Specifics of the clinical trials data life cycle

(momentum for providing access to patient-level data)

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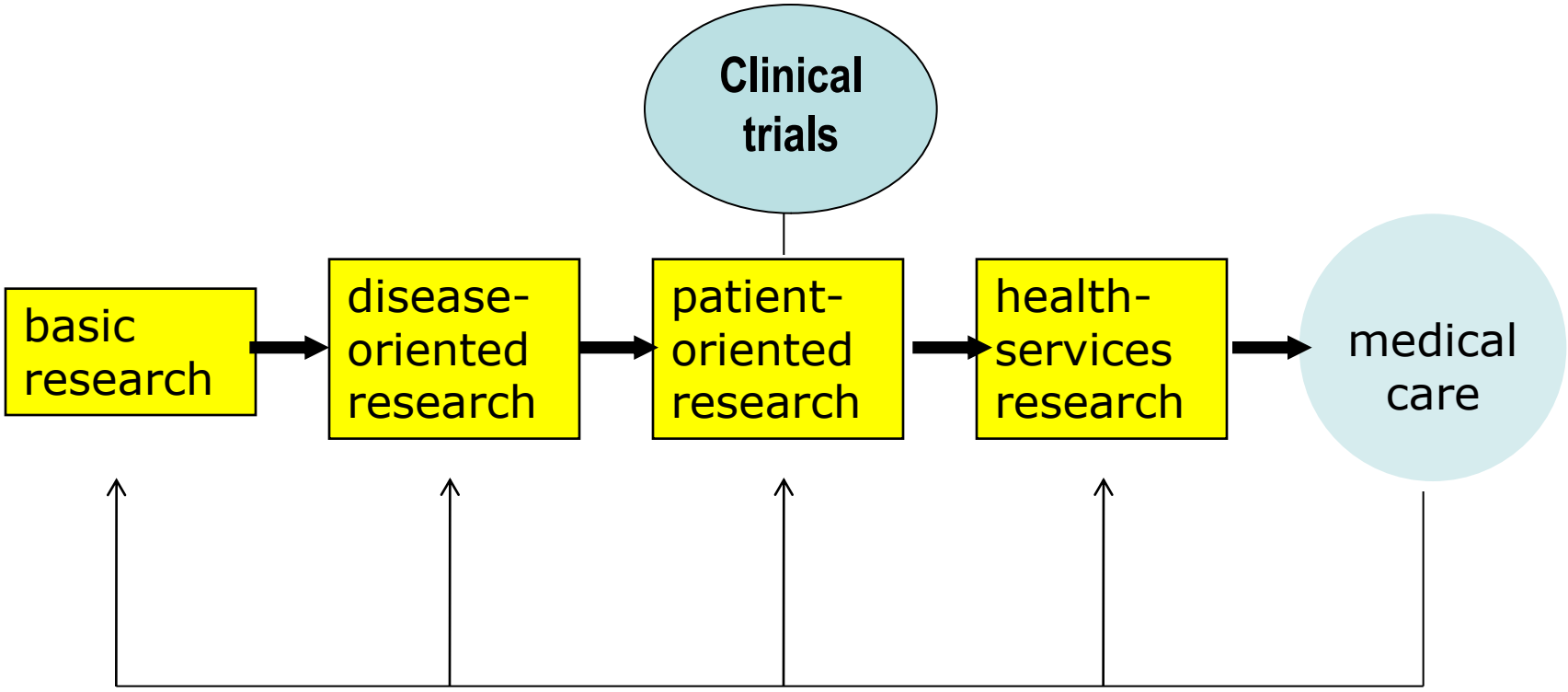
Prof. Dr. C. Ohmann
ECRIN-ERIC

Specifics of the clinical trials data life cycle

Major challenges in innovation transfer



Specifics of the clinical trials data life cycle

Clinical trial*

„Clinical trials are designed and carried out to address research questions about the safety and efficacy (or effectiveness) of one or more health interventions.“

**IOM, Discussion framework for clinical trial data sharing, Nat Acad Press, 2014*

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Framework conditions for clinical trials

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Clinical trials are performed in a highly regulated environment. This covers:

