Transparency in Clinical Trials: A New Paradigm Shift?

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Table of Contents

- ***Evolution***
- ***Rational***
- ***Insights***
- ***Challenges***
- ***Conclusion***

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We're in the middle of a major flu epidemic, and the CDC has recommended treatment with an antiviral for high-risk people.

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

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FUNDAMENTAL QUESTIONS….

- How and when will patient-level data be allowed to evaluate?

- And who decides on the data availability and for what purpose?

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The example gives rise to the need of what we call as....

Sharing Clinical Trial Data: Maximizing Benefits, Minimizing Risk

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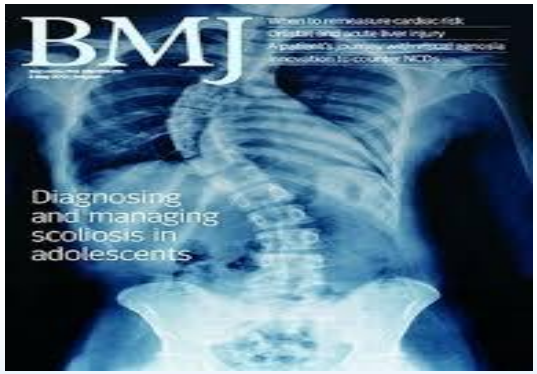
EVOLUTION:

- **Non-regulatory research**

- **The British Medical Journal (BMJ) supporting the cause. To provide detailed patient level data viz:**
  1) **mid-study protocol changes,**
  2) **negative efficacy outcomes and**
  3) **potentially life-threatening adverse effects.**



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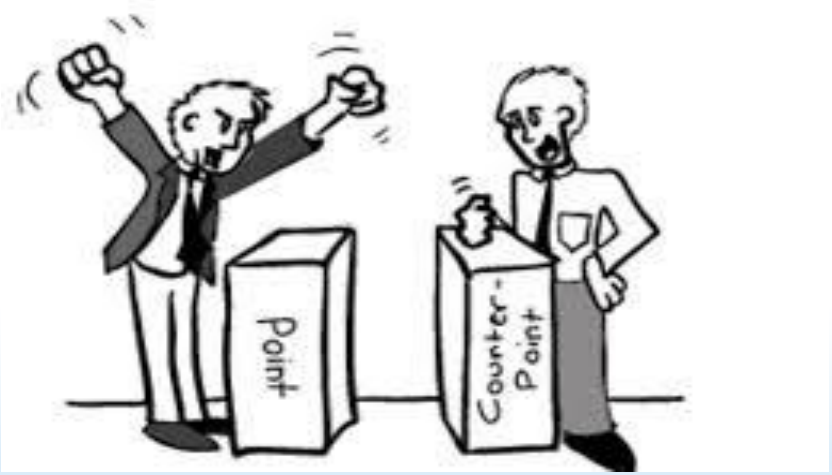
RATIONALE….

Pharmaceutical companies claim that:

- the data release could prompt a market advantage to peers, misinterpretation of data and
- breaches of patient confidentiality.

While others in the medical world feel publically sharing the data sets could serve to enhance disease research, drug development and most importantly, strengthen patient safety.



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IS THERE NO TRANSPARENCY NOW….

- Clinicaltrials.gov is a clinical trial registry and results database contains over 130,000 U.S. and international clinical research studies that are available for clinicians and the public to search.

- Clinical trial registry and summary information of FDA-approved medical products are freely available.

GOING FORWARD ….

- A significant difference will be the availability of detailed, anonymized patient data (de-identification) with primary focus on safeguarding the 'privacy of patients.'

- Some experts suggest even the full reliability of the clinical database also remains in question, which shall be answered.

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INSIGHTS ….

The path to responsible clinical trial data sharing revolves around 5 commitments:

- Commitment 1: To enhance data sharing with researchers
- Commitment 2: To enhance public access to clinical study information
- Commitment 3: To share results with patients who participate in clinical trials
- Commitment 4: To certify procedures for sharing clinical trial information
- Commitment 5: To reaffirm commitment to publish clinical trial results

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FULFILLING COMMITMENTS:

Eli Lily has shared clinical trial information since 1st January 2014 and joined ClinialStudyDataRequest.com from 1st June 2014.

Since March 2014, **NovoNordisk** has:

- Published CSRs completed after 2006
- Where feasible, old CSRs are made available on request
- Granted access to anonymised patient-level data from trials
- Older data can be requested.

