44 Conducting a Multicenter Trial: Learning from the JUPITER (Justifying Patellar Instability Treatment by Early Results) Experience

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44.1 Introduction

Multicenter trials are critically important in answering significant research questions in orthopedic surgery. Due to the nature of orthopedic injuries and treatment, it can be difficult for a single center to accumulate enough patients to have sufficient statistical power to address a clinical question. In addition, the patient population or the particular practice patterns of a single location can make generalizing the results of a single-site study difficult [3]. For example, in patellofemoral instability, surgical results based on an injury group consisting primarily of traumatic injuries to male military recruits in their 20s may not be applicable to atraumatic dislocations in skeletally immature female patients with trochlear dysplasia. A multicenter trial might help address diverse patient populations and practice patterns.

> Multicenter trials can provide important information by collecting sufficient numbers and varieties of patients to allow significant statistical power and generalizability. Challenges are related to the geographic separation and different locations that make trial coordination more difficult than in a single-site study.

There are unique challenges related to multicenter trials. The obvious one is that investigators are geographically spread apart, resulting in increased difficulty in communication and potential for increased variability in conducting the

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study. What is just as critical is the dedication of the group of investigators to be willing to be collaborative and compromise to achieve a collective goal.

44.2 Initiation of Multicenter Trial

Typically, a multicenter trial begins with a small group of investigators who share a common interest in a clinical research question. This is often based on results of a single institution's experience and the desire to identify how this may be further generalizable. In the JUPITER trial, the investigators have been motivated to initiate a multicenter study investigating the results of treatment of patellofemoral instability in a pediatric, adolescent, and young adult population. The standard of care for initial acute patellofemoral dislocation has historically been nonoperative [10]; however, it has been demonstrated that the rate of recurrent instability can be quite high and also that many patients have symptoms or loss of function related to the dislocation. In addition, recurrent instability has been associated with a significant rate of articular cartilage damage and long-term osteoarthritis [6]. Recent work done at several centers has identified specific risk factors for recurrent instability [1, 2, 5, 9]. Algorithms have been proposed for treatment [11], but questions still remain as to the natural history and results of treatment for different patients [7, 8]. JUPITER is a multicenter, multi-armed prospective cohort study aimed at addressing some of these questions, particularly which patients can do well with an isolated medial patellofemoral ligament reconstruction for stabilization and which patients need other procedures.

Initiation of the JUPITER trial was based on a pilot single-center study and was designed to identify risk factors for recurrent patella instability and treatment outcomes.

44.3 Discussion and Planning Phase

A discussion phase was initiated after some initial face-to-face and email contacts among members of a group of researchers interested in the area of patellofemoral instability, primarily as determined by attendance at the International Patellofemoral Study Group (IPSG) meeting in Chicago in 2015. Interest was gauged by a small group of initial investigators. In most multicenter trials, there is a project leader or leadership team that helps keep the trial on track. Key to the conduct of this and any multicenter study is significant commitment by this group of investigators.

Discussion and planning began with a small group. Essential statistical evaluation was performed, and a screening form was developed and circulated to evaluate site and investigator capabilities.

The research goals were identified, and after this was clarified, a statistician performed a power calculation for the study. A statistician or epidemiologist with statistical training is a critical partner in identifying the appropriate number of patients to ensure sufficient power to answer the proposed research question. Appropriate corrections should be made for patient dropout or loss to follow-up. The calculation of overall enrollment numbers will be compared to anticipated individual site enrollments for a given period of time to help determine the total number of sites and/or anticipated length of time for enrollment.

A screening form for potential sites interested in joining the study was developed and circulated. In this tool, sites and investigators provided information about level of interest, site and investigator experience and support (including financial support and research personnel such as research assistants/coordinators), estimated frequency of enrollment, and anticipated level of commitment. A sample screening form page from JUPITER is shown in Fig. 44.1 (Tables 44.1 and 44.2).

