MACRO update, 2011 - 2013


Overall, MACRO is doing well, with steady investigator demand and enrollment performance, no ethical or regulatory issues, and a sound cost center model. Major developments include expansion into project management, temporary staffing, provision of Research Associate (RA) support at UPMC Mercy, and new investigator clients.

Challenges and opportunities include more timely billing for our services, occasional under-enrollment, positioning ourselves for tight economic times (e.g., lowering client costs, maximizing internal efficiency), and maintaining RA quality while expanding the program. Our overall goal is to become the “FedEx” of clinical trials at UPMC – a valued service that everyone uses due to good service and price, stable financials, and a top organization to work for.

Respectfully submitted,

David T Huang, on behalf of the MACRO Executive Committee

August 26, 2013

I. Performance data

Facilitate clinical research

From June 2011 – May 2013, MACRO enrolled 418 patients in 20 interventional trials and 637 in 12 observational studies for 32 PIs in 8 Departments/Divisions across 4 hospitals. Overall, these numbers represent a similar level of activity compared to the previous 2010-2011 report.

Ethics and regulatory compliance

As before, we have had no significant ethical or regulatory issues. In particular, we successfully managed our first FDA audit (for the Octapharma trial, Site PI – Alarcon). This audit occurred as we were the highest-enrolling site.

Fiscal soundness

As of August 2013, we have an annual budget of just over $1M (approximately the same as in 2010-2011), and $626K in fully executed cost center agreements for 20 studies for FY 2013 (we are behind on our billing – see below). These funds come from studies based in CCM (25%), Surgery (30%), Emergency Medicine (5%), and Medicine (ID, GI, Pulm, Gen Med, Renal) (40%). 70% of our funding is federal.

As of August 12, 2013, we are approximately net-neutral on the books, but are behind on getting our bills out the door. We have met with Kim Kushon and John Kellum, and will claim increased time from Dan Unikel until these bills are sent (anticipated completion date October 2013)
II. Major Developments

Facilitate clinical research

Project Management

In addition to her duties as Coordinator Director, Barb Early serves as the Project Manager for PAMPER (PI: Sperry, Co-PI: Guyette), a multicenter, DOD funded study of prehospital plasma administration for trauma, and has obtained IRB approval for waiver of informed consent for emergency research, and facilitated obtaining an IND from FDA for the use of prehospital plasma. PAMPER was recently described in the Pittsburgh Tribune. http://triblive.com/news/allegheny/4052301-74/plasma-research-blood#axzz2Tq2KGalQ

In addition to her new duties as Associate Coordinator Director, Mary Stefanick serves as the Project Manager for two multicenter ID studies (PI: Singh). The first is ongoing, and is a NIH funded trial comparing CMV prevention strategies; the second has completed enrollment, and is a physician initiated, industry sponsored study comparing fungal prevention strategies. MACRO is also assisting with the completion of the SNAP acute pancreatitis study (PI: Whitcomb), for which we provided partial coordinating center support.

Our expansion into project management resulted from, as always, investigator demand. We believe such work is a natural extension of our core focus (screening + enrollment of acute care patients), and is natural “next level” work for experienced coordinators such as Ms. Early + Ms. Stefanick. We also recognize that such expansion brings challenges, primarily increased workload for two vitally important individuals. We will carefully evaluate future project management opportunities as they present.

Temporary staffing

For 2 trials, both in Internal Medicine (Renal and GI), MACRO provided as-requested temporary coordinator coverage. We recently agreed to provide temporary coverage for another GI study. Clients were pleased with the support:

“I want to thank you (Dan Unikel) and Barbara both for your help during this transition time. The Macro Coverage has been indispensable in keeping our research studies on track and we appreciate your flexibility and support”

- Operations Manager, GI Division

Expanded Research Associate (RA) program, primarily at UPMC Mercy

Due to investigator demand (EM, NETT, Pipeline study by Chris Seymour), we have significantly expanded the RA program, primarily to add coverage for the UPMC Mercy Emergency Department. In 2010 we had 13 RAs for one study. We currently have 24 RAs that provide 24/7 screening for the Presbyterian + Mercy EDs for 7 studies in Neurosurgery, Stroke Neurology, and our core 3 Departments. RAs also do data entry, informed consent for noninterventional studies, and blood collection and processing. Several have been certified to do complex tests such as endotoxin assay and TEG.

