Planning and Conducting Investigator Initiated Multi-Site Studies

Vera Hollen, M.A.
Grants Management Administrator
Carilion Clinic
vlhollen@carilionclinic.org

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Learning Objectives

- Define the key operational objectives for multi-site studies
- Describe best practices for successful multi-site studies
- Identify the review criteria used by multi-site study funders

Why Conduct Multi-Site Studies?

- Multisite studies provide large, diverse samples with sufficient statistical power to detect significant associations between health systems, care processes and outcomes.
- Findings are more generalizable than studies in a single institution and more likely to influence healthcare practices and policies.
- Can present challenges such as collaboration among participating institutions, assuring data integrity, and reaching consensus regarding authorship and dissemination of findings.

Investigator Initiated Multi-Site Studies

- Study is designed by the investigator
- Project may be unfunded or funded by NIH, industry, foundation

Sponsor and Investigator Roles

Sponsor Role	Investigator Role
Ensure qualified investigators are conducting the study	Conceives study design and writes protocol Ensure that the study team is following the investigational plan
Ensure the protection of human subjects Monitor progress of the study Monitor protocol amendments	Coordinates all aspects of the study Ensure data integrity Submits progress and financial reports
Document the disposition of the study	Analyzes data and writes study manuscript Submits journal article(s) for publication

Project Conceptualization

NIH review criteria…

- If the specific aims of the research are achieved, how critical will the information be with regard to addressing the evidence gap and advancing knowledge?
- How likely is it that the study results will contribute critical clinical knowledge?
- How likely are the results to contribute to the improvement of health or clinical care?

Innovation

- The study should challenge current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions

- A refinement, improvement, or new application of theoretical concepts, approaches or methodologies, instrumentation, or interventions may be proposed

- Does the design/research plan include innovative elements that have the potential to advance scientific knowledge or clinical practice?

Protocol Design

1. Principal Investigator(s), research team and study site(s)
2. Research synopsis
3. Background & Significance
4. Objectives
5. Study design/methodology
6. Study population
7. Study drug/Interventions
8. Study Schedule
9. Adverse Reporting
10. Statistical Analysis Plan
11. Informed Consent Process
12. Risks and Benefits to participants
13. Study Timeline
14. Data Safety monitoring
15. Conflict of Interest
16. Publications and Presentation Plans
17. References

Study Timeline

- Include a table or graph of the overall study timeline. A visual representation of key project management activities and core milestones (E.g., Gantt Chart)

NIH review criteria…

- Are the listed milestones for each phase appropriate for the goals of the project?
- To what extent are the Core Milestones relevant, measurable, achievable, result-focused and time-bound?
- Is the study timeline appropriate to complete the goals, meet the milestones, and address the scientific question(s)?

The Study Team

- Select Co-Investigators with strong research/ clinical trials experience
- Ensure that there is evidence the collaborating sites have the appropriate personnel implement the protocol
- Clearly define the roles and responsibilities of the Lead PI, Co-Is
- Strong project management expertise among the key personnel is a critical key to success
- Define the oversight, responsibilities, communication with, and coordination of all sites

The Study Team

- Designate an on-site study coordinator for each site
- Develop written guidelines and hold regular meetings of the research team, on-site coordinators and other members of the research collaborative
- Be prepared for the varied requirements of institutional review boards

IRB Considerations

- Commercial funding
  - May require a central IRB
- NIH
  - Requires a central IRB as of Jan 2020
- Unfunded
  - Carilion's IRB may recommend single IRB
  - Smaller multi-site studies may allow each individual IRB to review

Engage with Carilion's IRB early to ensure a smooth process

The Study Team

- Staff turnover (particularly CRCs) is a major hurdle and slows the rate of patient recruitment.
- Appoint an overall CRC that can lend support to the multisite CRCs.
- Secure a commitment from the collaborating sites for dedicated coordinator time for the duration of the study
- Coordinator cross-training

Facilities & Resources

- Ensure appropriate facilities and resources available to adequately coordinate a multi-site study
- Make sure that that the necessary agreements can be put in place in a timely manner to initiate the study and provide the necessary protections

Challenges and Solutions

Challenge	Solution
Poor communication across the multiple sites	Conducting periodic team research meetings (e.g., monthly)
Unanticipated clinical coordinator turnover	Appoint an overall CRC to help nurture a cohesive team, cross train CRCs
Multi-institutional coordinator training	Conduct centralized protocol training, if feasible. Overall CRC is available for support
Dealing with multiple Institutional Review Boards	Engage Carilion's IRB early to help navigate the process
Slow subject recruitment and/or poor retention	Set explicit monthly recruitment goals for each clinic

