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Best Practices for Budget Estimations

Site Enablement League

Budgets Working Group

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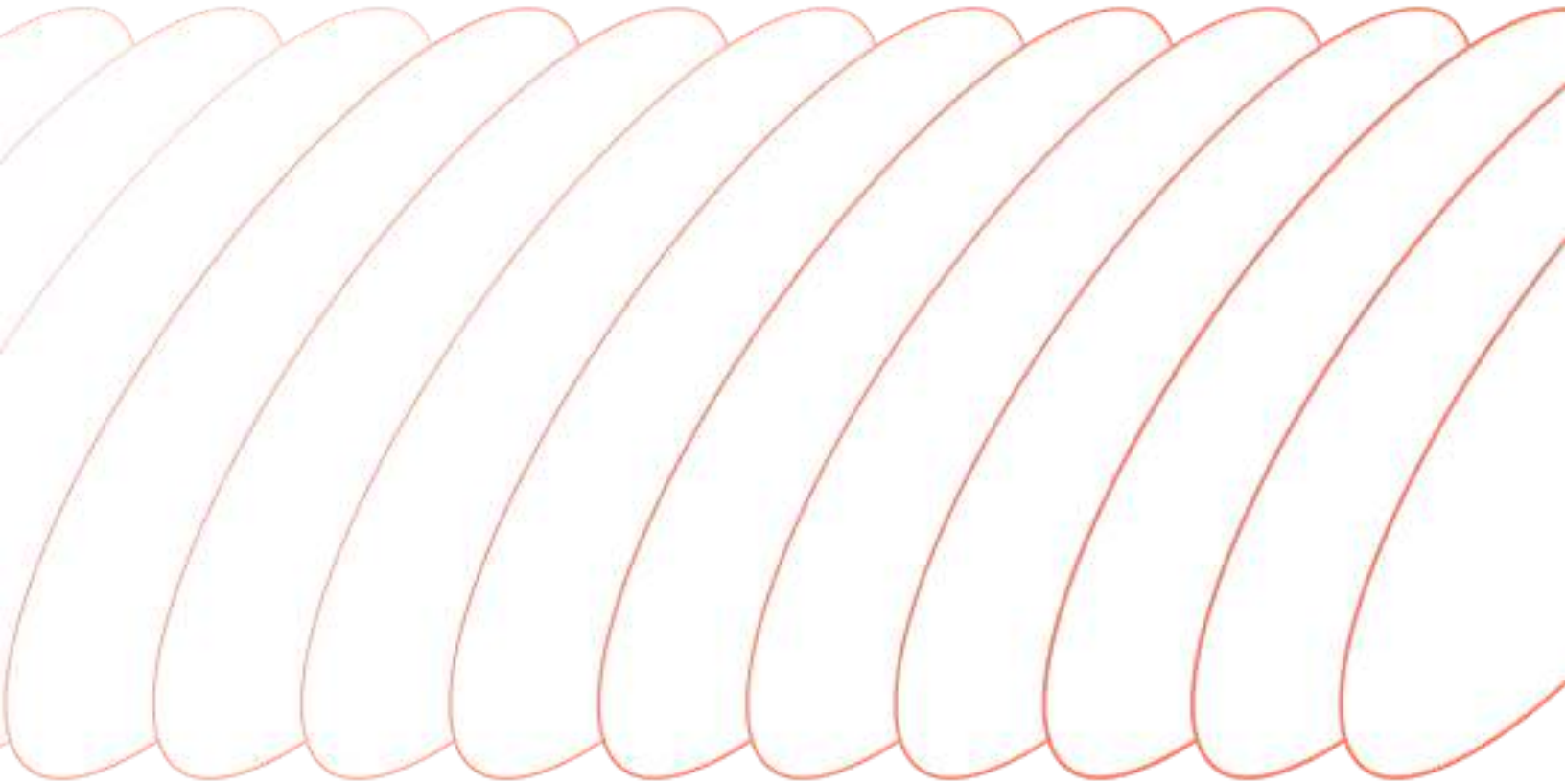

About this document

The clinical trial startup process is complex and involves many stakeholders. This document provides best practice recommendations for Budget Estimations from the Budgets Working Group of the Site Enablement League. By implementing these best practices, stakeholders can improve startup success rates, reduce timelines, and enhance overall trial efficiency.

