Biostatistics & Clinical Epidemiology Service: Office of the Chief Medical Officer

Empowering Clinical Research: The Essential Role of Statistics and Collaborative Partnership

08 April 2024

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NIH Clinical Center
America's Research Hospital

Agenda

- Objectives
- Mission
- Services
  - Key Statistical Functional Areas
  - Key Statistical Areas
  - Key Comprehensive Support Areas
  - Clinical Center Collaborations
  - Other IC Collaborations
  - Project Work Breakdown
- WHY/WHAT - Getting Started with BCES Collaborations (NEW PROCESS)
- HOW - Getting Started with BCES Collaborations (NEW PROCESS)
- Frequently Asked Questions
- Q&A

Objectives

1. **Statistical Integration in Study Design**
    - Empower PIs to collaborate with statisticians in designing studies, ensuring proper sample size determination, randomization, and control group selection while adhering to statistical best practices. This collaboration should extend to planning for eventual publication and regulatory submissions.
2. **Data Analysis Proficiency**
    - Enable PIs to work closely with statisticians to conduct robust data analysis, leveraging their expertise in advanced statistical techniques. Ensure that statistical analysis plans are comprehensive and align with regulatory or publications requirements for reporting.
3. **Ethical and Transparent Reporting**
    - Educate PIs on the ethical considerations of statistical analysis and emphasize transparent reporting practices, ensuring adherence to regulatory guidelines for comprehensive and accurate reporting in publications and submissions.

Amazing co-workers I met last week!

Introduction
BCES Mission

Promoting the practice of Statistics & Data Science in good clinical research to improve human health at the NIH

- To provide leadership and expertise in the design, data monitoring, analysis, and reporting of biomedical research studies
- To develop and implement innovative approaches for the design, monitoring, analysis, and reporting of biomedical research studies
- To collaborate with other scientists on the full spectrum of study conduct (i.e., protocol design, study execution, data quality, statistical analysis, interpretation of study results, and writing/presentation of findings) in the spirit of good interdisciplinary teamwork
- To provide education and training relevant to statistical, data science and epidemiological aspects of biomedical research

SERVICES PROVIDED BY CC-BCES

WHAT DO WE DO?

BCES supports research in these key statistical functional areas

- Study Design (Phases I/II/III clinical studies and other studies)
  - Including sample size and power estimation and analysis plan
  - Analysis, Reporting, Publications & Communications
  - Survey Design
  - Support clinical and non-clinical studies and other research protocol designs
- Data Management
  - Population-based and EHR research
  - Data Cleaning and data extraction
- Methodological support
  - Analysis planning & execution
  - Statistical Summary Report
  - Publications support / grant proposal support
  - Development of new methodology, tools, software
  - Biomarker Development
    - Personalized medicine using diverse biomarkers:
      - including radiological imaging, genomics, clinical chemistry profiles, immunological markers, and pathological features
- Results Interpretations
  - Draft/review papers, FDA communications, presentations need proper interpretation of results
- Education and training in Biostatistics & Epidemiology research methods

BCES covers these key statistical areas

- **Study Design**: Principles of study design, including randomized controlled trials (RCTs), cross-over trials, cohort studies, case-control studies, cross-sectional studies, and ecological studies.
- **Descriptive Statistics**: Methods for summarizing and presenting data
- **Inferential Statistics**: Techniques for making inferences and drawing conclusions from sample data, including hypothesis testing, confidence intervals, and p-values.
- **Regression Analysis**: Linear regression, logistic regression, and other regression models for analyzing relationships between variables and making predictions.
- **Survival Analysis**: Techniques for analyzing time-to-event data, including Kaplan-Meier curves, Cox proportional hazards models, and competing risks analysis.
- **Longitudinal Data Analysis**: Methods for analyzing repeated measures or longitudinal data, including mixed-effects models, generalized estimating equations (GEE), and growth curve models.
- **Categorical Data Analysis**: Techniques for analyzing categorical or nominal data, including contingency table analysis, chi-square tests, and logistic regression for binary outcomes.
- **Meta-Analysis**: Methods for combining results from multiple studies to generate summary estimates and assess overall effect sizes, including fixed-effects and random-effects models.
- **Bayesian Statistics**: Principles of Bayesian inference and Bayesian modeling techniques for incorporating prior information and updating beliefs based on observed data.
- **Machine Learning**: Introduction to machine learning algorithms and techniques, including decision trees, random forests, support vector machines, and neural networks, for predictive modeling and classification tasks.
- **Causal Inference**: Methods for assessing causal relationships and estimating causal effects from observational data, including propensity score matching, instrumental variables, and causal mediation analysis.
- **Epidemiologic Methods**: Principles of epidemiologic study design and analysis, including measures of disease frequency, measures of association (e.g., relative risk, odds ratio), and confounding and effect modification.
- **Public Health Surveillance**: Techniques for monitoring and analyzing health data to track disease trends, identify outbreaks, and inform public health interventions.