Subject Recruitment and Retention

- Support subject recruitment and retention plans with data to back accrual projections
- Create a table of the recruiting sites showing enrollment goals and number of potential participants available at each site
- Identify the primary and back-up recruitment strategies
- Participant retention and adherence strategies
- Possible competition from other trials for study participants

Standard Operating Procedures

Develop SOPs

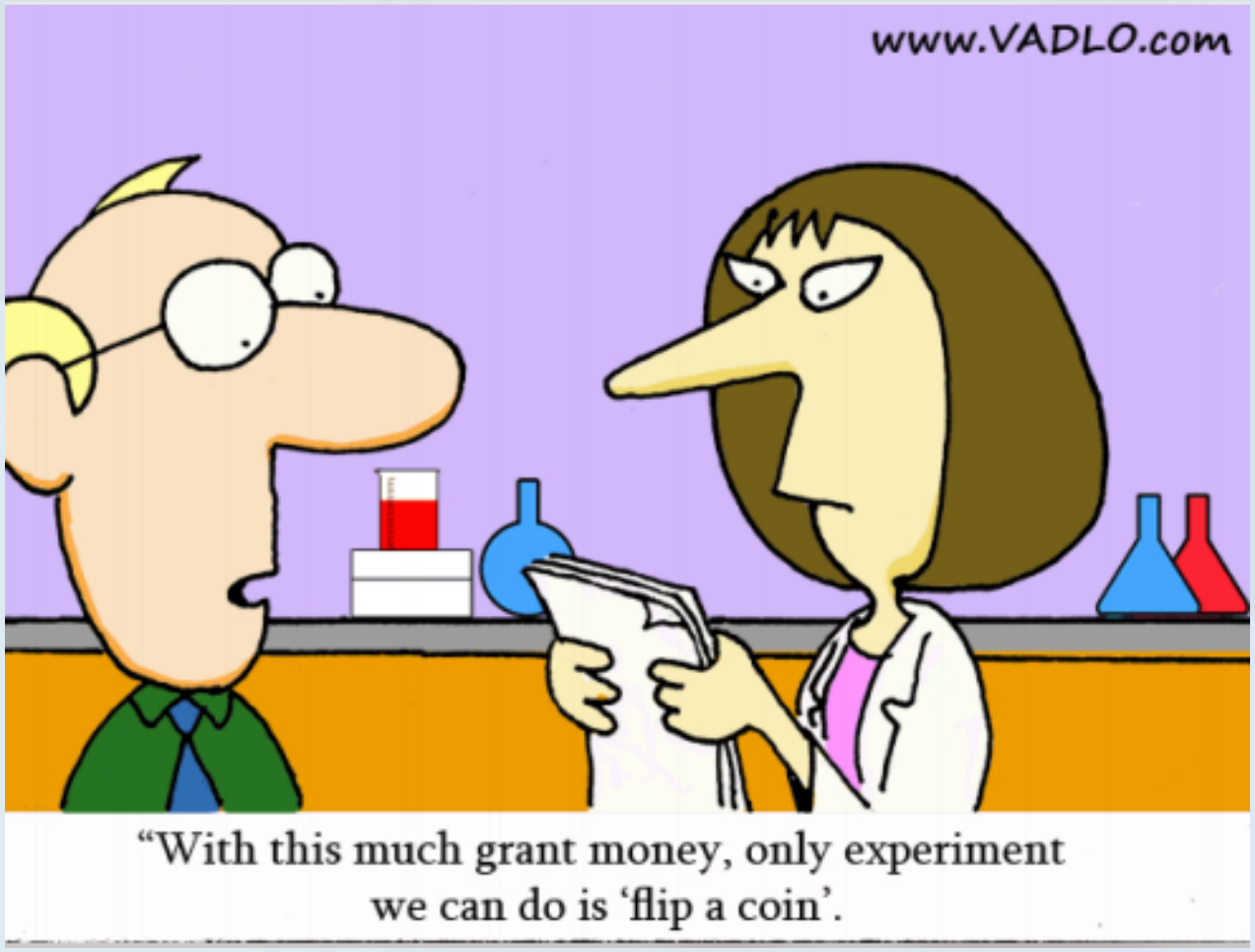
to share across sites

ICH GCP reference code	Standard Operating Procedures (SOPs)	Current version	
	Glossary		
4.0	Investigator Roles and Responsibilities	2.0	1
4.5	Protocol deviations and Violations	1.1	2
4.7.1	Randomisation	2.0	3
4.7.2	Unblinding	2.1	4
4.8	Informed Consent	1.1	5
4.9.2	File notes	1.1	6
5.1.1	SOP development	2.0	7
5.5.1	Electronic Data handling	2.0	8
5.5.2	Electronic Data transfer	2.0	9
5.5.4	Collection and transcribing of data	In Draft	10
5.5.5	Allocation of Participant ID Numbers	2.0	11
5.6.1	Site selection	1.1 Draft	12
5.14.1	Investigational Product Handling	2.0	13
5.17	Adverse Event Reporting	2.0	14
5.18	Monitoring	2.0	15
5.18.1	Site Closure	In Draft	16
5.18.2	Study Closure	1.0	17
5.19	Audit	2.0	18

