Funding Patient-Reported Outcomes (PROs) Assessment in Cancer Clinical Trials

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Costs of Quality-of-Life Research in Southwest Oncology Group Trials

Workshop on Quality of Life in Clinical Cancer Trials

2nd NCI-Sponsored Meeting for Cooperative Groups: Progress and Future Expectations

Bethesda, MD

March 1-2, 1995

Moinpour CM. Mon J Natl Cancer Inst 1996;20:11-16

Determination of Effort/Cost

- For 1 month in January 1995, key personnel were asked to keep a log of effort on trials with PROs
  - Studies could be in development, open, or closed but analyses occurring
  - Protocol development, monitoring of forms submission, and data analysis were emphasized

Table Footnotes

***Costs in 1994 dollars**

****Salaries include either a 22.5, 25, or 28 percent fringe benefit rate depending on position**

*****The PRO percentage (6%) of monthly operating costs for the Statistical Center includes secretarial and administrative staff salaries, two supply categories, postage, phone, and photocopying. PRO-related travel by the psychologist represents average monthly travel and does not involve the 6% calculation.**

Basis for 6%: There were 5174 Phase I,II,III and other (e.g., cancer control) patient registrations for 1994, of which 331 (SWOG trials + non-SWOG trials) had PRO registrations [(331/12)/(5174/12) = .06].

Moinpour, 1996

Estimated PRO Personnel and Operating Costs/Month

COST ITEM	COST/MONTH
PERSONNEL**	$5494
Operations Office Staff (15%)	$ 516
Statisticians/Psychologist (10 & 13%/25% = 48%)	$3089
Programmers (17%)	$ 968
Data Technicians (24%)	$ 514
Data Coordinator (12%)	$ 407
OPERATING EXPENSES***	$1810
DIRECT COSTS/MONTH	$7304

Moinpour, 1996

Estimated total costs of PRO data per PRO patient* (averaged over life of current and closed studies)

Direct PRO costs per month	$ 7,304
No. of PRO registrations/month	$ 28
Direct costs per PRO registration ($7304/28)	$ 261
Total PRO costs per month	$12,417†
Total costs per PRO registration ($12,417/28)	$ 443

* Costs in 1994 dollars.
† Total cost = 1.7 (direct cost).

Moinpour, 1996

Overestimate or Underestimate of Costs?

- Minimized data analysis effort because newly activated trials
- Did not overestimate protocol development because this is a continuing yearly effort with slight variations from year to year
- Overestimate because mostly companion studies requiring full protocol development
  - Subsequent trials were integrated into main protocol
- Underestimate overall because CRA time not included in estimates
- Does not include “donated” time of PRO Study Coordinators
- Variable costs: Each trial different: $\Rightarrow$ need for different PROs & assessment schedules
  - Length of questionnaires and number of assessments

Bruner Group Survey: Open CTEP trials w/ PROS

Group	Number	As a % of all open CTEP trials
ACOSOG	2	26-50%
ACRIN	7	26-50%
CALGB	2	1-5%
COG	5	1-5%
ECOG	8	6-10%
EORTC	40	26-50%
GOG	5	11-15%
NCCTG	18	51-75%
NCIC	23	51-75%
NSABP	5	51-75%
RTOG	18	51-75%
SWOG	6	6-10%

Summary: All Interviewed Groups

- Challenge: Spread limited resources across a number of trial responsibilities
- PRO effort is "bundled" with effort required for all clinical trial data
  - Only limited Group data on % effort required for including PRO assessments
    - Bruner Cooperative Group Survey: 92% said no estimate of the cost to conduct PRO research
- Variation in extent and types of outside funding used
- Extent to which CTEP and CCOP grants used to fund PROs varied by Group

Cooperative Group A

- CCOP grant
  - Statistician effort for cancer control trials including those with PRO data
  - Data management for cancer control trials including those with PRO data
  - Supports statistical effort for cancer control trials with or without a PRO
- Summary: CCOP grant primary funding source for statistical and data management for cancer control studies including PRO data

Cooperative Group A

- **CTEP Grant:**
  - **Data Management (Operations Office)**
    - **“Bundles” data entry/scanning, quality control, effort for treatment trials: clinical & PRO data**
      - **Programming for PRO or clinical outcomes not funded**
  - **Statistical support (Statistical Center)**
    - **For treatment trials, all statistical effort “bundled”: clinical & PRO data**
  - **CTEP funding for Committees**
    - **5% Vice Chair for Outcomes & Health ServicesCommittee**
    - **Covers treatment and cancer control research**
- **Summary: 2 CTEP grants fund data management & statistical effort for treatment trials**

