The Radiation Oncology Data Sharing Landscape: **Clinical Trials**

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Disclaimer

- While this presentation was created with care, please confirm your national and institutional recommendations and requirements prior to sharing, requesting, and publishing clinical trial data

The Value of Clinical Trial Data Sharing

Improve reliability and robustness of results

Inform development of clinical guidelines

Aid in developing new methodology

Support new clinical trial design

Vickers, *Trials* 2006

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Risks:

- Trial participant privacy and confidentiality of records

Challenges:

- Data collected, curated, and stored in standardized formats
- Technical transferring of data

Capture value and minimize risk

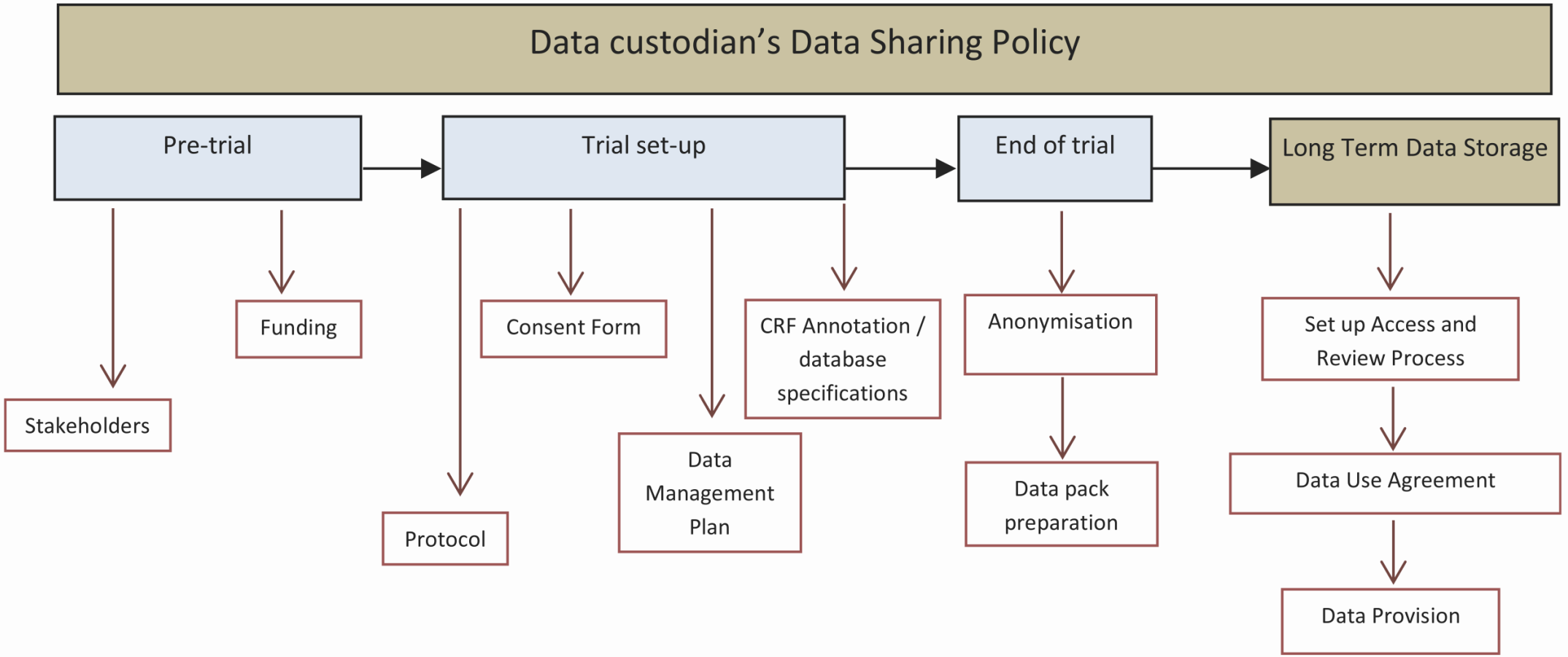
Design clinical trials and manage data with the expectation of sharing

Minimize privacy risk to individuals

If you wait until the end of a clinical trial to figure out how to share data, it is too late!

