Cooperative Group Financial, Organizational and Management Analysis

Clinical Trials and Translational Research

Advisory Committee

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Judith A. Hautala Ph.D.

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Project Goals

- Gain a comprehensive functional understanding of the financial, organizational and management structure of the Clinical Trials Cooperative Groups

- Identify organizational and funding strategies to improve operational efficiency and cost effectiveness

- Identify improved practices for shared strategic management of a complex goal-oriented research enterprise

Clinical Trials Cooperative Group Program

- Clinical trial infrastructure support grants to a nationwide network of 10 Clinical Trials Cooperative Groups
  - Four adult multi-disease, multi-modality Groups
  - Six disease, modality or population focused Groups
- Late phase efficacy trials
  - 100 trials, 20,000 patients
- Early phase exploratory trials
  - 200 trials, 4,000 patients
- Patients enrolled at Cancer Centers, other academic medical centers and community oncology practices
- Awardee institutions range from major universities to specifically created not-for-profit organizations

Cooperative Group Financial Structure

- Infrastructure support for designing and managing trials
  - Operational functions (administration, regulatory, protocol development/management, audits, QA, training, etc.)
  - Data management and statistical analysis
  - Scientific leadership
  - Specimen banks, reference laboratories and clinical reviews
- Reimbursement to sites for enrolling and managing patients on trials
  - Member Institutional U10 awards
  - Member site infrastructure subawards
  - Per case reimbursement

Project Scope

- Internal Group Organizational Structures
- Cross-Group Financial/Organizational Comparison
- Financial Structure
  - Unit Costs
  - Institutional Cost Sharing/Pro Bono Time
  - Non-NCI Funding
  - Indirect Cost burden
- Accrual Patterns and Funding Models
- Common Services and Tools
- Application and Review Processes
- System Governance

Analysis Methodology

- Mapped requested direct cost grant application budgets to a functionally-based Common Budget Outline framework
- Site visits with individual Groups
  - Assumptions underlying budget requests
  - Activities conducted under each budget category
  - Rationale for budget allocations and reallocations
  - Institutional cost sharing and pro-bono investigator time
  - Non-NCI funding – sources, amounts and uses
  - Group organizational and membership structure
  - Impact of common services and tools
  - Application and review processes
- Interviews with NCI and CTSU staff
- NCI trial, accrual, membership and award data

Key Data and Findings

- High-Level Cross-Group Budget Allocation
- Unit Costs
- Institutional Cost Sharing/Pro Bono Time
- Non-NCI Funding
- Accrual Patterns

High Level Cross-Group Budget Allocation Analysis

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High Level Functional Cost Categories

Infrastructure Costs	**Accrual Costs**
Group Leadership	Member Site U10
Group Administration	Non-U10 Member
Trial Operations	Per-Case Reimbursement
Special Funds	
Statistics/Data Management	
Scientific Leadership	
Scientific Services	
Travel	

Grant Application Analysis

- Mapping based on detailed analysis of budget forms, budget justifications and position descriptions
  - 1000's of pages
  - 1-20 funded institutions
  - 100-500 funded individuals
  - Budgets organized by institution not by function
- Mapped two applications per Group
  - Most recent competitive renewal
  - 2007 non-competitive renewal (2008 for NCCTG)
- Performed Cross-Group analysis based on percent allocation to various budget categories in non-competitive year

Infrastructure versus Accrual Costs

- Eight Groups allocate 50-60% to infrastructure costs
  - Budgets range from $15-30M
- Two Groups allocate ~75% to infrastructure costs
  - Low accrual costs due to low accrual volume
- Groups with small number of trials and low accrual volume inherently less cost-effective due to fixed infrastructure costs

Infrastructure Cost Allocation

- Percentage allocation to various cost categories remarkably consistent across the Groups
  - Wide range of budgets, institutional settings, nature of trials, accrual
  - Budgets constructed with percent time for 100-500 individuals
- Statistics and data management largest category at 37%
- Core services averages 21% but highly variable
- Scientific leadership 5-10% with two outliers
- Administration, trial operations, travel each 8-10% on average
- Group leadership 3.5% on average
- Special funds 2-7% if requested