Comprehensive Statistical Support Services for Medical Research and Beyond

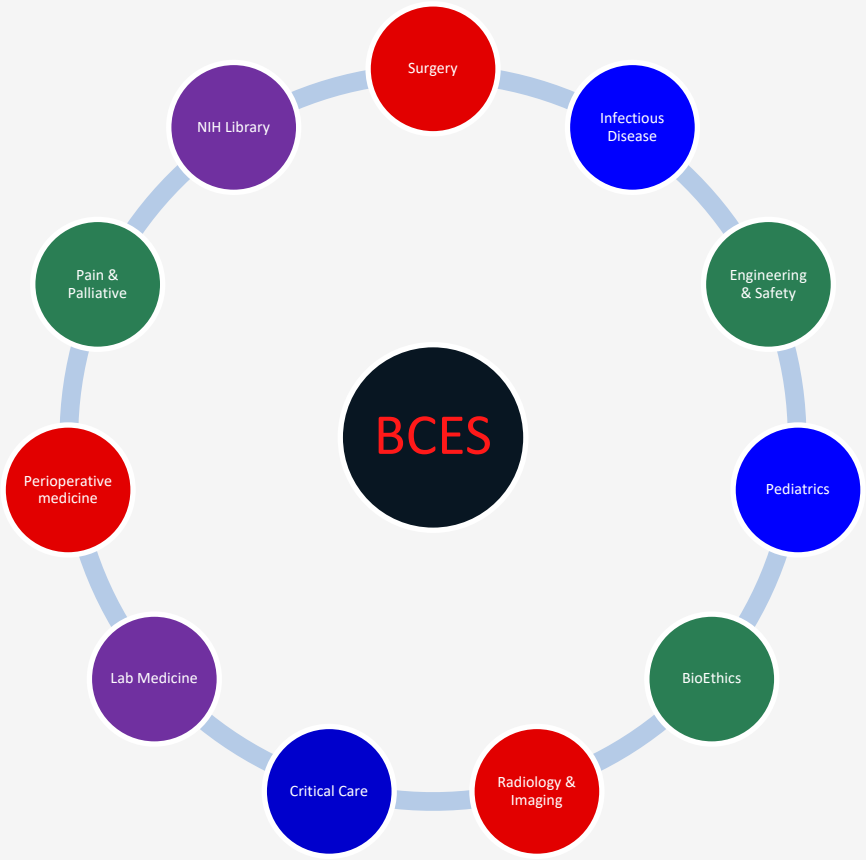
1. **Clinical Trial Design & Analysis**: Assistance in designing clinical trials, including sample size calculation, randomization procedures, and selection of appropriate statistical methods. Analysis. Publication.
2. **Survey Design**: Guidance on survey design principles, sampling strategies, and questionnaire development for epidemiological and health services research. And analysis of data.
3. **Epidemiological Studies**: Support for epidemiological research, including study design, analysis, and interpretation of findings to identify disease patterns, risk factors, and population health trends.
4. **Electronic Health Record (EHR) Analysis**: Analysis of EHR data to identify trends, associations, and outcomes related to disease management, treatment effectiveness, and healthcare utilization.
5. **Research Studies Design and Analysis**: Collaboration on the design and analysis of various research observational studies, including cross-sectional, cohort, case-control, and longitudinal studies across diverse fields.
6. **Pre-Clinical & Non-Clinical Studies**: Statistical support for pre-clinical studies (animal studies); non-clinical studies (such as building safety protocols or engineering) or non-clinical roles in clinical studies (such as serving as DSMB statistician). Services include a wide range of statistics: design of experiments, data analysis, and interpretation of results.
7. **Statistical consultation:** Service provides expert guidance and advice on statistical methodologies, study design, and data analysis to researchers, clinicians, and students seeking assistance with their projects.
8. **Collaborative Research**: Our core actively engages in collaborative research projects across various disciplines throughout the research process: from study design and data collection to analysis and interpretation of results. Through collaboration, we contribute to the advancement of scientific knowledge and the successful implementation of research studies.
9. **Review Committees**: We offer protocol review services as part of the CC-Scientific Review committee for human and animal studies. Our involvement in protocol review processes helps to safeguard the integrity of research studies and promote the use of sound statistical methods in scientific investigations. We participate in the NIH Prevention Research Committees.
10. **Training and Education**: Several courses offered in Biostatistics and Epidemiology throughout the year by BCES; also an *Invited Speaker Series* is added with reputable speakers in relevant topics at the NIH such as deep learning and other advanced statistical topics. The course and the invited speaker series are tailored to researchers, clinicians, and fellows in the NIH community.

