Baptist Health

Setting Up Your IIS Program for Success – From Ideation to Dissemination

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Agenda

01 Investigator-Initiated Study (IIS) Basics

02 Starting from the ground up

03 Who are the key players and committees?

04 What are the key performance indicators?

05 What does success look like?

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Investigator-Initiated Study (IIS) Basics

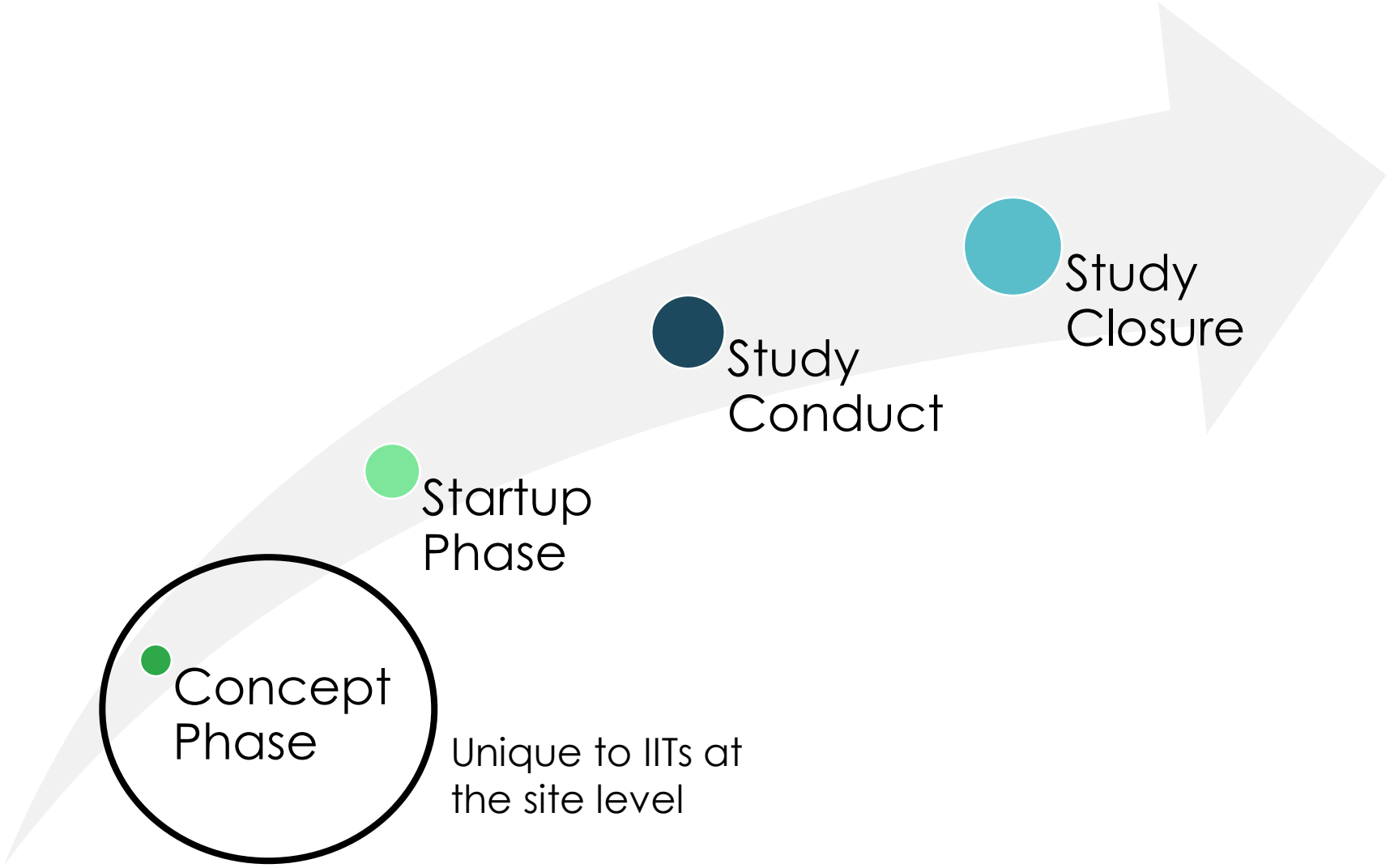
IISes are…

- Clinical studies **initiated and managed by a nonpharmaceutical company researcher(s)**
  - Individual investigator
  - An institution
  - Group of institutions
  - Collaborative study group or a cooperative group
- **IISes go by many names**, including:
  - Investigator-Initiated Trials (IITs)
  - Investigator-Sponsored Trials
  - Noncommercial Trials
  - Academic Clinical Trials
  - Physician-Led Studies, etc.

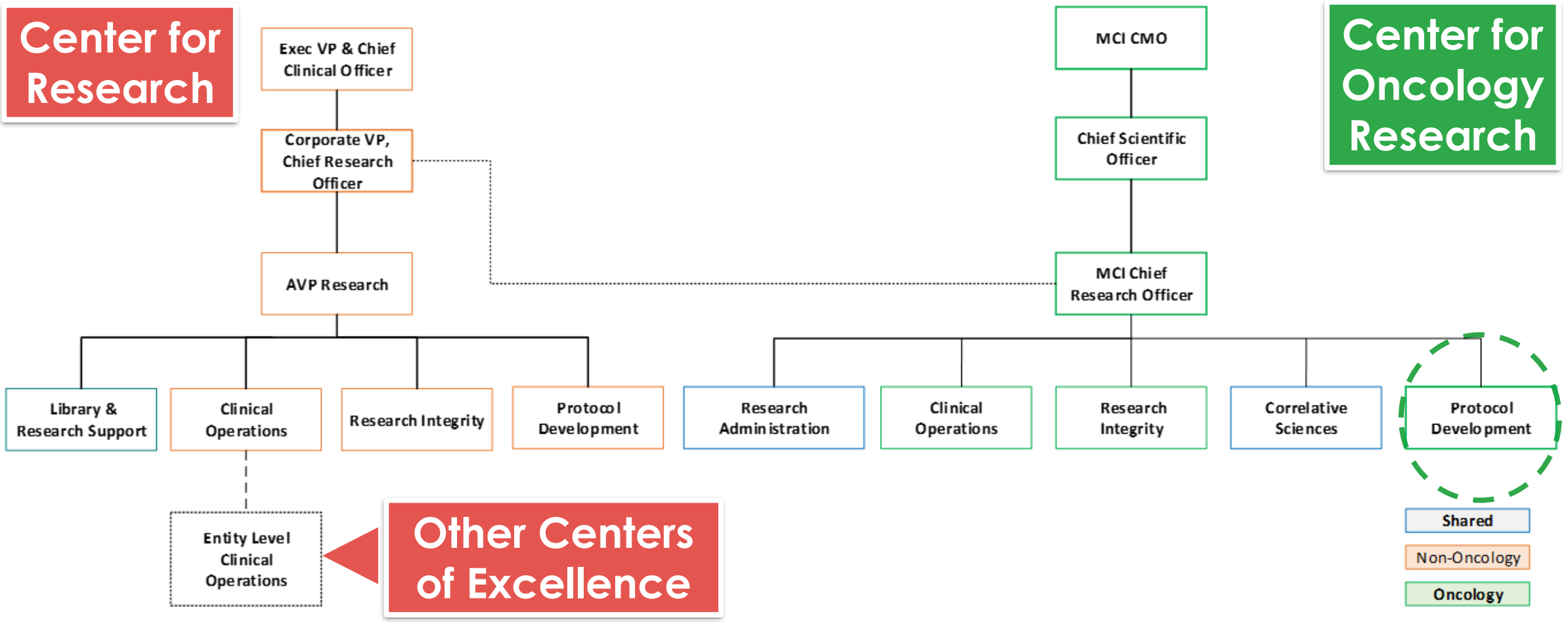
Konwar et al. 2018, *Perspect Clin Res*

Photo by National Cancer Institute on Unsplash

Investigator-Initiated Study (IIS) Basics



Baptist Health South Florida Research Enterprise



Starting from the ground up

Photo by Markus Spiske on Unsplash

What did I get myself into?

