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ClinicalTrials.gov: Updates and Modernization

NIH Collaboratory Virtual Steering Committee Meeting April 23, 2020

Stacey Arnold, PhD
Results Team Project Specialist, ClinicalTrials.gov [Contractor, ICF]

U.S. National Library of Medicine
National Center for Biotechnology Information

Agenda

- ClinicalTrials.gov Basics
- Recent Updates to ClinicalTrials.gov
- Modernization Effort
- Collaboration with OBSSR to Develop Proto-papers and Support Materials

ClinicalTrials.gov Basics

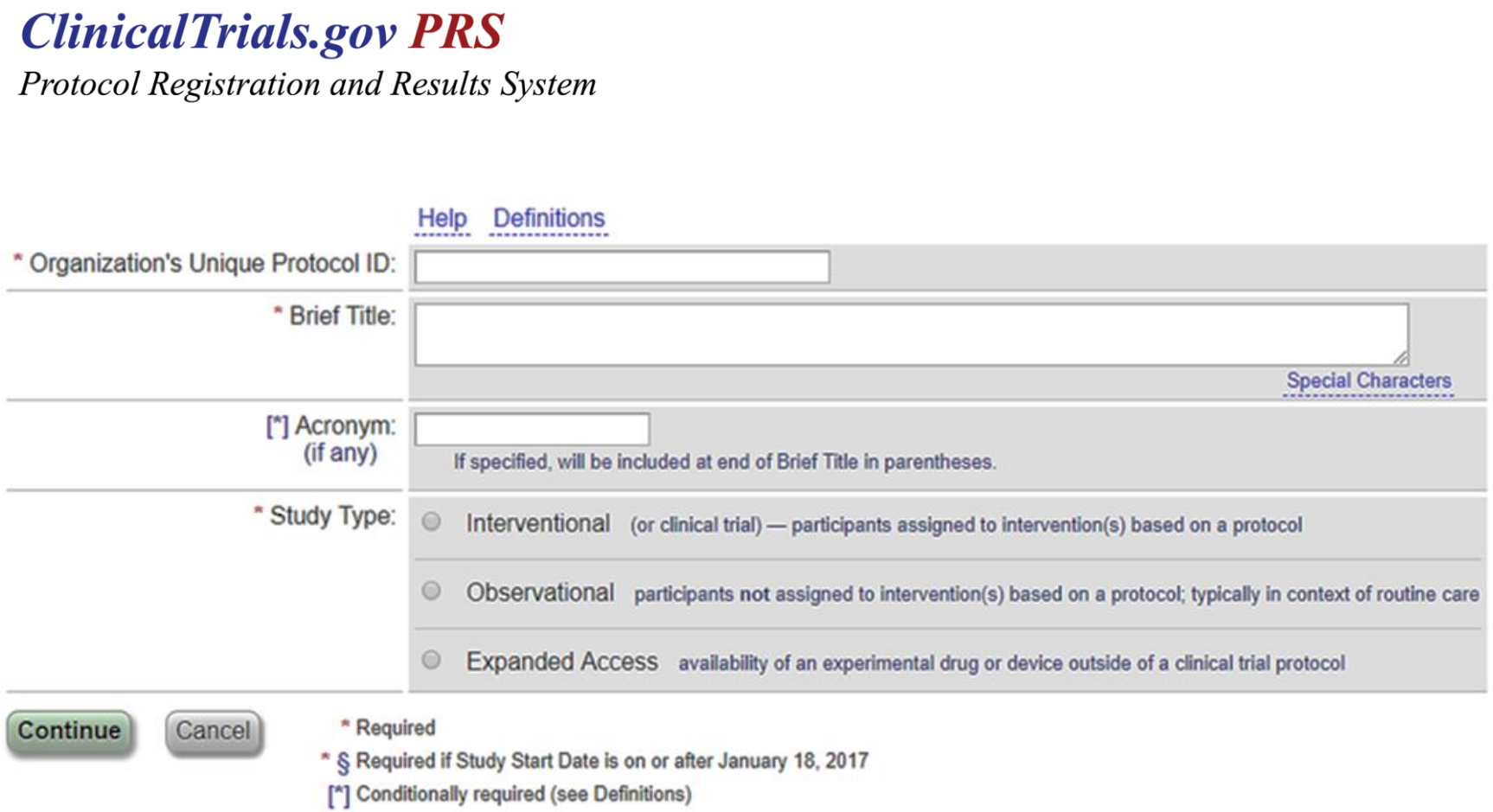
Benefits of Comprehensive Registration and Results Reporting

All contribute to increased public trust in clinical research

- 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

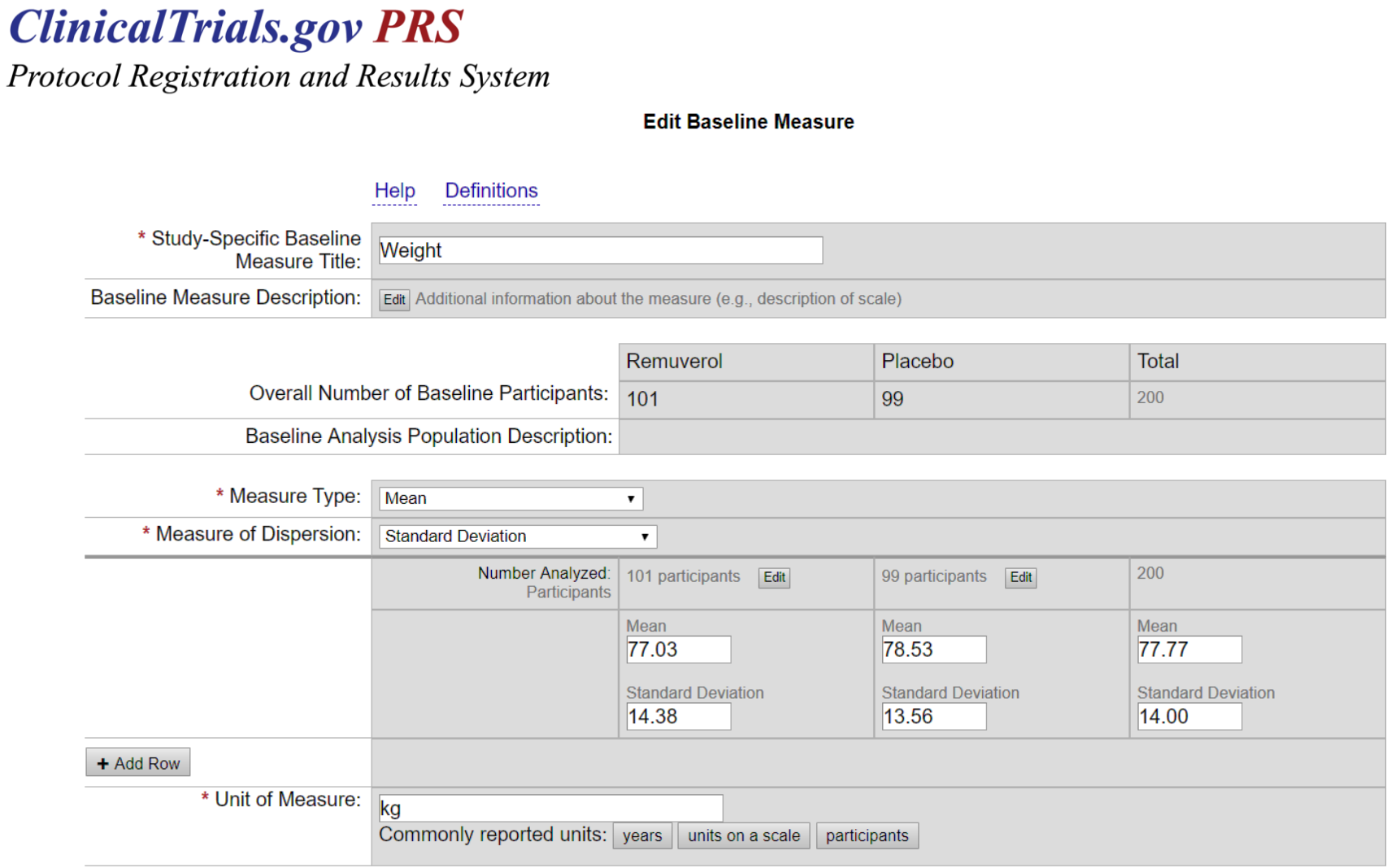
Basics of Registration Information Submission

- 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



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

Help Definitions

* Study-Specific Baseline Measure Title:	Weight
Baseline Measure Description:	Edit Additional information about the measure (e.g., description of scale)

