ClinicalTrials.gov: Updates and Modernization

NIH Collaboratory Virtual Steering Committee Meeting April 23, 2020

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Results Team Project Specialist, ClinicalTrials.gov [Contractor, ICF]
Agenda

• ClinicalTrials.gov Basics
• Recent Updates to ClinicalTrials.gov
• Modernization Effort
• Collaboration with OBSSR to Develop Proto-papers and Support Materials
ClinicalTrials.gov Basics
Benefits of Comprehensive Registration and Results Reporting

- Honor commitment to participants that their contributions will advance science; support enrollment
- Mitigate publication bias
- Advance stewardship and accountability
  - Identify unmet research needs
  - Facilitate complete reporting
  - Avoid unnecessary study duplication
  - Evaluate research integrity
- Support evidence-based medicine

All contribute to increased public trust in clinical research
Basics of Registration Information Submission

- Interactive data entry or automated upload
- Anyone can enter data, but “responsible party” must submit
- Content reflects:
  - Legal requirements
  - International standards
  - Good reporting practices
- NIH grant application aligns with subset of content

**ClinicalTrials.gov PRS**
Protocol Registration and Results System
Basics of Results Information Submission

- Structure supports:
  - Complete reporting
  - Efficient quality review
  - Consistent data display
  - Detailed search and integration of other NLM resources

- Aligns with good reporting practices (CONSORT)

**ClinicalTrials.gov PRS**
Protocol Registration and Results System

### Edit Baseline Measure

<table>
<thead>
<tr>
<th>Study-Specific Baseline Measure Title:</th>
<th>Weight</th>
</tr>
</thead>
</table>

**Baseline Measure Description:**
Additional information about the measure (e.g., description of scale)

<table>
<thead>
<tr>
<th>Overall Number of Baseline Participants:</th>
<th>Remuverol</th>
<th>Placebo</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>101</td>
<td>99</td>
<td>200</td>
</tr>
</tbody>
</table>

**Baseline Analysis Population Description:**

<table>
<thead>
<tr>
<th>Measure Type:</th>
<th>Mean</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Measure of Dispersion:</th>
<th>Standard Deviation</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Number Analyzed Participants</th>
<th>101 participants</th>
<th>99 participants</th>
<th>200</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>77.03</td>
<td>78.53</td>
<td>Mean 77.77</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>14.38</td>
<td>13.56</td>
<td>Standard Deviation 14.00</td>
</tr>
</tbody>
</table>

* Unit of Measure: kg

Commonly reported units: years, units on a scale, participants
ClinicalTrials.gov: Information Scaffold

- Journal Publications
- Results Database
- Conference Abstracts
- Clinical Study Reports
- Individual Patient Data (IPD) Repositories
  - Uncoded
  - Coded
  - Analyzable
- Summary Results
- Other information (e.g., press releases, news articles, editorials)

ClinicalTrials.gov

- NCT Number
- Full Protocols
- Statistical Analysis Plans
- Informed Consent Forms
- Other Study Documents
Results Posted Within 30 Days

1. Sponsor Account
2. Registration Information
   - Automated Validation
   - QC Review Comments
3. Manual Validation
   - Quality Control Review
   - No “Major” Issues
   - “Major” Issues
4. Public Posting
   - General Notice and Standard QC Review Comments

- Results posted after each QC review for applicable clinical trials (ACTs) with Study Start Date on or after 1/18/17
- Responsible party must correct or address major issues within 25 calendar days of review
Recent Updates to ClinicalTrials.gov
ClinicalTrials.gov Home Page

Update: COVID-19

1. New links added:
   - CDC – latest public health information
   - NIH – latest research information

2. Targeted ClinicalTrials.gov search results – studies related to COVID-19
Targeted Search Results: COVID-19

- Search results include those for related identifiers (e.g., SARS-CoV-2, 2019-nCoV)
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- Links to additional resources:
  - ClinicalTrials.gov — subset of federally-funded studies
  - WHO Trial Registry Network
  - CDC — information for clinicians
Targeted Search Results: COVID-19

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- Links to additional resources:
  - ClinicalTrials.gov – subset of federally-funded studies
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  - CDC – information for clinicians
Answers to Top Questions: COVID-19

- Links to responses available on What’s New and Support Materials pages
- Updated as needed
Answers to Top Questions: COVID-19

- Links to responses available on What’s New and Support Materials pages
- Will be updated as needed
PRS Guided Tutorials

- Results tutorials launched in Beta in August 2019
- Registration tutorials launched March 2020; tutorials taken out of Beta
- Tutorials can be accessed on ClinicalTrials.gov or from within the PRS
- Feedback has been collected
  - User testing: further updates are planned
- Fictional manuscript and example ClinicalTrials.gov record for Units Other Than Participants Study Design now online
Modernization Effort
ClinicalTrials.gov Modernization Overview