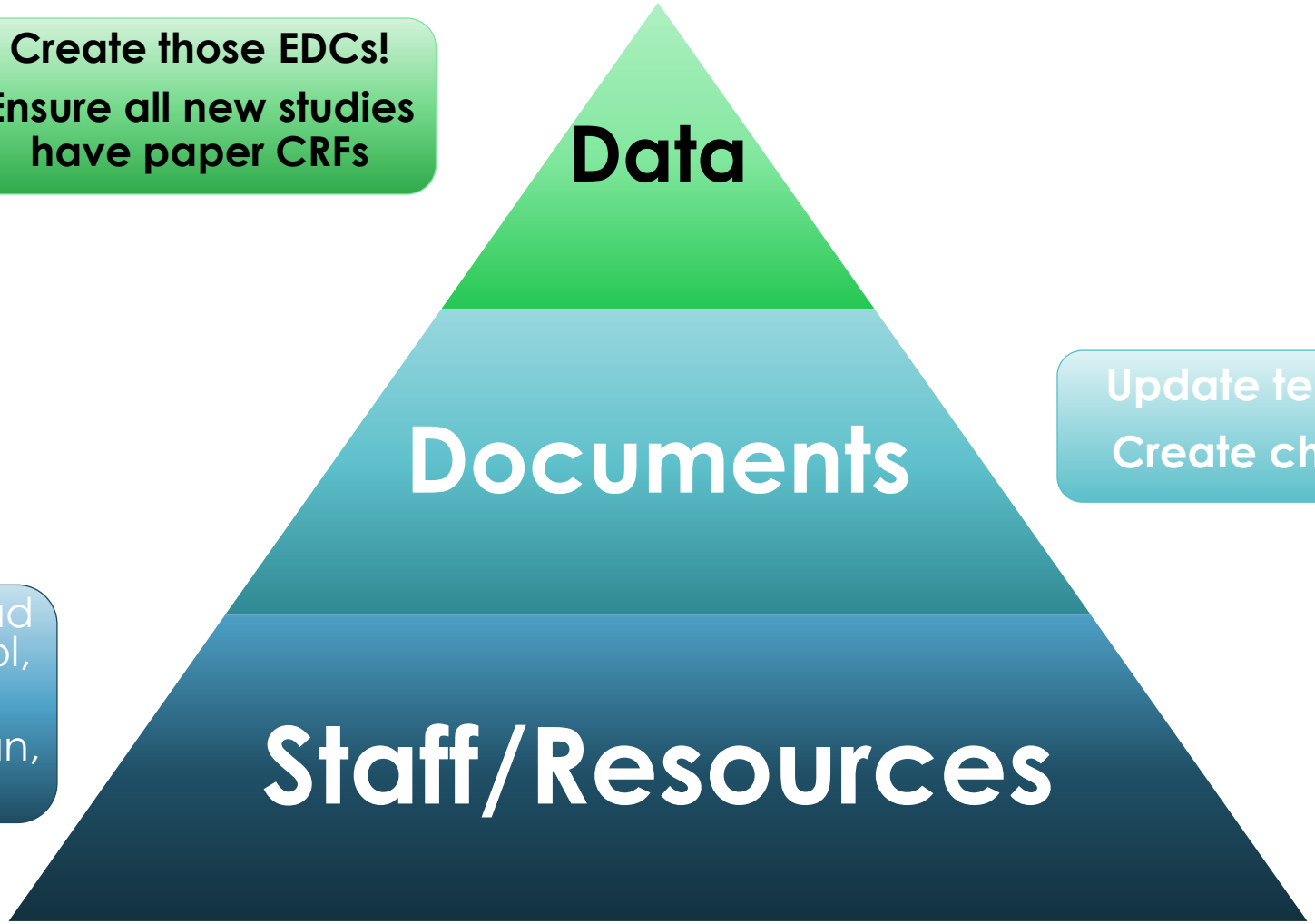
- ~17 IITs in startup or open; ~5 in development
- Poorly written protocols and ICFs
- Outdated document templates
- No paper CRFs, partially completed EDCs
- One statistician handling all power analyses & sample size calculations, statistical analysis plans, analysis, and data visualization
- Long timelines from concept approved to open to accrual (years in some cases)
- Multiple amendments before a study opened to accrual

In short…studies that were difficult to operationalize, monitor, and analyze.

Starting from the ground up: Needs assessment

Create those EDCs!

Ensure all new studies have paper CRFs



Update templates

Create checklists

Training: How to read and write a protocol, ICF

Add'l staff: statistician, data project mgr

Starting from the ground up: Team Purpose

Miami Cancer Institute's Concept Development & Data Management (CDDM) team *partners* with physician investigators to develop their research concepts into *well-designed, well-written scientific protocols* that address an important knowledge gap in the medical literature, with the *ultimate goal* of improving the lives of people with cancer.

CDDM provides a *collaborative environment* and a range of services to take a concept from *ideation through to activation*, and from *data analysis to dissemination*.

Who are the key players?

Miami Cancer Institute's Concept Development & Data Management Team (CDDM)

Collaborating Departments

Who are the key players?
Core Team

Biostatistics

Ideation: power analysis/sample size calculation, study design, statistical analysis plan

Study Conduct: data, safety, and endpoint monitoring

Study Results: data analysis and visualization

Closure & Dissemination: abstract, presentation, and manuscript

Medical Writing

Ideation: protocol and study document development

Study Conduct: protocol amendments and document version control

Closure & Dissemination: abstract and manuscript, study reports

Other: create templates and training, review/editing of departmental documentation (e.g., policies, SOPs, we content)

Who are the key players?
Core Team

Data Management

Ideation: develop paper case report forms (CRFs), and electronic CRFs and data capture systems (eCRFs, EDCs); create data management plans

Study Conduct: data management and monitoring, updates/changes to CRFs, eCRFs, and EDCs

Study Results: data aggregation, casebooks

Research Support

Can be research associates/fellows or project managers, for example

Assist investigators with research activities throughout the life cycle such as:

- Literature searches
- Cross-functional team collaboration
- Working on abstracts, presentations, manuscripts
- Keeping track of deadlines

Who are the key players? Best Friends

Monitors/CRAs

Ideation: review protocol and ICF for appropriate safety and monitoring language; review CRFs and test EDCs to ensure the study can be monitored appropriately

Study Conduct: relay issues from monitoring reports that may require amendments to protocol or changes to CRFs/EDC

Closure: final monitoring report required before freezing the EDC and downloading casebooks and final study data

Research Operations

Ideation: input into initial protocol development to ensure easy operationalization; review CRFs and test EDCs for data entry

