establish number of potential study candidates.§ Incorporate study manual or special instructions into EHR "clinical content" for study encounters |
| Study enrollment | <ul style="list-style-type: none">§ Implement study screening parameters into patient registration and scheduling.§ Query EHR database to contact/recruit potential candidates and notify the patient's provider(s) of potential study eligibility. |
| Study execution | <ul style="list-style-type: none">§ Incorporate study-specific data capture as part of routine clinical care / clinical documentation workflows§ Auto-populate study data elements into care report forms from other parts of the EHR database.§ Embed study-specific data requirements (case record forms) as special tabs/documentation templates using structured data entry.§ Implement rules/alerts to ensure compliance with study data collection requirements§ Create range checks and structured documentation checks to ensure valid data entry |

How EHR's could accelerate Clinical Trials (Back-end)



| Trial Step | EHR potential role |
|------------------------------|--|
| Submission & Reporting | <ul style="list-style-type: none">§ Provide data extraction formats that support data exchange standards§ Document and report adverse events |
| Evidence-based review | <ul style="list-style-type: none">§ Assess congruence of new findings and existing evidence with current practice and outcomes (incorporate into meta-analyses)§ Submit findings to electronic trial banks using published standards. |
| Evidence-based clinical care | <ul style="list-style-type: none">§ Implement study findings as clinical documentation, orders sets, point-of-care rules/alerts§ Monitor changes in care and outcomes in response to evidence-based clinical decision support§ Provide easy access to detailed clinical care data for motivating new clinical trial hypotheses |

Distinguishing system names & functions



| | |
|---|---|
| Electronic health record (EHR) | A system for collecting clinical signs, symptoms, problems, diagnoses, test results to support routine clinical care |
| Electronic data capture (EDC) | A system for entering clinical trial data directly from remote investigator sites. |
| Remote data capture | Conceptually same as EDC (An earlier term) |
| Clinical data management system (CDMS) | DBMS used to store and manage clinical trial data |
| Clinical trial management system (CTMS) | System used to track the status of a trial such as investigator site start-up tasks, IRB approvals, enrollment tracking, data submission tracking |
| Statistical analysis data set | Clinical trial data (usually file-based) used to perform statistical analysis |

The Regulatory Environment



| Trial Step | EHR potential role |
|----------------------------------|--|
| HIPAA | § Privacy & Confidentiality of health records |
| 45 CFR Part 2 | § Confidentiality of alcohol and substance abuse records |
| 21 CFR Part 50 21 CFR Part 56 | § FDA Protection of Human Subjects |
| 21 CFR Part 11 | § FDA electronic records & e-signature rules |
| 45 CFR Part 46 | § OHRP human subjects protection |

Roles in Clinical Trials



| | |
|-----------------------------------|---|
| Principal investigator | With an established clinical relationship |
| | With no established clinical relationship |
| Study subjects | |
| Local Institutional review boards | |
| Research subject advocates | |
| Funding sponsor | |
| Non-study clinicians | Standard care setting |
| | Emergency care setting |
| EHR users | |
| System managers | EHR |
| | Clinical trials |
| Data stewards | |
| Institutional managers | |
| Billing & compliance | |

Role-Based Restrictions?



| Role | EHR-related questions |
|---|---|
| Principal investigator with no pre-study clinical relationship to the patient/subject | <ul style="list-style-type: none"><li data-bbox="583 500 1890 662">§ For a study subject with EHR data obtained prior to study consent, what part of the pre-consent record can an investigator access?<li data-bbox="583 670 1921 833">§ If the PI is allowed to see pre-consent eligibility or screening attributes only, how can access to the rest of the record be suppressed?<li data-bbox="583 841 1942 1125">§ Can the PI access pre-consent data that are marked as confidential or have unique regulatory confidentiality rules? If such pre-consent data are screening or eligibility criteria, does permission to access change?<li data-bbox="583 1133 1932 1230">§ Can study consent waive confidentiality or regulatory access restrictions on sensitive pre-consent data? |
| Principal investigator with a pre-study clinical relationship to the patient/subject | <ul style="list-style-type: none"><li data-bbox="583 1263 1743 1312">§ Is EHR data access changed in a clinical trial? |

Role-Based Restrictions?



| Role | EHR-related questions |
|----------------|---|
| Study subjects | <p>§ If clinical trial specific data is co-mingled with standard care data, are those data discoverable for insurance purposes? For malpractice purposes? What is the “legal medical record” when both clinical trial and standard care data are commingled? How separable (physical/logical) do these data need to be to maintain legal “firewalls?”</p> <p>§ If a person’s only contact with the institution is as a study subject, should the patient’s identifying demographics be searchable/discoverable in patient registration system?</p> <p>§ When a study subject either completes a study or withdraws study consent, does their research-only data remain part of the permanent EHR database?</p> |

