EORTC
European Organisation for Research and Treatment of Cancer
The future of cancer therapy

Data Sharing: practical experience of EORTC

3rd KCE trials symposium
Brussels, Thursday 28th November 2019

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EORTC
European Organisation for Research and Treatment of Cancer
The future of cancer therapy

Mission

AIM: To increase cancer patients' survival and quality of life

Do this through:

- **Generating robust medical evidence**: design, coordinate and conduct multidisciplinary, clinical and translational trials, leading to therapeutic progress and new standard of treatment in care.

- **Setting Standards**: being a reference for methodological research and an authority in establishing the standards of treatment in care.

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EORTC is unique

Independent	• Not for Profit organization where research is done with **unwavering independence** and accountability for making all results public
Multidisciplinary	• Our research spans **all aspects of cancer management**: medical, radiation, surgical, imaging, and translational research
Multi-tumour	• Network of **over 5.500 oncology experts**. Our research is solution-driven, for all types of cancers, leaving no-one behind
International	• A network of **over 930 institutions** in **31 countries;** coordinated and managed from headquarters in Brussels with over **200 core staff**
Regulatory compliance	• Our experts ensure our activities meet the **strictest regulatory standards and quality assurance requirements**

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EORTC by the numbers (2018)

A world-class network	An expert HQ	Unique output
• 2770 patients screened 2412 patients enrolled in Clinical Trials • > 5,300 collaborators • 933 institutions • 37 countries • 19 active groups & task-forces • 118 collaborative groups • 76 peer reviewed papers	• 219 employees • > 200,000 patients in database • ± 27,000 patients in follow-up • 10 EORTC HQ peer reviewed papers	• **213 ongoing studies:** ○ 57 studies open to patients ○ 11 studies open in 2018 • **52 studies in development:** ○ 26 studies in protocol outline development ○ 15 studies in protocol development ○ 11 studies in regulatory activation

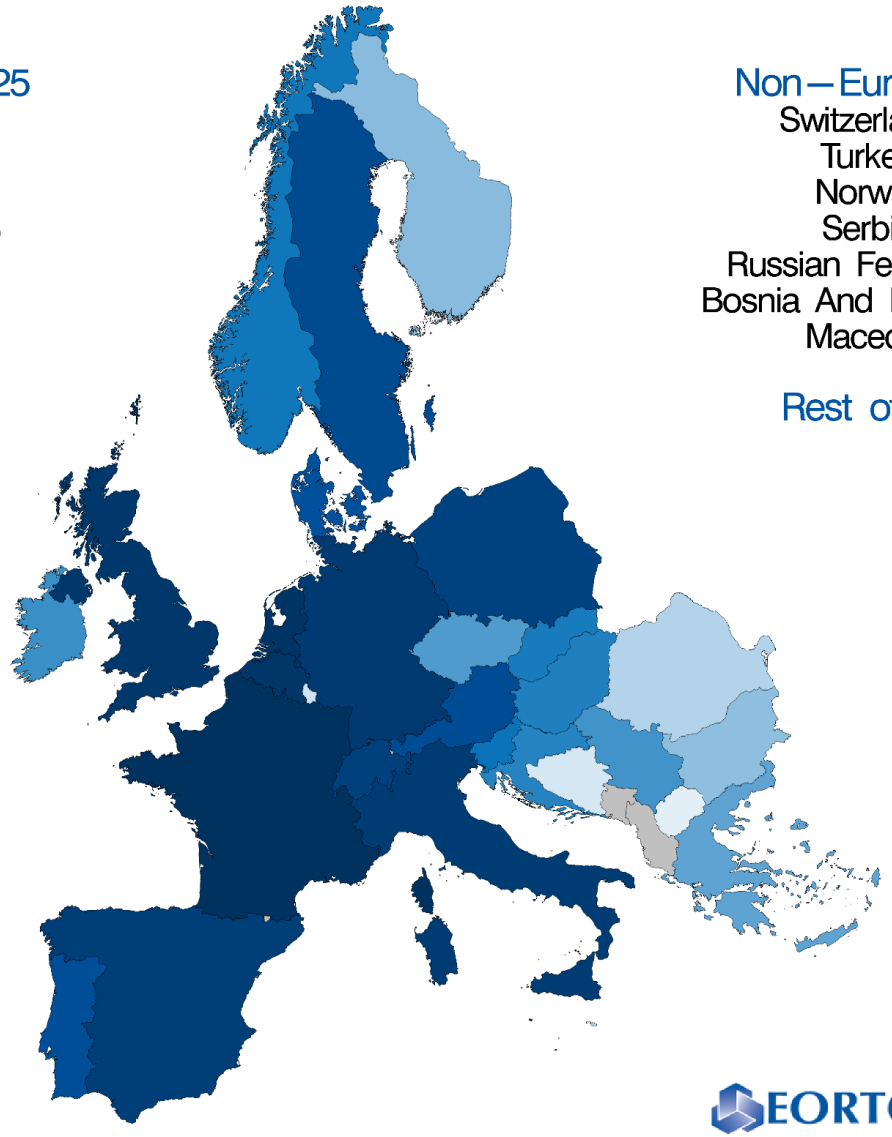
+ Research project defined by DOGs, partnerships