Study Conduct: relay when protocol amendments or changes to CRFs/EDC may be required

Closure: study closeout, preparation of all final reports, ensuring all study binders and hardcopy patient casebooks are accurate and complete

Pharmacy

Ideation: critical review of protocol for investigational drug receipt, storage, handling, administration, toxicities, drug interactions; create pharmacy manual

Study Conduct: may randomize participants

Who are the key players? Best Friends

Lab/Specimen Repository

Ideation: review of correlative objectives and endpoints in the protocol, provide input for their operationalization, create lab manual

Study Conduct: relay when protocol amendments or changes to CRFs/EDC may be required for the lab

Study Results: provide any data from correlative studies that may not be captured in the main EDC

Pre-Award/Post-Award

Ideation: grant/funding submission, initial concept budget, full study budget, review of protocol and ICF for appropriate billing and compensation language, coordination with CMS for investigational device coverage

Closure: submission of final reports for funding agencies

Regulatory

Ideation: review of protocol and ICF for key regulatory language (e.g., FDA reporting), navigation through committees (e.g., feasibility, scientific review, IRB), FDA submission, CT.gov registration

Study Conduct: amendments, interim IRB & FDA submissions, CT.gov updates

Study Results: posting results to CT.gov

Closure: study closeout, submission of all final reports, ensure regulatory binders are accurate and complete

Who are the key reviewers and committees?

- Feasibility/Logistics
- Scientific Review
- FDA
- IRB/Ethics
- CMS (for device studies)
- Data Safety & Monitoring

What are the Key Performance Indicators (KPIs)?

Productivity & Output

- Total number of requests
- Number/percent of requests that go to startup or are otherwise completed
- Number/percent of abandoned or withdrawn requests
- Number of publications
- Number of abstracts/podium/ presentations

Turnaround Times (TATs)

- Request received to startup or completed
- Request received to abandoned or withdrawn
- Startup to open to accrual

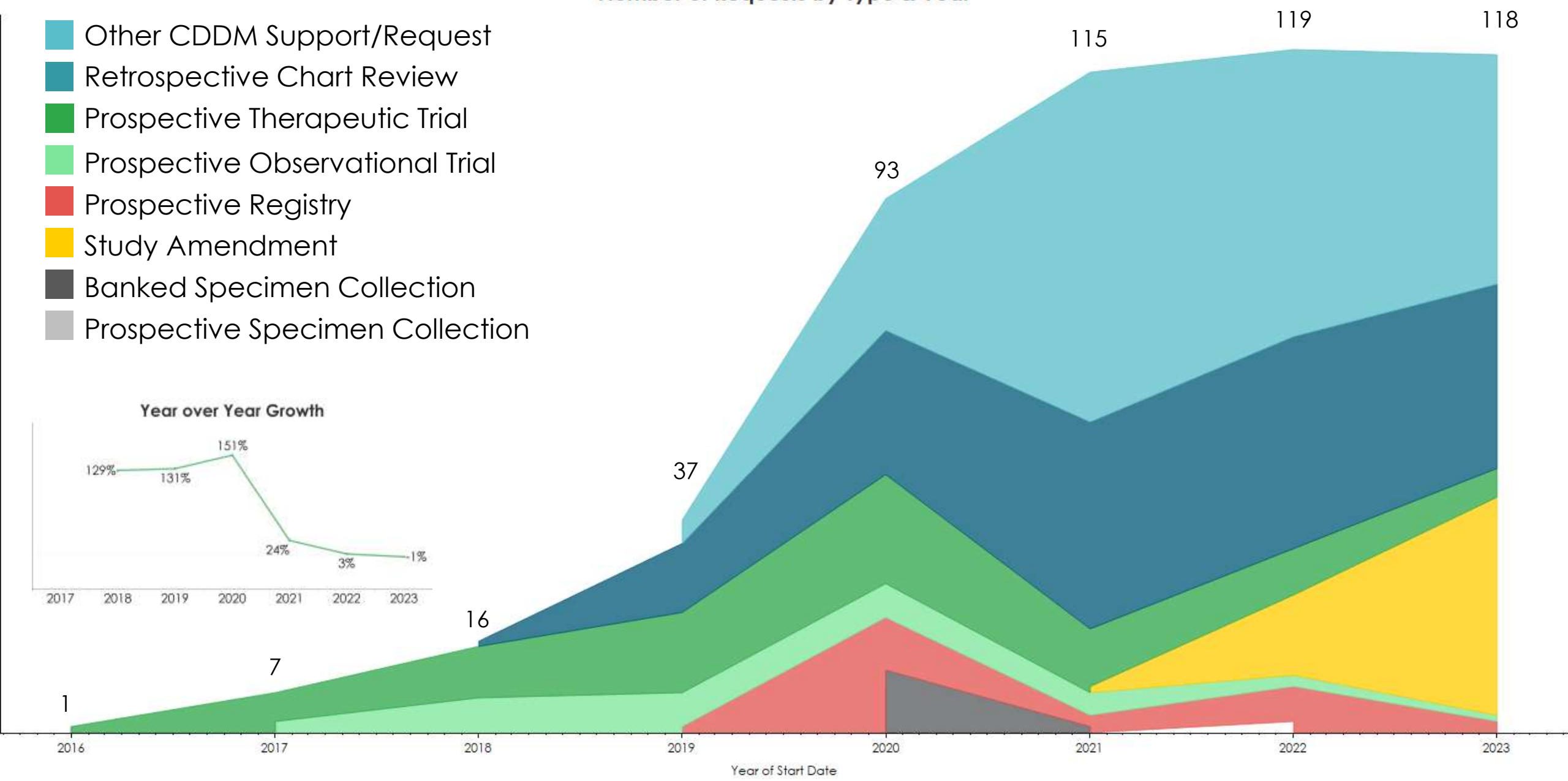
Other

- Number of amendments between IRB approval and opening

Data slicing

- Type of requests
- Oncology group
- Principal investigator
- Disease site
- Concept/study phase
- Request date (year/quarter/month)