Principal Inv

Group/ CC/ NIH

These services aim to support medical researchers at the NIH Clinical Center and beyond, as well as researchers in other fields such as building safety, by providing expertise in statistical analysis, study design, interpretation of results, and scientific review of study protocols to ensure methodological rigor and validity.

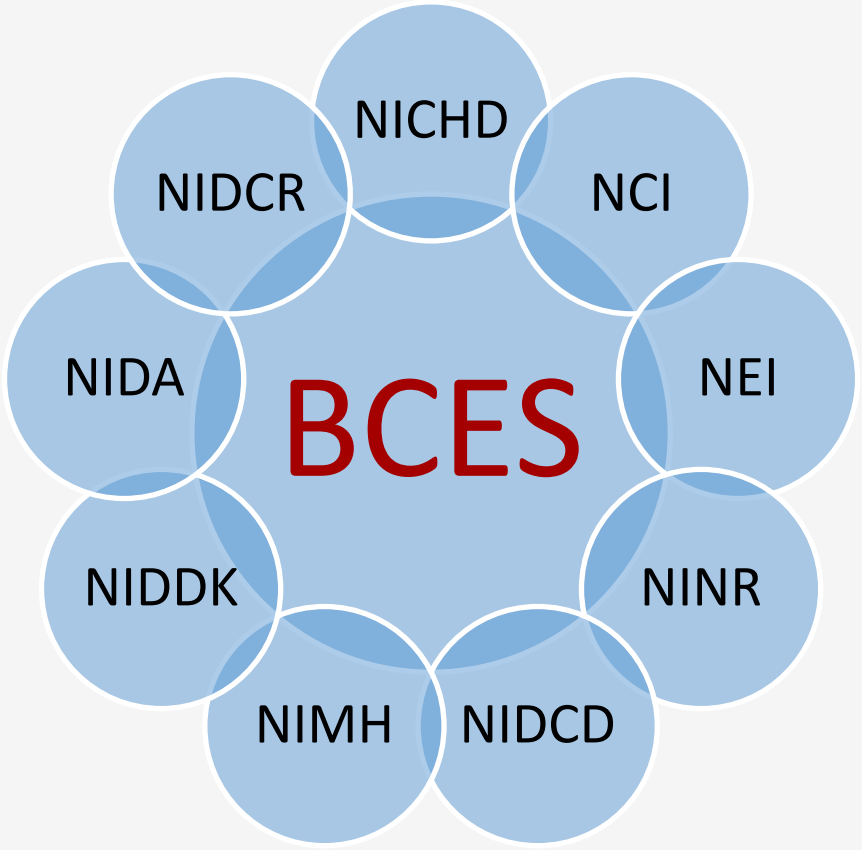
Some of the Clinical Center Collaborations



Few examples of collaborations: (pharmacy,rehab medicine,transfusion)