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Accrual of screened patients in EORTC clinical studies from 2001 to 2018: 94656 patients

European Union: 84525

France: 18549
Netherlands: 17681
Belgium: 10414
United Kingdom: 9038
Germany: 8705
Italy: 8011
Spain: 4297
Poland: 1426
Sweden: 1002
Austria: 992
Portugal: 796
Denmark: 680
Slovenia: 513
Slovakia: 481
Hungary: 416
Croatia: 379
Ireland: 320
Czech Republic: 260
Greece: 132
Cyprus: 101
Estonia: 94
Finland: 68
Bulgaria: 51
Latvia: 44
Lithuania: 26
Malta: 20
Romania: 20
Luxembourg: 9



Non–European Union: 3920

Switzerland: 2198
Turkey: 657
Norway: 501
Serbia: 296
Russian Federation: 254
Bosnia And Herzegovina: 8
Macedonia: 6

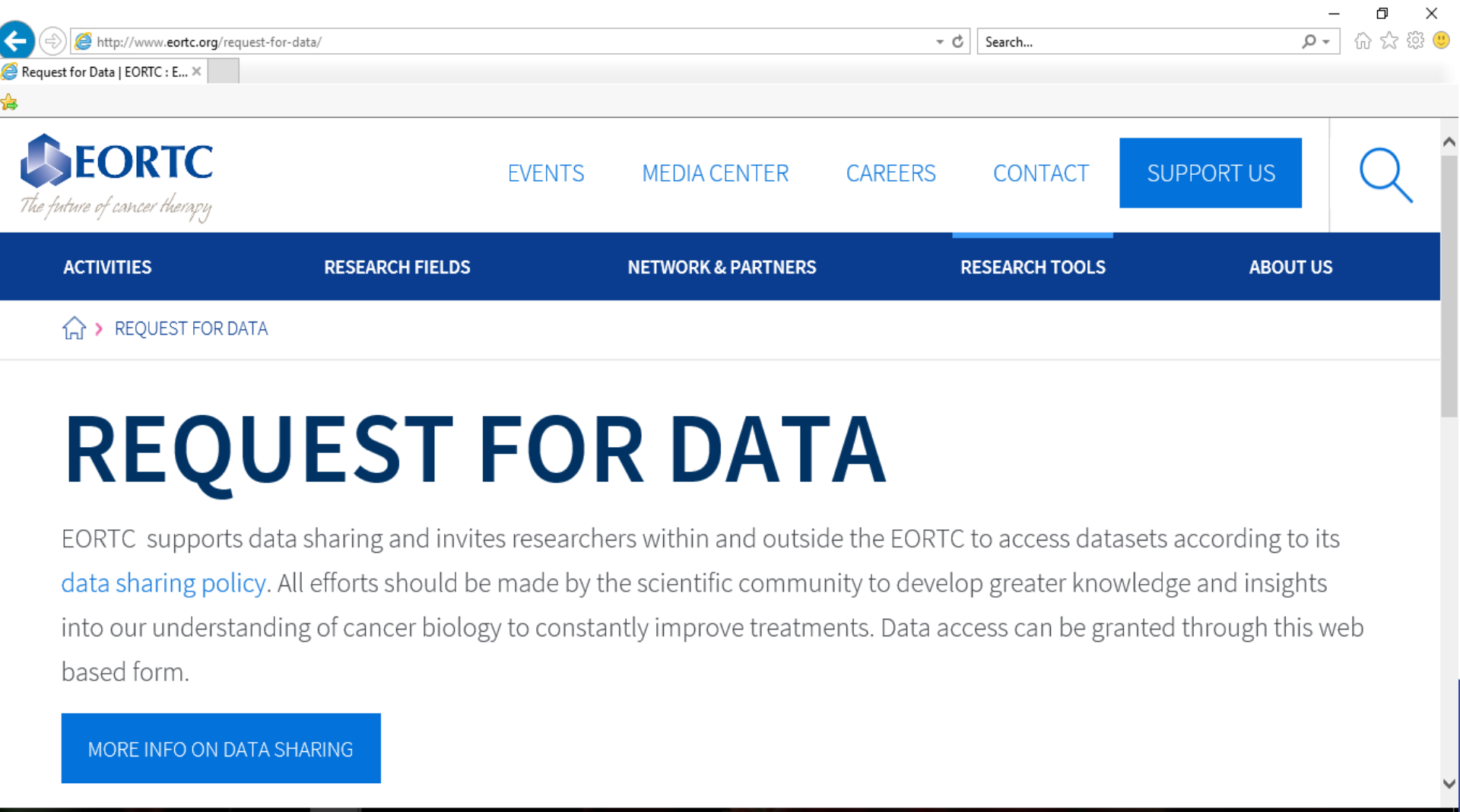
Rest of the world: 6211

EORTC *The future of cancer therapy*

And yes

we do share our data!