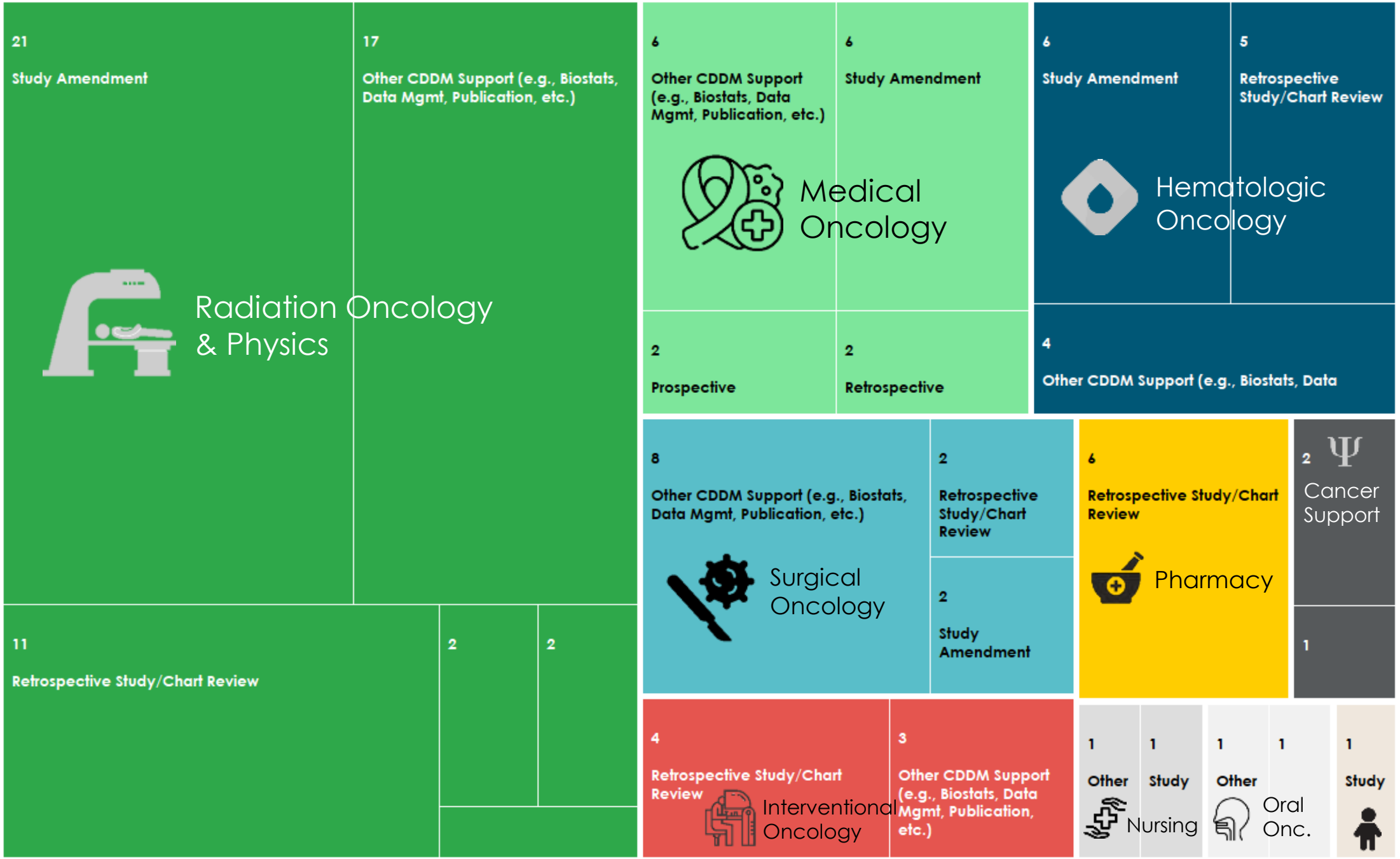
Number of Requests by Type & Year



Year over Year Growth

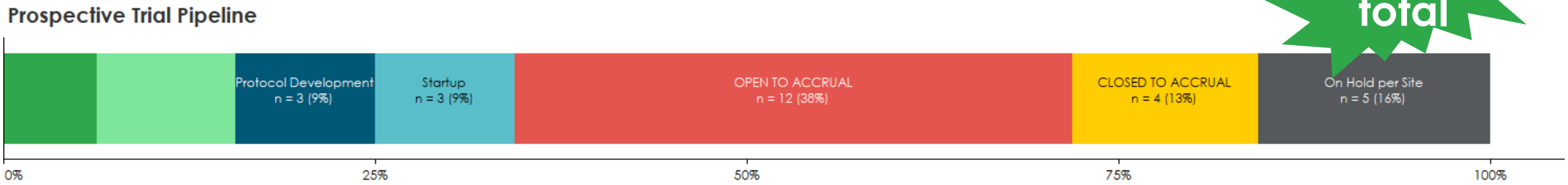
Data current through 25 Sept 23

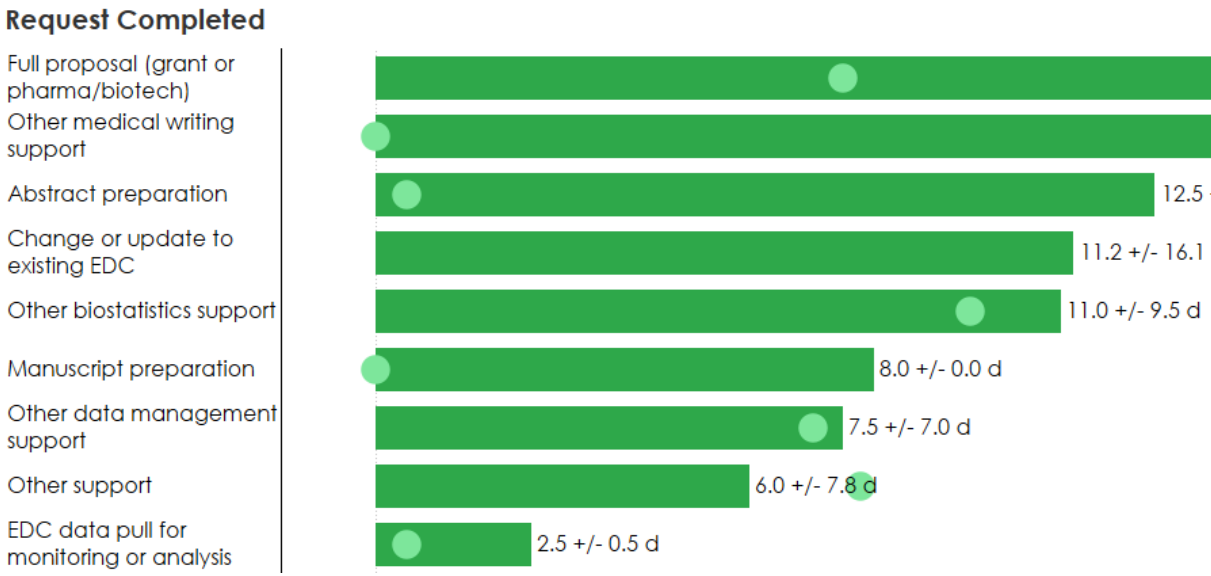
Requests by Type and Oncology Group (2023 CYTD Sept 25)