JUPITER (Justifying Pediatric Instability Treatment by Early Results)
SCREENING FORM

Name of surgeon: _____

Institution Name: _____

Affiliated University: _____

Phone No _____

Research Coordinator _____

Years in Practice: _____ years

Type of Practice: _____

Average no of Patellar Instability treated non-operatively per year: _____

Average no of Patellar Instability treated operatively per year: _____

Average no of Medial-sided repair per year: _____

Average no of isolated MPFL reconstructions per year: _____

Average no of TTO (Elmslie-Trillat, AMZ, distalization) per year: _____

Average no of Osteochondral fracture Rx following patellar stabilization per year: _____

Average no alignment osteotomies (femur/tibia, coronal/rotational) per year: _____

1. Of all operative patellar stabilization, how often do you do knee arthroscopy?

   Knee Arthroscopy _____%

2. Of all operative patellar stabilization, how often patients have open femoral physis?

   Open Physis _____%

Fig. 44.1 JUPITER Screening Form

44.3.1 Protocol Development

Protocol development was initially performed by the executive committee based on a pilot study initiated at one site. Multiple questions need to be answered during protocol development, including eligibility criteria and assessment. Assessment for clinical projects can include history, physical examination, and radiographic studies, as well as patient-reported outcome scores and standardized evaluation tools.

The specific aims of JUPITER were to evaluate the safety and effectiveness of (1) nonoperative treatment, (2) isolated medial patellofemoral ligament (MPFL) reconstruction, and (3) MPFL reconstruction combined with bony procedures (osteotomy, trochleoplasty). Subject recruitment was planned for a 1 year time period at ten

Table 44.1 JUPITER authorship criteria (adapted from PRISM https://www.prismsports.org/)

Eligibility criteria for authorship in JUPITER manuscripts (adapted from PRISM)
I. All of the following criteria must be met to be considered for authorship:
1. Maintain good standing in JUPITER, as defined in the manual of operations
2. Respond with all of the following within *2 weeks* for each manuscript
(a) Comments/edits of manuscript (or an "all good" response)
(b) Completion of all disclosure forms
(c) Completion of all copyright transfer forms, etc.
II. In addition, investigators must have met a set of the following criteria (by receiving **at least 3 points**)
1. Participated in protocol development and study design—1 point
2. Participated in writing the original manuscript—2 points
3. Reviewed a rough draft of the article with substantial suggestions and editing—1 point
4. Patient enrollment with complete data used for this study:
(a) 1–9% of patients in study with sufficient follow up data—1 point
(b) 10–29% of patients in study with sufficient follow up data—2 points
(c) ≥30% of patients in study with sufficient follow up data—3 points
5. Participated in grant writing for study group funding—2 points
III. Authorship order will be determined by Executive Committee based upon:
• Good standing in JUPITER
• Amount and quality of manuscript drafting/edits/review
• Number of patients entered into the registry
IV. If you wish to perform a research sub-study utilizing the multicenter database, you need to complete a "Research Proposal Form"
• The form will be reviewed by the investigators and coordinators at Cincinnati Children's Hospital and the Hospital for Special Surgery to assure:
– No conflict with existing study proposals
– Compliance with the "FINER" criteria: Feasible, Interesting, Novel, Ethical, and Relevant
• If the study is approved, all participating Investigators in the group will be notified about the study. Centers with clean and complete data related to the topic will be invited to participate
• Preliminary authorship criteria and order will be established with a PI and one other representative from the proposing institution and a PI only from other participating institutions. The tag line "JUPITER study group" will be added to the list of authors on all publications

JUPITER-Version 1—February 2018

centers. Posttreatment outcome assessment was to be performed at 6, 12, and 24 months, including assessment of function, activity level, health-related quality of life, patellar stability, knee motion, and complications.

44.3.2 Clinical Assessment

In JUPITER, a draft assessment tool for data collection was developed. The initial tool was relatively lengthy, and multiple conference calls were made by the group of investigators to help further refine and develop the protocol. Critically, it was felt that it was important to simplify the initial form to minimize the burden on the investigators located at multiple sites. A simplified assessment tool also allows for improved patient compliance and reproducibility of data. Validated tools are important to use to make sure the data appropriately reflects desired outcome evaluation; we use Pedi-IKDC, Kujala, HSS Pedi-FABS, Banff Patellofemoral Instability instrument 2.0, and KOOS Knee survey. Initially, the assessment tool was a paper document; however, specialty society grant funding was received allowing investigators to use a Web-based system for data collection and management (Oberd™, Columbia, Missouri USA), and the study transitioned to this during the course of enrollment. Other investigators have used REDCap (Research Electronic Data Capture), which is a free, research data management system sponsored by Vanderbilt University and supported by the National Institutes of Health. The advantages of using electronic databases are multiple: (1) can allow for remote col-