EORTC Data Sharing Policy (POL008) effective since October 2001



EORTC data sharing principles

- Ensure the good use of the data and, whenever possible, translation into patient benefit.
- Safeguard intellectual property, the privacy of patients and confidentiality.
- In accordance with the EU data protection rules and other applicable European legislation.
- No data release until the primary study results have been published.

How we are willing to share data

- **Collaboration model**
- Clinical trials are complex
  - Study protocol and amendments
  - Data coding conventions
  - Updates since final publication
  - Statistical analysis plan
- We want our data to be used for good research
  - Close collaboration is needed to ensure that the data are well understood
  - There are so many ways of making the data speak…



How we share the data technically

- The data are ***de-identified***
- A copy of the database is **physically sent to the researcher**

  via a secure password protected portal (eg. Filebox)
- We follow-up the projects closely to avoid
  - further dissemination of copies of the data
  - uncontrolled use of our data



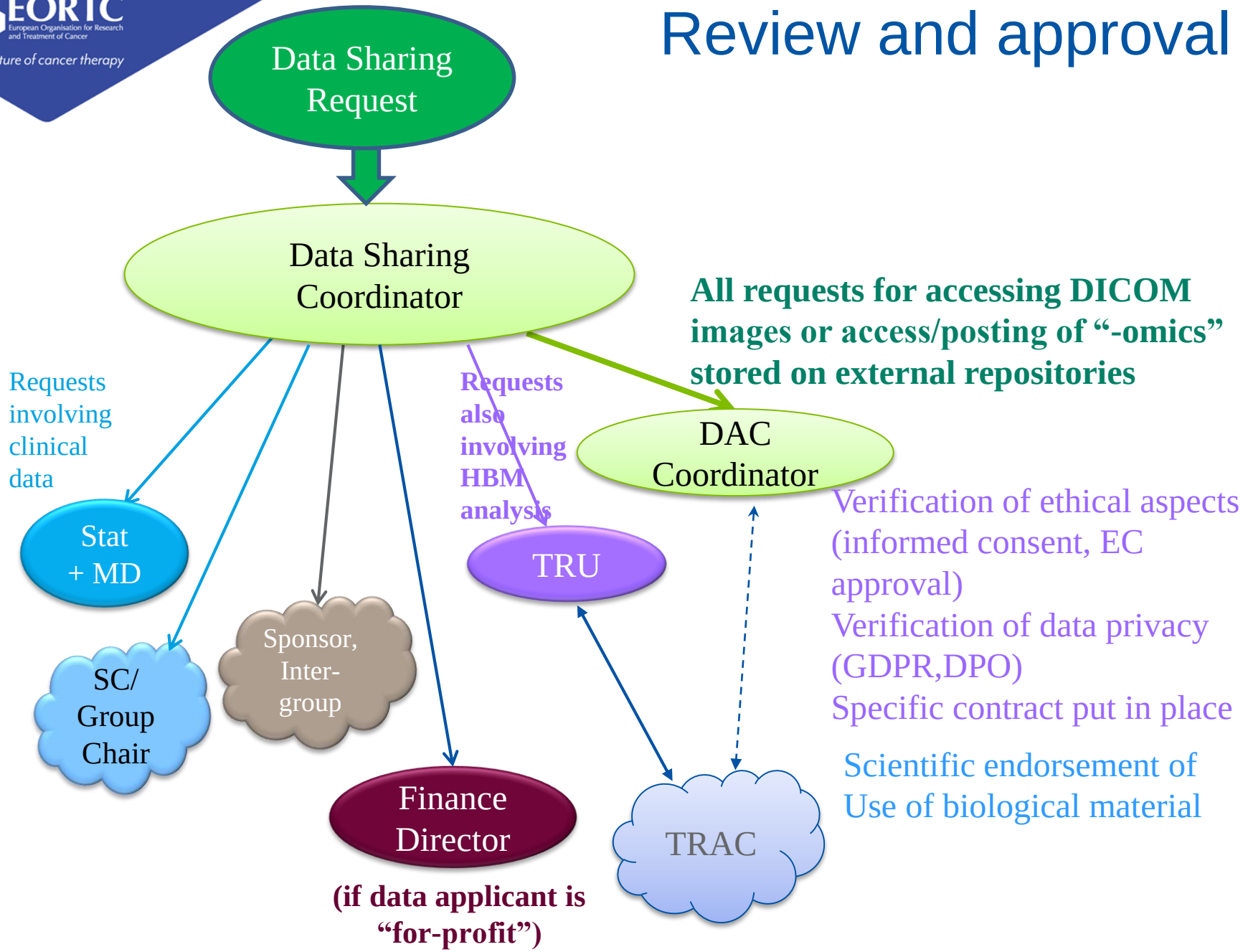
Data sharing at EORTC

Studies are available AFTER primary publication

Formal data request (online form)