SOME MORE:

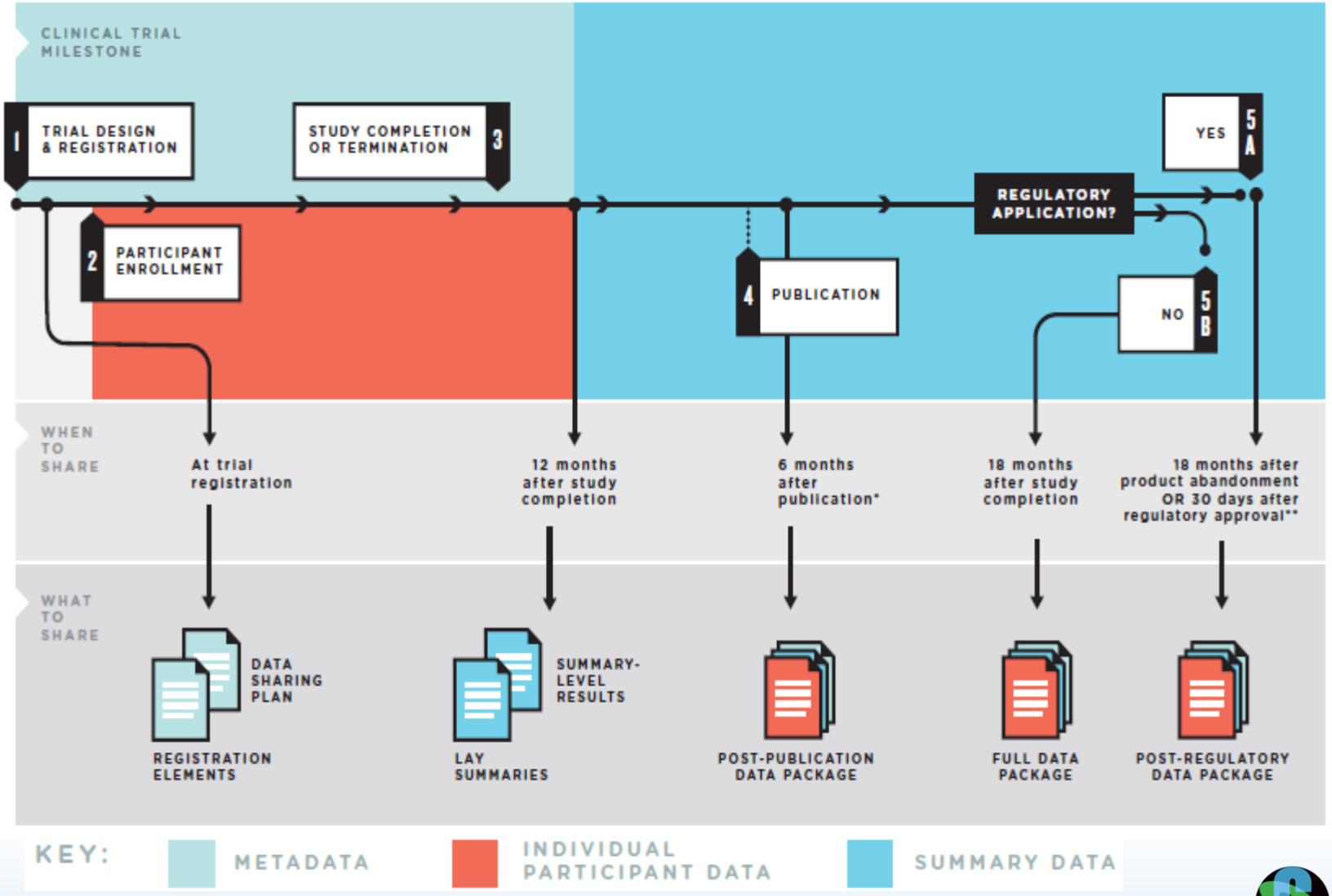
GSK too has decide to be a part of ClinialStudyDataRequest.com

- GSK request site: including a list of studies already available, request submission form.
- Independent review panel: to check the validity of requests.
- Data sharing agreement: in accordance with the charted published on the site.
- GSK access system: developed by SAS, providing read-only access for requesters to conduct research and download their analyses.

Novartis will provide access to anonymised patient-level data and commits to providing expanded information about clinical trial results on company website.