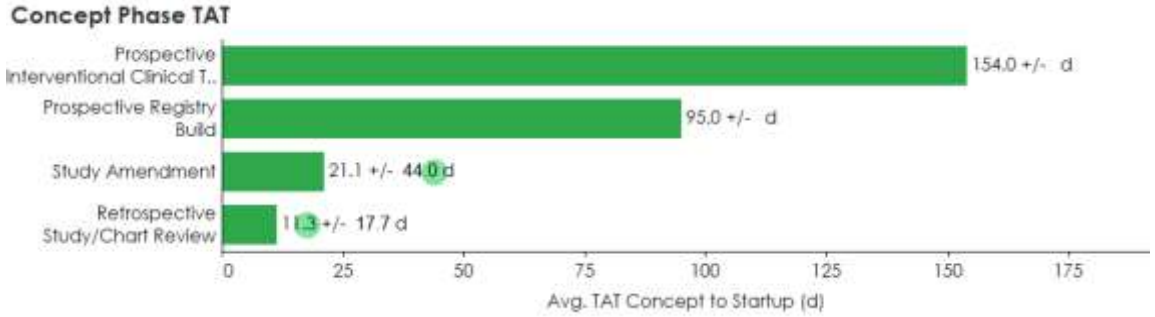


Study Statuses and TATs

32 total

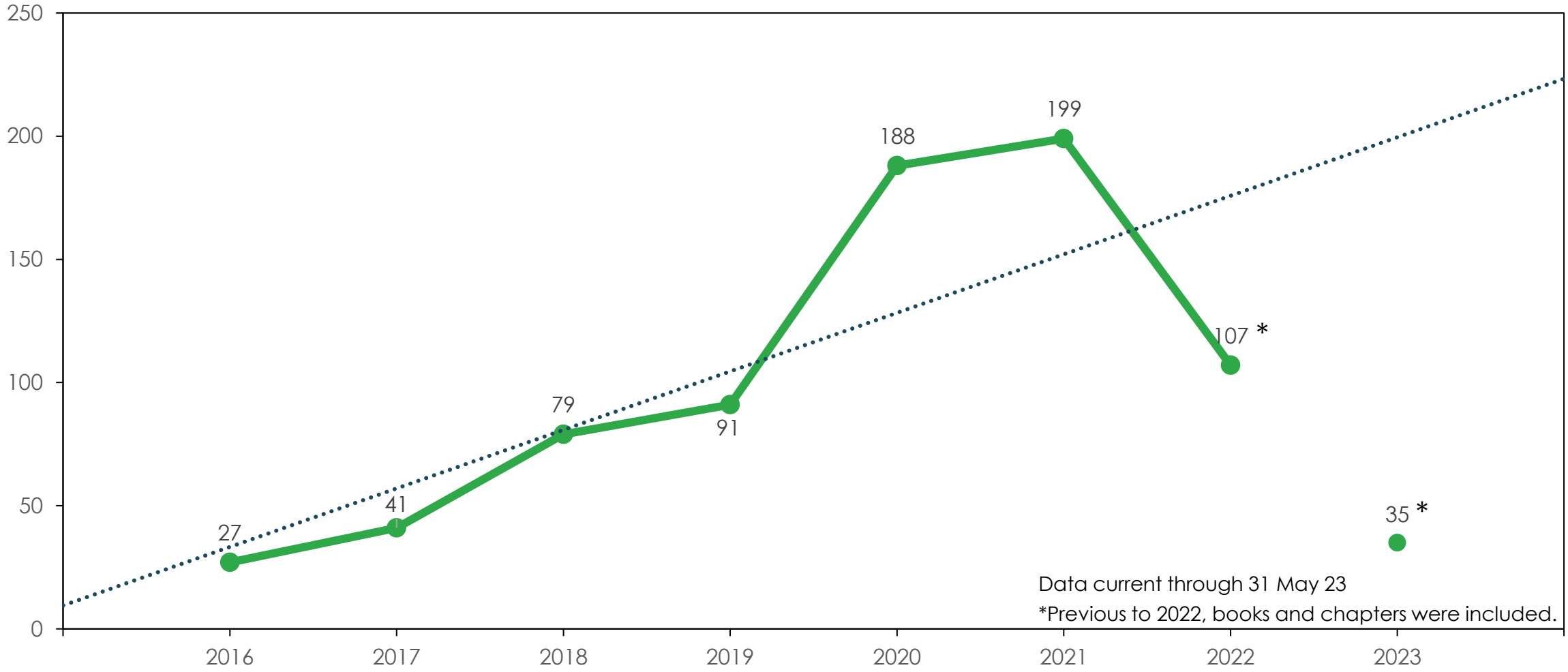






Data current through 25 Sept 23

Scholarly Output: Publications 2016-2023



What does success look like?

Engaged PI: It takes a lot of work to conduct an IIS – PIs who understand the extraordinary time and effort are crucial

Strong Foundation: "Core team" and "best friends" help create a solid protocol to ensure smooth operationalization and monitoring

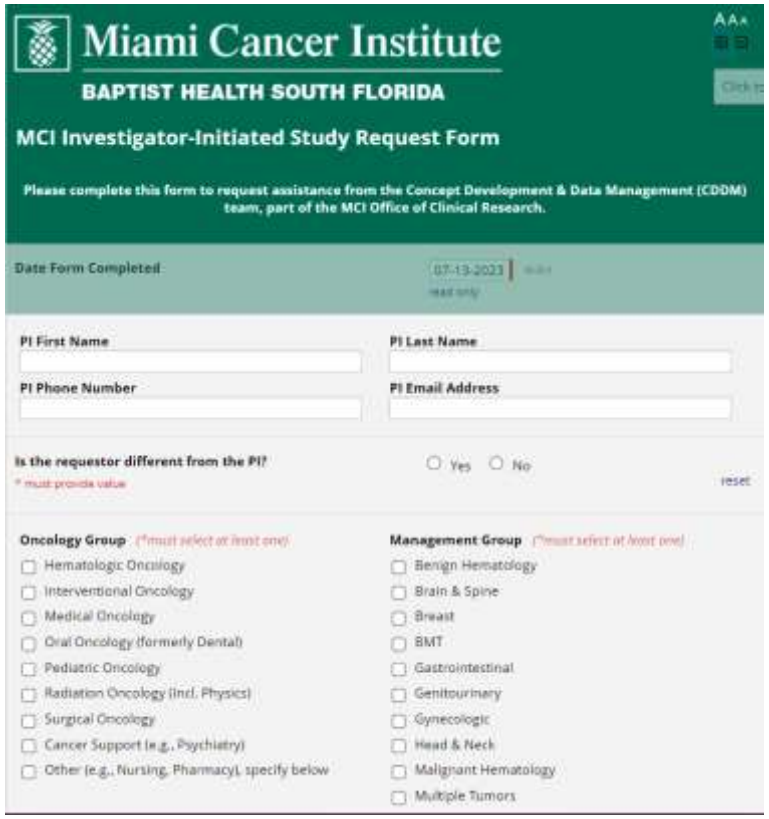
Meeting TAT Goals: Having TAT goals and monitoring them regularly will ensure your program is running smoothly

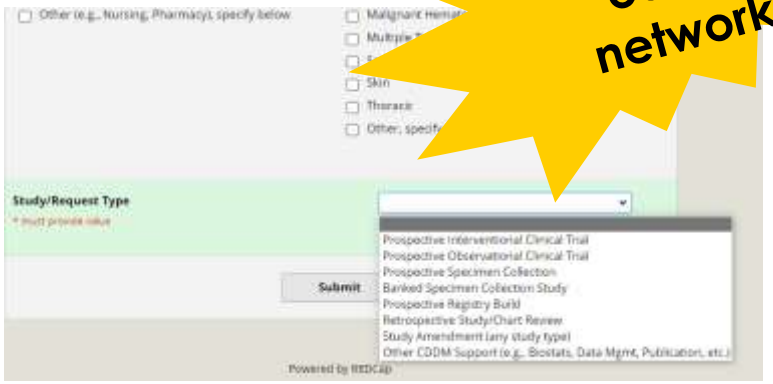
Minimal Amendments, Safe and Compliant: Multiple amendments can affect patient safety and compliance, a strong foundation is key