No evidence for major <u>differential</u> cost efficiency or inefficiency across the Groups

Unit Cost Analysis

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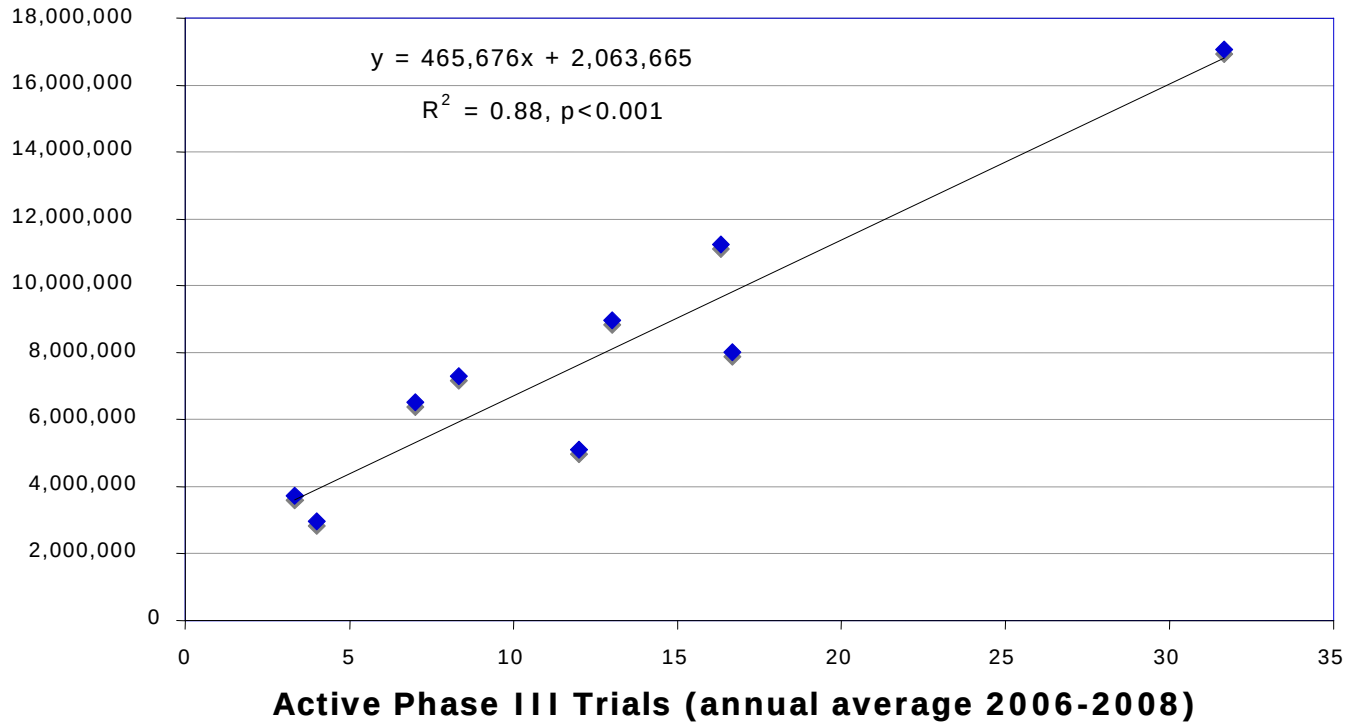
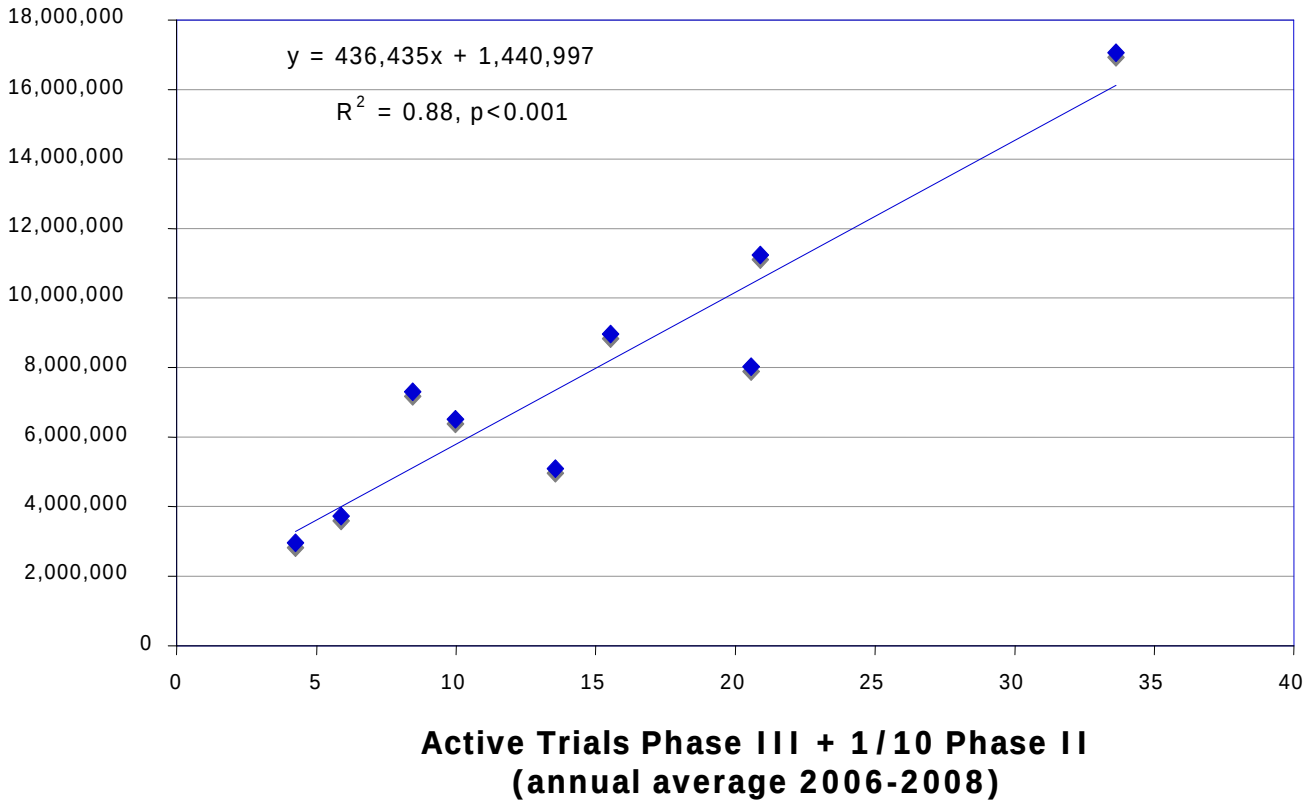
Correlation of Infrastructure Cost with Trial Activity