- Description of the research
- Brief statistical analysis plan (SAP) and/or research protocol
- Curriculum Vitae of the methodologist in charge
- Publication plan
- Terms of use (contract) agreed and signed
    - Data to be used solely for the purpose of the defined project
    - Publications sent to EORTC prior to submission
    - Acknowledgement to EORTC
    - Protection of the confidentiality of the data!!
    - **Contract** if request of tissue/images/sensitive data
- So far at no cost if academic applicant

Review and approval



MINDACT Review Process Workflow
For Internal use

0 months

MINDACT form submitted to mindactRP@eortc.org

MINDACT EXCO INFORMED – to express interest in the RP or straight rejection

Email – 1 week to react

FIRST FEASSIBILITY CHECK AT EORTC HQ

- RAU: Ethical /Legal feasibility
- COM/Stat: Availability of data / Additional data collection/ Contract

1 month

First feasibility – 2 weeks to assess

Directors/bundle owner greenlight – 2 weeks

For projects with only data sharing – MINDACT bundle owner greenlight

For projects with extended EORTC HQ recourses needed (anything apart from pure data sharing) - directors evaluation

2 months

Scientific review (1 month to collect the TRAC feedback)

FEASIBILITY CONFIRMED

ERP number granted

RP number granted

FEASIBILITY NOT MET

Any major obsticules identified (regulatory/data avialbility/legal)

If no directors greenlight granted due to funding/recourses - recommendation to ExCo/SC for change for pure data sharing project or additional funding required to be able to run the project within EORTC HQ

3 months

Scientific assessment (ExCo every 6 weeks + 2 weeks for SC confirmation) MAX 8 weeks in total

SCIENTIFIC REVIEW

(TRAC/ODAC/Stat dep/TAC whatever applicable)

- For any project 1 MINDACT specific reviewer
- For TR projects, 1 TRAC reviewer
- For genomic data projects, ODAC to review

EORTC HQ Full feasibility check

4 months

SCIENTIFIC ASSESSMENT

1. MINDACT ExCo
   - receives MINDACT form and any comments from the feasibility check and scientific review
   - issues recommendation: project update to be done/conditional approval/ approval/rejection
2. MINDACT SC – endorsement
   - receives project title and MINDACT ExCo recommendation
   - endorses MINDACT ExCo recomendation

REVIEW AND APPROVAL CAN BE COMPLEX !

DECISION BY MINDACT EXCO/SC

1. MINDACT ExCo
   - receives MINDACT form and any comments from the feasibility check
   - issues recommendation: project update to be done/cancellation/ recategorization
2. MINDACT SC
   - receives project title and MINDACT ExCo recommendation
   - endorses MINDACT ExCo recomendation

5 months

HQ greenlight

6 months

contract

Requestor to provide EC approval

HQ GREENLIGHT

(based on SC endorsement; by MINDACT bundle owner(?))

7 months

Release of data – for data sharing

EXECUTION OF PROJECT

1. Applicable contracts to be put in place
2. Applicable regulatory approvals received at EORTC HQ
3. Samples/data shipment and analysis

* If disagreement between MINDACT ExCo and MINDACT SC – MINDACT SC decision prevails

* Any project, rejected at any stage, can be resubmitted to mindactRP@eortc.org, providing the project has been adjusted accoridng to raised blocking comments. Depending on nature of the adjustments, either the full evaluation process will have to be done (scientific changes), or not (administrative changes or data/HBM sharing/RP change)

Terms related to authorship

At time of request, declare

- Publication and posting plan
- Whether the publication will be **published on behalf of EORTC and/or co-authored by an EORTC staff (depending on level of involvement**

