The Evolution of Clinical Trial Transparency (Registries)

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Publication bias - concerns

• How do we know if all studies are published?

• Do publications accurately reflect the conduct of studies?

Protocol registration

- Pioneered by ICMJE, WHO and others
- Enables studies to be tracked to publication
- Enables review of submitted manuscripts against the protocol summary
- Helps reduce duplication
- Provides opportunities for participation
Publication bias - concerns

• How do we know if all studies are published?

• Do publications accurately reflect the conduct of studies?

• What happens when a study is not published in a peer-reviewed journal?

Results registration

- Pioneered by industry
- Results in the public domain irrespective of outcome and whether or not studies are accepted for publication

GSK Clinical Study Register
Launched October 2004

Lilly Clinical Trials
Launched December 2004
Providing access to protocol and result summaries

Current GSK Approach – Posting on Registers and Databases

Protocol summaries and result summaries posted for:
- Clinical trials (phase I-IV)
- Observational studies that evaluate medicines
- Meta-analyses that evaluate medicines
- Results posted:
  - At the time of approval
  - Within 12 months of termination
  - Within 12 months of LSLV for phase IV studies
Posting Clinical Study Information

What Information is Posted?

Pre-determined scientific non-promotional information.

- Study title/rationale/objectives/phase
- Study design/treatment schedule/location(s)
- Statistical methods
- Study period
- Study population/demographics
- Results for primary and secondary endpoints defined in the trial protocol
- Adverse events (including all serious adverse events)
- Names of principle investigators
- References to publications in the medical literature
What Does it Look Like?

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Current GSK Approach – Publication in the Scientific Literature

Commitment to seek peer-reviewed publication AS MANUSCRIPTS of all:
- Clinical trials (phase I-IV)
- Observational studies that evaluate medicines
- Meta-analyses that evaluate medicines
- Submission within:
  - 12 months of approval
  - 12 months of termination
  - 18 months of LSLV for phase IV studies
- Should publication not be possible, context and interpretation will be added to the result summary on our register

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Where next?

We don’t have all the answers.

We welcome dialogue and constructive discussion with stakeholders.

Study Results Posting for Patient Benefit

**Audiences that use Results Posted on Registers**
- Academic researchers
- Meta-analysts
- Journal editors
- Third party payers
- Lawyers
- Healthcare practitioners?
- Patients?

**Uses**
- To conduct meta-analyses and reviews
- Re-analyze individual study data
- By industry to inform clinical programs
- By editors when reviewing manuscripts
- Guide/inform treatment decisions at the physician and patient levels?
Need for harmonisation

Sponsors of multinational trials

Country A
Register A
Information A

Country B
Register B
Information B

Country C
Register C
Information C

Country D
Register D
Information D

Country E
Register E
Information E

Country F
Register F
Information F

Timing of Disclosure

European Commission has issued a Communication that would require the public disclosure of results from phase II-IV clinical trials with 12 months of completion of the trial irrespective of the approval status of the medicine.

In the US, the FDA Amendments Act (FDAAA) includes language regarding the potential for study results posting for unapproved products at some point in the future.
Getting the balance right for patient benefit

Framework that rewards innovation

Public disclosure of clinical research

New medicines

Appropriate use of medicines

Scientific advance

Study Results Posting: Interpretative (Lay) Summaries

- Title VIII of the FDA Amendments Act stipulates that not more than 3 years after enactment the HHS Secretary will expand the NIH study results database by rulemaking to provide:

  “A summary of the clinical trial and its results that is written in non-technical, understandable language for patients, if the Secretary determines that such types of summary can be included without being misleading or promotional.”

- Public meetings held in 2009
  - Determine need
  - Identify a process for producing summaries
Interpretative (Lay) Summaries
Key Issues to be Addressed

- Determining need
  - NEJM was not supportive because of the authorship issues
  - Others (e.g. Consumer's Union) felt they were critical

- Authorship
  - How can we ensure they are non-promotional and accurate?
  - How can we ensure they are understandable – reading level?
  - Who will write the summaries? – Independent writing groups?
  - Who will review the summaries? – Regulators?
  - Who will pay for writing and review?

Summary

Current Approach → Future Challenges

Audiences for postings and publications

Need for harmonisation

Timing of disclosure

Posting interpretative (lay) summaries