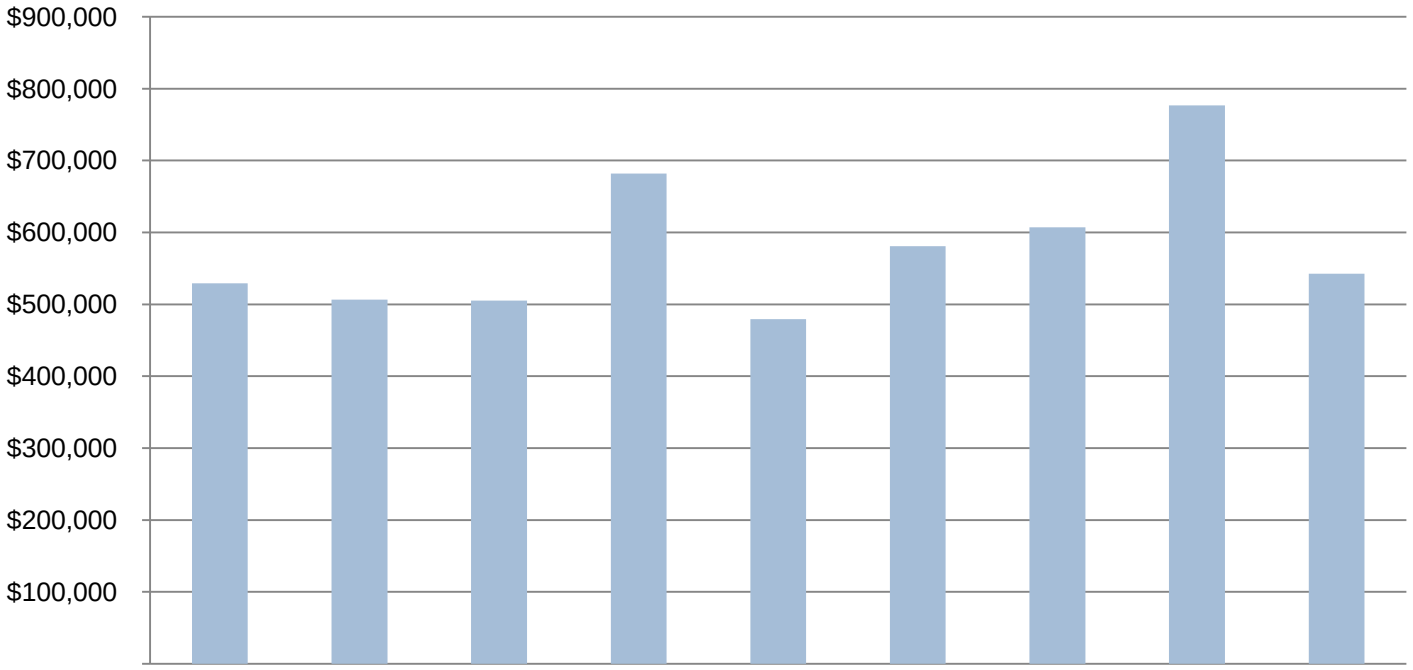
- **Strong correlation of infrastructure costs with number of Phase III trials led by the Group**
- **Weaker correlation with total trials led by Group or total Lead Group accrual**
- **Phase II trial activity does not substantially impact overall infrastructure costs**