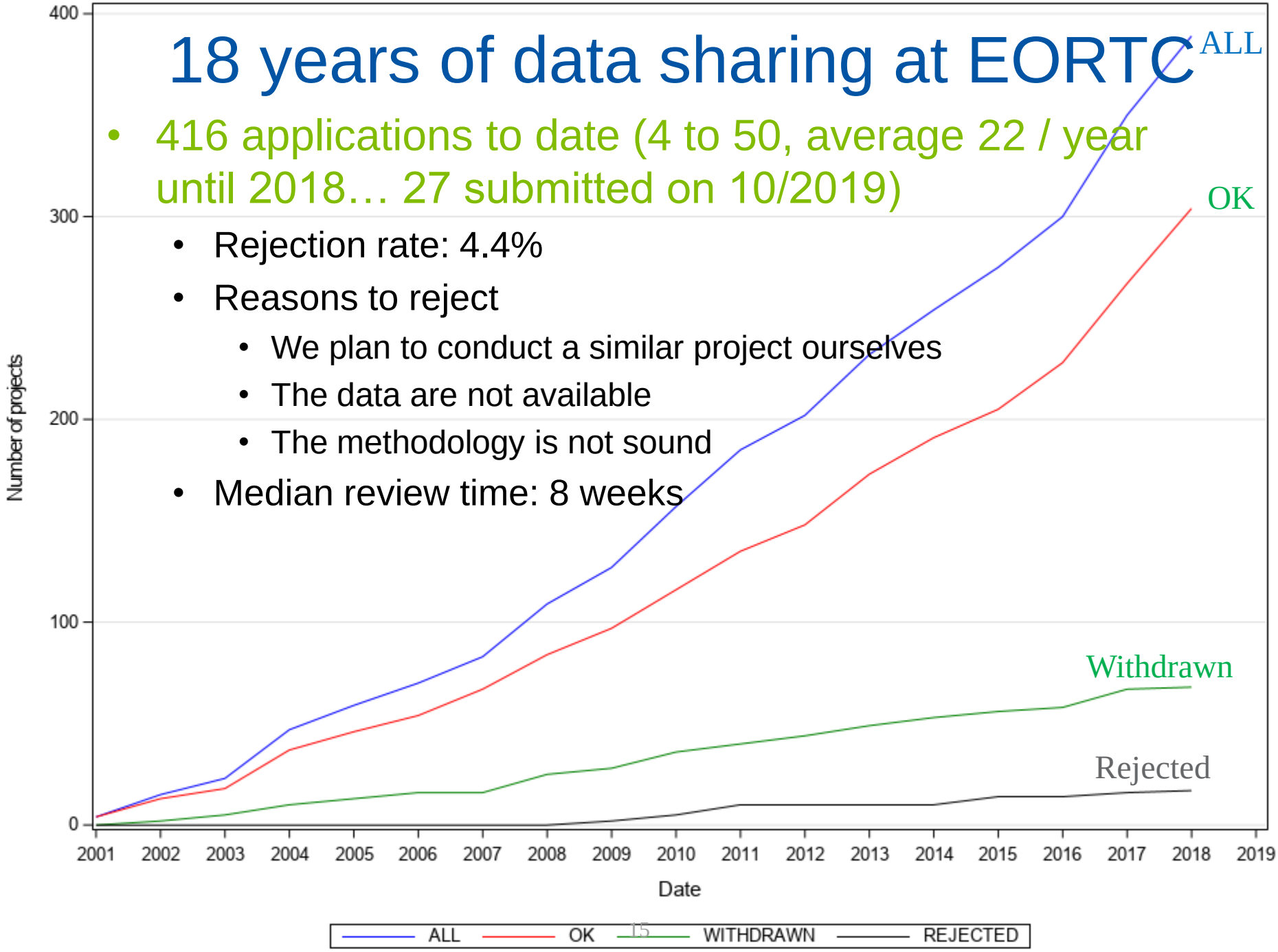
NO → **Triggers terms of use with respect to inclusion of disclaimers that work not done at EORTC and does not reflect official view of EORTC (If not)**
+ follow-up to publication
+ HQ review of the draft prior to publication

YES → **Publication follows standard path of EORTC publications (EORTC POL009)**

- Changes to the declared plan require additional approval

18 years of data sharing at EORTC

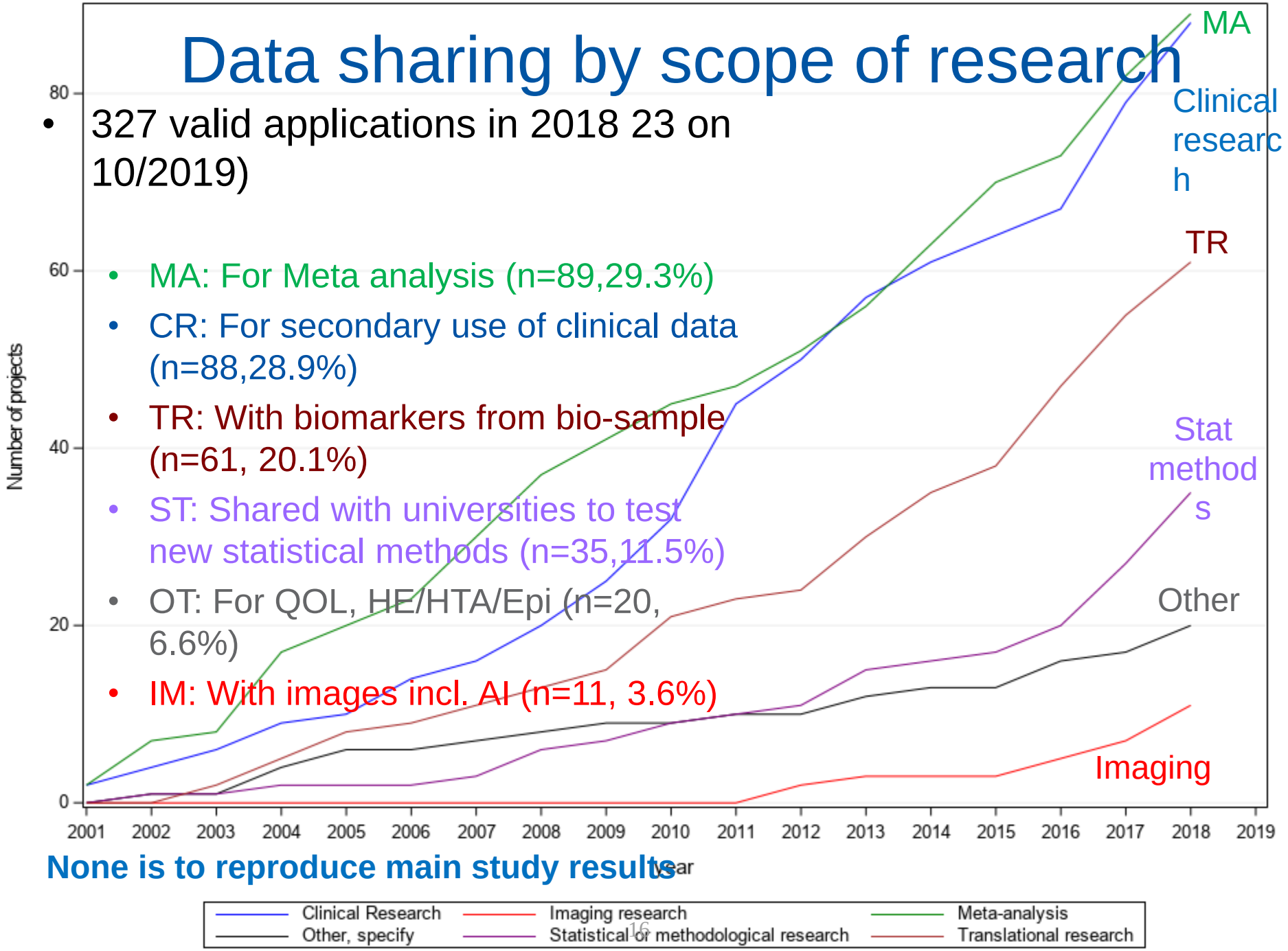
- 416 applications to date (4 to 50, average 22 / year until 2018… 27 submitted on 10/2019)
  - Rejection rate: 4.4%
  - Reasons to reject
    - We plan to conduct a similar project ourselves
    - The data are not available
    - The methodology is not sound
  - Median review time: 8 weeks