1. BioEthics –
    - Survey Design, propensity score matching
2. Perioperative Medicine
    - Animal studies
3. Engineering
    - Design of Experiments
4. Radiology & Imaging –
    - Machine Learning

Other Center Collaborations



Project Work Breakdown

- **Clinical Research Studies** (*statistics wide in scope*) – 80%
  - Observational of patients who came for care
  - Recruited patients
  - Survey
  - BIG data study
    - Eg: critical care (DB: cerner (EHR), etc)
    - ALLOFUS
- **Clinical Trials** for new drug or diagnostic or device or procedure (educational or consent) (*statistics is more regimented*) – 15%
  - (i) Protocol/SAP/analysis (ii) randomization (iii) DSMB
  - FDA trials
    - Eg of (i) : Current ph II study recent (NIAMS arthritis auto-immune)
      - FDA interaction – estimand framework in Protocol → SAP in future
      - Industry sponsored clinical trial and IC PI initiated
    - Submission of study data to the FDA (ADaM/SDTM+TFL in XML format) by sponsor
    - Trials initiated by other Ics: role of other CC staff involvement limited
  - Eg of (ii): unblinded statistician TBD
  - Eg of (iii): NINDS central DSMB committee

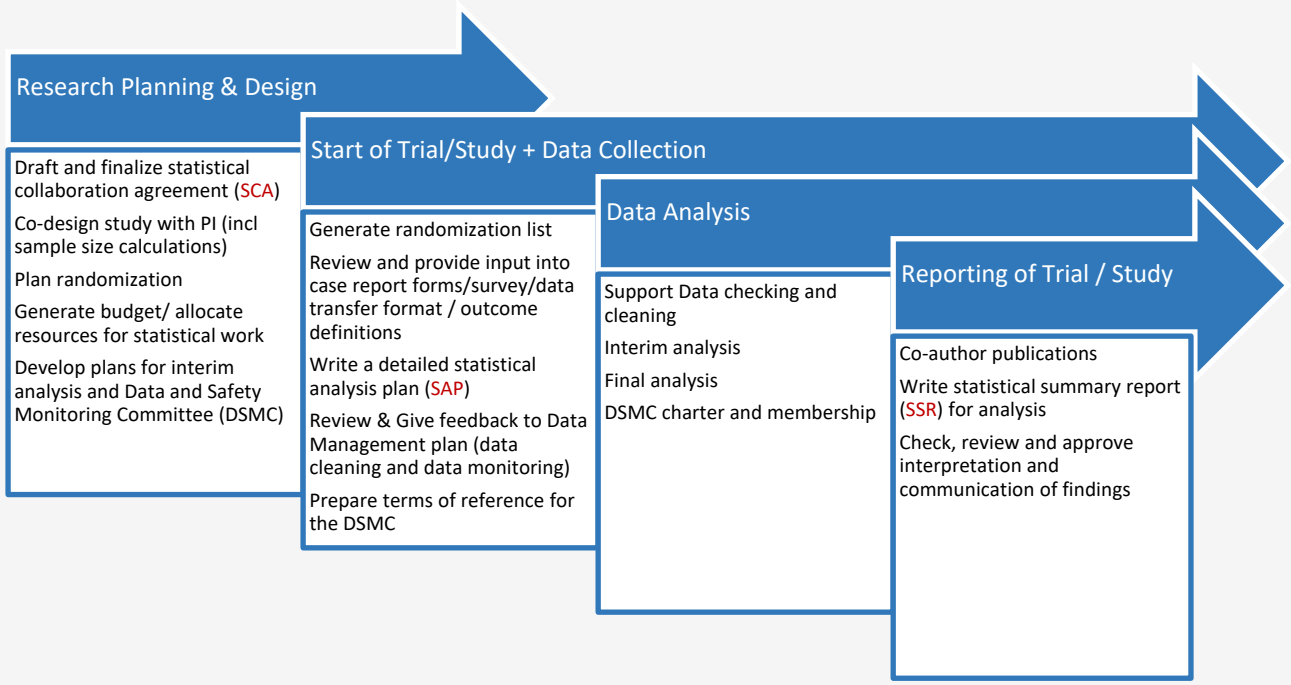
- **Non-Clinical Studies** – 5%
  - Building safety (stat: DOE/Epi)
  - Engineering (stat: DOE/Epi)
  - Animal studies (stat: DOE)