Correlation of Infrastructure Cost with Trial Activity



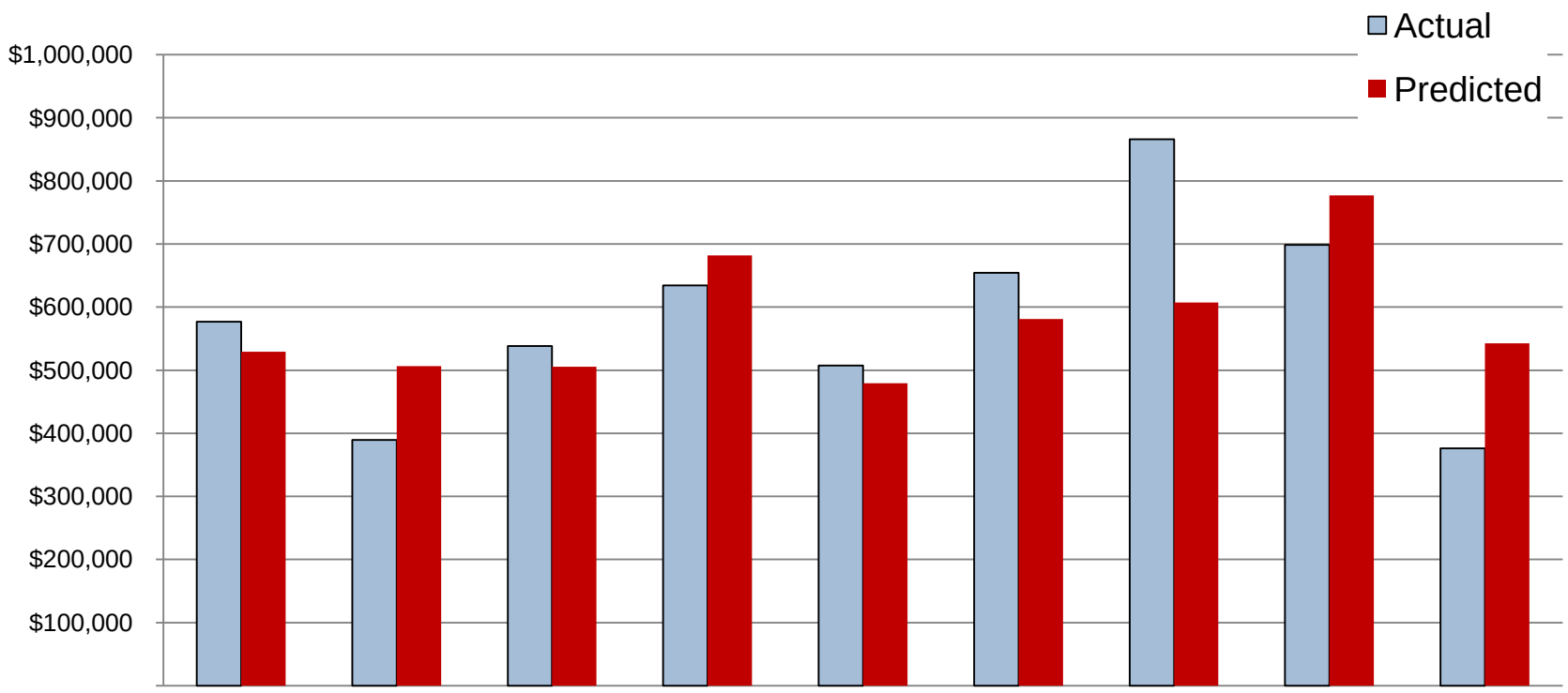
- **Regression model predicts**
  - **$1.5M fixed cost to establish and operate a Group**
  - **$450K variable cost per trial**