To help manage this expansion, we have hired a RA graduate (who is currently applying to PA school) to take point on Mercy RA operations as a “Super-RA”. Stacy Stull continues to be the overall RA leader. The expansion to Mercy offsets our pulling out of the VA Oakland, which had newly required our nurses to become clinically certified at the VA.

New investigator clients
Neurology (Reddy) and Neurosurgery (Okonkwo), in conjunction with EM (Callaway) and a new CCM client (Shutter), recently hired MACRO for RA (Mercy and Presbyterian) and coordinator coverage (Presbyterian) for three studies within the NIH funded NETT trials network, as well as other brain injury biomarker studies. With NETT, and a new EM investigator client (Suffuletto), these activities represent a significant increase in EM studies with MACRO vs. in 2011.

New investigators to clinical research

We also welcomed 4 new investigators into their first forays into clinical research with prospective human subjects enrollment (Gomez, Daly, Seymour, Clermont), and are working towards more (Forsythe). For some, their work with MACRO was their first research experience. Although new investigators require more MACRO effort, only some of which is billable, we believe this effort is well worth it to further spread a culture of research, especially amongst junior faculty with significant clinical loads.

Efficiency

In June 2012 we designated 2 CRCs as “super-screeners”, to take advantage of these 2 individuals’ particular strength in screening. We recognize that sub-specialization of duties has its drawbacks, but thus far this move seems to have improved enrollment performance. We will continue to monitor monthly. We will also soon modify Research Rounds such that David Huang will accompany each CRC ~ monthly to their designated ICU, but in the context of routine CRC work.

Ethics and regulatory compliance

Novel technology-assisted consent mechanisms

In collaboration with the IRB and Dr. Ryan, we have worked out novel ways for informed consent that leverage the changing ways people communicate and use technology. Specifically, we have obtained approval for use of Apple Facetime videoconferencing when physician consent is required, and texting/emailing a picture of the signature page (as many have readier access to a smartphone than a fax machine). We are creating standard procedures for these processes. Vera Iouchmanov continues to take point on regulatory compliance.

Fiscal soundness

Cost to clients

We continue to revise our cost center model to lower costs to clients, while maintaining fiscal soundness. Specific revisions we’ve instituted are: a new lower cost administrative tier for minimal work studies, elimination of the monthly “access” fee for the RA service line, reduction of physician director stipends, reduction of coordinator ACRP certification test reimbursement. We also cautiously deploy RAs instead of CRCs where appropriate, to lower client costs.

<table>
<thead>
<tr>
<th>Fiscal Year</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRC $ / hour</td>
<td>55</td>
<td>61</td>
<td>64</td>
</tr>
<tr>
<td>RA $ / hour*</td>
<td>14</td>
<td>13</td>
<td>15</td>
</tr>
<tr>
<td>U. Pitt fringe benefit rates</td>
<td>33.6%</td>
<td>33.9%</td>
<td>41.5%</td>
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* plus $100/month access fee.

The above chart shows our main cost center charges over time since inception (The other 3 service lines are much smaller financially – Lab, CRC On-Call, Admin). As can be seen, the RA charge has remained stable. The $6/hour CRC increase from FY 2011 to 2012 was largely due to our decision to decrease projected CRC billable hours based on actual time card data accrued in the interim year (i.e., for our first cost center model in 2011, we underestimate billable hour time. For example, non-billable hours include administrative meetings,
both internal and study-specific, short-term disability, etc.). The $3/hour CRC increase from FY 2012 – 2013
was largely due to the large increase in Pitt fringe benefit rates.

Financial independence

For FY 2013, we will reduce Barb Early’s % effort billed to CCM from 20% to ~5%. We continue to fund 50% of
Dan Unikel’s time. CTSI provides a modest % effort to David Huang, which we have in effect used to fund an
administrative assistant.

Internal operations

Mission clarification

We will continue to focus on our core strength of screening and enrollment into acute care studies, but keep
our minds open to other opportunities. In 2012 we were asked to assist in an outpatient hypertension study.
We accepted the work, largely to bring in funds during a relatively quiet period, but having one coordinator
physically gone from Scaife, Monday – Friday, negatively affected daily operations (call schedule, core group
dynamics and collaboration, etc.)