- statements of research ethics and international standards *(e.g. Helsinki)*
- regulations for drugs and medical *devices (drug law, medical device law)*
- prespecified trial protocol to be followed
- specific informed consent from participants
- intellectual property protection
- requirements for data protection and confidentiality
- Specific contracts between trial partners *(involving grant givers, sponsors, CROs, etc.)*
- rules for data handling, data cleaning and data archiving
- rules for publication

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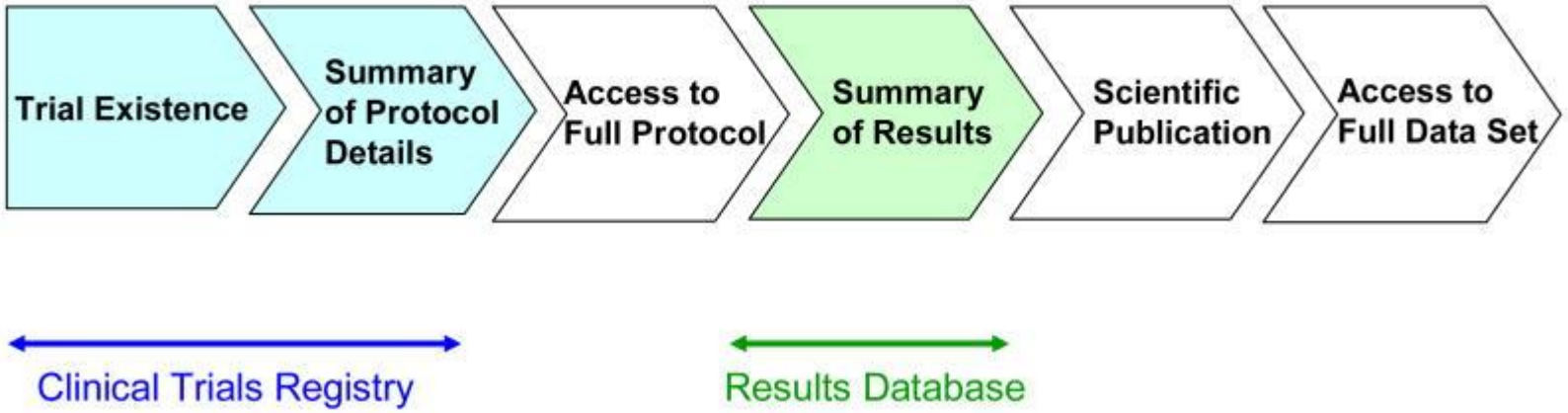
Chain of transparency from trial registration to access to patient-level data*