Predicted Infrastructure Cost per Trial from Regression Model



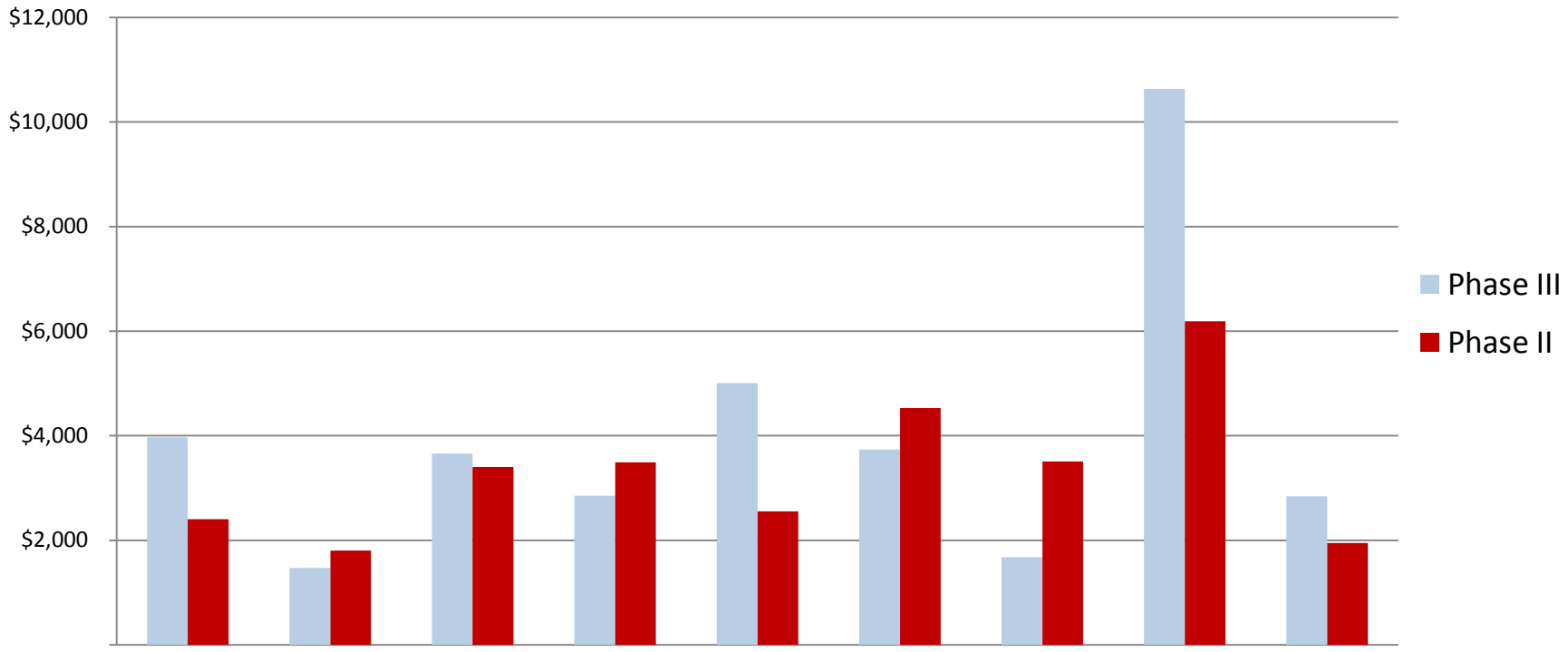
- **Seven Groups cluster in $500-600K range**
- **Two high outliers at $680K and $775K due to small trial volume**

Predicted versus Actual Infrastructure Cost per Trial



- **Actual 2007 costs allocated by assuming that Phase III trial costs 10 times that of a Phase II**
- **Actual cost per trial within 10% of that predicted for six Groups**
- **One high outlier at $866K actual cost per trial, 42% above that predicted**
- **Two low outliers at ~$400K actual cost per trial, 23% and 31% below that predicted**

Infrastructure Cost per Lead Group Accrual



- **Infrastructure costs allocated by assuming that Phase III trial costs 10 times that of a Phase II**
- **Per accrual cost highly variable**
- **On average, each Phase III and Phase II accrual represents ~$3000 in infrastructure costs**

Analysis of Institutional Cost Sharing and Pro-Bono Time

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Scientific Leadership Time Commitment Estimated by Groups

- Scientific Committees
  - Chairs 20% time
  - Vice-Chairs 5-10% time
- CRA/Nursing Committees
  - Chairs 15% time
- Administrative Committees
  - Chairs 5-10% time
- Committee Members
  - 1% time commitment from each active member
- Protocol Chairs
  - 10% time for Phase III trial
  - 5% time for Phase II trial

Cost Sharing/Pro-Bono Time Calculation Methodology

- Committee Leadership
  - Calculated total FTEs based on estimated time and number of committee Chairs/Vice-Chairs
  - Subtracted FTEs supported with U10 funds
  - Multiplied non-supported FTEs by $190,000

- Committee Members
  - Determined median number of members per committee across Groups – 24 members/committee
  - Calculated total FTEs per Group based on 1% time
  - Multiplied total FTEs by $175,000

- Protocol Chairs
  - Calculated total FTEs based on estimated time and average number of trials open per year in 2006-2008
  - Subtracted FTEs supported with U10 funds
  - Multiplied non-supported FTEs by $190,000

Scientific Leadership
Cost Sharing and Pro-Bono Time

- 77% of the time required for Scientific and Administrative Committees and Protocol Chairs provided pro-bono by investigators or covered by their home institutions

