ELECTRONIC HEALTH RECORDS FOR CLINICAL RESEARCH

BioMedBridges Annual General Meeting

Dipak Kalra, EuroRec
Christian Ohmann, ECRIN
on behalf of the EHR4CR Consortium
Healthcare needs have been changing

There is a requirement for new, safer, more effective medicines in areas of changing medical need

This need has driven Life Science innovation

A large number of medicines are in development in order to…

- leverage new science
- expand treatment options
- improve quality of life
- provide value for money

### Medicines in Development in 2012

<table>
<thead>
<tr>
<th>Disease</th>
<th>Cancer</th>
<th>Colorectal Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer’s Disease</td>
<td>72</td>
<td>85</td>
</tr>
<tr>
<td>Cardiovascular Disorders</td>
<td>252</td>
<td></td>
</tr>
<tr>
<td>Arthritis</td>
<td>76</td>
<td>141</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>88</td>
<td></td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>212</td>
<td>139</td>
</tr>
<tr>
<td>Mental Disorders</td>
<td>255</td>
<td></td>
</tr>
<tr>
<td>Skin Cancer</td>
<td>85</td>
<td></td>
</tr>
<tr>
<td>Rare Diseases*</td>
<td>460</td>
<td>132</td>
</tr>
<tr>
<td>Respiratory Disorders</td>
<td>398</td>
<td></td>
</tr>
</tbody>
</table>

Source: PhRMA 2012 Profile of the Pharmaceutical Industry

Sequencing of the Human Genome

personalised medicine

CURRENT CHALLENGES IN CLINICAL RESEARCH
Clinical research is costly, long, complex

Allocation of R&D investments by R&D phase (by %)

- Pre-human/Pre-clinical: 21.5%
- Phase I: 8.3%
- Phase II: 12.5%
- Phase III: 35.7%
- Approval: 8.7%
- Pharmacovigilance (Phase IV): 9.8%
- Uncategorized: 3.5%

Source: EFPIA. The Pharmaceutical Industry in Figures. 2013
Patient recruitment a major cause of trial delays

- With no searchable patient database, identifying and recruiting suitable patients and trial sites are principal causes of trial delays
- Delayed trials waste costly resources and slow access to new drugs

The percentage of studies that complete enrolment on time:

- **18%** in Europe,
- **7%** in the US¹

Almost **23%** of all trial delays caused by patient recruitment problems²

Each day a drug is delayed from market, sponsors lose up to **$8m**³

50% of today’s clinical trials fail to achieve the target recruitment rate⁴

---

There is growing recognition of the value of re-using EHRs for Clinical Research

- In 2010, OECD Health Ministers met in Paris to discuss how to improve value in health care. In their final communiqué, they underlined the importance of better health information systems and called for more and effective use of health data that has already been collected.

"Health data constitutes a significant resource in most OECD countries and it makes economic and ethical sense to use this data as much as possible: to improve population health and to improve the effectiveness, safety and patient-centeredness of health care systems."

OECD, 2013
A unique initiative

- Mandated by IMI
- One of the largest European public/private partnership projects in this area
- 4-year project (2011-2015)
- Budget of € >16m

For further information see [www.ehr4cr.eu](http://www.ehr4cr.eu) or contact Geert Thienpont (EuroRec) geert.thienpoint@ramit.be
Brings together key stakeholders

Overcoming barriers that limit access to EHRs for research

Developing a platform and services to re-use EHR data

Moving towards deployment of a sustainable ecosystem

Offering a new paradigm for clinical research in Europe
Requirements informed by stakeholders

- 95% in favour of reuse of EHR data (internal & external stakeholders)
- Identified issues that need to be addressed
- Priority services: protocol feasibility, patient identification and recruitment, exchanging data with EHRs for clinical trial data collection, adverse event reporting
- Interviews with stakeholders helped inform software requirements (Protocol Feasibility Service and Patient Identification and Recruitment Service)

95% rated compliance with ethical, legal and privacy requirements as the highest, or equal highest driving force for success of EHR4CR

EU survey

- 203 respondents from 23 EU countries
- Pharma, academia, CROs, Patient advocacy groups, Health agencies, IT providers

A win-win for all stakeholders is critical

- **Pharma, academia, CROs**: Clinical trial development will become more efficient by reducing the time it takes to bring new drugs to market, thus generating substantial value.