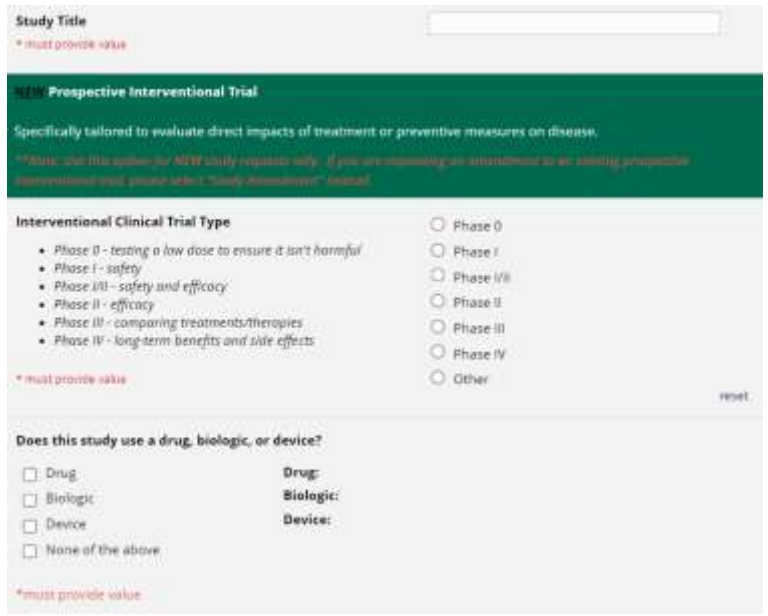
Contributing to science and medicine: The ultimate goal is to effect change in practice and clinical care

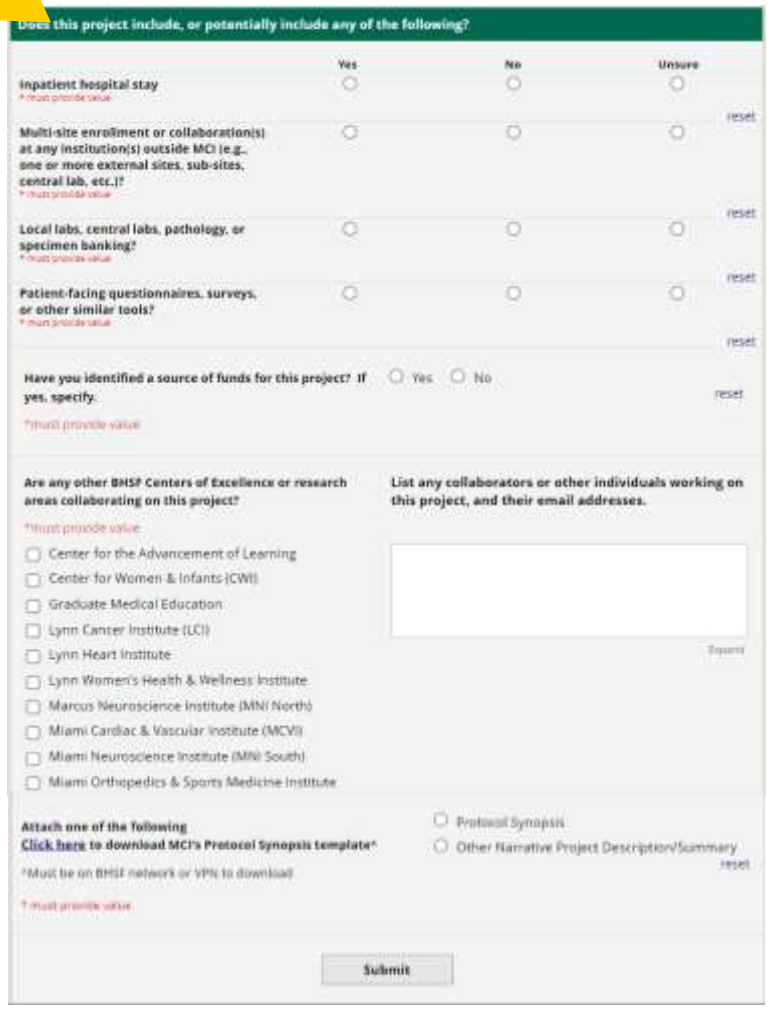
Extra tips for success: Intake Form

Intake accessible out of network









Extra tips for success: Templates and Workflows

Resources for Investigators:

- Concept Development and Data Management
  - Investigator Initiated Research Templates
  - Investigator Initiated Research Workflows
- Expanded Access and Emergency Use

Concept Development and Data Management (CDDM)

How to Request Support:

To request CDDM support for your project, please visit the following link: https://redcap.link/MCI-CDDM-intake. You may select a type of study, a study amendment, or select "Other Support" for specific support from one of our cores.

Investigator Initiated Research Templates

- Prospective Interventional Clinical Trial Protocol
- Prospective Interventional Clinical Trial Synopsis
- Prospective Observational Clinical Trial Protocol
- Prospective Clinical Trial Informed Consent Form
- Prospective Biospecimen Collection Protocol Template
- Prospective Registry Protocol Template
- Prospective Registry Informed Consent Form
- Retrospective Manual Chart Review Protocol Template
- Retrospective MCI Data Repository Protocol Template
- Retrospective Data Collection Sheet Template
- Retrospective Data Linkage Log Template
- National Cancer Database (NCDB) Participant User File (PUF) Request Template

Investigator Initiated Research Workflows

- Prospective Interventional IIS Concepts Phase
- National Cancer Database (NCDB) Participant User File (PUF)

Other Resources:

NIH/FDA Electronic Protocol Writing Tool

Available on Intranet

Example Workflow

Prospective Interventional IIS Concepts Phase

Miami Cancer Institute
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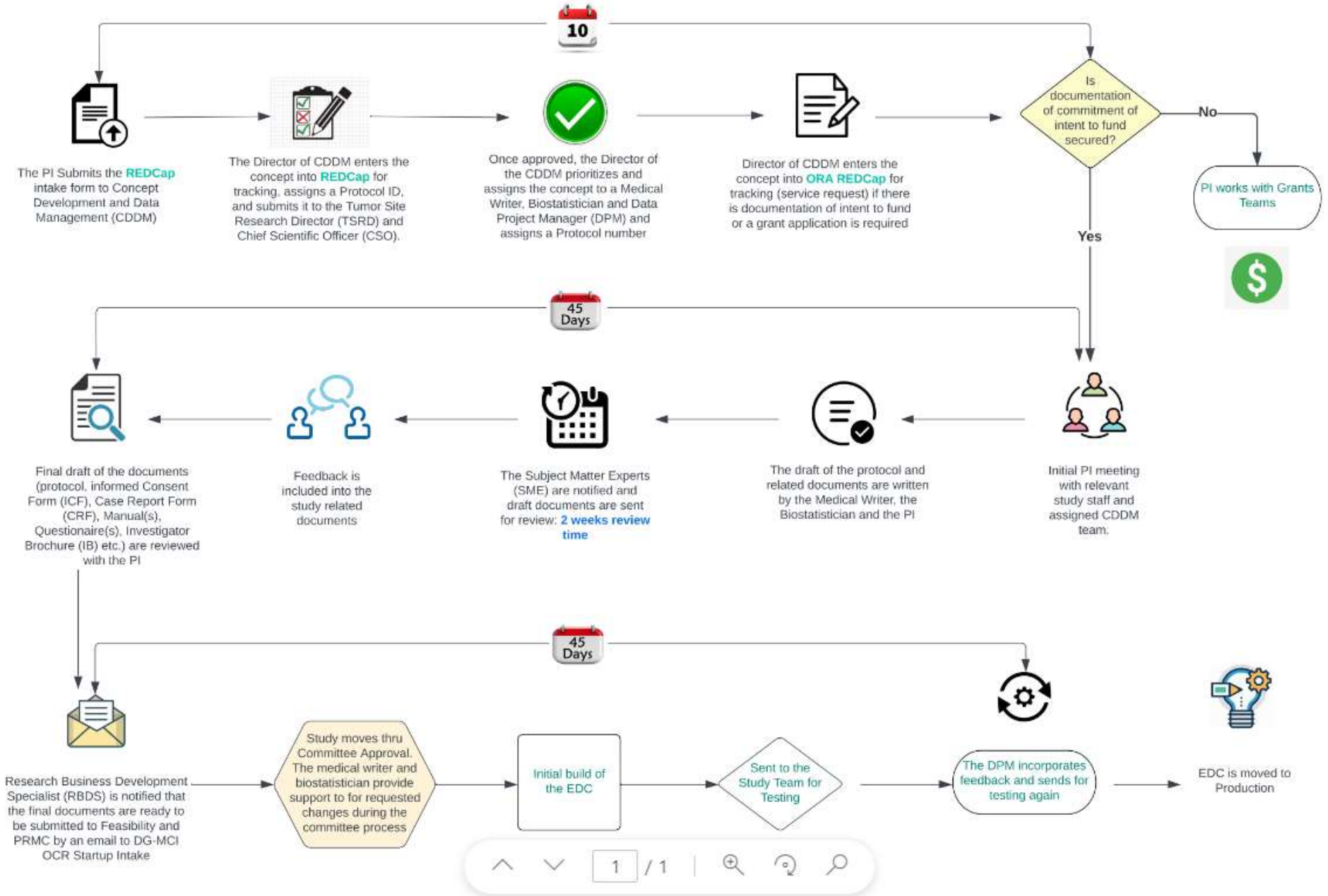
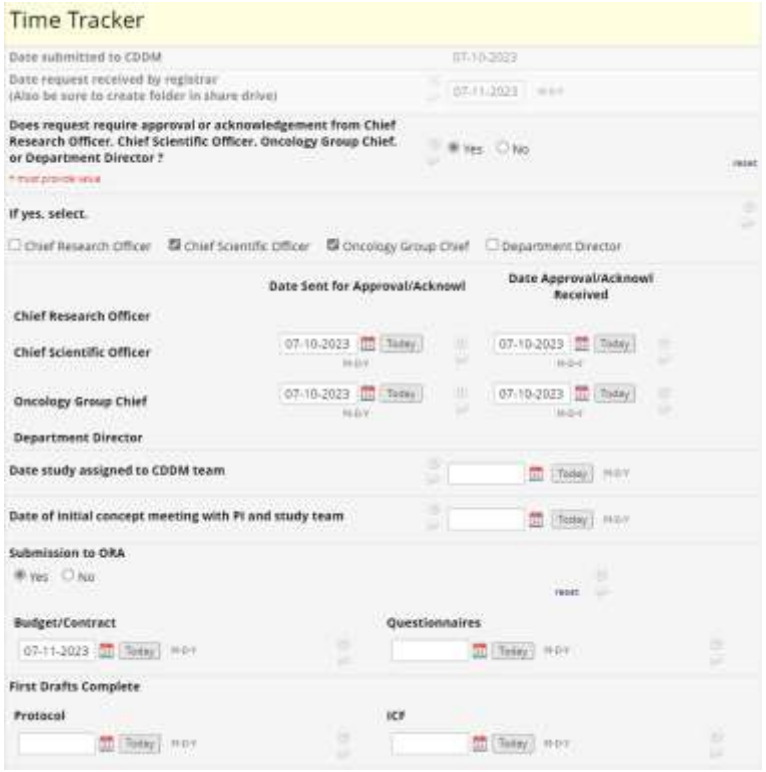
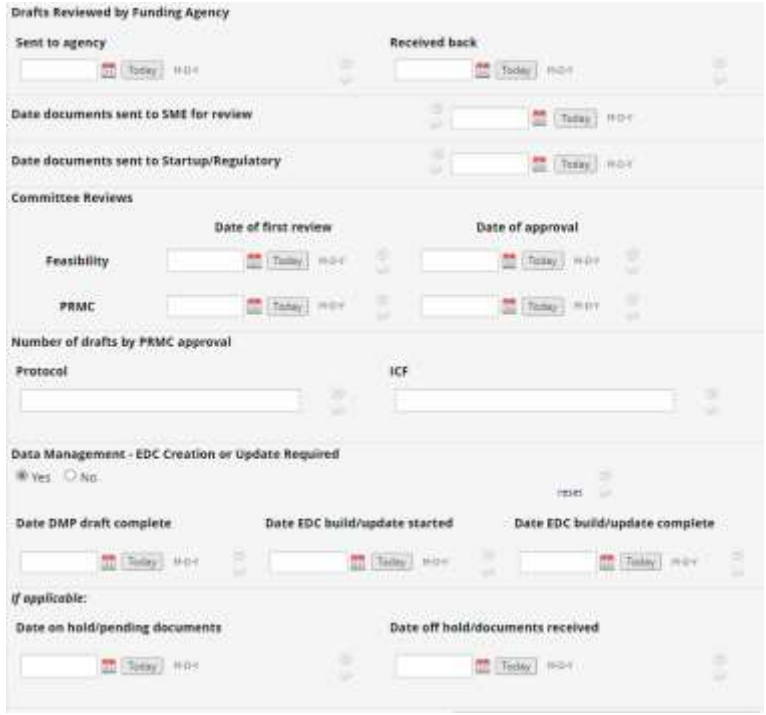
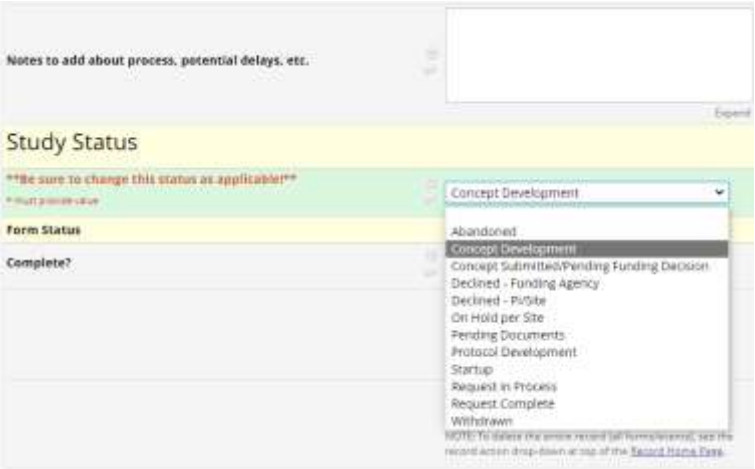


Extra tips for success: TAT Tracker





Linked to Intake Form



Extra tips for success: Medical Writing Checklist for Protocols & ICFs

Scientific Review

Is the protocol written to address the research question(s) and hypothesis(es)?