Data sharing by scope of research

- 327 valid applications in 2018 23 on 10/2019)

- MA: For Meta analysis (n=89,29.3%)
- CR: For secondary use of clinical data (n=88,28.9%)
- TR: With biomarkers from bio-sample (n=61, 20.1%)
- ST: Shared with universities to test new statistical methods (n=35,11.5%)
- OT: For QOL, HE/HTA/Epi (n=20, 6.6%)
- IM: With images incl. AI (n=11, 3.6%)



None is to reproduce main study results

Publication

- 97% of the completed projects resulted in publications
- 25% of the ongoing projects already led to some publication
- We co-author 87% of the publications, reflecting collaborative work

Data Sharing at EORTC (summary)

- The process is in place and functions well
  - We are faster than many other organisations
  - Fosters collaboration
  - Increases the number of publications
- Few instances of data abuse to date
- The process deeply involve EORTC resources:
  - Logistics of reviews, administrative support needed
  - Training statistician to complex (old) trials
  - Involves several departments (notably contracts)
  - Burden of data sharing increases
  - Sharing of more sensitive data
  - Complete de-identification (may take up to 5 days for old studies)
    - Removal of dates (offset or time intervals), text fields with narrative,…
    - Removing/changing any data that makes a patient unique (e.g. age > 89y)
    - This might restricts the analyses that can be done with the data
    - Whole genome data and some images can identify patients
  - Preparation of data documentation.
- **As of today the process is free of charge**

- Availability described on https://www.eortc.org/data-sharing/

More and more support for data sharing

- More recognition of data sharing benefits but perceived risks are also present *
- More interest in data sharing (with development of AI, DL,…)
- More funders requiring data sharing plans
- More journals requiring data availability statements (DAS)

Mello et al. N Engl J Med. 2018 Jun 7;378(23):2202-2211,
Bauchner et al. JAMA. 2019 Nov 21.

David Simpson VP of ASCO Clinical Trial Data Transparency Forum Sixth Installment June 2019

DAS elements?

- Who should be contacted to request data or for questions?
- What is available (code, statistical plan, etc.)?
- When can the data be accessed (immediately or embargoed, limited time period)?
- Where can it be accessed (data platform, funder, author)?
- Why can it not be shared?
- How were the data analyzed?
- Data set unique identifier?
- Other?