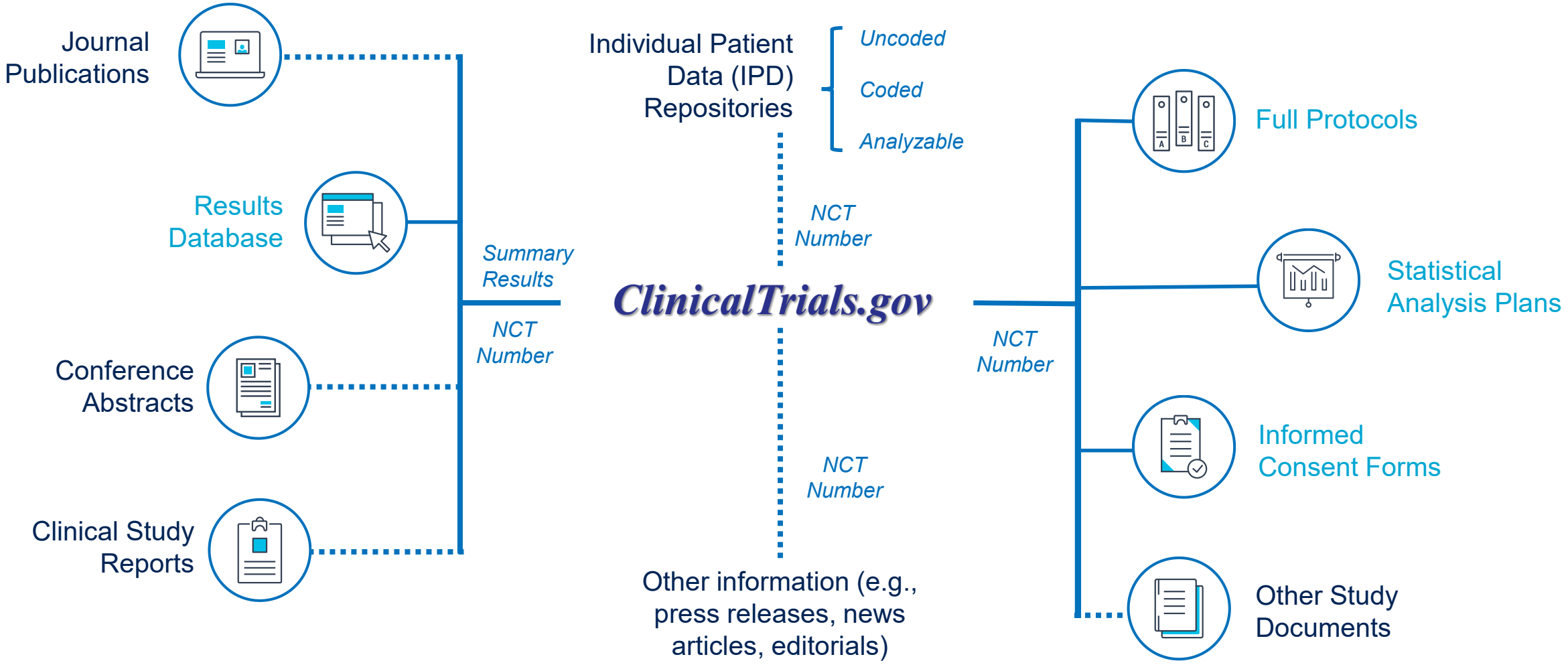
	Remuverol	Placebo	Total
Overall Number of Baseline Participants:	101	99	200
Baseline Analysis Population Description:			

* Measure Type:	Mean		
* Measure of Dispersion:	Standard Deviation		
Number Analyzed: Participants	101 participants Edit	99 participants Edit	200
	Mean 77.03 Standard Deviation 14.38	Mean 78.53 Standard Deviation 13.56	Mean 77.77 Standard Deviation 14.00

+ Add Row

* Unit of Measure:	kg Commonly reported units: years | units on a scale | participants