Current year: Engagement
- Engage with stakeholders to determine and validate approach and specifications
  - Request for Information (RFI) and Public Meeting
  - NLM Board of Regents Working Group
- Develop modernization roadmap
- Enhance internal business processes

Future (years 2 – 5):
Implementation of Roadmap
- Conduct user evaluation and continue engagement
- Make improvements to support compatibility across trial lifecycle (seamless end-to-end process)
- Upgrade system infrastructure components
Request for Information (RFI)

• Solicited input on key modernization-related topics to guide planning for infrastructural enhancements:
  1. Website functionality
  2. Information submission
  3. Data standards

• Received over 260 Comments from a 75-day comment period (December 30, 2019 - March 14, 2020)

• NLM’s modernization effort aims to deliver an improved user experience on an updated platform to accommodate growth and enhance efficiency

• Note: RFI was not intended to modify existing legal and policy requirements for clinical trial registration and results submission
Public Meeting

Goals of the public meeting

• Share high-level summary of RFI comments and key themes
• Gather diverse stakeholders to collectively share synergistic and competing needs
• Obtain further information on certain themes/topic areas

To register, visit: https://events-support.com/events/ClinicalTrials-gov_Modernization_Public_Meeting

April 30, 2020, Virtual Meeting
9:30 am - 12:30 pm
Collaboration with OBSSR to Develop Proto-papers and Support Materials
OBSSR Materials Development

- Fictional manuscripts and example ClinicalTrials.gov records for 4 designs:
  1. Cluster Randomized
  2. Fractional Factorial
  3. SMART
  4. Micro-randomized

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### Cluster Randomized Study Design Example (With Results)

**Methods**
- **Study Design**: This was a pragmatic, three-group, cluster randomized trial designed to compare strategies for preventing *P. ovale* infections in adult intensive care units (ICUs) in the Southern Innovative Clinical Health System (SICHS). ICUs were randomly assigned to one of three groups. All ICUs located within a hospital and all adults in those ICUs were assigned to the same group. There was a 12-month baseline period from January 31, 2016, to January 30, 2017. The 12-month intervention period immediately followed, from January 31, 2017, to January 30, 2018.
- **Eligibility Criteria**: Inclusion criteria for participation in the study were: commitment by the hospital's administration to have all its ICUs randomized for the trial, less than 30% of patients in participating adult ICUs currently receiving either intranasal 2% No-Bug cream or 4% No-Scrub (hydrogen peroxide) sanitizing cloths at baseline, and stable use of infection-prevention initiatives and products during the baseline period. The exclusion criteria were: adoption of new infection-control initiatives that would conflict with the study protocol.

**Data Sources**
- We obtained hospital-specific, individual patient data for ICUs from the SICHS data system for both the baseline and intervention periods. Participants with repeat visits to a hospital over the course of the study contributed data for only their first ICU visit. Consequently, there were unique, non-overlapping samples in the analyses for these hospital ICUs during the baseline and intervention periods. We randomized the ICUs so that the three intervention groups included a similar proportion of patients.

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### ClinicalTrials.gov Data Table

<table>
<thead>
<tr>
<th>Condition or Disease</th>
<th>Intervention/treatment</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>P. ovale</em> Infection</td>
<td>Drug: 2% mushroom cream</td>
<td>Phase 4</td>
</tr>
<tr>
<td></td>
<td>Drug: 4% hydrogen peroxide sanitizing cloth</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diagnostic Test: PD screening</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Transmission-based precautions</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Room disinfection</td>
<td></td>
</tr>
</tbody>
</table>
OBSSR Materials Development

- Fictional manuscripts and example ClinicalTrials.gov records for 4 designs:
  1. Cluster Randomized
  2. Fractional Factorial
  3. SMART
  4. Micro-randomized

- Supplementary Materials:
  - Question and Answer documents
  - Annotated Participant Flow tables
  - Cross-walk of PRS data elements to OBSSR Protocol Template
OBSSR Materials Development

• Subject matter experts within and outside of OBSSR reviewed the proto-papers and provided invaluable feedback

• Goal is to share materials on the ClinicalTrials.gov website this summer
  • Content will be incorporated into the PRS Guided Tutorials

• Working with OBSSR to promote availability of tutorials via:
  • OBSSR Webinar
  • Clinical & Translational Science Awards Program (CTSA) Presentation
Thank You

Questions? Submit to the ClinicalTrials.gov Information Team, National Library of Medicine
register@clinicaltrials.gov

ClinicalTrials.gov Modernization Information
https://clinicaltrials.gov/ct2/about-site/modernization