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Introduction

The process of building a clinical trial budget can be daunting for someone new to the task. The procedures and hospital/clinic costs must be accounted for, of course, but the operational aspects of the protocol must also be considered or the budget will not cover the cost of actually implementing the protocol. These operational aspects include the staff TIME and EFFORT required to operationalize the protocol in a compliant way while also maximizing patient enrollment, retention and data quality. Estimating the time and effort actually requires a deep understanding of the protocol requirements, which is often overlooked or not well understood.

The goal of this document is to educate all stakeholders on the budget estimation process, identify common pitfalls, and suggest best practices for improving the process. If all stakeholders understand each other's perspectives, improving transparency in the process, then collaboration can be improved.

To assess a clinical trial budget, the responsible person must review each activity in the protocol with as much granularity as possible to understand if that activity is a Procedure or Hospital cost and/or if there is an operational component. The budget costs are then built around these detailed activities. The initial budget is a forecast, of course, and may have to be adjusted later as the study progresses.

Procedure and Hospital Costs

Some costs in a protocol are the same for any study:

- Tasks, tests, activities, or procedures that have a CPT code for hospital procedures and professional fees
- Money paid out to others for research services for protocol requirements/tasks that are NOT covered by CPT code, such as pharmacy services, imaging review (RECIST criteria assessment), etc.

These costs are often more obvious in the protocol and easier to assess than operational costs. Whether they are considered research costs or billable costs depends on Medicare Coverage Analysis and other factors (See the Best Practices for Budget Justifications document for more details), but the cost for each activity is objectively based on clinical care billing codes and costs.

Many sites document and maintain these costs in a Research Chargemaster, which:

- Is agreed on with their hospital or any facility that they use for protocol activities
- Covers anything with a CPT code - actual tests, procedures and physician charges
    - Ensure that the chargemaster DOES cover physician time to there is no double billing for physician time

The chargemaster does NOT cover research staff time and effort for these tests/procedures.

As a tangible example; if a study requires a 6 Minute Hall Walk Test, the test itself has a CPT code for billing (94618), but that does not cover the cost of the research coordinator coordinating the test with the clinical staff, coordinating any specific protocol requirements for the test, getting the patient from the waiting room to bring them to the testing location, ensuring protocol compliance during the test, etc. The time for those activities is not covered by the clinical reimbursement and is the operational cost that should be included in the study budget.

Operational Costs

Operational costs cover fixed research costs and the research staff time and effort for ALL protocol activities, including those that are also billed for procedure and hospital costs. The operational costs of a protocol are less obvious and vary from site to site because they capture the TIME and EFFORT required to run the study. The time and effort costs account for a larger portion of the budget than the procedure/testing costs (typically captured in the research chargemaster), and they are very often underestimated, which leads to challenges for sites in covering their costs. They are typically the most negotiated items in a budget because they are often not explained or justified and because they vary so much from site to site.

Fixed operational costs include costs such as:

- Standard research fees (IRB submission fee, monitor change fee, etc.)
- Dry ice fees, freezer storage fees, etc.
- Technology fees (CTMS, ISF, etc.)

Time and effort operational costs include things such as:

- Time spent scheduling visits and procedures, especially imaging or other testing
- Time spent with participants during study visits - escorting them around the site, waiting with them, checking on them, etc.
- Time spent collecting and uploading images, shipping samples, entering data, etc.

Many sites use a “Master Fee Schedule” to document fixed operational costs and a “Rate Card” to establish and document standard time/effort rates for different staff personas: RC, PI or Sub-I, administrative staff, etc. This terminology is not consistent across the industry and some sites may have different names for these tools.