Objective:
Physicist's role in clinical trial data sharing

- What are the steps that require thought and what can the physicist do to enable data sharing
  - Trial design and registration
  - Data management
  - Publication
  - Formal policy of clinical trialist groups
- Time points throughout trial life cycle

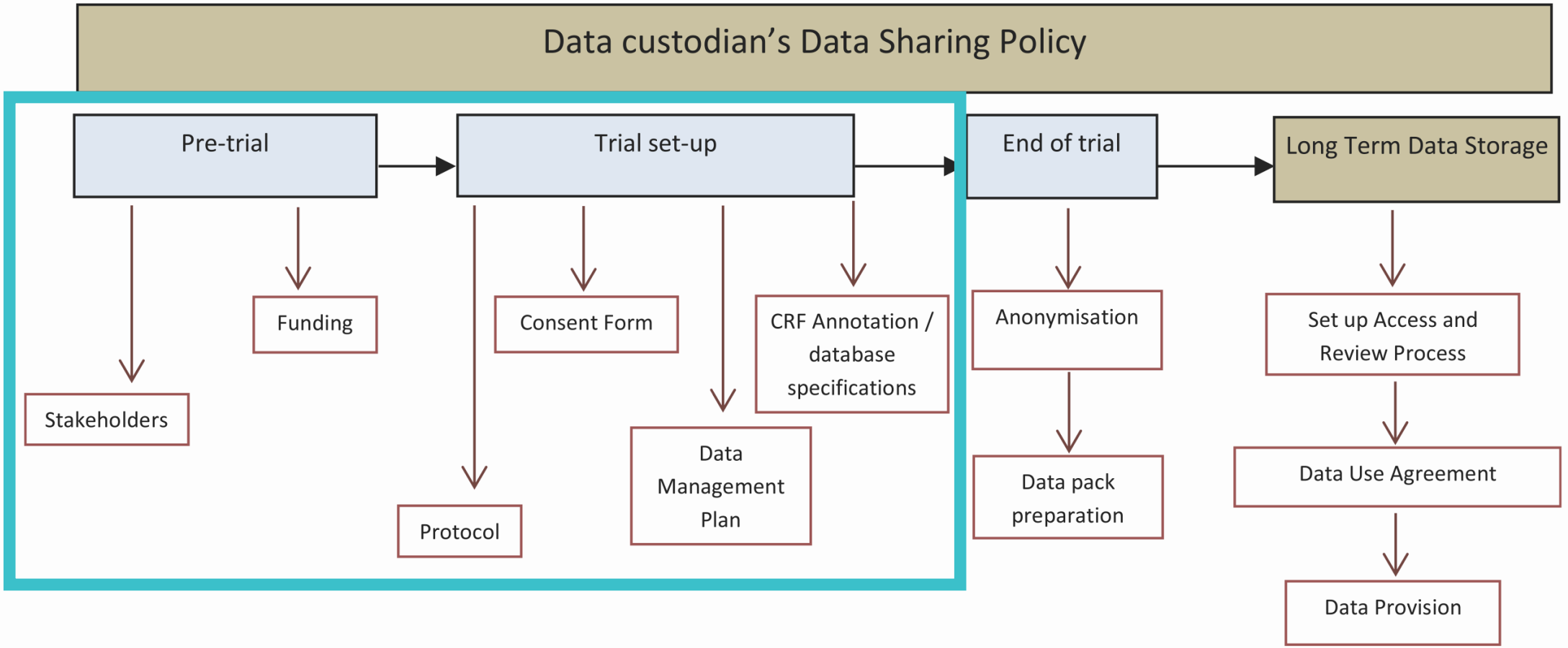


Key:

Consideration at the Data custodian (e.g. CTU) level

Consideration at the individual trial level

Tudur Smith *et al. BMC Medicine* (2015) 13:298



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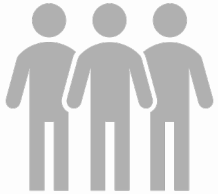
Trial design and registration:

Stakeholders



Participants:

Individual patients and healthy volunteers

Funders:

Public/non-profit

Industry sponsors

Investigators

Clinical trialists

Secondary users

Participants - Informed Consent

- Informed consent is required of all individuals that volunteer to participate in a clinical trial

- Include:
  - What data available and how shared
  - Potential risks of sharing
  - How participants' data will be protected

- Institutional ethics review boards will provide guidance

Participants - Informed Consent

Historical data:		
Consent may be limited for data sharing	Consent may be expressly disallowed or very limited	Data may be uninterpretable or internally inconsistent

Waiver of consent is often possible if research poses no more than minimal risk to the participant AND cannot be practically conducted

Participants - Compound Consent

- Should data sharing be a condition of trial participation or should consent forms include a separate provisional?