Role-Based Restrictions?



| Role | EHR-related questions |
|---------------------------|--|
| Standard care clinicians | § Are clinical trial data accessible to clinicians who provide standard care only? |
| Emergency care clinicians | § What are the “break the glass” (treatment unblinding or trial-specific-data exposure) requirements when serious adverse events are suspected by non-trial clinicians? |
| EHR users | <ul style="list-style-type: none">§ Assuming access to trial-specific data is allowed, can a non-trial clinician change trial data that they feel are incorrect?§ Can a clinical trial clinician change non-protocol / standard care data that they feel are incorrect?§ Is there a difference in access or update rights between standard care data that will be included in the research data extract versus standard care data that will not be included in the research data extract?§ Who “owns” data quality for shared (research & non-research) data elements? |

Role-Based Restrictions?

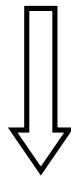


| Role | EHR-related questions |
|---------------------|--|
| EHR system managers | <ul style="list-style-type: none"><li data-bbox="449 526 1892 630">§ Should research data be separated from standard clinical care data?<li data-bbox="449 643 1934 857">§ How to maintain different user roles & permissions for clinical versus research roles – especially if the same person can play dual roles simultaneously during the same encounter?<li data-bbox="449 870 1934 1029">§ Who can create study-specific documentation / case report forms screens? If new terms or value sets are required, who controls these additions to the master tables?<li data-bbox="449 1042 1948 1485">§ Should unusual, unapproved or study-specific laboratory data be entered into the EHR? Are there any special rules for genomic or proteomic data? If entered manually, what level of clinical training is required for the data entry personnel? Are these data part of the legal medical record? Should these unapproved data elements be visible to non-research clinicians? |

Narrowing the question



How can electronic health record systems (EHRs) accelerate clinical trials?



Can EHRs be used to capture clinical trial data?

- n As an electronic data capture (EDC) system

CRF variables vs EMR Data Dictionary Terms



Classified all Case Report Form (CRF) variables used in 3 Pediatric studies

1. Pulmonary hypertension
2. Duchenne Muscular Dystrophy
3. Anorexia nervosa

Question: How many CRF variables are defined in the EHR data dictionary?

[In data dictionary ¹ available for charting]

CRF vs EMR: Results



**Classified all Case Report Form (CRF) variables
used in 3 Pediatric studies**

| Clinical domain | Elements on CRF | Elements in EMR | %Probable coverage |
|-----------------|--------------------|--------------------|-----------------------|
| Total | 1093 | 503 | 47% |

CRF vs EMR Results



**Classified all Case Report Form (CRF) variables
used in 3 Pediatric studies**

| Clinical domain | Elements on CRF | Elements in EMR | %Probable coverage |
|--------------------------------|--------------------|--------------------|-----------------------|
| Pulmonary hypertension | 455 | 251 | 55% |
| Duchenne Muscular Dystrophy | 184 | 101 | 55% |
| Anorexia Nervosa | 454 | 157 | 35% |
| | | | |
| Total | 1093 | 503 | 47% |

CRF vs EMR Results



Classified all Case Report Form (CRF) variables
used in 3 Pediatric studies
Drill-down by Data Domain Type

| Variable type | Trial Admin | Demo | Medical | Family Hx | Diagnostic Tests | Lab | Meds | Questionnaires | Total |
|-----------------------------|----------------|----------------|----------------|---------------|------------------|-----------------|---------------|----------------|-----------------|
| Pulmonary Hypertn | 34% (n=29) | 100% (n=36) | 50% (n=52) | 100% (n=7) | 20% (n=88) | 100% (n=138) | 73% (n=22) | 0% (n=83) | 55% (n=455) |
| Duchenne Muscular Dystrophy | 6% (n=34) | 100% (n=37) | 35% (n=48) | 100% (n=1) | 20% (n=10) | 100% (n=20) | 65% (n=34) | N/A (n=0) | 55% (n=184) |
| Anorexia Nervosa | 27% (n=44) | 82% (n=11) | 75% (n=76) | N/A (n=0) | 0% (n=16) | 100% (n=44) | 81% (n=43) | 0% (n=220) | 35% (n=454) |
| Total | 22% (n=107) | 98% (n=84) | 57% (n=176) | 33% (n=24) | 20% (n=98) | 100% (n=202) | 74% (n=99) | 0% (n=303) | 47% (n=1093) |

Conclusions



Overlapping regulations, competing institutional responsibilities, and unclear role boundaries are difficult to untangle

EMRs configured to support non-protocol care do well with demographics & lab but do poorly with diagnostic tests and questionnaires