ClinicalTrials.gov: Information Scaffold



Results Posted Within 30 Days

Update study record

Submit study record

Backend Processing

Responsible Party

QC Review Staff

1 **Sponsor Account**

2 Registration Information

Results Information

Automated Validation

3 Manual Validation Quality Control Review

ClinicalTrials.gov

No "Major" Issues → 4 **Public Posting**

"Major" Issues → General Notice and Standard QC Review Comments

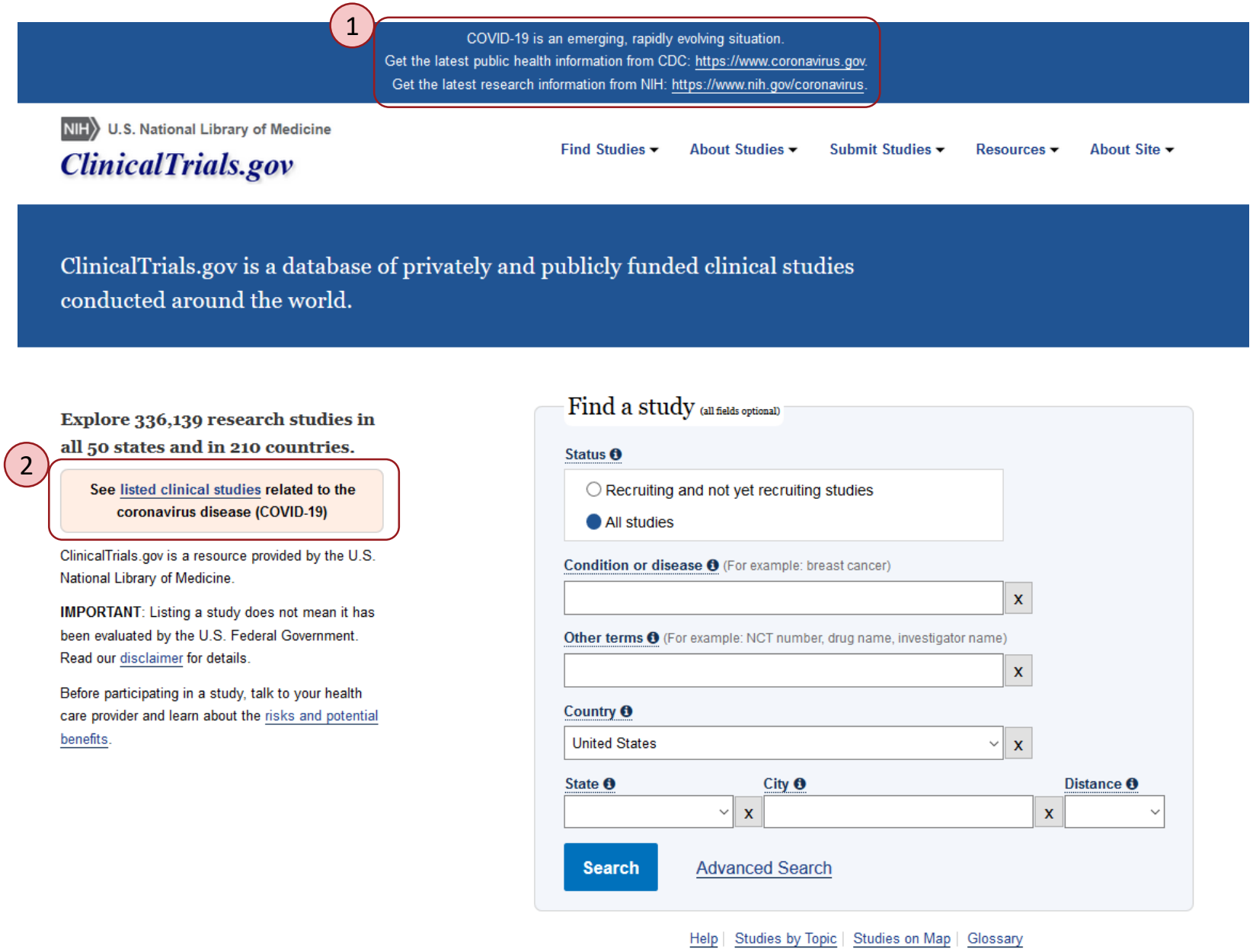
QC Review Comments

- 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

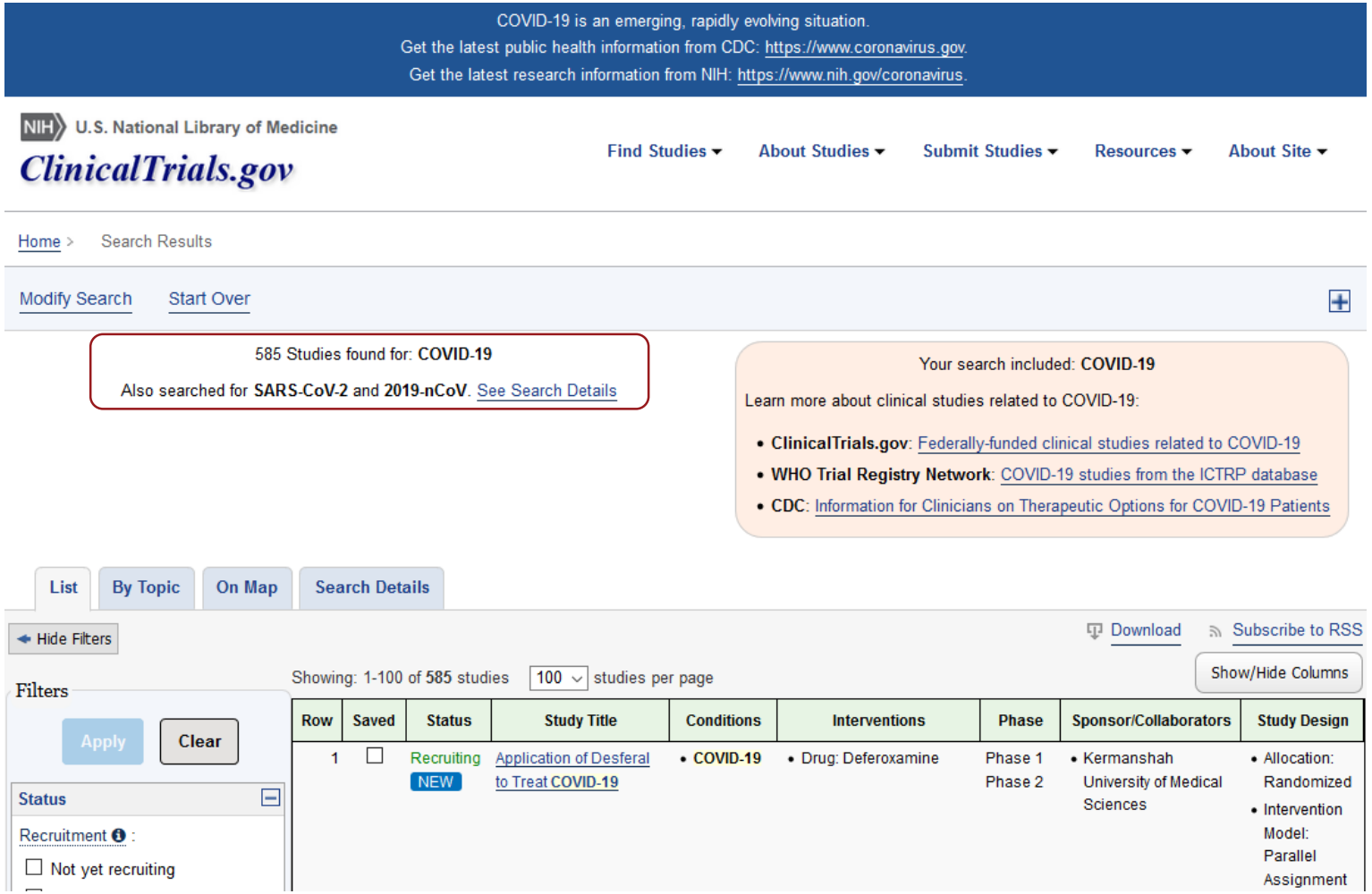
ClinicalTrials.gov Home Page Update: COVID-19

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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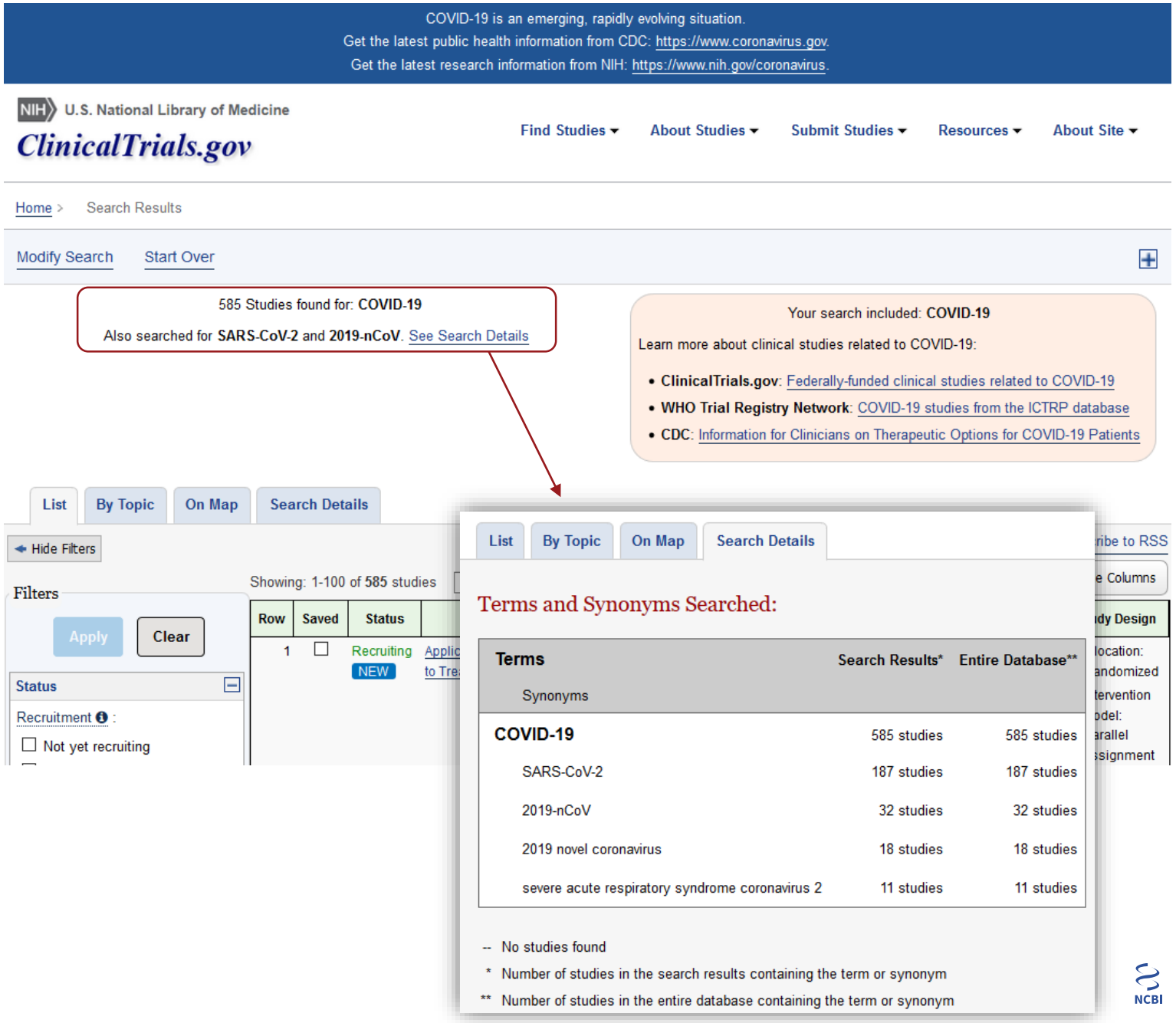
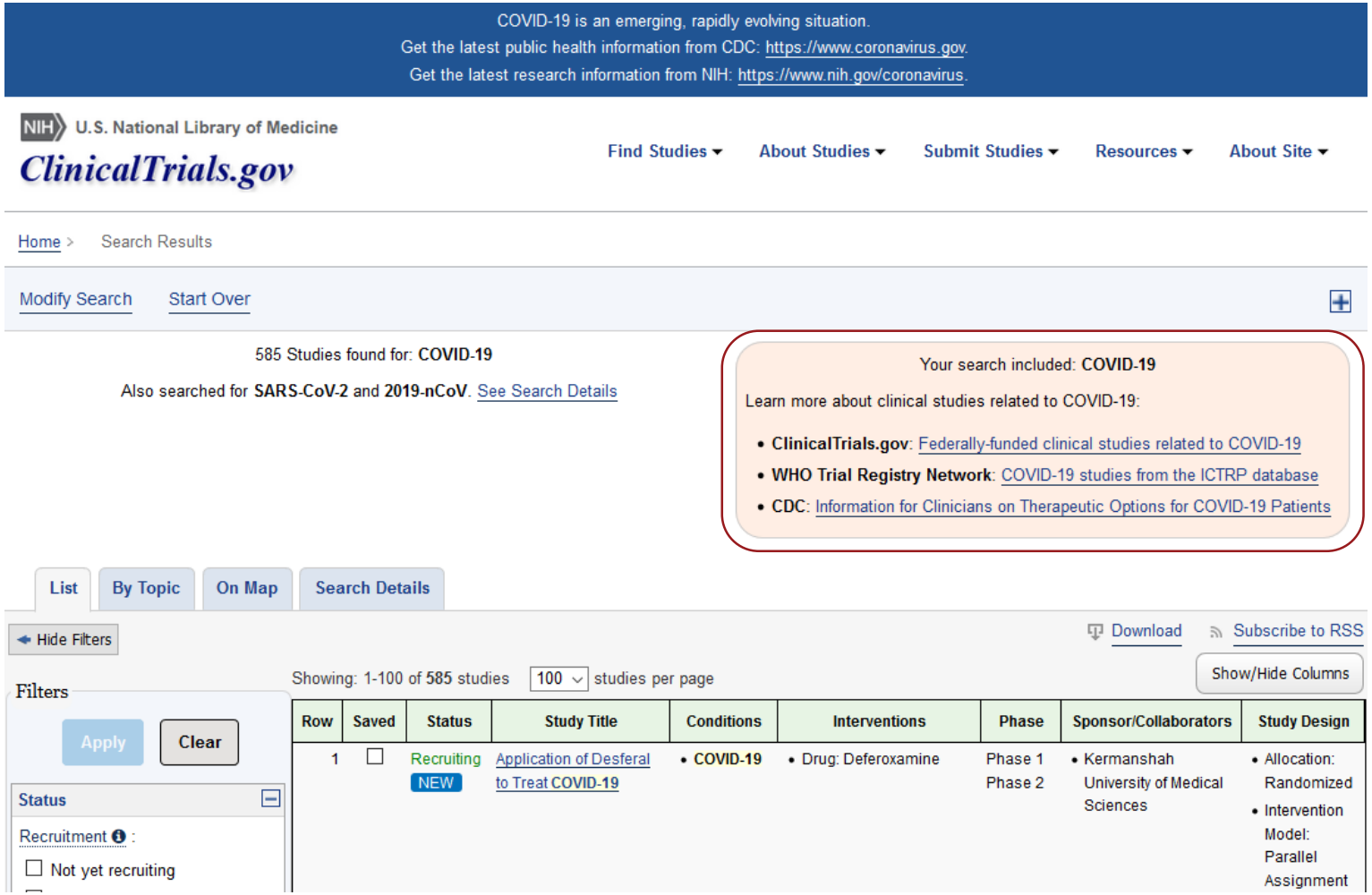