*Zarin, Science 2008; 319:1340

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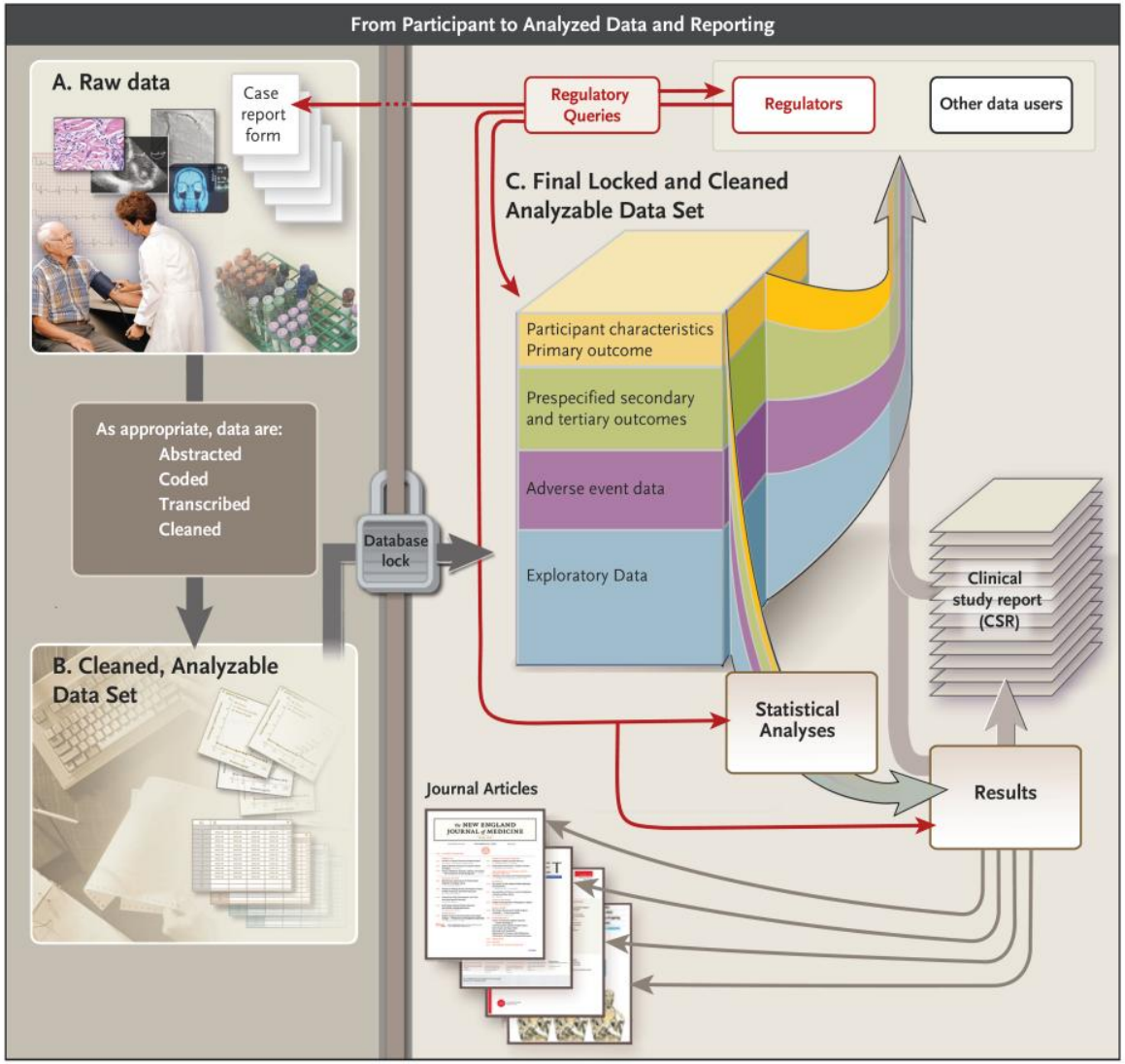
Data flow from participant to analyzed data and reporting*



IOM, Discussion framework for clinical trial data sharing, Nat Acad Press, 2014

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Problems with clinical trials

- problems with trust in the scientific process of generating data and in the validity of reported findings
- problems with transparency by the pharmaceutical industry *(e.g. Paxil, Vioxx, hormon replacement therapy)*
- practice standards rely on goodwill and collaboration of industry
- misrepresentation & over-representation of positive trials in the literature
- duplication of trials that have already been performed
- significant discrepancies between data submitted to regulatory authorities and public presentation in the literature
- no transparent and accountable system of medical knowledge production due to restricted access to clinical trial data *(e.g. incomplete registries)*

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Advantages of providing access to patient-level clinical trial data

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- ensure data quality and robustness of analyses
- improve accuracy of estimates of benefits from a treatment
- optimise the use of clinical trial data for re-analyses, secondary analyses, systematic reviews, meta-analyses, analysis of rare events, subgroup analysis

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Groups/organisations interested in access to patient-level clinical trial data

- meta-analyses *(Cochrane, HTA-authorities)*
- trial methodology *(Society for Clinical Trials)*
- transparency/clinical trial registration
  (WHO ICTRP, NIH ClinicalTrials.gov, OpenAIRE)
- public/charity funding bodies *(H2020 Health, IMI, Wellcome Trust)*
- medical journal editors *(BMJ)*
- medicines agencies *(EMA)*
- patient representations *(EPPOSI)*
- representatives of Ethics Committees, experts on informed consent
- experts on data protection, intellectual property, confidentiality
- IT-experts *(EUDAT)*
- standardisation bodies *(CDISC, OASIS)*
- clinical data management systems (CDMS)-providers

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Challenges to implement access to patient-level clinical trial data

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- rights and responsibilities of the data holder
- restrictions to share data *(e.g. de-identification)*
- invasion of privacy or breaching of confidentiality
- confidential commercial information
- risk to damage vulnerable populations
- administrative and financial burden
- appropriate recognition to the original investigator
- multiple analysis may lead to conflicting/invalid conclusions
- need for further information and metadata

**IOM, Discussion framework for clinical trial data sharing, Nat Acad Press, 2014*

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Possibilities of data sharing*