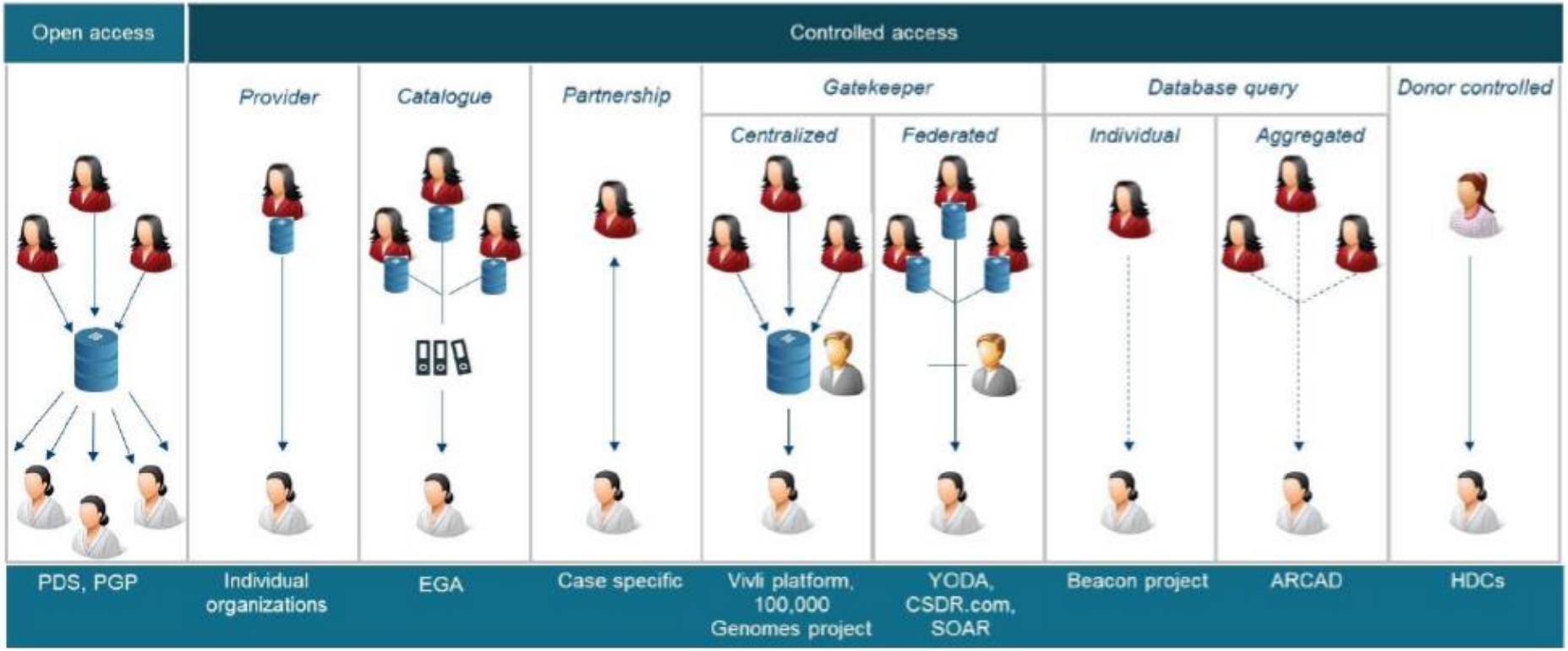
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More and more support for data sharing

- DASs are one more burdensome task for researchers
- DA policies are different across journals
- Awareness of data repositories (platforms) is low among researchers in some disciplines, e.g. clinical research
- Not all data can be open access e.g. due to commercial or “proprietary” embargoes.

David Simpson VP of ASCO Clinical Trial Data Transparency Forum Sixth Installment June 2019

9 models to share data and samples



Mello et al. N Engl J Med (2013) 369:1651–8.10.1056

Broes S, Towards a tiered model to share clinical trial data and samples in precision oncology, Frontiers in Medicine, 2018

9 models to share data and samples

	Controlled access strategy	
Provider EORTC	Pre-specified set of criteria should ensure a transparent system; possibility to appeal to an independent board	Lack of full transparency or assurance of impartiality; difficult to identify data holders
Catalog EGA	Clear overview of types of data held by different study teams; allows data generators to maintain autonomy	Datasets obtained on different consent forms complicated reuse
Partnership	Conduct of research in accordance with requirements of both parties; benefit-sharing strategies	Complex negotiations; increased timelines before project start

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9 models to share data and samples

	Controlled access strategy	
Gatekeeper VIVLI	Data provider cannot veto a request; transparent procedure; full assessment of scientific request and requester; apply benefit-risk balance test data sharing and share minimum data necessary for the request; communication portal between data provider and data requester	Costly (infrastructure, administration, maintenance; curation costs; human resources; opportunity costs); potentially time-consuming procedure
Database query Beacon project/ARCAD	No direct data sharing, thus can be applied for (personal or commercially) sensitive data; analyses are conducted by original study team who are most familiar with the nuances of the dataset; not limited by particular formats	Little control and transparency on executed queries; resource-intensive for data holders; potentially considerable wait times for requesters.
Donor controlled HDCs	Patient engagement and empowerment; effective reuse of data with explicit consent of the donor	Additional burden (increased resources for health literacy; infrastructures to manage patient preferences…)