Targeted Search Results: COVID-19

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



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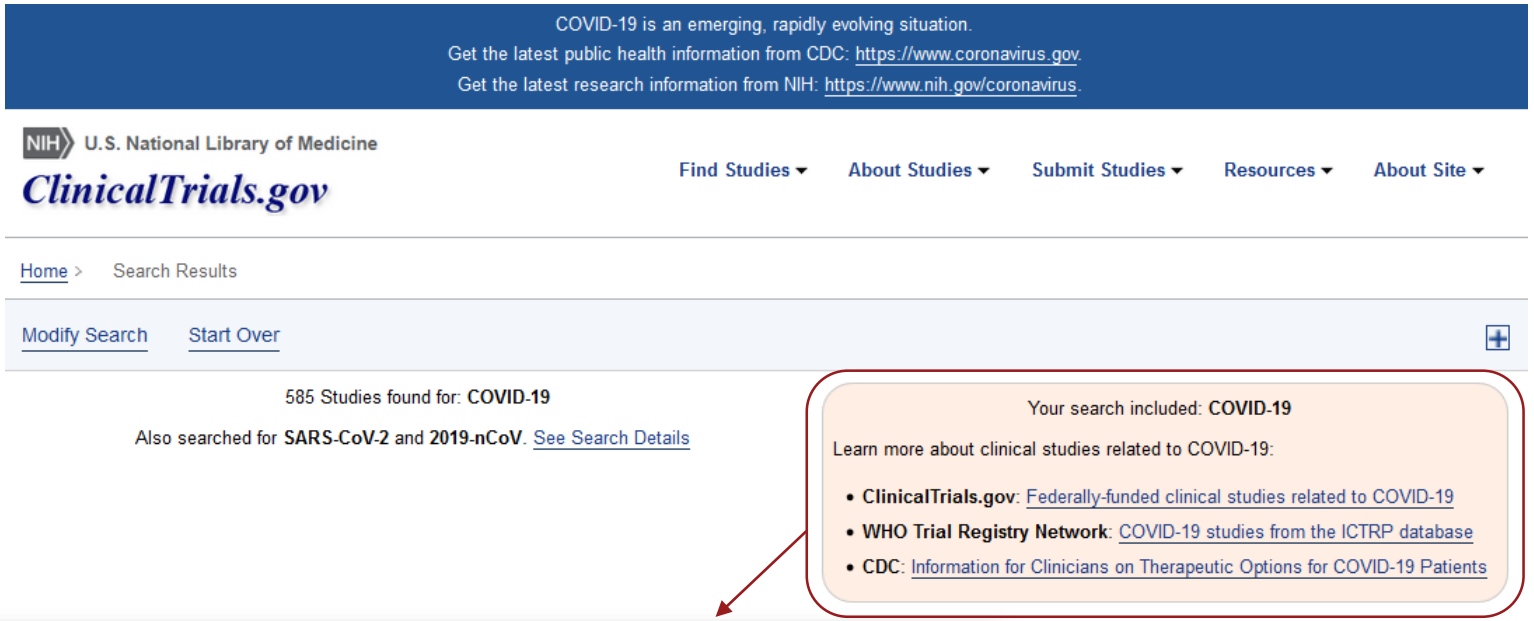
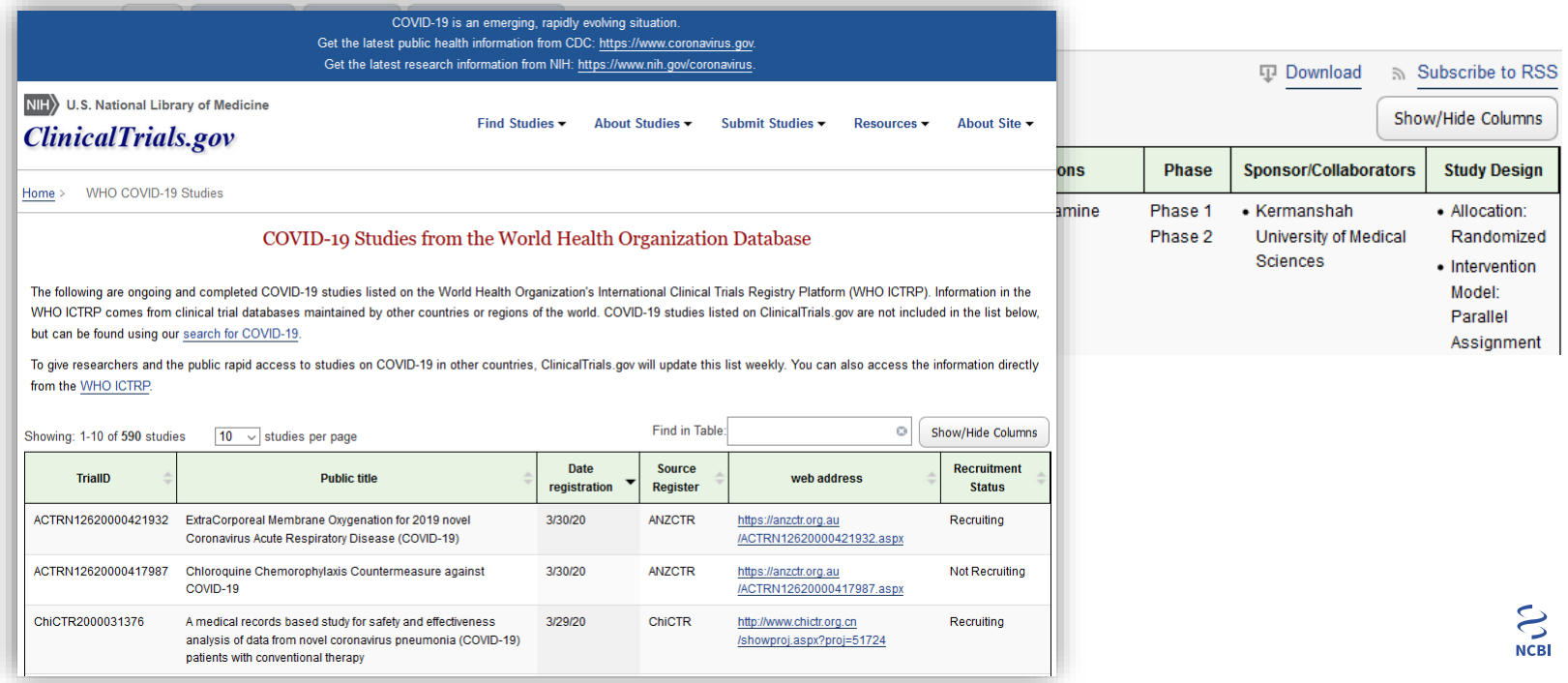
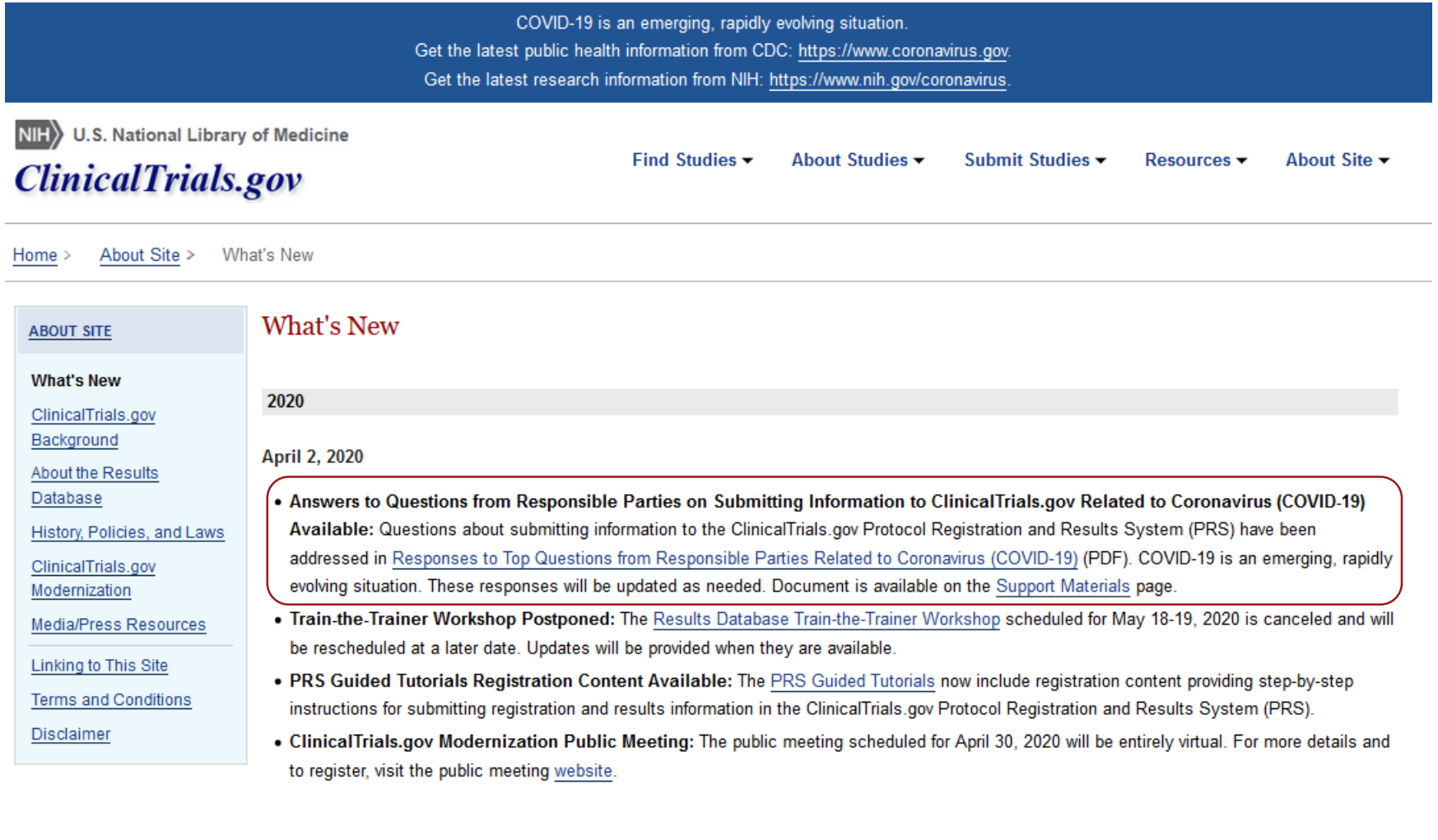