- Open access

- Controlled access with a data use agreement (DUA):

  - prohibitions on re-identification
  - requirements to acknowledge the data providers
  - requirements to send copies of submitted manuscripts/publications
  - restrictions on further sharing of data
  - assignment of intellectual property rights
  - requirements to publish or post findings from the data
  - requirements to notify industry sponsors of findings that raise safety concerns

**IOM, Discussion framework for clinical trial data sharing, Nat Acad Press, 2014*

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First thoughts on the EUDAT reference model for clinical trials*

Entities	**Attributes**	**Description**	**Standards** (examples)
originator	work ownership	investigator/patient sponsor or principal investigator	- -
depositor	data metadata - - PID access rights	CRF, adverse events data metadata study metadata (trial protocol) reports, publications unique study identifier need to be defined	- CDISC ODM, BRIDG CDISC TDM GCP ICH E3 EudraCT, ISCRTN, CT.gov -
repository			
user			

**EUDAT, Deliverable D4.1.1, 2012*

Specifics of the clinical trials data life cycle

European Clinical Infrastructures Network (ECRIN)

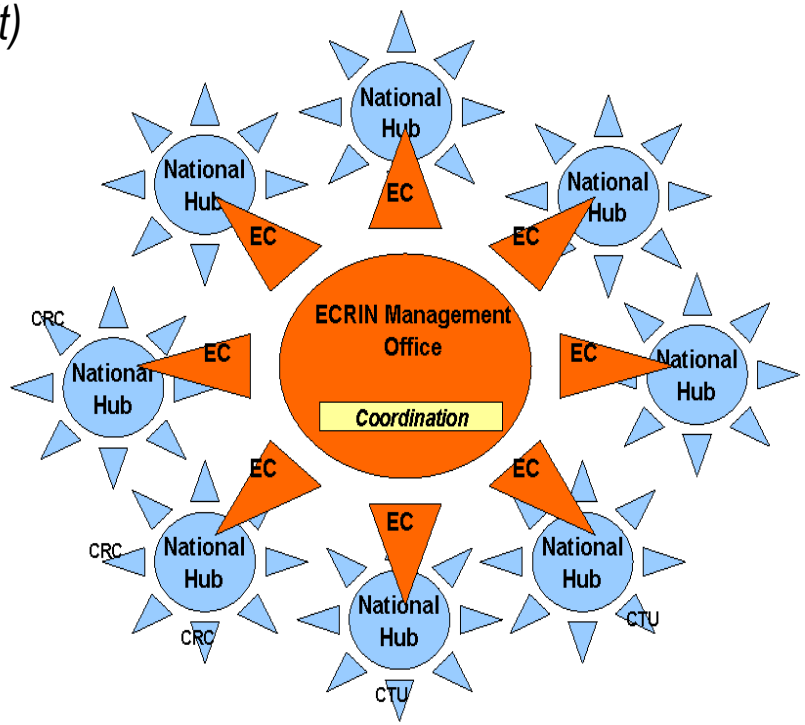
- ECRIN started in 2004, on the ESFRI roadmap in 2006, 3 previous and 1 ongoing funded EU-project with 21 countries, recently implemented as ECRIN-ERIC with 5 countries

- pan-European, distributed infrastructure providing consulting and coordinated services to multinational clinical trials in Europe *(mainly non-profit)*

- consulting and services for multinational clinical trials via an ECRIN management team with a central office in Paris, European Correspondents in the member countries *(as liaison officers)* and national networks of clinical trial units/clinical research centres

- ECRIN in operational phase *(21 multinational trials supported)*

- large impact of ECRIN on data management, legislation, education, IT-systems and patients/ citizens



CRC= Clinical research centre
CTU= Clinical trial unit

EC= European Correspondent

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Next steps

„Providing access to patient-level clinical trial data“

Working task within the CORBEL-proposal (Coordinated Research Infrastructures Bulding Enduring Life-science Services); INFRADEV-4-29014/2015: Implementation and operation of cross-cutting services and solutions for clusters of ESFRI and other relevant research infrastructures intiatives; proposal with 35 partners)

„Providing a solution for scientific communities requirements regarding management of the life cycle of data, including dynamic data and sensitive data“

Proposal for Joint Research Activity (JRA) between EUDAT and ECRIN within EUDAT 2020