COLLABORATING WITH CC-BCES IN A NEW PROCESS

THE WHY & THE WHAT

BCES Biostatisticians will help you in design, execution, completion and translational stages of your research

Biostatistics



Clinical Research Stage

Some challenges faced by BCES

1. Clinical Center initiated clinical trials
   - At times do not involve statistician in protocol writing, review or data collection / initiation step
   - At times, do not have a SAP* developed by a BCES statistician
     - Asks statistician to do adhoc analysis for publication purposes
     - Data collection mechanism/vehicle not tied to SAP
   - *RISK: Research and conclusion may not be interpretable or reproducible*
2. Clinical Center initiated research studies
   - At times contact us for analysis 2 weeks prior to abstract submission
   - *RISK: Research and conclusion may not be reproducible*
3. Clinical Center PIs & groups & other IC's
   - At times seem unaware of the range of services BCES offers

*SAP=statistical analysis plan

Getting Started with BCES

1. How can I meet with BCES to discuss my project?
   - BCES offers biostatistics and epidemiological consulting and collaboration to enhance the quality and rigor of scientific research conducted at the Clinical Center and other IC's
     - Send e-mail with project details to CC-BCES@mail.nih.gov
     - For administrative or strategic or other questions about BCES, send email to CC-CC-BCES-admin@mail.nih.gov to Nusrat Rabbee, BCES Director
     - You will receive an email reply from the Director
2. Do you have walk-in clinics?
   - BCES will offer virtual walk-in clinics for short consultations support **Tuesdays 2-3p ET beginning on May 7, 2024** at: Click here to join the meeting
     - Meet with a biostatistician without an appointment and obtain quick advice on your project
3. How about longer-term collaborations/MOUs?
   - Appointments with staff statisticians are available by appointment only. Send email to CC-BCES-admin@mail.nih.gov

Terms for Working with BCES

To submit a request, email CC-BCES@mail.nih.gov. Please provide as much detailed information as possible concerning your request. The BCES Chief, Nusrat Rabbee, PhD nusrat.rabbee@mail.nih.gov will reply.