It is important to note that this operational time and effort should be budgeted separately from site overhead cost. Overhead expenses should include the cost of doing business, such as rent, utilities, printers, central IT infrastructure charges, etc. For many sites, especially academic medical centers, overhead costs are dictated by the parent organization and are non-negotiable.

There is not alignment about this across the industry. Some sites, typically smaller sites, budget for the overhead cost to support their staff. This makes it difficult to compare budgets from site-to-site and can create more scrutiny and skepticism during budget negotiations. Furthermore, it makes it very difficult for any site to analyze a study budget to understand where they are making or losing money. A better approach for the industry would be for overhead to cover the cost of doing business and for operational costs to be documented as time/effort per study activity.

Budget Templates

Sponsor/CRO template budgets are sometimes written to show a cumulative payment per visit without detailing specific payment amounts for the required visit tasks.

Example: Visit 1 = $300/patient

Lumping sum payment amounts make it hard to estimate the costs for the actual tasks and effort that go into a visit. The budget should be expanded to include details on each line item, including time and effort and justification for those details. It should be the first step a site takes when they receive a consolidated budget template. Sometimes this happens at the sponsor level before the template is sent to sites, in which case the template might look like:

Example: Visit 1 includes (per patient):

- EKG, $50
- Vitals, $50
- Inclusion/exclusion criteria review, $50
- Informed consent, $150

Estimating Operational Costs

The idea of deeply analyzing a clinical trial protocol to predict all logistics and estimate time and effort during budget negotiations likely feels very daunting. To make the process more complex, the person negotiating the budget is often not responsible for any actual trial execution, meaning that they need to spend time collaborating with research staff to understand the time and effort requirements. This study specific planning and problem solving requires operational input and knowledge of site-specific workflows. It's very common to underestimate the time spent on logistics and administrative details, especially if the activity details are not clear or have not yet been provided by the sponsor or vendors. Although this task can be overwhelming, it is necessary to ensure that costs are covered during study execution.

These steps will help establish a process for the assessment:

- Consult with the staff who will be doing the work to support this process
    - They will know the operational details better than anyone and can help make sure nothing is overlooked
- Evaluate the protocol and all associated manuals (lab, pharmacy, imaging, etc.) to identify ALL protocol tasks (administrative and clinical)
- Consider the way the tasks are completed:
    - Do you have to train other departments/people?
    - Where do you have to go?
    - Who do you have to talk to?
- Analyze difference between standard of care and the protocol requirements
- Give time estimates for EACH person for EACH task (including very detailed steps like walking, redaction, uploading, copying, working with witness/LAR, oversight, etc.)
    - Include RC time, staff time, oversight time, etc.
- Estimate time for other hospital staff (pharmacy, lab, imaging techs, etc.)
- Do not negotiate subject costs until you have done medicare coverage analysis (for all qualifying clinical trials)
    - Refer to Medicare National Coverage Determination Guidance 310.1 to determine if this is a "Qualifying Clinical Trial"
    - If a trial does NOT meet Medicare's criteria for a QCT, then the sponsor is responsible for all costs, including:
        - Investigational product

        - Routine care associated with the trial
        - Procedures, tests, and monitoring
    - If a trial DOES meet Medicare's criteria for a QCT, then conduct a complete Medicare coverage analysis. Medicare may pay for certain costs associated with the trial, including:
        - Routine costs (Office visits, standard lab tests, items/services used to administer the investigational drug/device)
        - Care that is medically necessary or considered standard of care for the specific patient population
    - For pediatric studies NCD guidance and Medicaid coverage assessment should be completed
    - For quality management and consistency across studies, this documentation should exist for all studies even if you're sure it's not covered trial
- Ensure there is a way to include time/effort in invoiceable items
    - Example: Unscheduled visits/tests that are invoiceable, such as an EKG at an unscheduled visit, may have RC time/effort that needs to be invoiced

Getting Started

The working group discussed tactics that have been successful in starting and navigating this process:

- Develop a Master Fee Schedule and/or Rate Card for operational costs and use these on every negotiation for all sponsors:
    - Include standard institution startup fees for each study type/phase/TA
    - Include common administrative items and costs that are not study specific, such as pharmacy startup, lab startup, technology fees (ex: eReg, sample management software), etc.
    - Include standard time/effort rates for different staff personas: RC, PI or Sub-I, administrative staff, etc.
    - Revisit this list annually to ensure it stays up to date with increasing costs
    - Maintain this as an internal even if it is not shared with sponsors
- Share the Master Fee Schedule with the sponsor/CRO FIRST, before working on the rest of the budget, in case there are non-starters on the list for either party

    - Include any study-specific administrative/effort charges that might be unusual, if they have been identified, such as pharmacy or laboratory costs needed to meet protocol requirements
    - It's better to get to "NO" as fast as possible if that is a potential outcome
- For sponsors/CROs that do repeat studies at your institution, consider negotiating this as a master budget agreement with the sponsor to reduce negotiation time for each study
    - Remember to update the agreement if internal annual review results in changes
- Educate sponsors/CROs that costs really vary from site to site and with proper justification they should be accepted
    - This is more appropriate than using any "fair market value" assessment
- Thoroughly assess the TOTAL operational cost so you know what it is even if some costs are negotiated out or down during budget negotiations
    - This effort helps the institution assess profitability and allows for a sound financial decision to be made
    - The results of the assessment may also be used to identify and improve inefficient processes or areas where sponsors commonly underpay and costs exceed income
- Be professional and remember the goal is to cover your effort and be fiscally responsible on behalf of your institution
- Always provide justification for time and effort
    - See the Best Practices for Budget Justifications document from this working group for more information

- Establish an institutional SOP that explains that all research costs must be covered in order for the institution to accept participation in a clinical trial

Pro Tips

The working group shares important considerations and examples from their experience estimating time and effort required to run a protocol:

- Ensure that you account for complex visit logistics
    - Example: some tests occur only at one facility and the RC will have to spend time traveling to that site

    - Example: Sample shipment requires dry ice and the RC will have to go across campus to pick it up
    - Example: Long study visits that take all day for RC - waiting, walking, hospitality, etc.
    - Example: RC time walking across campus for a visit
- Consider if there is any variance across sites/facilities/locations
- Include time and effort for institutional/local system set-up effort
    - Example: CTMS, eBinders, recruitment sources, drug accountability forms, EHR source capture, pharmacy, etc.
- Remember to include all startup items
    - Feasibility, PSSV, SIV, budget creation, etc.
- Consider participant effort, costs (parking, lunch, etc.) and comfort (snacks for a long visit, etc.) when determining a fair stipend
- Consider the impact of regulations and institutional requirements that impact startup time, recruitment efforts, or visit logistics:
    - Example: New vendor training, new committees, new technology
    - Example: Patient parking locations that are far from the visit location and require staff to escort/assist patients to the visit
    - Example: DEI recruitment goals that require new recruitment efforts (geographic data, etc.)
    - Example: R3 requirements for sample tracking that require additional time/tools
    - Example: Startup time required to coordinate sample logistics to obey a state rule that samples shipped have to go to a CLIA certified lab in the same state

The working group also shares some items that are commonly overlooked:

- Time for administrative tasks
    - Examples: copying, scanning, uploading, redacting, scheduling, shipping, filing, collecting signatures, creating source, visit preparation, etc.
- Participant-facing time
    - If a staff member needs to remain with a participant for the duration of a visit that is time and effort that must be accounted for
- PI/Investigator oversight time (ICF review, AE review, CRF signoff, etc.)
- RC interactions with the pharmacy
    - Drug accountability, drug transport, shipment reconciliation, etc.