Table 44.2 JUPITER institutions and investigators

Institutions	Investigators
Cincinnati Children's (Coordinating Center)	Shital Parikh, PI Eric Wall
Hospital for Special Surgery (Coordinating Center)	Beth Shubin Stein Dan Green Sabrina Strickland Peter Fabricant
Boston Children's	Yi-Meng Yen Dennis Kramer Benton Heyworth Matthew Milewski
Columbia University	Charlie Popkin Lauren Redler
Mayo Clinic	Diane L. Dahm Todd Milbrandt Aaron Krych
NorthShore University Health System	Jason L Koh David Roberts Verena Schreiber
OrthoIndy	Jack Farr Kosmas Kayes
Oregon Health Sciences University	Jackie Brady Dennis Crawford Matthew Halsey
Ohio State University	Robert Magnussen
Texas Scottish Rite	Henry Ellis Philip Wilson
University of Minnesota/TRIA	Elizabeth A. Arendt Marc Tompkins
University of Missouri	Seth Sherman

lection of PRO by any electronic media, (2) can send automated updates related to follow-up and incomplete data, and (3) can help with data analysis due to advanced data output functions.

> Protocol development was conducted by a team, and clinical and radiographic assessment tools were selected. Assessment is aided by use of Web-based data collection and management for clinical outcomes and centralized radiographic evaluation. Data is collected centrally.

44.3.3 Radiographic Evaluation

Regarding radiographic evaluation, an extensive amount of time was spent in investigator meetings to develop standard radiographic methods. Given the relative complexity of radiographic evaluation (e.g., for the measurement of anterior tibial tubercle–trochlear groove distance on MRI) in the JUPITER study, it was important that training to establish common standards for imaging evaluation was necessary. Training was performed by using a standard set of images reviewed at in-person meetings and also distributed electronically. Ultimately, concerns still remained about variability in image interpretation across sites, and part of the way through enrollment, the investigators were able to obtain sufficient funding to have images electronically sent to a central site to be interpreted by a specifically trained team of musculoskeletal radiologists. For this aspect, REDCAP was used to collect and store the data. This evolution to centralized radiographic evaluation and repository for image assessment is expected to improve consistency of this aspect of evaluation and also reduced the time commitment of individual sites. If there is a potential for significant variability in radiographic interpretation, then centralized imaging analysis at a single site is preferred.

44.3.4 Centralized Data Repository

The data from multiple sites must be collected and aggregated at a centralized site. This data management can be time-consuming and expensive; however, it is critically important to be able to have the data in a secure location that remains accessible to appropriate researchers. This typically requires financial support, which can be either provided by the sponsoring institution or external grants.

44.3.5 Funding and Grants

Once the research protocol has been established, it is often valuable to submit for research grants from various funding sources. In many cases, the initial pilot study is self- or institution-funded; however, extrapolating the study to multiple sites requires an additional level of funding. In most nonindustry-sponsored research, support for

research personnel at each individual site is typically that site's responsibility. Individual sites may have limited resources to participate in the trial, and obtaining grant support may be critical to active site enrollment. Investigators should be active in pursuit of local support as well as from larger organizations. Using data from the pilot study, the JUPITER executive group successfully submitted an application for research funding from one of the orthopedic specialty societies to support patient-reported outcome data collection. Additional grant funding from university/departmental research funding allowed for single-site radiographic review. Ultimately, it is hoped that the JUPITER experience will allow competition for NIH-funded grants that provide multi-institutional support.

Grant funding plays an important role in supporting the research project.

44.3.6 Institutional Review Board (IRB) Approval

In a clinical trial, institutional review board (IRB) ethics approval for human research must be obtained. This can often be a complex and time-consuming effort. The process is even more complex when multiple sites are involved, and data must be transmitted between different institutions. In JUPITER, the pilot site had developed an IRB-approved protocol that served as a template for IRB protocols at the other sites. This speeded up site-specific protocol development; however multisite approval resulted in delays in initiating study at several sites, for many months in some cases. In the future, the authors would consider utilizing a central IRB for the trial for as many sites as possible, which would hopefully speed gaining the appropriate ethical approval for multiple sites and decrease time to full enrollment. Recently, the NIH has released a policy on using a single IRB for multicenter trials, which may help with this process. This can be found at https://grants.nih.gov/policy/clinical-trials/single-irb-policy-multi-site-research.htm.