- Pros:
  - Freedom to participate
  - Reduce (potentially) restricting participation from specific groups of people
- Cons:
  - Discrepancies between original data set and secondary use data

Funders

- Can set standards and encourage data sharing

- Public/non-profit:
  - Often support clinical trials by providing research grant money to Universities
- Industry sponsors:
  - Directly sponsor a clinical trial of product
  - Example: Elekta Unity MRL Momentum project

MOMENTUM creates a data repository for tracking outcomes of combining imaging and treatment of different cancer types. It will help to define, per tumor site, which patients can benefit the most from this approach.

Investigators – trialists and researchers

Trialists

Investigators that design and conduct the trial

Secondary users

Investigators of reanalysis, ancillary analyses, and meta-analyses

Investigators – Manuscript preparation

Data availability statements on original trial publication:

Whether individual deidentified participant data will be shared

What data specifically will be shared

What related documents will be available (protocol, statistical analysis plan, etc.)

When data will be available and for how long

Secondary analyses publications:

Must attest use was in accordance with terms

Provide appropriate credit to those who generated data

Explain how analysis is different than original

The Role of Journals

- Recommendations

1. As of 1 July 2018 manuscripts submitted to ICMJE journals that report the results of clinical trials must contain a data sharing statement as described below.

2. Clinical trials that begin enrolling participants on or after 1 January 2019 must include a data sharing plan in the trial's registration. The ICMJE's policy regarding trial registration is explained at www.icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html.

ICMJE INTERNATIONAL COMMITTEE of MEDICAL JOURNAL EDITORS

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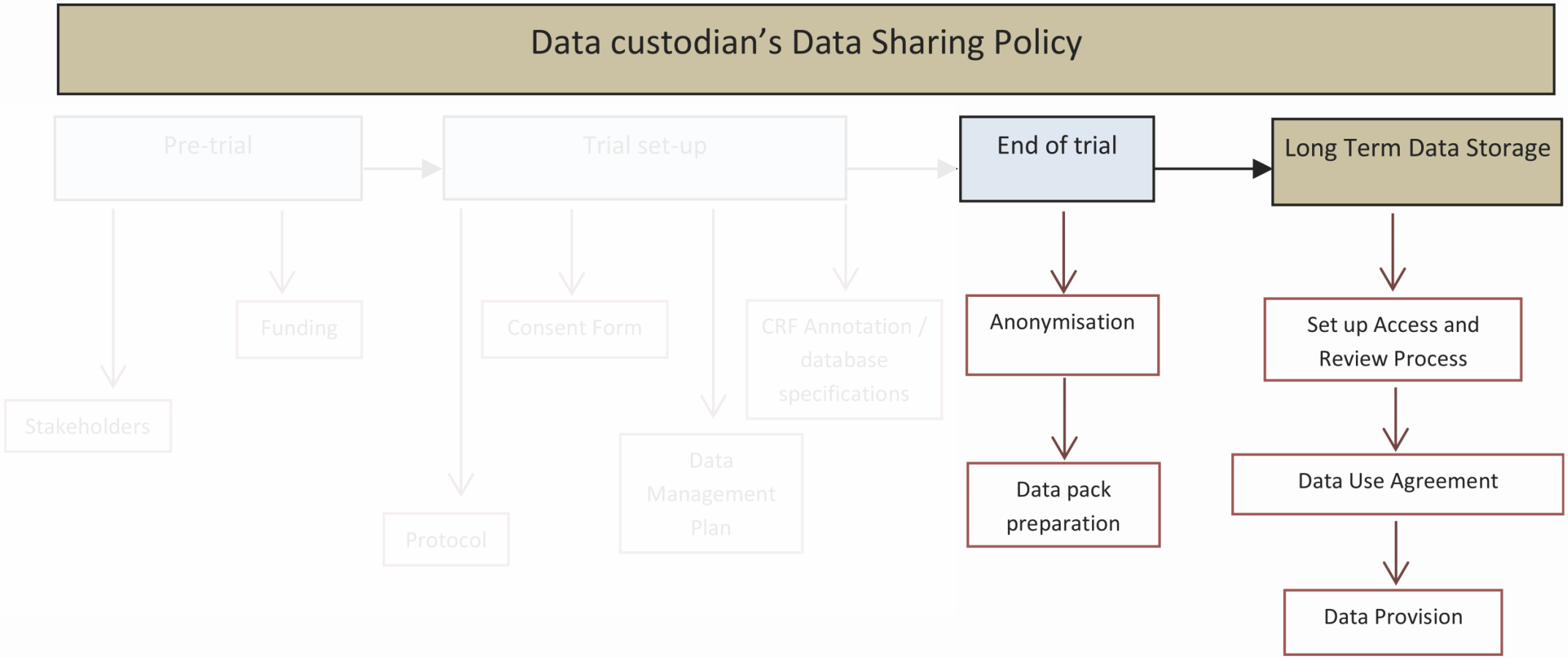