Human Resources

Two coordinators left (1 lost to the above outpatient study due to easier hours / no call, 1 left for a better suited
position), two new coordinators were hired, and a new administrative assistant (Meghan Buck) was hired to
help manage growing administrative needs. We also appointed our most experienced coordinator to a new
Clinical Coordinator Manager position (Mary Stefanick), to help with daily coordinator operations and be a
resource to new coordinators. The new Executive Committee now also meets bimonthly for efficiency, and
focuses on issues that affect all studies MACRO-wide. Significant synergy is achieved thereby (eg, posting of
PAMPER on DEM’s acute care research website, shared waiver of informed consent knowledge).

CTSI

We continue to be part of the CTSI clinical trials core. We also have recently asked CTSI to assist with basic
research teaching of our now much larger Research Associate (RA) program.

III. F/u to Challenges listed in previous Annual Report

Moving to electronic systems

We did not construct a management database as we could not find a suitable vendor. The administrative
assistant helps to compensate. We are working with a WPIC individual to create an electronic ED screening
system for the RAs. If this move from paper succeeds, we will consider soliciting a bid from this individual and
CRISMA for a database that covers other essential MACRO functions. In the meantime we have moved the
RA screening log to EXCEL files, and off of paper. We also participated in Chris Seymour’s sepsis EHR effort.

Visibility and “PR”

We have undertaken a variety of efforts to increase visibility, though impact is hard to measure. We have
received multiple positive responses regarding our quarterly newsletters, mostly created by the administrative
assistant. A draft “lease vs own”, “Who is MACRO?” brochure is attached; it is targeted to potential new clients.

Administrative processes + new investigators

We did finalize CCM “leftover funds” arrangements + did recruit multiple new investigators.
IV. Challenges + Future

Under-enrollment

For the first time in our history, we had significant difficulty with enrollment, in 2 trials (GRAIL, cellulitis trial), due to a number of factors (first PI trial in a new Division, incorrect choice of specialty for the PI). In response, we shifted GRAIL back to CCM and have since enrolled significantly more patients (currently in 2nd place for enrollment nationwide), and have redoubled our level of scrutiny before accepting a new study – in particular focusing on enrollment feasibility across multiple domains (PI access to patients, enrollment window, $, clinical and non-clinical barriers, etc.).

Lower client costs, while maintaining salaries and staff

We see project management and temporary staffing requests as the likely next phase of work that comes our way. We need to position ourselves such that we can nimbly take on such work, without harming overall operations.

We need a salaried employee financially between a CRC and RA. Thus, we will likely make our next hire a paramedic. We had good success with 1 in the past. We will also likely make the current “Super-RA” position permanent.

We will also further reduce non-salary expenditures, and consider accepting more well-funded industry studies. As we move to full financial independence, we will also need to reject thinly funded studies from investigators that require significant time.

Mission creep

We wish to build on our core strength, while staying open to new opportunities. We also wish to facilitate small, thinly funded studies, but not spend disproportionate amount of time doing so. Our approach for the coming year is to assess, at the Executive Committee level, new opportunities on a case-by-case basis.

Risks

Our RA expansion could harm quality. We have taken several measures to ensure quality control.

Our delay in getting bills out on time is a serious financial risk. We may need to hire Dan Unikel at > 50% for MACRO.

Future

Our overall goal is to become the “FedEx” of UPMC clinical research – a good product at a good price, steady financial performance, and a great place to come to work.
Appendix – MACRO brochure (DRAFT)

1. What is MACRO?

MACRO (Multidisciplinary Acute Care Clinical Research Organization) is a non-profit, University of Pittsburgh cost center, clinical trials group, run by the Departments of Critical Care Medicine, Surgery, and Emergency Medicine, and is part of the U. Pitt CTSI clinical trials core.

[ need logo ]

Our core service is provision of 24/7 screening and enrollment of acutely ill and injured patients. This is made possible by a group of dedicated coordinators (most RNs) and research associates (Pitt premed students), an experienced and expert coordinator director, multidisciplinary physician directors, and a dedicated financial accountant. We also provide regulatory and budget development assistance, as well as project management for a few studies.

Think of us as “leasing” coordinator services, with similar pros/cons to leasing vs owning a car.

2. What studies / investigators currently use MACRO?

Most of the studies we facilitate come from investigators in our parent departments. We also facilitate studies from Infectious Disease, GI Medicine, Neurology, and Neurosurgery.