Answers to Top Questions: COVID-19

- Links to responses available on What's New and Support Materials pages
- Updated as needed



COVID-19 is an emerging, rapidly evolving situation.
Get the latest public health information from CDC: https://www.coronavirus.gov.
Get the latest research information from NIH: https://www.nih.gov/coronavirus.

NIH U.S. National Library of Medicine
ClinicalTrials.gov

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Home > About Site > What's New

ABOUT SITE

What's New
ClinicalTrials.gov Background
About the Results Database
History, Policies, and Laws
ClinicalTrials.gov Modernization
Media/Press Resources
Linking to This Site
Terms and Conditions
Disclaimer

What's New

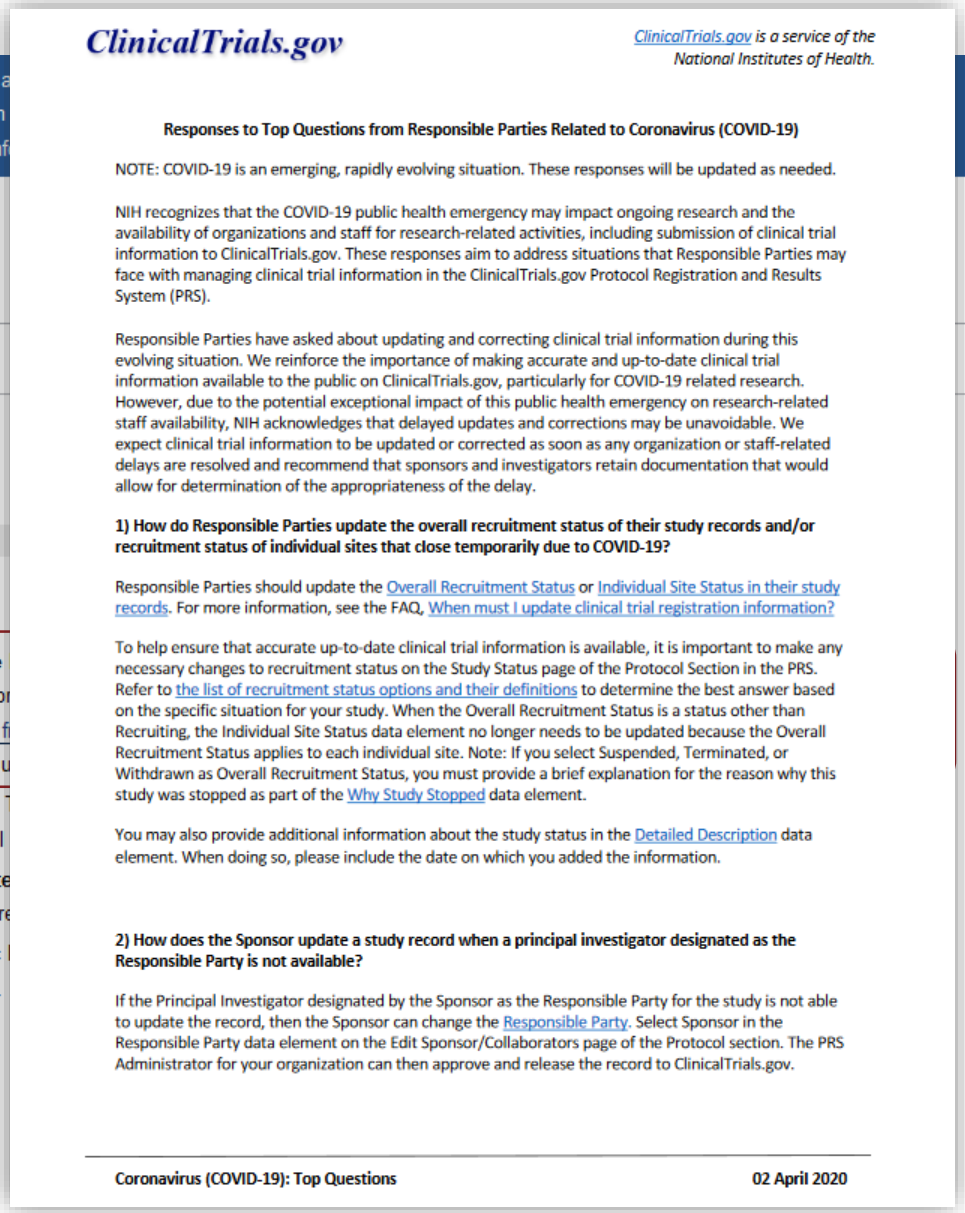
2020

April 2, 2020

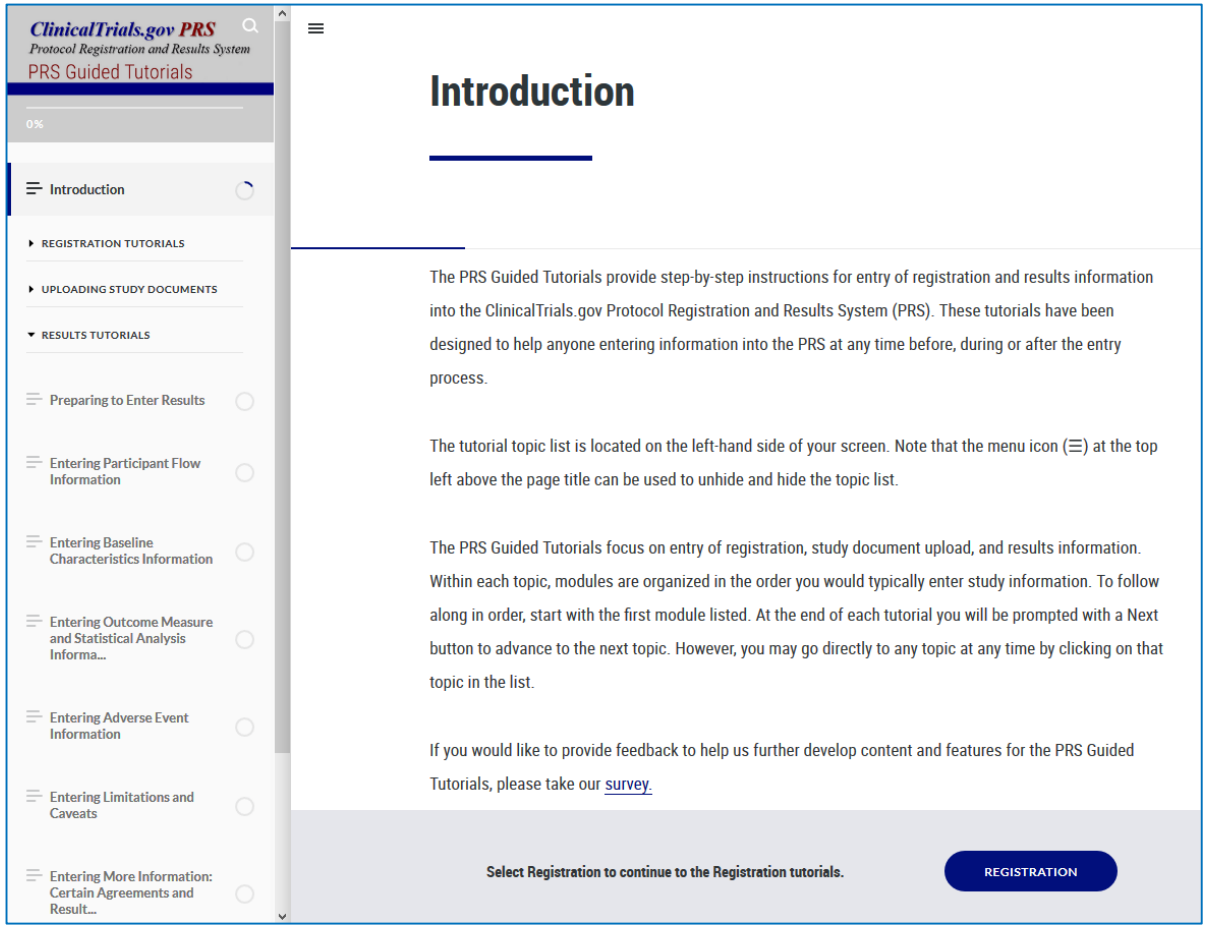
- **Answers to Questions from Responsible Parties on Submitting Information to ClinicalTrials.gov Related to Coronavirus (COVID-19) Available:** Questions about submitting information to the ClinicalTrials.gov Protocol Registration and Results System (PRS) have been addressed in Responses to Top Questions from Responsible Parties Related to Coronavirus (COVID-19) (PDF). COVID-19 is an emerging, rapidly evolving situation. These responses will be updated as needed. Document is available on the Support Materials page.
- **Train-the-Trainer Workshop Postponed:** The Results Database Train-the-Trainer Workshop scheduled for May 18-19, 2020 is canceled and will be rescheduled at a later date. Updates will be provided when they are available.
- **PRS Guided Tutorials Registration Content Available:** The PRS Guided Tutorials now include registration content providing step-by-step instructions for submitting registration and results information in the ClinicalTrials.gov Protocol Registration and Results System (PRS).
- **ClinicalTrials.gov Modernization Public Meeting:** The public meeting scheduled for April 30, 2020 will be entirely virtual. For more details and to register, visit the public meeting website.

Answers to Top Questions: COVID-19

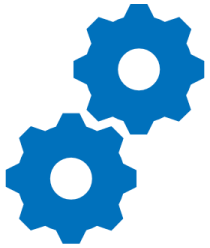
- Links to responses available on What's New and Support Materials pages
- Will be updated as needed



PRS Guided Tutorials

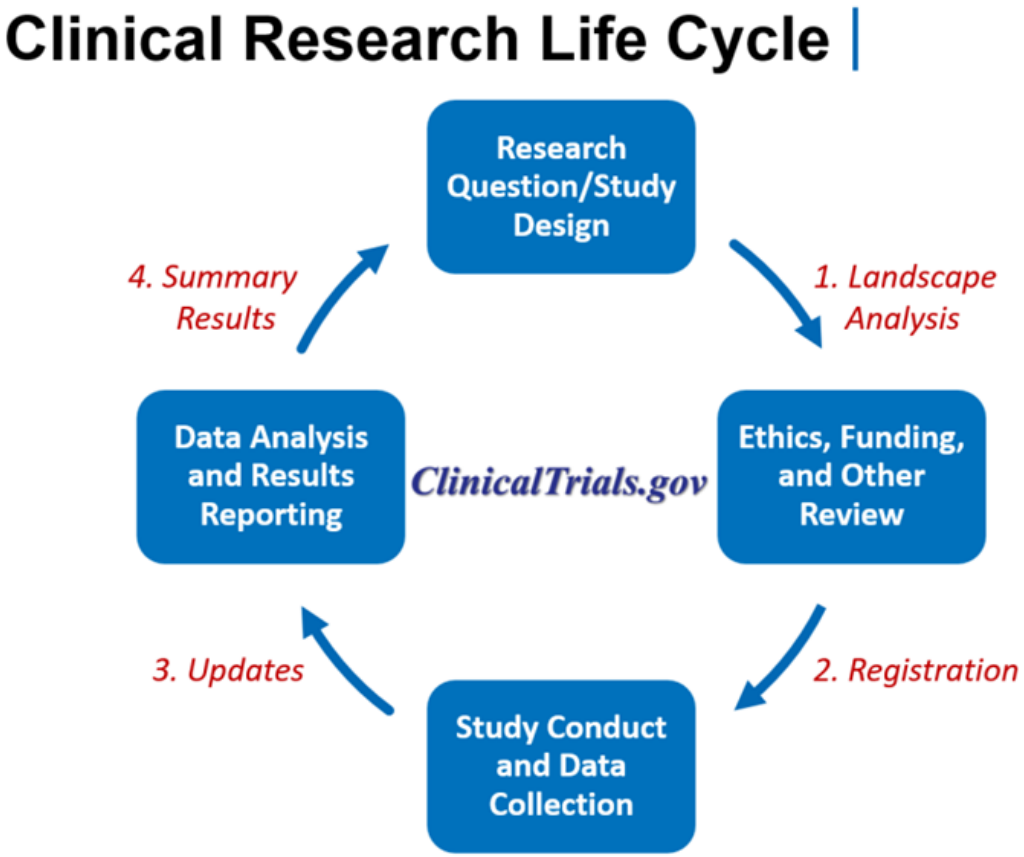


- Results tutorials launched in Beta in August 2019
- Registration tutorials launched March 2020; tutorials taken out of Beta
- Tutorials can be accessed on ClinicalTrials.gov or from within the PRS
- Feedback has been collected
  - User testing: further updates are planned
  - Survey (continuing): https://bit.ly/2N1mMHV
- 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