- **Hospitals**: Able to participate in more clinical research programmes, benefiting their patients.

- **Health authorities**: Access to new and better evidence to underpin health policy, strategy and resource planning.

- **Health community/governments**: Able to offer improved quality of healthcare with reduced healthcare costs.

- **EU**: More attractive for R&D investment.

- **Patients**: Faster access to safe and effective medicines, improving health outcomes across Europe.
Results

**Technical Platform**

**A Set Of Tools And Services**

1. Protocol Feasibility
2. Patient Identification and Recruitment
3. Clinical Trial Data Exchange

**Validated Through Pilots**

- Different therapeutic areas (*e.g.* oncology, neuroscience, diabetes, CVS…)
- Several countries (*under different legal frameworks*)

**Business Model**
Scenario 1: Protocol Feasibility

Protocol design based on estimates and not optimised

- With no, or limited access to actual patient data, trial design is based on discussions with expert clinicians

- Increased amendments, slower than expected enrolment, costly changes to add new sites and countries, even failed trials

A third of protocol amendments are avoidable\(^1\), at a cost of $0.5m per amendment.\(^2\)

How long will the trial take?

Will we find sufficient numbers of the right patients?

Do the inclusion/exclusion criteria make sense?

2. Industry Standard Research, 2010
EHR4CR information flows for protocol feasibility

Diagram:
- **EHR4CR Platform services**
  - Cross-mappings
  - Query transformation
  - Query results transformation and aggregation
- **Hospital A**
  - EHR
  - local CDW or I2B2 or iSOFT etc.
  - query listener and query performer
- **Hospital B**
  - EHR
  - ETL
  - EHR4CR CDW dedicated repository
  - query listener and query performer

**Query results transformation and aggregation**
- **Cross-mappings**
  - cross-maps standard to local
  - cross-maps local to standard

**Results visualization**
- **Protocol manager**
  - query composer
  - results visualizer

**Query transformation**
- **query orchestrator**
  - store of queries & cache of result sets

**ETL**
- **AUDIT**
  - store of queries & cache of result sets
Example result set for protocol feasibility

<table>
<thead>
<tr>
<th>Hospital A</th>
<th>Age 40-60</th>
<th>--------</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+ Heart failure</td>
<td>275</td>
</tr>
<tr>
<td></td>
<td>+ Not on diuretics</td>
<td>123</td>
</tr>
<tr>
<td></td>
<td>+ Normotensive</td>
<td>84</td>
</tr>
<tr>
<td></td>
<td>+ Have had angioplasty</td>
<td>5 or less</td>
</tr>
<tr>
<td></td>
<td>+ BMI &gt;35</td>
<td>443</td>
</tr>
<tr>
<td></td>
<td>+ etc.</td>
<td></td>
</tr>
</tbody>
</table>

| MEETING ALL CRITERIA | 3 |
…Deployed Across 10 Pilot Sites
EHR4CR Protocol Feasibility Services...
A European inventory of common electronic health record data elements for clinical trial feasibility

Justin Doods, Florence Botteri, Martin Dugas, Fleur Fritz and on behalf of EHR4CR WP7

Trials 2014, 15:18
http://www.trialsjournal.com/content/15/1/18

![Heat map image]

**Figure 3** Heat map of the data exports from the data inventory current version. The first two columns describe the ISO 11179 data element concepts (data group/data item). The third column shows the average usage of the data element over all sites while the following columns (site 1 to site 9) display the frequency at the individual sites. The Data Inventory is ordered by the average usage sorted in descending order from most available to least. The frequency ranges from 100% (dark green) to 0% (dark red). Data elements that are not available at a site are shown as Not Available (NA) (black).
Ensure an environment for trustworthy re-use

Segregation…
of EHR4CR data from EHR

Control…
lock/unlock access by hospital

De-identification…
individual patient anonymous

Consolidation…
only aggregated patient numbers leave the hospital

Governance…
independent institute ensures data are accessed in a trustworthy way
Our key design principles

- Analyse de-identified health records at participating hospital sites
  - Platform only connected to dedicated repository approved by each hospital for EHR4CR use
- For protocol feasibility and patient identification/recruitment, only patient counts (totals and sub-totals) are returned from each hospital to the central EHR4CR Platform, never patient level data
  - Platform never stores or communicates data about single data subjects
- Data about individuals, who might be invited into a study, remain internal to the hospital and abide by its local governance rules
  - Only treating physicians can re-identify candidate patients
- EHR data is only shared - within the hospital - with a clinical research team if the patient has given that specific consent
Ensuring robust governance