    - Which physical pharmacy location has the drug - does the research staff need to walk there to get the drug?
    - Are there specific pharmacy requirements that limit where the drug can be held?
- Staff training (SIV, clinical staff training, additional protocol, vendor/technology, etc.)
- Communications
    - Engagement Calls, IT support for tech, document/log submission to sponsor/CRO staff
    - Site management calls
- Cleaning patient rooms between visits
- Monitoring preparation time
- Remote monitoring visit time
    - Still have prepare and follow up from the visit
    - Any “Over the shoulder” time required during the visit
- CRA turnover - time/effort to onboard a new monitor
    - Introduce staff, tour the facility, get system access, re-monitoring fees, etc.
- Technology fees
    - Study websites that they maintain, recruitment services, eReg, eConsent, eSource, etc.
    - Sponsors sometimes push back or limit this budget item, so be sure to explain how they benefit from this technology to justify the cost
- Administrative work for imaging/samples
    - Deidentifying, downloading, uploading, shipping, storage, preparation, transport, shipping (dry ice), etc.
- Sponsor vendor IT security review, set-up, training and education
- Data entry/data cleaning/query resolution
    - Could be invoiced above a certain threshold or could be included in visit time/effort, should scale with visit complexity
    - Special requests for database lock, interim data analysis, etc.

These examples illustrate how deep protocol knowledge and understanding of site operations are critical to correctly estimating the costs required to run a protocol. This can be complex and overwhelming, especially for someone with no expertise in protocol execution. Fortunately, the output of this operational analysis is content that can be continuously reviewed and reused by documenting the decisions in a living document. Use the results to CREATE A PLAYBOOK! Document what is successful, note any tips or tricks that help, and also

note what to watch out for and things that do not work during negotiation. Often this institutional knowledge resides in one or two humans and is not shared or documented.

Note that sponsor and CRO staff can learn a LOT about the operational aspect of the study protocol by reviewing a detailed site budget. There are likely operational aspects of a protocol that are more complex or time consuming than intended. The working group encourages sponsor and site staff to be open minded to the site perspective on operations. Protocol compliance is the shared goal and sites need to execute the logistics to make that possible.

Budget History

Often sponsors/CROs assume that a new study budget will be the same as a previously negotiated budget, but the reality is that operational costs depend on:

- The study phase
- The study complexity (therapy area, study design, etc.)
- The study type (observational vs. interventional)
- The facilities, staffing model, and workflows of each site and the department/team at that site running this study
- The billing rates for various clinical trial staff depending on seniority and experience

If sponsors/CROs want to use a site's historical budget as a starting point for a new study, they should recognize that things change and be flexible, taking the time to consider new justifications, annual fee increases, changes in teams, study complexity differences, etc.

Conclusion

Improving industry knowledge of how to conduct budget estimations is key to ensuring costs are covered for study sites AND increasing the speed of budget negotiations. With proper documentation and justification, these detailed budget estimations have the power to decrease budget negotiation cycles because sponsors/CROs can be more confident in accepting budget requests knowing WHY the budget request is needed.

Finally, parties on both sites must realize that budgets must be renegotiated if/when new information about study conduct is received. This often occurs if site feasibility or site startup happens before all protocol/pharmacy/laboratory/vendor documents are finalized [Reference: https://www.sciencedirect.com/science/article/pii/S2451865424000383?via%3Dihub].

Controversial Ideas

As an industry, we might collectively consider if the dollars we save in lengthy negotiations are worth the time we lose for enrollment and the resulting delays in study completion. WCG data from 2022 shows that budget negotiation time is not improving and there is still a big differential between the starting point and final budget (*www.wcgclinical.com/insights/clinical-trial-budgets-current-trends-questions-answered-part-1/*).

If the final budget ends up being significantly higher than the starting budget it begs the question of if the starting point for the budget should be higher, which would likely reduce the negotiation time. Time lost during lengthy budget negotiation delays recruitment/enrollment start and leaves less time for sites to enroll. A mindset shift toward considering a more mutually agreeable budget starting point and less negotiation cycles would dramatically increase startup times in the industry. If sponsors/CROs are willing to consider this change, and sites are better at estimating their time/effort and justifying their requests, we could make huge progress in reducing startup times and decreasing study durations.