April 30, 2020, Virtual Meeting
9:30 am - 12:30 pm

Goals of the public meeting

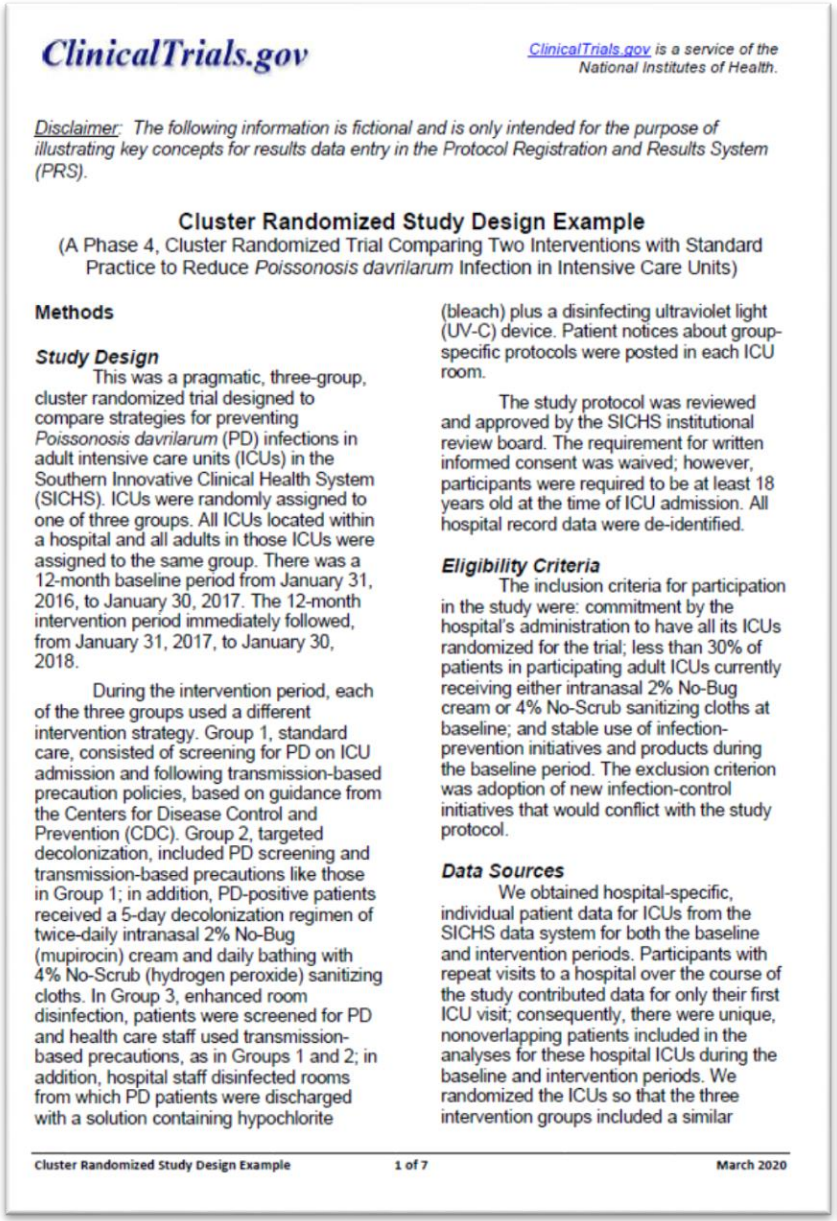
- Share high-level summary of RFI comments and key themes
- Gather diverse stakeholders to collectively share synergistic and competing needs
- Obtain further information on certain themes/topic areas

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

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



ClinicalTrials.gov

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Disclaimer: The following information is fictional and is only intended for the purpose of illustrating key concepts for results data entry in the Protocol Registration and Results System (PRS).

Cluster Randomized Study Design Example

(A Phase 4, Cluster Randomized Trial Comparing Two Interventions with Standard Practice to Reduce *Poissonosis davrilarum* Infection in Intensive Care Units)

Methods

Study Design

This was a pragmatic, three-group, cluster randomized trial designed to compare strategies for preventing *Poissonosis davrilarum* (PD) 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.

During the intervention period, each of the three groups used a different intervention strategy. Group 1, standard care, consisted of screening for PD on ICU admission and following transmission-based precaution policies, based on guidance from the Centers for Disease Control and Prevention (CDC). Group 2, targeted decolonization, included PD screening and transmission-based precautions like those in Group 1; in addition, PD-positive patients received a 5-day decolonization regimen of twice-daily intranasal 2% No-Bug (mupirocin) cream and daily bathing with 4% No-Scrub (hydrogen peroxide) sanitizing cloths. In Group 3, enhanced room disinfection, patients were screened for PD and health care staff used transmission-based precautions, as in Groups 1 and 2; in addition, hospital staff disinfected rooms from which PD patients were discharged with a solution containing hypochlorite (bleach) plus a disinfecting ultraviolet light (UV-C) device. Patient notices about group-specific protocols were posted in each ICU room.

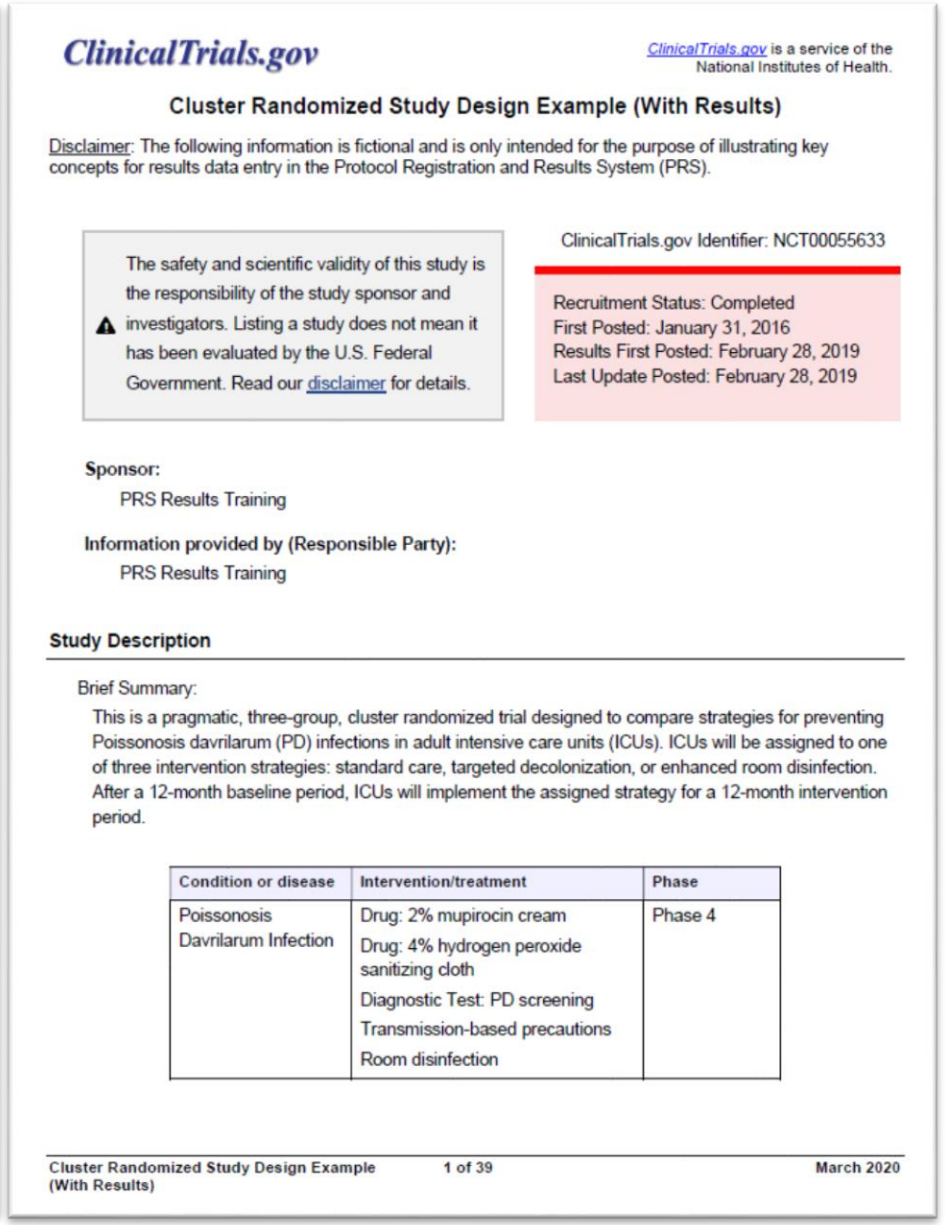
The study protocol was reviewed and approved by the SICHS institutional review board. The requirement for written informed consent was waived; however, participants were required to be at least 18 years old at the time of ICU admission. All hospital record data were de-identified.

Eligibility Criteria

The 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 sanitizing cloths at baseline; and stable use of infection-prevention initiatives and products during the baseline period. The exclusion criterion was 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, nonoverlapping patients included 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



ClinicalTrials.gov

ClinicalTrials.gov is a service of the National Institutes of Health.