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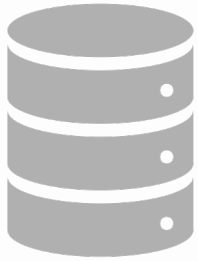
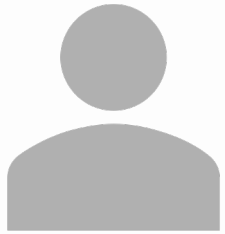
Physicists in the post-trial process



Data preparation and storage team

Anonymization

Standardization adherence



Data requester team

Determine specific variables requested

Trials within national clinical trial organizations (NRG, etc.) often handle data management & anonymization

Data preparation & Anonymization

- Practical guidance on anonymizing trial datasets
  - References:

    Moran et al. AAPM TG 113
    Keerie et al. Trials 2018
    Hrynaszkiewicz et al. BMJ 2010

- Data should be:
  - Accurate, standardized
  - Actually unidentified

Table 1 Aggregated list of potential patient identifiers in datasets (Hrynaskiewicz [15])

Direct identifiers	Indirect identifiers
01. Name	A. Place of treatment or health professional responsible for care
02. Initials	B. Sex
03. Address, including full or partial postal code	C. Rare disease or treatment
04. Telephone or fax numbers or contact information	D. Sensitive data, such as illicit drug use or 'risky behaviour'
05. Electronic mail addresses	E. Place of birth
06. Unique identifying numbers	F. Socioeconomic data, such as occupation or place of work, income, or education
07. Vehicle identifiers	G. Household and family composition
08. Medical device identifiers	H. Anthropometry measures
09. Web or internet protocol addresses	I. Multiple pregnancies
10. Biometric data	J. Ethnicity
11. Facial photograph or comparable image	K. Small denominators – population size of < 100
12. Audiotapes	L. Very small numerators – event counts of < 3
13. Names of relatives	M. Year of birth or age
14. Dates related to an individual (including date of birth)	N. Verbatim responses or transcripts
Superfluous	
02. Superfluous information (audit trail data, administration data)	

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Clinical trialist groups: Formal policies

- NRG, TROG, CCTG, etc. have data sharing and ancillary analyses policies

- Data sharing formal request (NRG):
  - Conduct analysis of anonymized clinical data from **published** NRG Oncology study
  - Identify: specific NRG Oncology Trial(s), goals/objectives, summarize statistical analysis, identify specific requested variables
  - Ethics approval and associated paperwork