3. What has been their experience?

From June 2011 – May 2013, positive comments we’ve received include:

- Dr. Nina Singh, Chief of Transplant Infectious Diseases, VA Pittsburgh Healthcare System: “I have had the opportunity to work as a PI with Mary Stefanick and Vera Iouchmanov for almost a year now. I wanted to let you know how outstanding these coordinators are. They are enthusiastic about their work, reliable, knowledgeable, and diligent. I have never had to repeat a task request to them. It is a pleasure and a privilege to have them on my projects.”

- Dr. Lou Alarcon, Medical Director, Trauma Surgery, Associate Professor of Surgery and CCM: “I just wanted to thank everyone for their extraordinary efforts on the PROMMTT trial. It was a real pleasure working with all of you. It was especially gratifying to work with the students, and I hope this experience has been rewarding for them and solidified their interest in bio-medical careers.”

- Dr. Alain Corcos, Medical Director, Division of Multisystem Trauma, UPMC Mercy, for helping Mercy maintain Level 1 Trauma certification: “We were told at our exit interview that research is no longer considered a "significant issue" for our program. Your contributions to that end cannot be overstated.”

We also have had negative comments (eg, simultaneous ED studies leading to temporary under-enrollment in one ED study), and always rapidly institute a corrective action plan.

4. Which investigators might use MACRO?

- Those that can benefit from our core service and strengths
- Prefer “leasing”
- Lack funds to hire a full-time coordinator, or
- Would prefer to "outsource" human resources, admin aspects of all / part of their research
• Want to be a Site PI, but lack infrastructure and/or knowledge
• Are new to clinical research that requires prospective human subjects enrollment

5. Which investigators might NOT use MACRO?

• Do not need 24/7 screening and enrollment
• Prefer “owning”
• Want direct oversight of their research coordinator
• Require a full-time coordinator

4. How much does MACRO charge?

As a U. Pittsburgh cost center, we charge the same rates for all clients. The bulk of the cost are $/hour charges for coordinator (mid 60s) and RA time (mid teens). You will only pay for hours of worked actually used. There are also administrative fees, that vary from nominal for simple studies to significant for multi-center, interventional, studies. We will work with you to figure out the most cost-effective way MACRO can aid your study, and can provide everything from minimal support to complete support. Eg, for some studies we only provide screening and notification of potential subjects, while for others we handle all logistical tasks including IRB, patient consent (when allowed – eg, for observational studies), blood draws, etc.

As when hiring a contractor for your house, if you do some work yourself, you can save funds, and then only hire the contractor for specific tasks. Or, you can ask the contractor to do it all. It’s the same with us. We will also track your monthly “burn rate”, so you can keep track of how your funds are being spent. Below, are four Figures to visually display how your study + MACRO would work together.
Components of MACRO Costs

In order to provide 24/7 coverage, costs are billed in three separate components. Fixed costs include administrative start-up costs and screening time. Per-subject costs are only charged when work is done on an enrolled subject.

**Per-Subject Costs**

**Fixed Costs**

When another study is also screening at some site, cost to each study goes down.

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Why do screening costs go down when there are more studies?

When RA’s or CRC’s are working on subjects, that time is per-subject cost billed to the individual studies.

Screening time is billed in equal portions to all studies that are screening at that site.

The remainder of every 24 hours is spent screening.

For example, four studies at a site will share equally the time spent screening.

If a new study starts, the share of screening hours billed to each study will go down. (And the time spent with subjects should go up).
Most studies have some fixed reimbursement per subject. Total revenue is directly proportional to number of subjects enrolled. Some studies have a small infrastructure or start-up payment as well.

MACRO budget will be favorable for a project if
(1) Orange Bar (per-subject revenue) increases faster than Red Bar (per-subject time expense), AND
(2) The study enrolls enough subjects to make break-even scenario.

The break-even number of subjects should be projected at the outset of the study.

When does MACRO make more sense than single study coordinators?

The key advantage of MACRO model is shared cost of on-call coverage and screening. When a single study employs enough coordinators to cover 24/7 or on-call time, the Blue Bar (screening) fixed cost will be higher. The Break-even number of subjects for a given study may be much higher.
5. How do I contact MACRO?

Clinical coordinator director: Barbara Early, MSN, CRC, earlybj@upmc.edu

CCM: David T. Huang, MD, MPH, huangdt@upmc.edu

Surgery: Jason Sperry, MD, MPH, sperryl@upmc.edu

EM: Clifton Callaway, MD, PhD, callawaycw@upmc.edu