Cooperative Group A

- 40 active trials: 19 include a PRO (48%)
- External funding (non-CCOP/CTEP)
  - Grants (1 trial with PRO)
    - Foundation
      - Supports FTE for trials but PRO not specified
    - Disease Funders Collaborative
      - PROs and institutional reimbursements supported but not specific FTE
  - Industry (1 trial)

Cooperative Group A

- **Institutional reimbursement for trials with PRO**
  - **CCOP grant if CC credits**
    - **CCOP institutions receive CC credits**
    - **Non-CCOP institutions receive $1000/full CC credit**
  - **If no CC credits, no payments**

Cooperative Group B:

- CCOP grant
  - CCOP grant: Data Center
    - Data Control Tech (primarily scanning/verification)
    - Data Coordinator (quality control)
  - Budgets “bundle” data entry/scanning, quality control, programming effort
    - Perception that PRO data takes more time, especially when there are every-cycle assessments
  - Summary: CCOP grant support for PRO/cancer control data management FTE is small but primary source

Cooperative Group B

- CCOP grant (cont.)
  - 100% of the Statistical Center CCOP budget is for cancer control/PRO FTE
    - Designated %FTE for 3 statisticians: cancer control
      - Contribute additional FTE to CTEP treatment trial effort
  - Behavioral scientist PRO FTE "bundled" with cancer control
    - Current time allocation: 35% cancer control
  - Summary: CCOP grant primary funding source for PRO/cancer control statistical/behavioral science FTE

Cooperative Group B

- CTEP grant
  - Major funding source for treatment trial data operations
  - Statistical support requested for treatment trials
    - Statisticians analyze treatment trial PRO data with assistance from cancer control statisticians
  - Behavioral scientist FTE: None

Cooperative Group B

- **Use of external funding (non-CCOP/CTEP) for PROs**
  - **Grants**
    - **DOD grant (Telephone counseling intervention)**
    - **U10 grant (3 elderly treatment trials with baseline PROs & pharmacokinetic studies): 1 currently open**
    - **R01 funding for molecular epi trial with epi risk factors questionnaire: open**
    - **Supplemental funds to CTEP & CCOP grants ($$ for institutions to cover a long fu period for PROs): closed**
    - **Small foundation grants for special PRO data projects (closed), and to fund CRA time in a limited institution study (open)**

Cooperative Group B

- **Pharmaceutical company funding**
  - **Of 9 active trials with a PRO:**
    - **2 funded with industry $$**
      - **1 open and accruing**
      - **1 closed to accrual, analytic effort ongoing**
  - **In general, attempt to obtain pharmaceutical $$ to supplement data operations, data analysis, and institutional reimbursements**

Cooperative Group B

- **Institutional Reimbursements for PROs**
  - **CCOP grant if CC credits**
    - **CCOP institutions receive CC credits**
    - **Non-CCOP institutions receive $2000/full CC credit; $200/.1 CC credit**
  - **If no CC credits, no institutional reimbursement for either CCOPs or non-CCOPs**
  - **CTEP grant does not fund institutions beyond treatment reimbursement/patient**
  - **Seek pharmaceutical $$ to support institutional PRO effort**
    - **1 hour for Nurse/CRA time for each PRO assessment**

Cooperative Group C

- **Cancer Control and Health Outcomes Committee has 4 subcommittees**
  - **Quality of Life Subcommittee Chair funded by CTEP U10 grant**
    - **Funds Chair of QOL Comm (25%FTE)**
    - **Funds "cadre" member of QOL Comm**
      - **Performs services for "QOL Centralized Service" for Group**
  - **Health Services Subcommittee Chair funded by CTEP and Foundation $$**
  - **100% FTE PRO data manager/interviewer funded by CTEP grant**

Cooperative Group C

- CCOP grant does not provide funding for PROs except through
  - Cancer control credits [see below]
  - Some support for Symptom Intervention Subcommittee and Cancer Control and Health Outcomes Committee Chairs

Cooperative Group C

- 80 – 100 studies open at any time
- Successful grant funding effort
  - At least 3 trials funded by foundation or R01 support
  - 3 funded with pharmaceutical support
  - 3 Symptom Intervention studies with foundation or industry $$ (1 study has both types)
  - PROs included even if no outside funding but constant effort to obtain outside funding

Cooperative Group C

- Institutional support for PRO effort
- Funded by both CTEP and CCOP grants
  - If CC credits, CCOPs receive credits; non-CCOPs receive per case $$ reimbursement from CCOP grant
  - If no CCOP credits, non-CCOPs paid from CTEP grant; CCOPs don't receive credits or $$
    - Try to obtain industry funding to pay CCOPs when no CC credits
  - CTSU pays $250/case for PRO companion studies for non-CCOPs