iTHRIV Resources

- integrated Translational Health Research Institute of
- iTHRIV.org
- Community Engaged Studio: a facilitated round table discussion that brings together health researchers and patients/consumers/other non-academic stakeholders
- Recruitment Enhancing Resources Program: Supporting Diversity and Inclusion in Research Participation
- CTSA Recruitment Innovation Center

Budgeting

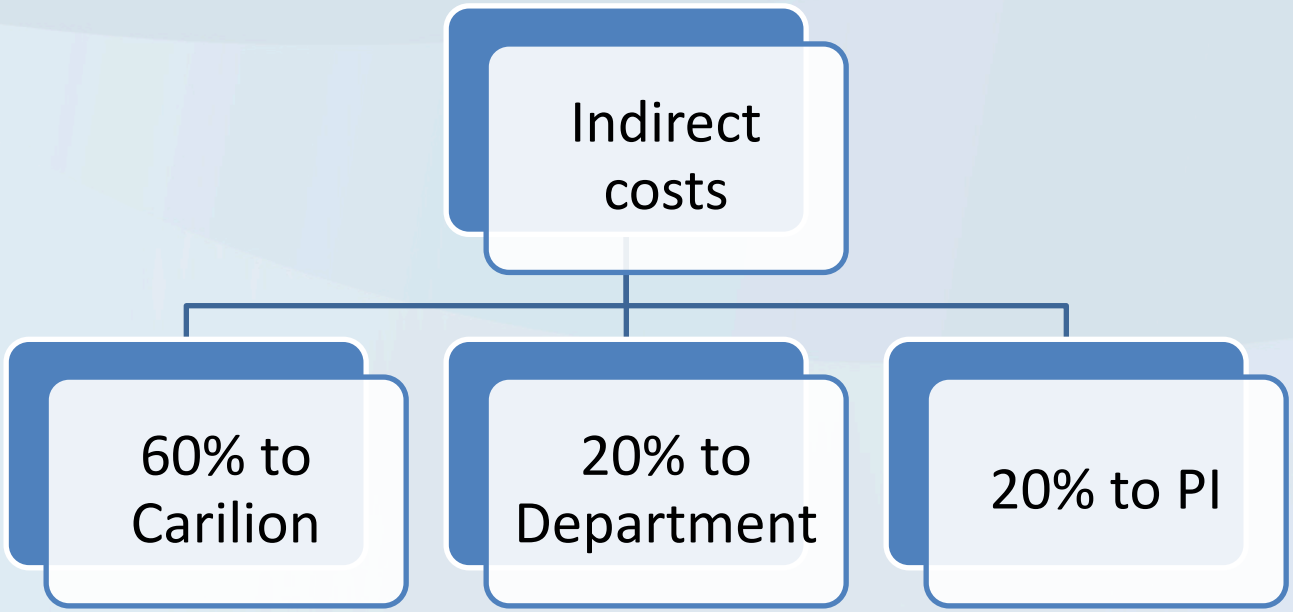

www.VADLO.com
"With this much grant money, only experiment we can do is 'flip a coin'.

Budget

- Administrative and Start up Costs
- Staffing/Salary Costs
- Fringe benefits
- Supplies
- Equipment
- Patient Care Costs
- HART fees
- IRB fees
- Travel
- Publication fees
- Subcontracts
- Overhead costs

Overhead

- Is overhead allowable from the sponsor?
- Is there a cap?



Subcontracts

- Budget for collaborating sites will be a subcontract
- Costs will vary among sites
- Administrative and Start up Costs are non-refundable. Plan wisely!
- The primary institution is accountable to the sponsor for money spent
- Minimize financial risk when planning cash flow

Dissemination

- Once the study has concluded, it’s time to disseminate the results
- General dissemination plans should be established at the start
- Develop strategies to ensure that key findings of your study are disseminated to key stakeholder groups
- How do you make your study findings publicly available in an efficient and timely manner – data analysis can take months/years
- For publications, consider authorship and scope of the manuscript
- What secondary analyses will be done and why

Keys to success

- Common management strategy among all sites
- High degree of control in protocol implementation, data collection & reporting
- Qualified and experienced study team
- Regular communication
- Meticulously managed budget
- Regular and open communication with the sponsor

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References

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