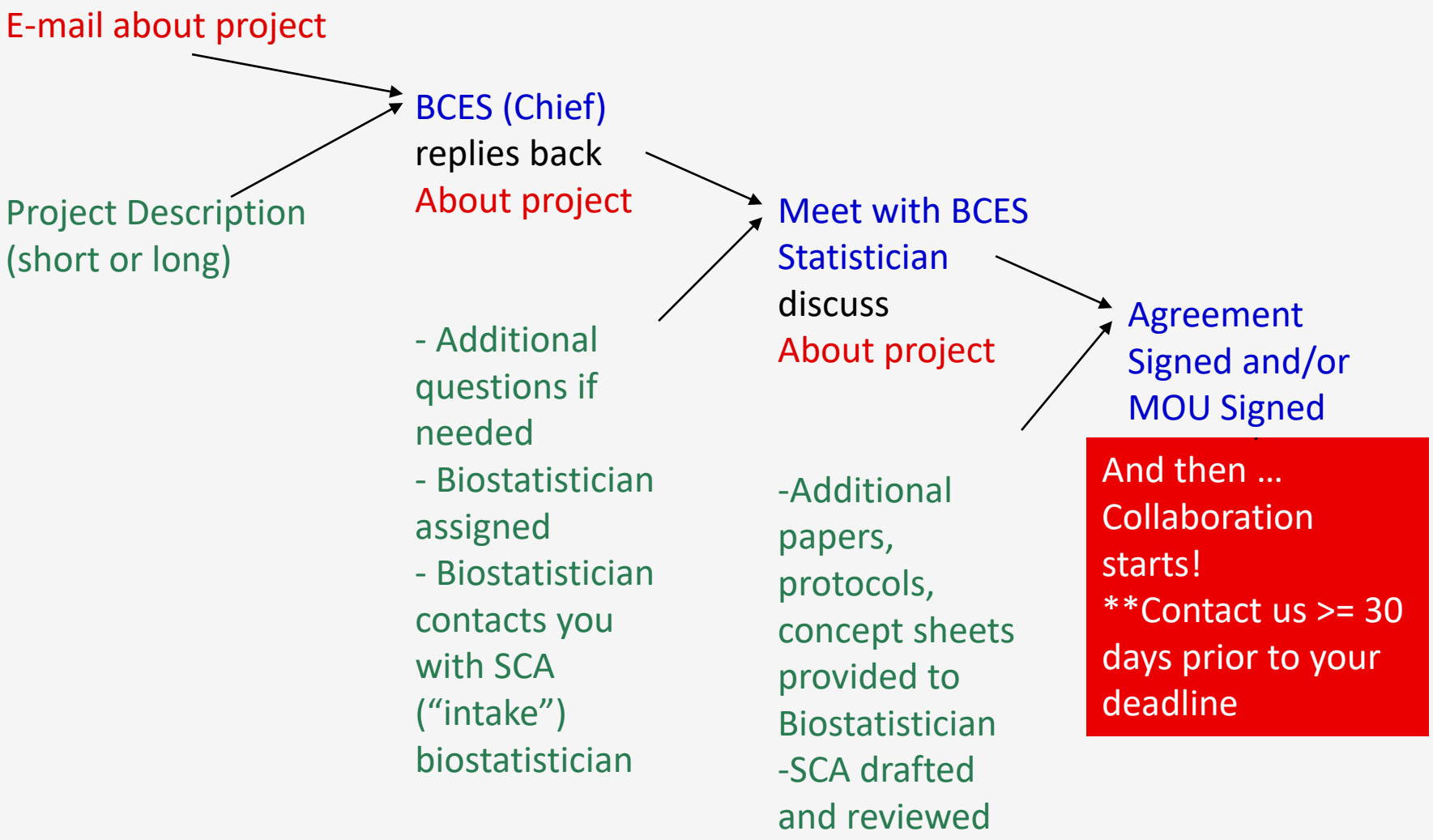
Terms for receipt of statistical support from the Biostatistics and Clinical Epidemiology Services

- Support is provided to all departments within Clinical Center for clinical and non-clinical research where study design, data management and statistical analysis is required
- NIH Investigators outside of the Clinical Center will establish a Memorandum of Understanding (MOU) as needed with CC-BCES to compensate for project work to be done
- BCES should be credited in the acknowledgments section of grants, presentations and/or the biostatistician should be included as a co-author of any publication resulting from support received.
- BCES members encourages collaborators and affiliates to contact us as early in the planning or analysis process as possible and well in advance of the desired completion date. For requests requiring a considerable time commitment, we ask that you contact us at least 30 days prior to the project completion date.