Cooperative Group D

- CCOP grant does not fund PRO effort at central office
- CTEP grant funds Behavioral & Health Outcomes or PRO research
  - 3 statisticians
  - Lead statistician budgeted 30% FTE for all Behavioral & Health Outcomes (BAHO) Comm studies
    - E.g., Functional measurements (arm function), breast cosmesis studies, menses records, cardiac
    - PRO effort ranges from 30-70%
  - 10% effort for BAHO Chair

Cooperative Group D

- PRO “Compliance Officer”: 40% FTE
- Time spent by regulatory, nurse (protocol development, telephone resource for institution staff), and MDs at Operations Office

Cooperative Group D

- CCOP credits fund institution staff time supplemented by industry funding if available
- When no industry funding, most trials with PRO conducted only in CCOP institutions
- Industry funding used to supplement about 30% of trials with PROs

Other Funding Contexts

Cross-Group Harmonization Effort: Group Payments for Ancillary Studies

- Payment amount varies as well as which type of institution paid for cancer control/PRO activities
  - Mostly based on cancer control credits
  - Some Groups also pay non-CCOPs from CTEP grant
  - Not clear whether includes CCOP + non-CCOP institutions or CCOPs only
- Similar effort beginning for Group/industry funding guidelines

The Current Status of Clinical Research in the U.S.

ASCO Survey

Emanuel EJ, Schnipper LE, Kamin DY, Levinson J, Lichter AS. The costs of conducting clinical research. J Clin Oncol 2003;21:4145-4150.

ASCO Survey on Costs of Conducting a Clinical Trial

- 21 clinical sites surveyed re: time spent doing 13 activities involved in clinical research
  - Hypothetical Ph III trial for HRPC comparing placebo vs. new drug
  - 11 weeks of treatment; 12 months of follow-up
    - Total of 17 office visits
  - PROs included but # of assessments not clear & no specific time/cost reported
  - Data reported as estimates

ASCO Survey

- To examine accuracy of estimates, staff at 4 sites were “shadowed” to observe actual time
  - Conclusion: Staff underestimated time
  - But not “real time” because observing how staff spent time doing research BUT protocol of interest was hypothetical
- Average non-treatment cost was $2000/pt
  - 32% of hours spent on clinical trial activities
  - Substantial variability within & across practice sites and government vs. industry sponsorship

Costs of Doing Clinical Research

- **Survey data: in general, only 22% of oncologists have calculated the costs associated with doing clinical research**
  - **Bruner data above: only 8% (1 group) have attempted to see how much PROs cost**
- **Those who have either directly calculated the costs of doing clinical research or recently negotiated contracts for clinical research provide significantly higher estimates of costs:**
  - **Calculated costs: $3,400**
  - **Not calculated costs: $2,150**

Roche et al., 2002: CRA Time Spent in Clinical Trials Research

- Prospective study
  - 83 CRAs from 24 NCIC CTG sites
  - Tracked time for 30 consecutive days over 3 month period
  - 41 tasks with 156 subtasks
  - Examined 4 stages of trial activity
    - Protocol management
    - Eligibility & trial entry
    - Treatment
    - Follow-up
  - Included PRO assessments (questionnaire & diary)

Roche et al., 2002

- Reported substantial variability site to site (same trials) and within sites (different trials)
- Industry trials required more time
  - Not found in ASCO survey
  - Roche et al.: Industry trials increased workload at every stage and don't reflect supplemental funding
    - Rather "…that more money is rightly being paid for more work".

Roche et al.

- Mean time for PROs usually one of the lowest reported
  - Across tasks, usually ~¼ hour
  - Depending on stage of trial, much less than Special Procedures such as blood draws
    - Eg, during the treatment phase: 14.6 min vs. 35.9 min
  - PRO effort not commented on in paper

Funding PROs: 2006 PROACT Meeting: Conclusions

- Goal was to survey 6 cooperative groups: “Data” reported for 4
  - Very little detail re: specific costs associated with including PROs in clinical trials
  - Most data operations “bundle” FTE for traditional clinical and PRO effort
  - More specification re: statistician time but if so, usually “bundled” with cancer control effort

Funding PROs: 2006 PROACT Meeting: Conclusions

- Roche et al. data indicate that at the institution level, PROs not as time-consuming as other clinical outcomes such as special procedures (blood draws)
- ASCO survey indicates that don't really know what it costs to do a clinical trial
  - Under-estimates from respondents who had not based estimates on real-time calculations
- Similarly, no solid basis for cost of PROs
  - SWOG 1995 estimate reflects preliminary work