Regulatory issues (such as IRB issues and safety monitoring) can be challenging and delay site initiation. The use of a centralized IRB may be helpful but may require extensive back and forth with a primary site. Standardized protocols and procedures help with consistent and safe data collection.

Notably, audits from IRB during trials are common, and one has to organize and prepare everything such that complete transparency and responsibility could be proven at any point during the study. Recently, one of our coordinating centers had their IRB audit the entire JUPITER study. There were some omissions and some minor lapses, which have since been corrected.

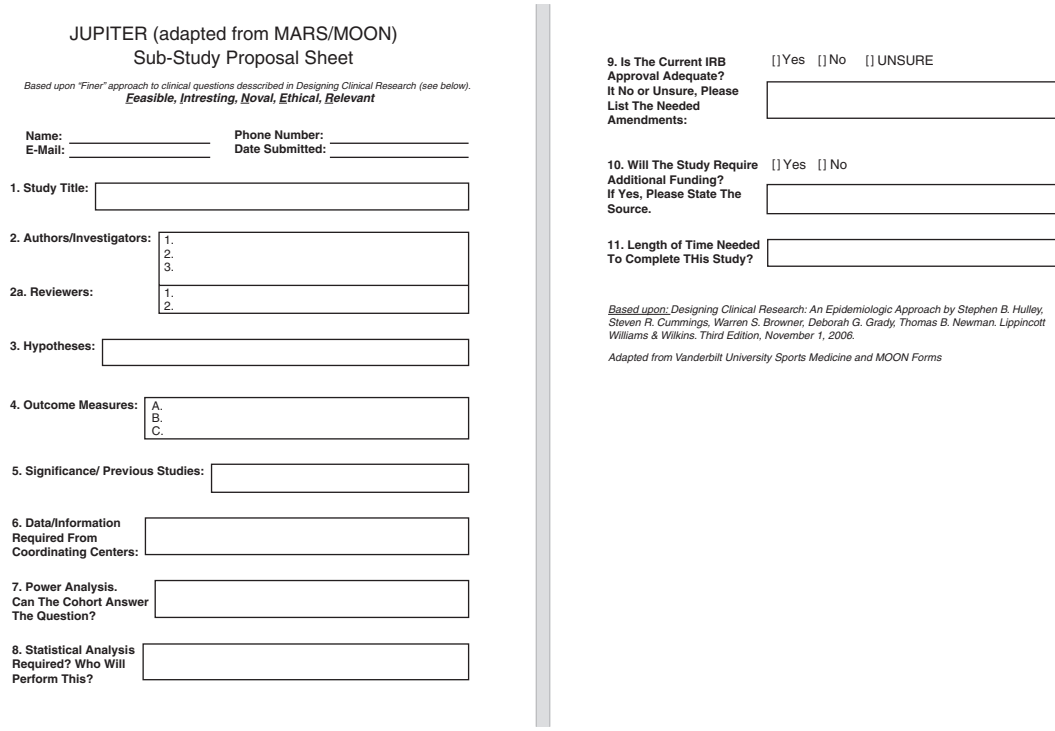
An additional component of any clinical trial for publication in most major journals is registration with a clinical trial database. In the United States, www.clinicaltrials.gov is free and is the most commonly used registration.

44.3.7 Data Safety and Monitoring Board

As part of most clinical trials, a data safety and monitoring board is often required by funding agencies. The purpose is to maintain subject safety and data integrity but also to recommend cessation of the trial for ethical reasons (e.g., failure to meet enrollment or interim analysis showing dramatic differences). Protocol deviations are also evaluated. Research coordinators at key sites can help monitor compliance and are in charge of data cleaning. Periodic audits at each institution would help ensure complete data collection.

44.3.8 Standardized Operating Procedures/Training

Once a clearly defined research protocol and standardized assessment tools have been created, a manual of operating procedures (MOP) can be developed. This can help with creating



JUPITER (adapted from MARS/MOON)
Sub-Study Proposal Sheet

Based upon "Finer" approach to clinical questions desscribed in Designing Clinical Research (see below).
Feasible, Intresting, Noval, Ethical, Relevant

Name: _____ **Phone Number:** _____
E-Mail: _____ **Date Submitted:** _____

1. Study Title:

2. Authors/Investigators: 1. 2. 3.

2a. Reviewers: 1. 2.