COLLABORATING WITH CC-BCES IN A NEW PROCESS

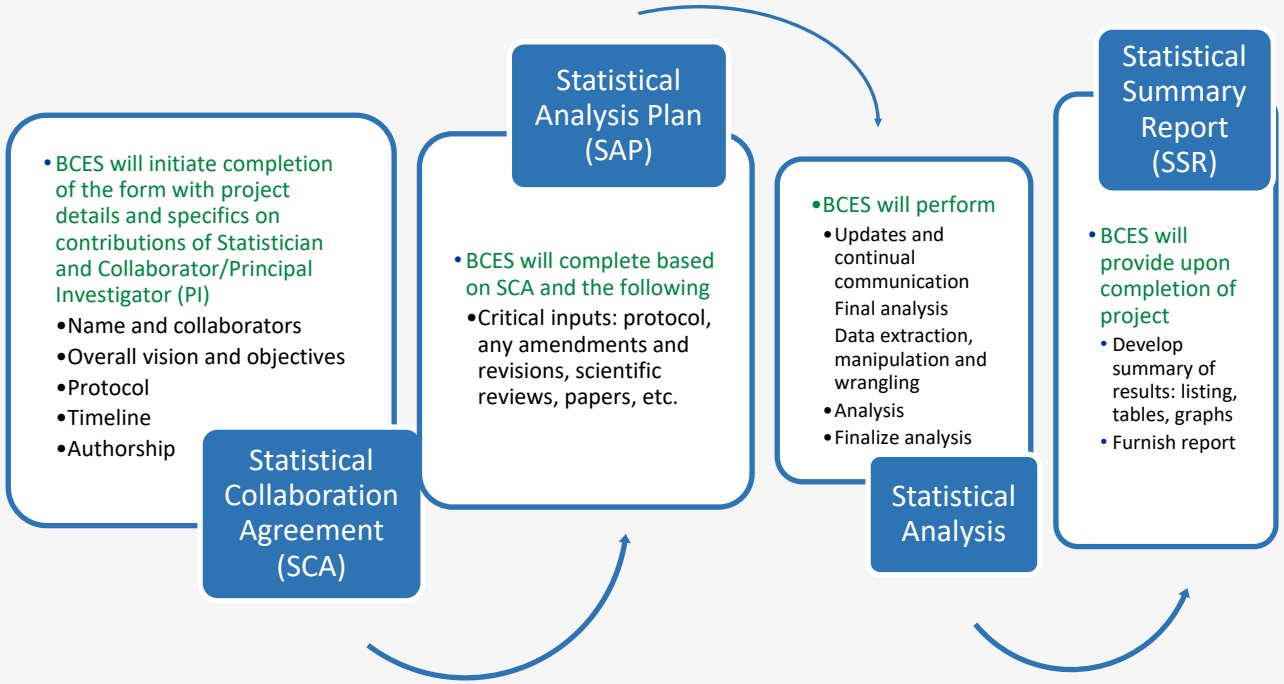
HOW THE PROCESS WORKS

Getting Started – Visual Approach



HOW THE PROCESS WORKS

COLLABORATING WITH CC-BCES



Frequently Asked Questions

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In a nutshell…

What we do well and often

PI-driven research studies within and outside CC

What we would like to aspire to

Become involved in CC clinical trials (phase I/II/III) from start

Become involved in clinical trials (phase I/II/III) with regulatory interaction

Be part of more NIH-wide or Clinical Center wide research initiatives

Be part of more DMC or DSMB committees

"Statistics is the grammar of science."

- Karl Pearson

"Alone we can do so little; together we can do so much."

- Helen Keller

The End

Questions / Discussion

Questions/Answers

Q1. Have you presented to the Chief Scientific Officer?

A1: We are presenting at the Investigator Series; and also will be presenting to the CC - Chief Science Officer

Q2: How do you resolve differences/pushback from PI?

A2: Two avenues: (i) co-design with PI in iterative process (ii) clinical center scientific review committee

Q3: Interpretation of results?

A3: This is critical. Could be around statistical significance. Or the design does not lead to desired conclusions. Multiple tests. Statisticians can contextualize and interpret results appropriately.

Questions/Answers

Q4. What is the turnaround time?

A4: Will depend on the data dimensions and analysis required. These are captured in the SCA. At least 4 weeks. Short projects vs long projects.

Q5: How can BCES work together with the Protocol Navigation community?

A5: PN works with investigator from the start. So it is very important to get statistician involved from the start to define endpoints

Q6: Do statisticians need to be co-authors in publications?

A6: Yes. Many journals now require this.

Questions/Answers

Q7. Can anyone in NIH use BCES services?

A7: Yes. We are dedicated to CC research needs and also have MOUs with other IC's. We need to raise awareness of BCES services within CC

Q8: Can you present these slides re: BCES services and capabilities throughout the NIH?

A8: We will try. This is why we are doing this presentation.

Q9: Does the IC requiring help need to be located within the CC?

A9: No.

Questions/Answers

Q10. When is the estimand analysis framework needed?

A10: New FDA mandated analysis framework for later phase clinical trials. Led by statisticians and co-led by clinicians. Even if not an FDA trial, this estimand framework should be used in clinical trial

Q11:Will you present at the MEC?

A11: Medical Executive Committee. Yes we will try to present there.

Q12: OHSRP avenues are important too?

A12: Great. We can present at the Investigator Series.