- Individual Groups range from 50-98% cost shared/pro-bono time

- Translates into $27.7M of “donated dollars” including fringe and indirect costs

- 17% of the annual total cost NCI Cooperative Group budget

Accrual Institutional Cost Sharing

- Analysis of four accrual funding categories
  - Institutional U10 awards supporting accrual
  - Group U10 sub-awards to sites to support accrual
  - Per case reimbursements
  - CCOP accruals

- Total funding supplied to sites by these four approaches was calculated and compared to the estimated real cost at $6000 per accrual

- Difference represents the dollar value of the institutional cost sharing in support of accrual

Total Accrual Cost Sharing

Accrual Type	Total
Institutional U10 Funded Accrual[1]	$ 5,431,043
U10 Sub-Award Funded Accrual[1]	$ 11,769,316
Per Case Reimbursement Accrual[2]	$ 51,836,000
CCOP Accrual	$ 19,120,000
Total Cost Sharing	**$ 88,156,359**
Total Accrual Cost[3]	$143,256,000
Cost Sharing Percentage	**61.54%**

[1]Main Members only
[2]Main Member and Affiliates
[3]Total accrual at $6000/case.

Total Institutional Cost Sharing and Pro-Bono Time

Component Activity	**Total Costs**[1]
Group Leadership	$ 787,312
Committee Leadership	$ 7,279,875
Committee Members	$ 14,148,750
Protocol Chairs	$ 6,229,461
Statistics/Data Management	$ 1,500,000
Accrual	$ 88,156,359
Total	**$118,101,757**

[1]Labor costs include 25% fringe and 50% indirect

Non-NCI Funding Analysis

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System Wide Non-NCI Funding

- $56M annually in non-NCI funding for Cooperative Group trials
  - $41M from industry
  - $6M from philanthropy
  - $9M from parent institutions, state funds, etc.
- 25% of annual Cooperative Group cash expenditures from non-NCI sources
- Groups highly variable, generating from 0% to 50% of their funding from non-NCI sources

Overall Cooperative Group Funding Structure

Funding Component	**Total Costs**[1]
Cooperative Group Awards	$161 M (45%)
CCOP Accrual Support	$ 10 M (3%)
CTSU Contract	$ 18 M (5%)
Accrual Cost Sharing	$ 88 M (24%)
Pro-Bono Investigator Time	$ 28 M (8%)
Industry Support	$ 41 M (11%)
Philanthropic Support	$ 6 M (1.5%)
Other Support	$ 9 M (2.5%)
Total	**$361 M**

[1]Direct and indirect costs

Accrual Analysis

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Accrual Distribution Analysis

- Main Members and their affiliates provide 75% of accrual
- Cancer Centers and their affiliates provide 40% of accrual
- Main Members with infrastructure funding contribute 3-4 times more accrual
- 60% of Main Member/CCOP networks contribute 90% of accrual
  - Low-accruing sites represent ~50% of sites (primarily affiliates and CCOP components)
  - Financial and operational burden of maintaining low accruing sites is minimal

Cross-Group Membership

- Institutions rarely members of only a single Group
- Large institutions generally Main Members of CALGB, ECOG or SWOG and one or more specialty Groups
- ~60% of Cancer Centers are Main Members of four or more Groups, all but two are Main Members of more than one Group
- High accruing CCOPs are members of at least one large adult medical oncology Group and one or more of the specialty Groups

Cross-Group Accrual

- "Within Group" accrual is often "cross-Group" accrual from the site's perspective due to cross-Group membership

- Concept of cross-Group accrual only truly relevant to three large adult medical oncology Groups

- ~50% of CALGB, ECOG and SWOG accrual is to trials led by other Groups (2006-2008)

Focus of Major Recommendations

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- Internal Group Organizational Model
- Accrual Funding Model
- Subcommittee H Review Criteria
- System Governance

Currently under analysis by NCI management

Potential involvement of Clinical Trials Advisory Committee Working Group