- Relevant background
- Rationale
- Study design (# arms, placebo or comparative tx, length of follow-up, randomization, schematic, etc.)
- Objectives with matching endpoints (and associated timeframe – important for CT.gov)
- Sample size
- Study population and eligibility
- Study intervention (incl. how many doses/cycles can be missed and still be valid)
- Tests and assessments (specify tests in each lab panels, assessment frequency, duration)
- Correlatives (type, when, how, which lab)
- Statistical analysis

Human Subjects Protection

- Is the risk of harms contrasted to probability of benefits?
- Explanation of risks/benefits in protocol and in informed consent form
- AEs, SAEs, and UPs
  - General definition, protocol-specific
  - Protocol-specific time points for collection
  - Protocol-specific reporting instructions and to whom (e.g., IRB, funding agency, regulatory agencies)
- Protocol and ICF clearly state which activities are standard care vs. research, by study visit?
- Privacy and confidentiality information is included
- ICF written in 6th to 8th grade language – check samples of you text in a readability calculator (bullet points help with improving readability)

Extra tips for success: Medical Writing Checklist for Protocols & ICFs

Completeness

- Include all abbreviations from the document in the abbreviation table
- PI signature page is included; for multi-site, site PI signature page included
- Are required sections included according to the protocol and ICF templates?
- Are multiple consent forms required? e.g., pregnancy, pregnant partner, child assent, LAR, etc.
- If pharmacy or lab manuals are required, have they been completed by their respective teams?
- If questionnaires or surveys are required, have licenses been requested through ORA?
- If participant diaries are required, have the templates been completed?
- Information about monitoring, privacy and confidentiality is included

Formatting

- Tables fit within margins
- Tables and figures are clear and appropriately sized (not blurry, stretched, smushed, i.e., use high-res, keep aspect ratio locked)
- Table and figure captions are used; figure & table list included after table of contents
- Linked cross-references as needed throughout
- Consistent fonts, sizes, line spacing throughout

Personnel, Sites, and Collaborators

- Co-I/Co-PI requires a separate 1572
- If a Co-I or Sub-I is at another institution, what research activities will be taking place at that institution? Do they need to have their own IRB approval or will one IRB cover their work?
- Special considerations for multi-site studies

Extra tips for success: Medical Writing Checklist for Protocols & ICFs

Consistency

Protocol consistent throughout entire document. Ensure consistency after each revision.

- Version number and dates on title page match page headers and file name
- Synopsis matches relevant protocol sections
- Study design schematic matches text
- Schedule of Activities matches Dosing and Administration, Study Assessments and Procedures, Safety and Other Assessments
- Protocol sections for Dosing and Administration, Preparation/Handling/Storage/ Accountability, Concomitant Therapy match the pharmacy manual
- Study endpoints included in Statistical Analysis Plan
- Double check titles of all tools/QOLs/assessments are correct and consistent throughout
- Update the Table of Contents with each update

Reference consistency – consider using a reference manager like EndNote

- All references cited in the text are listed in the reference section
- All references listed in the reference section are cited in the text
- Include PubMed ID (PMID) for ease with registering the trial on ClinicalTrials.gov

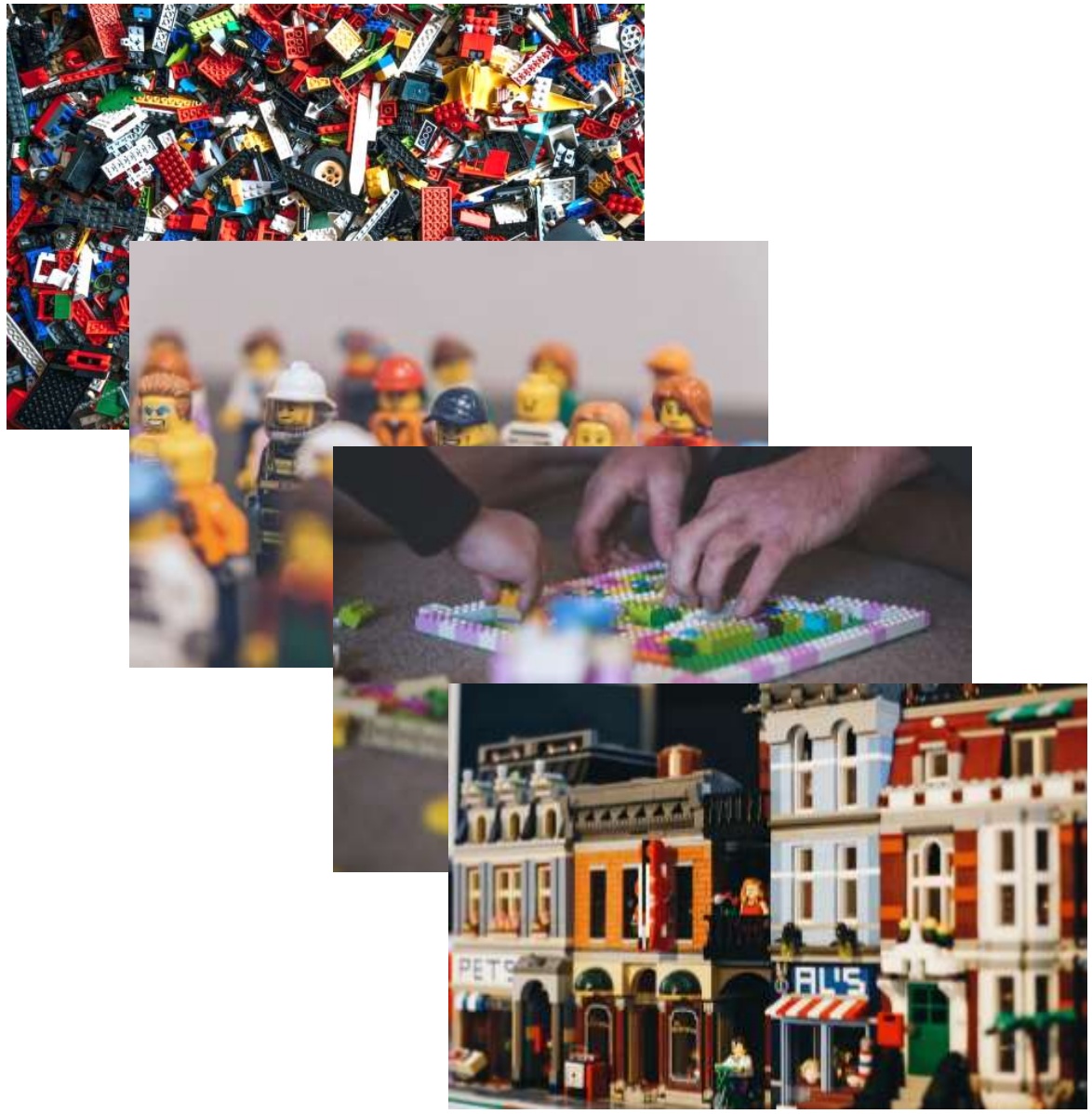
Cross-document consistency

- Protocol synopsis matches ICF summary
- Schedule of events in protocol matches in ICF
- Protocol drug dosing and administration section matches pharmacy manual
- Protocol correlative section matches lab manual
- Titles of tools/QOLs/assessments match across documents

Takeaways

No matter what your program looks like currently…

- First, start with your people and your resources
- Next, build your foundation of a solid protocol and consent form
  - Remember your best friends plus your core team
  - Use the various committees to improve your product before IRB approval
- KPIs help keep track of your final product
  - Overall volume, TATs, amendments before opening
- Marker of success: Contributing to science and medicine through dissemination and practice change
- Tips for success: Workflows, templates, checklists



Top: Photo by Markus Spiske on Unsplash
Second: Photo by Kenny Eliason on Unsplash
Third: Photo by Dan Burton on Unsplash
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Thank You.

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