3. Hypotheses:

4. Outcome Measures: A. B. C.

5. Significance/ Previous Studies:

6. Data/Information Required From Coordinating Centers:

7. Power Analysis. Can The Cohort Answer The Question?

8. Statistical Analysis Required? Who Will Perform This?

9. Is The Current IRB Approval Adequate? It No or Unsure, Please List The Needed Amendments: [ ] Yes [ ] No [ ] UNSURE

10. Will The Study Require Additional Funding? If Yes, Please State The Source. [ ] Yes [ ] No

11. Length of Time Needed To Complete THis Study?

Based upon: Designing Clinical Research: An Epidemiologic Approach by Stephen B. Hulley, Steven R. Cummings, Warren S. Browner, Deborah G. Grady, Thomas B. Newman. Lippincott Williams & Wilkins. Third Edition, November 1, 2006.

Adapted from Vanderbilt University Sports Medicine and MOON Forms

Fig. 44.2 JUPITER Sub-Study Proposal Sheet

standardization of enrollment and assessment. It will also help with training of research personnel. During the course of enrollment, it is not unlikely that there may be some change of research personnel at several of the sites where they may lose their research coordinator. A manual can assist in helping sites when research assistants or coordinators change. Training can be performed either in person, through documents, or by phone or online. Regularly scheduled phone or in-person meetings can keep personnel updated.

44.3.9 Research Questions

During the course of the trial or afterward, it is common to have additional research questions emerge. How to prioritize these questions and choose which ones to pursue can be difficult. It is best practice to develop criteria for the governing committee to evaluate these proposals. The FINER (feasible, interesting, novel, ethical, relevant) criteria [4] are often used to evaluate proposed research questions. A modification of this has been used by the MOON (Multicenter Orthopedic Outcomes Network) and MARS (Multicenter ACL Revision Study) groups, and this was adopted by the JUPITER group to determine which studies to pursue (Fig. 44.2).

44.3.10 Presentation and Publication

One of the potentially more challenging aspects of multicenter trials is how results will be presented and published. It is best to address questions of authorship and publication credit and priority before study initiation and certainly before publication submission. We feel that authorship should follow International Committee of Medical Journal Editors (ICME) criteria, which is actually required by many of the premier medical journals. Authorship must meet several criteria, including significant contributions to study design, execution, assessment, and

writing and editing. Up-to-date criteria with additional detail are provided online at http://www.icmje.org/recommendations.

Research questions are evaluated using the FINER (feasible, interesting, novel, ethical, relevant) criteria. Presentation and publication guidelines should be developed in advance so that there is a clear understanding about authorship.

With respect to multicenter trials, authorship questions become more complex. Fortunately, several existing models for publication authorship and priority exist. Historically, many journals limited the number of named authors; however, with the advent of electronic publication and indexing, it has become easier to credit multiple authors on a publication. In many cases, papers will be published with several principal authors and the rest of the investigators credited as a group, with each individual investigator's name listed and searchable electronically. For JUPITER, authorship criteria were first discussed among the executive committee and then circulated among the larger group of investigators for comment. Criteria were modeled after the PRISM (Pediatric Research in Sports Medicine) group criteria and included assessment of active participation in data collection, as well as ICMJE criteria. To encourage multiple author participation, it was recommended that principal authors from different sites be listed on each research paper. Publications would be submitted to the group for editorial review and input as required by ICMJE.

44.4 Execution

44.4.1 Communication and Coordination

Throughout the conduct of the trial, it is critical to keep investigators and sites engaged in the research process. Too often, multicenter trials lose focus and energy since geographic distance and limited face-to-face engagement can result in investigator focus being directed elsewhere. JUPITER has successfully addressed this with regularly scheduled monthly conference calls that include clinical research staff (such as research assistants and coordinators) as well as investigators. During these calls, critical operational updates can be provided to the group and especially the personnel that are typically performing much of the day-to-day enrollment and data collection activity. There is also time for investigators or coordinators to bring up and discuss questions or areas where further clarification is needed. Summary minutes provide valuable information that can provide updates to an existing standardized protocol.