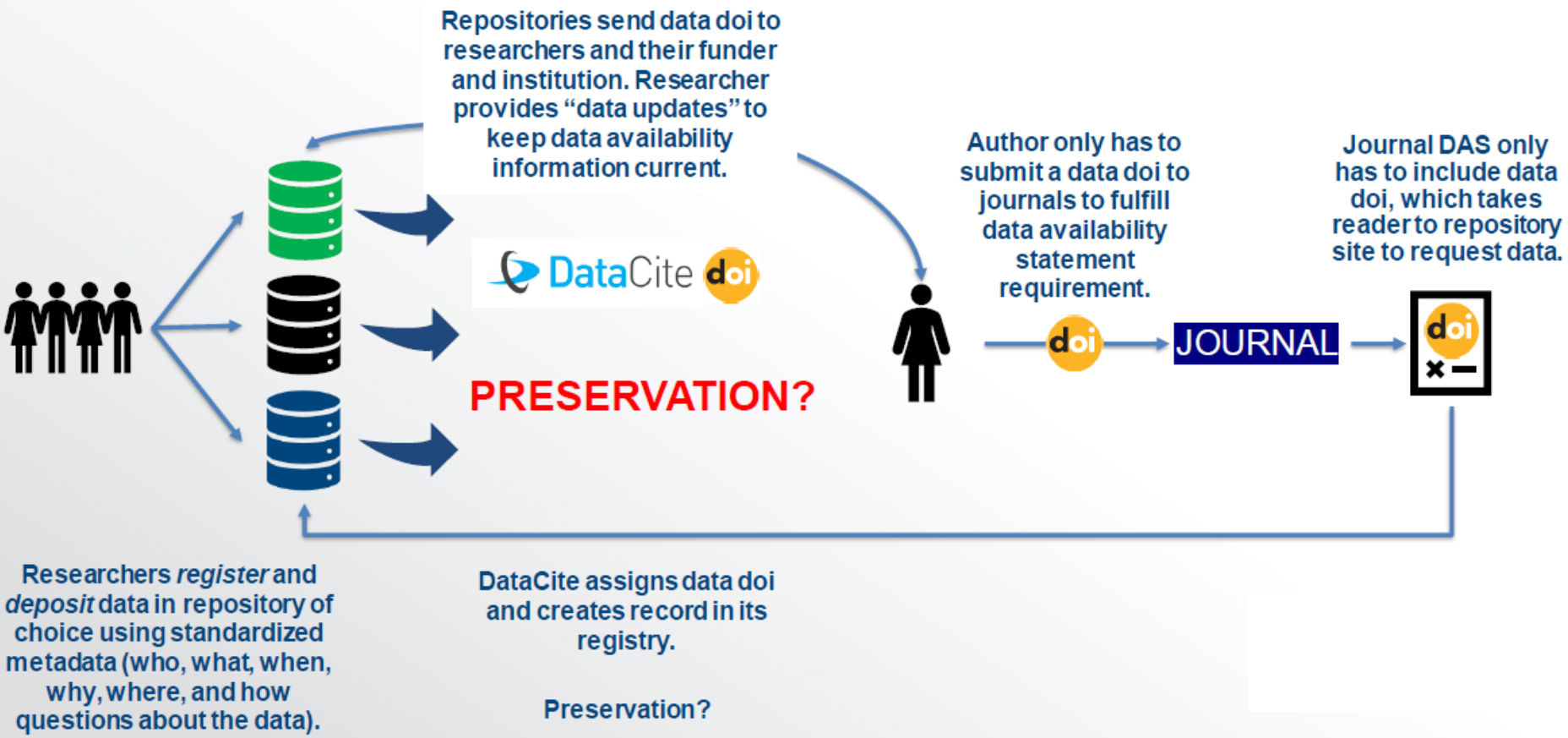
Broes S, Towards a tiered model to share clinical trial data and samples in precision oncology, Frontiers in Medicine, 2018

Alternative ways of sharing for EORTC ?

- Provider to Gatekeeper ?
- Online repositories such as https://clinicalstudydatarequest.com/ i.e. consortium of clinical study Sponsors/Funders.
  - Avoid sending physical copies
  - Assume administrative and financial burden of data management
  - Improve discoverability of data
  - Serve a critical governance role for clinical data, e.g. vetting data requests
  - **Make it easy for authors and publishers**

David Simpson VP of ASCO Clinical Trial Data Transparency Forum Sixth Installment June 2019

Make it easy for authors and publishers



Costly ! Solutions for Academic organization ?

Extracted from a presentation of David Simpson VP of ASCO at Clinical Trial Data Transparency Forum Sixth Installment, hosted by SAS in Heidelberg, Germany,

Any solution for Academic organization ?

- **Project Data Sphere (PDS) ?**
- You only know who downloaded the data, no access control
- Works for the data which investigator is willing to make available without any thresholds apart from a registration (open access).
- Big advantage that it's for free
- **Sensitive data need to remain under controlled access.**
- **Projects of or approved by EORTC disease oriented group is first priority**

Conclusions

- EORTC, 18 years of data sharing (DS)
- DS administrative and financial burden for academic organization
- DS generally cost not included in trial/research project funding.

Not all EORTC data can be made open access

- **Not or less sensitive trials data (to be determined on a case per case basis) could go to PDS (GDPR)**
- **For sensitive trials data :**
  - **Stay provider, develop partnership (SPECTA, IMMUCAN,…).**
  - **Keep control on data access and continue review of scientific of project**
  - **Priority to research projects/programs of EORTC disease oriented group**
  - **Find funding for DS. Admin cost coverage.**
- **Need EORTC board approval to change EORTC policy**

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Thanks