Cluster Randomized Study Design Example (With Results)

Disclaimer: The following information is fictional and is only intended for the purpose of illustrating key concepts for results data entry in the Protocol Registration and Results System (PRS).

⚠ The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our disclaimer for details.

ClinicalTrials.gov Identifier: NCT00055633

Recruitment Status: Completed
First Posted: January 31, 2016
Results First Posted: February 28, 2019
Last Update Posted: February 28, 2019

Sponsor:
PRS Results Training

Information provided by (Responsible Party):
PRS Results Training

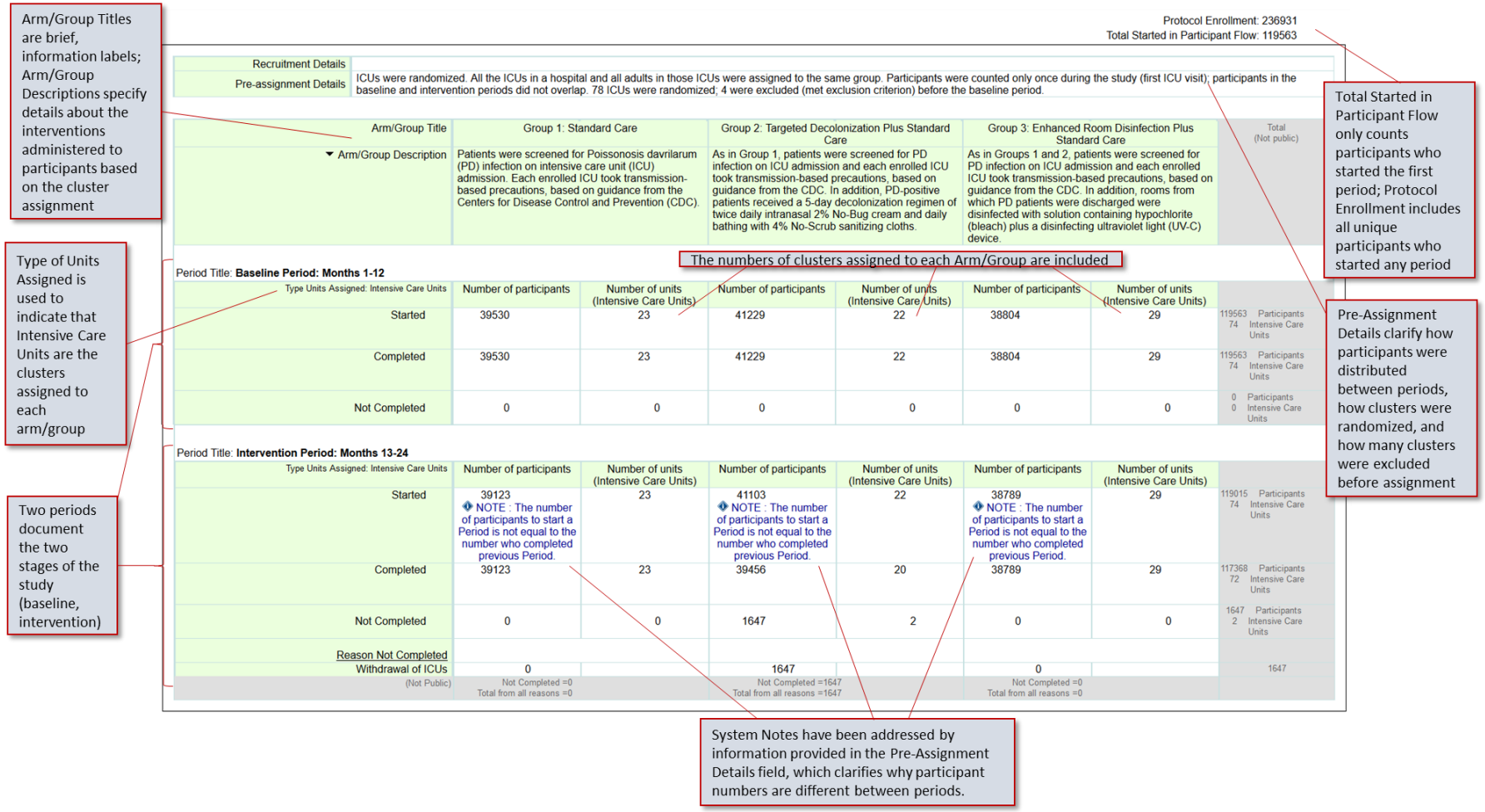
Study Description

Brief Summary:
This is a pragmatic, three-group, cluster randomized trial designed to compare strategies for preventing Poissonosis davrilarum (PD) infections in adult intensive care units (ICUs). ICUs will be assigned to one of three intervention strategies: standard care, targeted decolonization, or enhanced room disinfection. After a 12-month baseline period, ICUs will implement the assigned strategy for a 12-month intervention period.

Condition or disease	Intervention/treatment	Phase
Poissonosis Davrilarum Infection	Drug: 2% mupirocin cream Drug: 4% hydrogen peroxide sanitizing cloth Diagnostic Test: PD screening Transmission-based precautions Room disinfection	Phase 4

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



Protocol Enrollment: 236931
Total Started in Participant Flow: 119563

Recruitment Details	
Pre-assignment Details	ICUs were randomized. All the ICUs in a hospital and all adults in those ICUs were assigned to the same group. Participants were counted only once during the study (first ICU visit); participants in the baseline and intervention periods did not overlap. 78 ICUs were randomized; 4 were excluded (met exclusion criterion) before the baseline period.

Arm/Group Title	Group 1: Standard Care	Group 2: Targeted Decolonization Plus Standard Care	Group 3: Enhanced Room Disinfection Plus Standard Care	Total (Not public)
Arm/Group Description	Patients were screened for Poissonosis davrilarum (PD) infection on intensive care unit (ICU) admission. Each enrolled ICU took transmission-based precautions, based on guidance from the Centers for Disease Control and Prevention (CDC).	As in Group 1, patients were screened for PD infection on ICU admission and each enrolled ICU took transmission-based precautions, based on guidance from the CDC. In addition, PD-positive patients received a 5-day decolonization regimen of twice daily intranasal 2% No-Bug cream and daily bathing with 4% No-Scrub sanitizing cloths.	As in Groups 1 and 2, patients were screened for PD infection on ICU admission and each enrolled ICU took transmission-based precautions, based on guidance from the CDC. In addition, rooms from which PD patients were discharged were disinfected with solution containing hypochlorite (bleach) plus a disinfecting ultraviolet light (UV-C) device.	

Period Title: **Baseline Period: Months 1-12**

Type Units Assigned: Intensive Care Units	Number of participants	Number of units (Intensive Care Units)	Number of participants	Number of units (Intensive Care Units)	Number of participants	Number of units (Intensive Care Units)	
Started	39530	23	41229	22	38804	29	119563 Participants 74 Intensive Care Units
Completed	39530	23	41229	22	38804	29	119563 Participants 74 Intensive Care Units
Not Completed	0	0	0	0	0	0	0 Participants 0 Intensive Care Units

Period Title: **Intervention Period: Months 13-24**

Type Units Assigned: Intensive Care Units	Number of participants	Number of units (Intensive Care Units)	Number of participants	Number of units (Intensive Care Units)	Number of participants	Number of units (Intensive Care Units)	
Started	39123 NOTE : The number of participants to start a Period is not equal to the number who completed previous Period.	23	41103 NOTE : The number of participants to start a Period is not equal to the number who completed previous Period.	22	38789 NOTE : The number of participants to start a Period is not equal to the number who completed previous Period.	29	119015 Participants 74 Intensive Care Units
Completed	39123	23	39456	20	38789	29	117368 Participants 72 Intensive Care Units
Not Completed	0	0	1647	2	0	0	1647 Participants 2 Intensive Care Units
Reason Not Completed							
Withdrawal of ICUs	0		1647		0		1647
(Not Public)	Not Completed =0 Total from all reasons =0		Not Completed =1647 Total from all reasons =1647		Not Completed =0 Total from all reasons =0		

Arm/Group Titles are brief, information labels; Arm/Group Descriptions specify details about the interventions administered to participants based on the cluster assignment

Type of Units Assigned is used to indicate that Intensive Care Units are the clusters assigned to each arm/group

Two periods document the two stages of the study (baseline, intervention)

The numbers of clusters assigned to each Arm/Group are included

Total Started in Participant Flow only counts participants who started the first period; Protocol Enrollment includes all unique participants who started any period

Pre-Assignment Details clarify how participants were distributed between periods, how clusters were randomized, and how many clusters were excluded before assignment

System Notes have been addressed by information provided in the Pre-Assignment Details field, which clarifies why participant numbers are different between periods.

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