Communication and monitoring are critical to study progress. The use of regularly scheduled meetings improves communication and consistency; transparency about site-specific trial milestones helps monitor progress and encourages continued investigator participation.

Another successful tool has been to send out frequent regular score cards indicating progress to specific trial milestones, including investigators and sites, IRB status, and their current enrollment numbers. Subject visit and follow-up compliance are additional measures to be potentially added. The score cards serve several functions. First, they update the entire group of investigators as to the current status with respect to overall enrollment in the project. It is motivating to see the progress being made across the different locations as the trial progresses. Secondly, it allows the group to identify and learn from the sites that are most successful in terms of enrollment. Finally, it can spur some friendly competition and additional engagement to increase enrollment activity.

Face-to-face group meetings are also valuable to engage the group and continue active participation. We have tried to have face-to-face meetings at major medical conferences where it is anticipated

that there will be multiple investigators available. This can be challenging since not all investigators will be at every conference, and even if investigators attend the conference, they may have other commitments that limit their availability. Some authors have suggested to address this issue, separate investigator meetings are helpful; however, this can be a significant time and expense burden.

44.4.2 Data Monitoring

Enrollment, ongoing participation, and continued follow-up need to be monitored during the course of the trial. In this way, accurate progress to milestones can be assessed and communicated. We recommend significant transparency throughout this process as there can be loss of trial participation at every step. Digital forms can significantly help in monitoring progress.

44.5 Publication

As previously noted, discussion of authorship and priority should be performed as early as possible, including in the planning phase of the study. Multiple papers typically emerge from a multicenter trial. Commonly, a methods paper is a first publication and is based primarily on the research protocol. Elements of the main paper (particularly the introduction and methods) can be written prior to obtaining complete data and analysis. Secondary studies can also be proposed prior to trial completion and evaluated as previously discussed using FINER criteria.

> Multiple papers often arise from a multicenter trial. Authorship should follow guidelines. Initial components of paper writing (such as the methods section) can proceed in parallel with study recruitment. Authors should respond in a timely fashion.

The data analytics team should be notified when collection is complete so that they can begin to work in a timely fashion. Appropriate involvement of a biostatistician in planning the study design can make the analytical work more straightforward when the data has been collected. Trying to make sense of a pile of data after the fact without appropriate preparation can be challenging.

Paper drafts should be completed promptly, and coauthors should commit to providing rapid review and comments to the drafts, hopefully within 1–2 weeks. The main author/s should assess and appropriately incorporate these comments and prepare for submission. Determination of the appropriate journal to submit to should involve the lead authors.

Following submission, it is not uncommon for high-quality journals to either reject or request significant revisions to the article. The lead author/s should take the responsibility to respond to comments and revise the article for resubmission or submission to a new journal. It is appropriate for the group to celebrate after publication!

44.6 Tips for Multicenter Trials

Multicenter trials have unique challenges in that there are additional layers of complexity due to the multiple parties involved. It is critical to have a highly motivated core group of investigators that are committed to the project. An important aspect is the inclusion of an epidemiologist/statistician in study design and planning. To simplify the process, centralization is helpful. A central IRB may help decrease time to initiation of the trial in multiple centers. Centralized image analysis can improve consistency and decrease investigator burdens. Centralized data collection is critical to a successful trial.

It is important to be aggressive in seeking out funding opportunities. Multicenter trials typically require funding of the central coordinating site and also funding of resources at each of the contributing sites. Early preparation and submission of grants can help significantly in getting the research off the ground.

Tips for Multicenter Trials

- Unique challenges due to multiple parties.
- Include epidemiologist/statistician in study design and planning.
- Centralized IRB and data collection and analysis are helpful.
- Funding can be challenging but is often needed to support the central coordinating site.
- Take advantage of others' knowledge; the MARS/MOON and PRISM multicenter trial groups were very helpful in setting up JUPITER.
- These are complex, so anticipate challenges to enrollment.
- Communication and transparency maintain consistency and encourage investigators.
- Multicenter trials have unique benefits—not only to answer research questions but also to build collegiality and collaboration with investigators from multiple institutions.

It's very helpful to take advantage of opportunities to discuss with other groups that have initiated and successfully executed multicenter trials. In orthopedic sports medicine, the MARS and MOON groups have been very helpful and have been generous with their advice. The pediatric PRISM (Pediatric Research in Sports Medicine) group has also provided models of how to address some of the questions about authorship.