- **Access to patient-level data** from trials of innovative medicines approved through www.clinicalstudydatarequest.com.
- **Simplified language summaries** and **additional data interpretation** on www.novctrd.com

Clinical Trial Life Cycle: When To Share Data



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Data Sharing Mechanisms:

Clinical trial IPD (individual-level participant data) can be shared either as: *micro data* or through an *online portal*.

MicroData

- downloaded as a raw data file
- on a disc, or transferred electronically

- access the data only through a remote computer interface
- all analysis performed is on the sponsor's computers.

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SAS Data sharing model:

SAS CLINICAL TRIAL DATA TRANSPARENCY

Dashboard and Reports

SPONSOR MANAGEMENT AND ADMINISTRATION

By User:

Last Updated: 17-APR-14 12:58:46 EDT

User	User ID	Role	Organization	Size	Involved Companies
Researcher, Lead (LRES)	ctdt_leadresearcher	Lead Researcher	State U	54.307366 MB	• ACME • ABC Pharma

Company: ABC Pharma | Start Date: 02-MAR-2014 | End Date: 01-MAY-2014 | View

By Company:

Last Updated: 17-APR-14 12:58:46 EDT

Company	Type	Status	Size
ABC Pharma	Large	Active	63.976562 MB

Research Projects : ABC Pharma

Study Size (GB) : ABC Pharma

Workspace Size (GB) : ABC Pharma

User Access Summary: 4 record(s)

Last Name	First Name	User ID	Role	Status (Request)	Status (Portal)	Status (Repo)	Company	Groups	Studies	Related Companies	History
Admin	ABC Pharma	ctdt_abcadmin	ABC Pharma Admin	Account Created	✓	✓	ABC Pharma	• CTDT ABC Pharma Admin	• ABCP-66890 • ABCP-66877	• ABC Pharma	
Barnes	Karen	barnesk	Lead Researcher	Account Created	✓	✓	Pharma Research	• CTDT RP-USERTEST - Full	• ABCP-66890 • ACME-12345 • ACME-12987 • CTDT RP-USERTEST	• ABC Pharma • ACME	
Researcher General		ctdt_researcher	Researcher	Account Created	✓	✓	State U	• CTDT RP-12345 - Full	• ABCP-66890 • ACME-12345 • ACME-12987 • CTDT RP-12345	• ABC Pharma • ACME	
Researcher Lead		ctdt_leadresearcher	Lead Researcher	Account Created	✓	✓	State U	• CTDT RP-12345 - Full	• ABCP-66890 • ACME-12345 • ACME-12987 • CTDT RP-12345	• ABC Pharma • ACME	