- Only approved users are formally registered and given secure log in credentials.
- Users have no means of requesting or obtaining patient level data through the services.
- Even patient numbers are suppressed if the numbers are very low.
- State of the art information security measures are used throughout.
- Audit logs are captured at key communications points:
  - Pharma sites, within the Platform and at hospitals.
- A Code of Practice and Standard Operating Rules will govern the actions of all parties using the EHR4CR services.
Scenario 2: Patient recruitment
A major cause of trial delay

- With no searchable patient database, identifying and recruiting suitable patients and trial sites are principal causes of trial delays
- Delayed trials increase the burden for sites, waste costly resources and slow access to new drugs

The percentage of studies that complete enrolment on time:
- 18% in Europe
- 7% in the US

Almost half of all trial delays caused by patient recruitment problems

Each day a drug is delayed from market, sponsors lose up to $8m

3. Beasley, "Recruiting" 2008
EHR4CR Patient Recruitment Services…

Site tools to…
- Re-use / adapt feasibility query
- Identify potential candidates
- Contact treating physicians
- Evaluate and recruit patients
EHR4CR information flows for patient identification and recruitment

- Recruitment query for an approved protocol
- Queries are stored and may be re-run periodically to identify new patients
- Accrual rates are periodically returned to the sponsor
- Suitable patients contacted by treating clinician
- Re-identified by treating clinicians and EHRs reviewed for suitability
- Recruitment workbench
- Pseudo-identifier list grouped by treating clinician
- Local CDW or i2B2 or iSOFT etc.
- EHR
- Hospital A
Scenario 3: Data capture/exchange

Divided patient care & clinical research information leads to inefficiencies

The result...
- Cumbersome and slow processes
- Redundant data entry
- Transcription inconsistencies
- Source issues

Over 40% of clinical trial data are entered into the patient’s health record, the clinical trial EDC system, and, possibly, a third paper copy. Over 70% of data are perceived by sites as duplicated between EHR and clinical trial systems.

1. Integrating Electronic Health Records and Clinical Trials: An Examination of Pragmatic Issues, Michael Kahn, University of Colorado.
Results

Towards Sustainability

1. A self-sustaining economic model
2. A roadmap for pan-European adoption
EHR4CR Economic Analyses

- EHR4CR Cost-Benefit Assessment (CBA)
  - To establish the value of EHR4CR services to pharmaceutical industry
    - Perspective of the primary payers
    - Assesses and compares EHR4CR conditions to current practices
    - Central to the EHR4CR value proposition

- EHR4CR Business Model Simulation
  - To forecast the business results from a EHR4CR service provider perspective
    - Estimated expenses and revenues
    - Results expressed as:
      - Balance sheets (revenues minus expenses)
      - Profitability ratio (revenues divided by expenses)
Model: A free market ecosystem

- **Data Provider**: An organisation that contributes data for EHR4CR e.g. hospital
- **Service Provider**: An organisation that provides EHR4CR services to Service Users
- **Service User**: An organisation that uses EHR4CR services such as a pharmaceutical company or an academic institution
Role of the EHR4CR Institute

- The Institute will promote and govern the use of routinely collected patient-level data for clinical research purposes
- It will maintain the EHR4CR technical specifications, and contributing some into future standards
- Through EuroRec it will establish certification procedures for EHR4CR Service Providers and for the capability of EHR systems to support clinical research
- In partnership with ECRIN and UKCHIP it will accredit clinical research organisations and personnel
- A formal business model for the Institute shows that this can be sustained and operate with a viable income stream for at least its first five years
Sustainability: seeding the ecosystem

At project end, there will be

- A growing network of data providers
- First Service Provider(s)
- Committed service users
- Institute based in Belgium
  - Oversight and governance
  - Specifications
  - Shared IP
  - Standards
  - Certification of systems
  - Promotion
Summary: The EHR4CR project is a large-scale initiative...

- Bringing together multiple stakeholders
- Tackling barriers that limit access to EHRs for research
- Developing a platform and services for the trustworthy reuse of EHR data for clinical research