One should expect that there will be difficulties in conducting the study. Sites may have difficulty with IRB approval or after beginning may lose their coordinator. It is helpful to anticipate this so build in additional sites and/or time for recruitment and enrollment.

Communication is critical throughout the process, for several reasons. It maintains the interest of geographically separated investigators. It improves the creation and conduct of the trial. Transparency with score cards regarding completion of trial milestones also is important to engage ongoing enrollment.

Finally, multicenter trials are critically important for medicine, but they are also a great way to build collegiality and friendship with investigators across multiple institutions. A critical part of medicine is shared knowledge, and working together with like-minded, interested investigators builds the community of scholars that contributes to the advancement of clinical care.

Clinical Vignette/Case Study

The JUPITER (Justifying Patellar Instability Treatment by Early Results) study is an example of how a multicenter trial is initiated, developed, and executed. After an initial pilot study at a single institution, a small group of investigators was established to develop a protocol. Additional investigators were invited to participate, and the protocol was further developed, including the decision to centralize data collection and analysis. Input was received from investigators from other multicenter studies, such as MOON, MARS, and PRISM. It was decided to use the FINER criteria for evaluation of proposed research questions, and authorship guidelines were developed as well. Some challenges were encountered with obtaining local IRB approval at several sites, and others had difficulty with research coordinator recruitment, but ultimately enrollment goals were able to be achieved, and longitudinal data is in the process of being gathered.

Take-Home Messages

- Multicenter trials have unique advantages in obtaining large numbers and increased generalizability of results but have coordination challenges.
- Careful research design, including an epidemiologist/statistician, is critical.
- Centralized data storage and analysis can improve consistency.
- Other orthopedic multicenter trials and their investigators are a valuable resource.

- Challenges are likely to arise during the IRB process and conducting the study, so additional leeway should be included for possibly delays.
- Communication between investigators is critical.
- Multicenter trials can build collegial relationships and further collaborations.

References

1. Askenberger M, Janarv PM, Finnbogason T, Arendt EA. Morphology and anatomic patellar instability risk factors in first-time traumatic lateral patellar dislocations: a prospective magnetic resonance imaging study in skeletally immature children. Am J Sports Med. 2017;45(1):50–8.
2. Christensen TC, Sanders TL, Pareek A, Mohan R, Dahm DL, Krych AJ. Risk factors and time to recurrent ipsilateral and contralateral patellar dislocations. Am J Sports Med. 2017;45(9):2105–10.
3. Chung KC, Song JW, Group WS. A guide to organizing a multicenter clinical trial. Plast Reconstr Surg. 2010;126(2):515–23.
4. Hulley SB, Cummings SR, Browner WS, Grady DG, Newman TB. Designing clinical research: an epidemiologic approach. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2006.
5. Jaquith BP, Parikh SN. Predictors of recurrent patellar instability in children and adolescents after first-time dislocation. J Pediatr Orthop. 2017;37(7):484–90.
6. Koh JL, Stewart C. Patellar instability. Orthop Clin North Am. 2015;46(1):147–57.
7. Krych AJ, O'Malley MP, Johnson NR, Mohan R, Hewett TE, Stuart MJ, et al. Functional testing and return to sport following stabilization surgery for recurrent lateral patellar instability in competitive athletes. Knee Surg Sports Traumatol Arthrosc. 2018;26(3):711–8.
8. Sanders TL, Pareek A, Hewett TE, Stuart MJ, Dahm DL, Krych AJ. High rate of recurrent patellar dislocation in skeletally immature patients: a long-term population-based study. Knee Surg Sports Traumatol Arthrosc. 2018;26(4):1037–43.
9. Tompkins MA, Arendt EA. Patellar instability factors in isolated medial patellofemoral ligament reconstructions—what does the literature tell us? A systematic review. Am J Sports Med. 2015;43(9):2318–27.
10. Vavken P, Wimmer MD, Camathias C, Quidde J, Valderrabano V, Pagenstert G. Treating patella instability in skeletally immature patients. Arthroscopy. 2013;29(8):1410–22.
11. Weber AE, Nathani A, Dines JS, Allen AA, Shubin-Stein BE, Arendt EA, et al. An algorithmic approach to the management of recurrent lateral patellar dislocation. J Bone Joint Surg Am. 2016;98(5):417–27.