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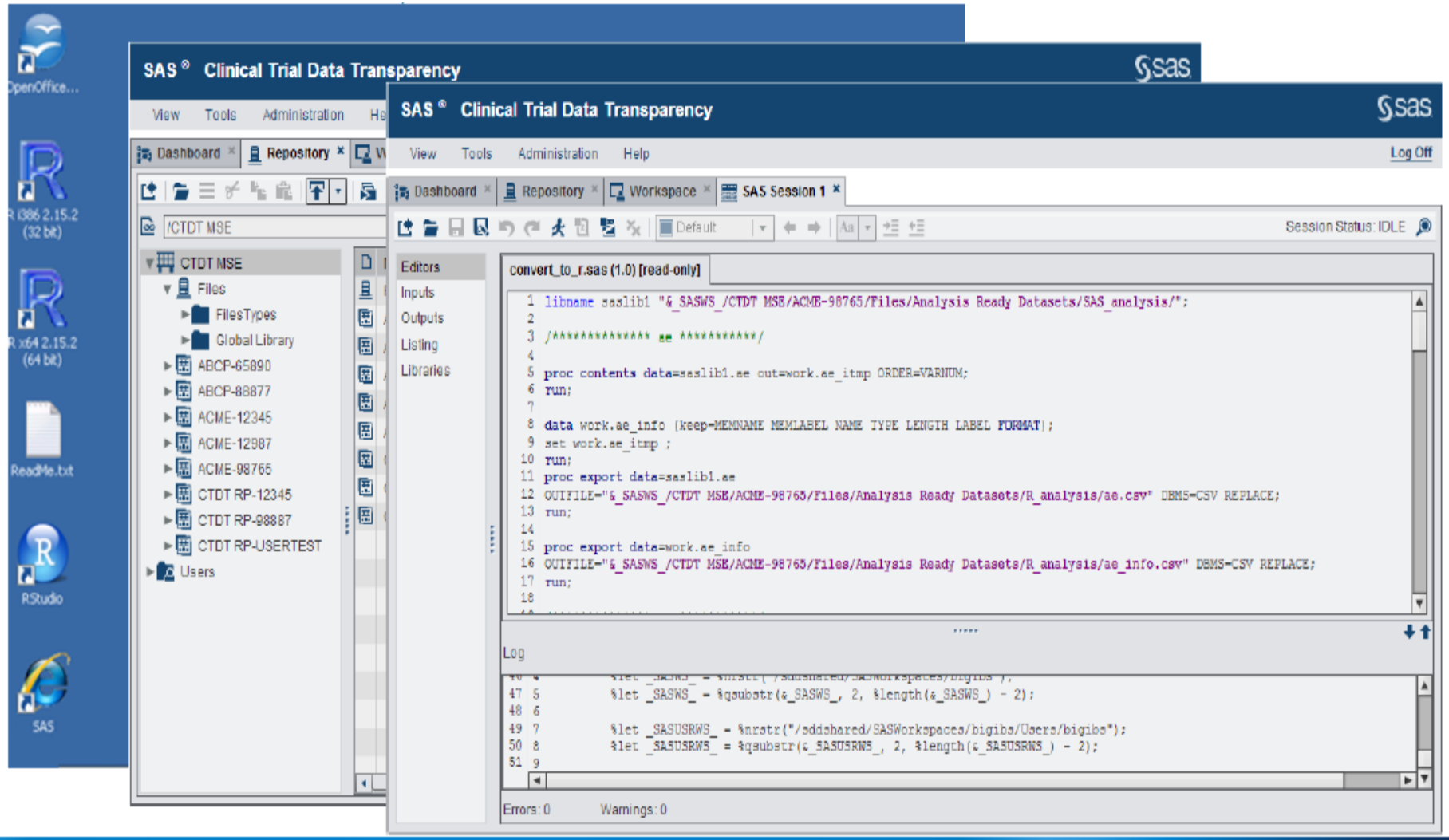
SAS Data sharing model:



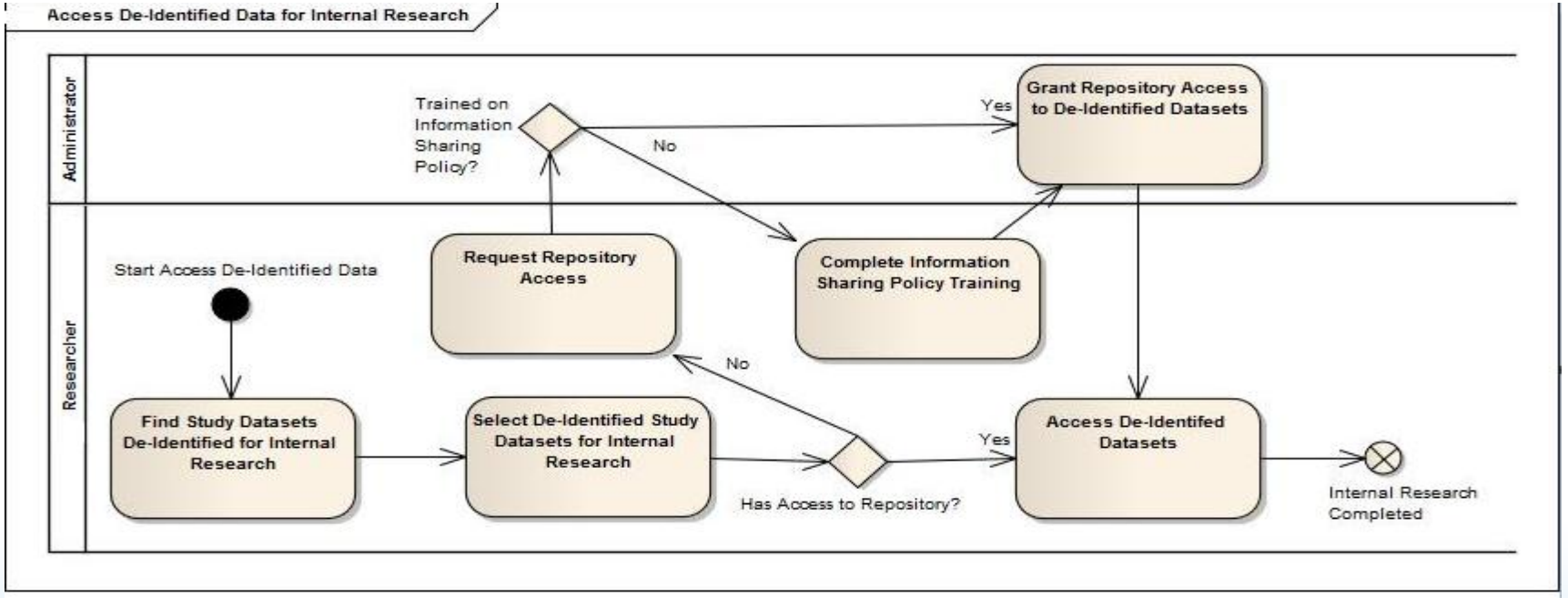
Futuristic Thoughts:

Setting up an environment to support De-identification which will be a:

Platform to effective information sharing across the partner and external parties keeping data privacy intact,

Robust, compliant with the legal requirements, risk assessed but also simple to understand.

Governance, Traceability, Re-identification, Access Management – **PROCESS and TOOLS**



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Futuristic Thoughts (Stakeholders):

Role	Description
Internal Researcher	Researcher functioning within internal processes requesting or granted access to use the internal de-identified clinical data repository.
External Researcher	Researcher functioning outside of processes and roles requesting or granted access to access data for analysis and reporting outside of the internal de-identified clinical data repository.
Programmer	Clinical programmer capable of configuring and running SAS Macros on data that existing in the de-identified clinical data repository.
Administrator	Responsible for establishing group and individual accounts and access rights.
Compiler	Responsible for compiling all supporting documents made available to external researchers, such as the CSR, SAP, and protocol.
QA Reviewer	Responsible for reviewing the de-identified datasets produced for external research.

Futuristic Thoughts (How to de-identify data):

Internal Research:
The system shall de-identify the following variables for internal use:
SUBJECT (replace Using random functionality)
PATIENT(replace using random functionality)
USUBJID (replace using random functionality)
SUBJID (replace using random functionality)
CENTRE (replace using random functionality)
Note: The system shall create a de-identified copy of the source dataset that is identical to the source except for the changes executed in support of de-identification.

External Research:
The system shall de-identify the following variables at a minimum for external use:
SUBJECT (replace Using random functionality)
CENTRE (drop if not needed for analysis)
PATIENT(replace using random functionality)
USUBJID (replace using random functionality)
SUBJID (replace using random functionality)
AGE (replace and aggregate ages into 5-year bands)
Remove All Verbatim Terms, keep only coded term.
ALL date variables should only contain YEAR
Update AGE over 89 should be set to 90 (business rule)

CONCLUSION….

To the Flu example

If the data regarding the already available anti-viral was made transparent before, it could have:

- Eliminated duplicative efforts, and perhaps stimulating further ideas for research rather than just one epidemic focus.
- May also would have aided in HEOR (Health Economic and Outcome Research)
- Most important patient safety would have been improved.

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CHALLENGES….

With a paradigm shift in **clinical trial transparency**:

- Will other peer-reviewed journals follow BMJ's lead and require transparency from all clinical research authors?
- Can patient-level data still remain secure?
- And most importantly, will individual patient care and safety be improved?

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These matters, and others, will be important to answer as the debate towards clinical trial openness and transparency evolves.

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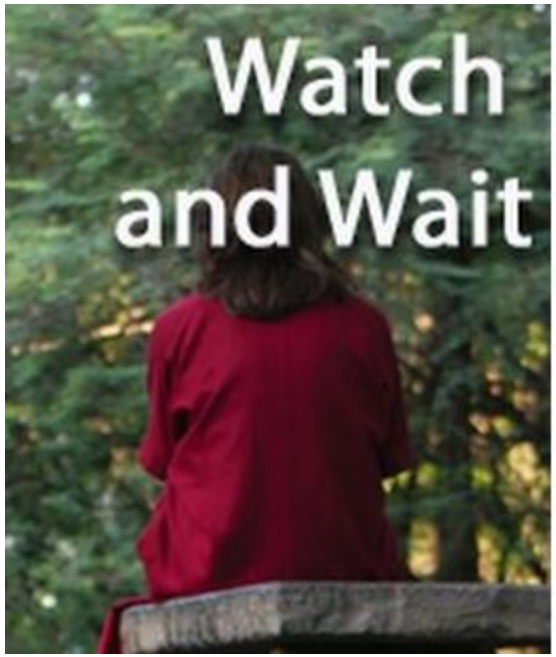
So let us….



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