Process of requesting data

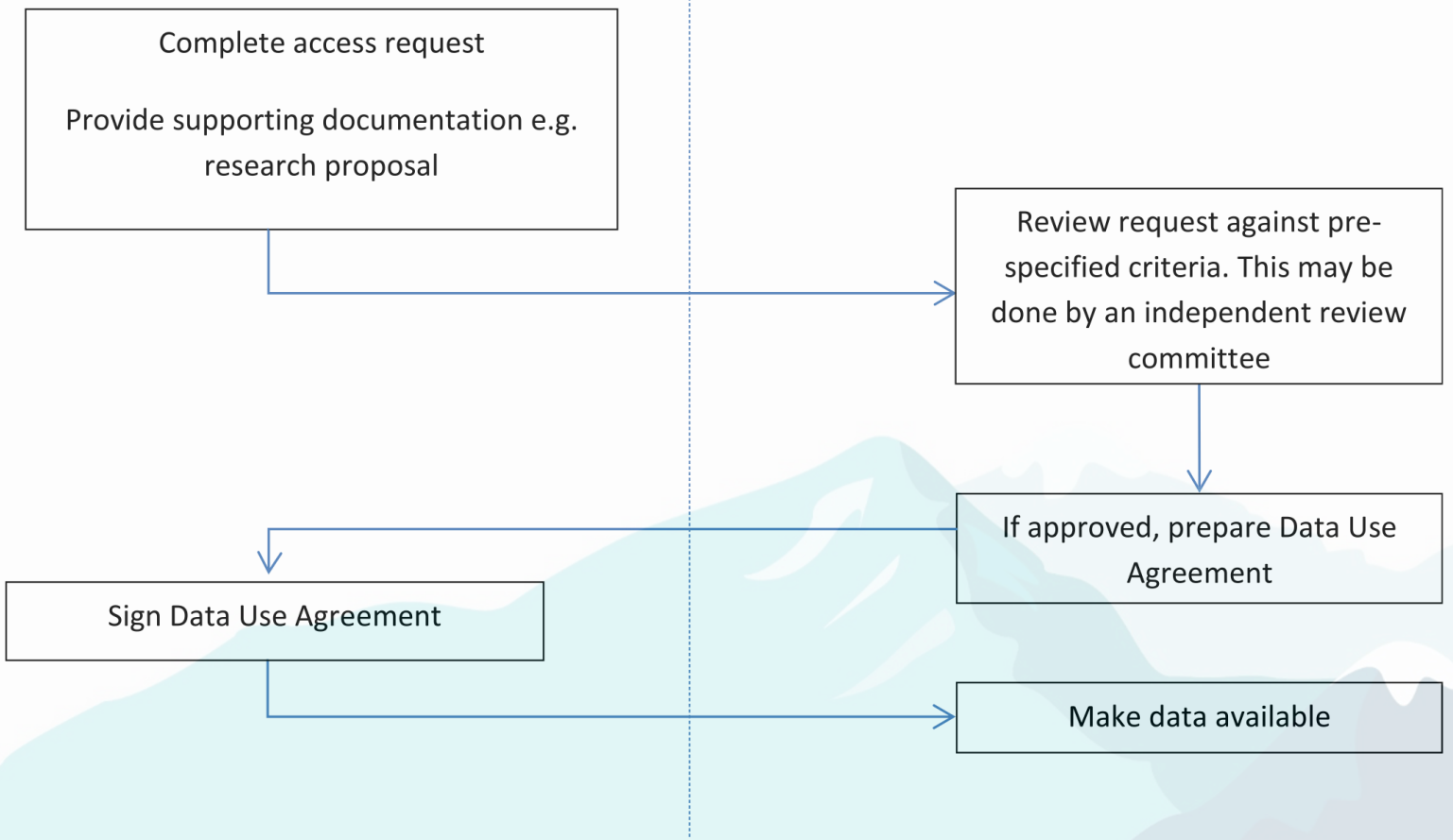
NRG, TROG, CCTG, etc.

Data Requester (e.g. researcher wishing to access IPD for research project) Tasks

Data Custodian (e.g. CTU) Tasks

Institutional clinical trial units

- Goals/objectives
- Statistical analysis
- Specific variables



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How is the medical community doing?

Data sharing and reanalysis of randomized controlled trials in leading biomedical journals with a full data sharing policy: survey of studies published in *The BMJ* and *PLOS Medicine*

Florian Naudet,[1] Charlotte Sakarovitch,[2] Perrine Janiaud,[1] Ioana Cristea,[1,3] Daniele Fanelli,[1,4] David Moher,[1,5] John P A Ioannidis[1,6]

Objective: To explore the effectiveness of data sharing by randomized controlled trials (RCTs) in journals with a full data sharing policy

Design: Survey published RCT

Results: 37 RCT, only 46% satisfied data availability

Conclusions: Data availability is not optimal

RT could do better too

BMJ 2018;360:k400

What does the future hold?

Implementing a Cloud Based Method for Protected Clinical Trial Data Sharing

Gaurav Luthria* and Qingbo Wang*

Oncology and Informatics – Review

Oncology

Oncology
DOI: 10.1159/000504325

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Applications of Blockchain Technology for Data-Sharing in Oncology: Results from a Systematic Literature Review

Alevtina Dubovitskaya[a, b] Petr Novotny[c] Zhigang Xu[d] Fusheng Wang[e]

Conclusion: Physicist role

- *Engage* the clinical trials design and registration process
  - Contribute to patient consent forms
- *Encourage* data sharing statements when publishing clinical trial results
- *Resources:*
  - NRG, CCTG, TROG, etc.
  - Institutional research ethics boards

Select References

- Sharing Clinical Trial Data: Maximizing Benefits, Minimizing risk, Institute of Medicine, Board on Health Sciences (book)
- Roelofs et al., *International data-sharing for radiotherapy research: An open-source based infrastructure for multicentric clinical data mining,* Radiotherapy and Oncology 110 (2014) 370–374
- Tudur Smith et al., *How should individual participant data (IPD) from publicly funded clinical trials be shared?,* BMC Medicine (2015) 13:298
- ICMJE recommendations: http://www.icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html
- NRG: https://www.nrgoncology.org/Resources/Ancillary-Projects-Data-Sharing-Application
- CCTG: https://www.ctg.queensu.ca/docs/newinv/2017/DataSharing_[illegible]estigators.pdf

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