Postmortem on a Non-Discussed NIH R01 Application:

Lessons Learned — the Hard Way

David DuBois, Ph.D.

Research and Professional Development Brown Bag Series
Institute of Health Research and Policy, University of Illinois at Chicago
April 16, 2019

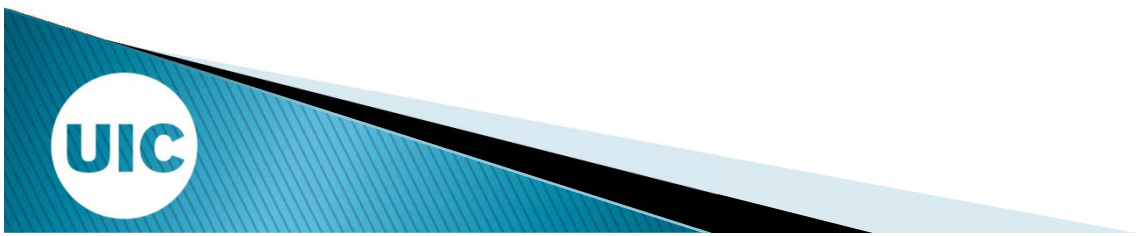
INSTITUTE FOR HEALTH RESEARCH AND POLICY

UIC

www.IHRP.UIC.edu

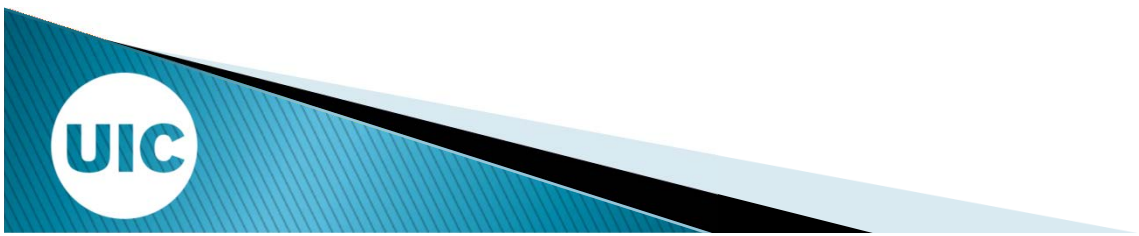
Background

- Extramural research funding is very challenging to obtain
  - Especially for **investigator-initiated research** that does not respond to a particular request for proposals or, if you are so fortunate, a specific request from a funder for you personally to submit a proposal on a given topic
    - For these kinds of unsolicited applications, for NIH you will likely be applying to a "Parent Announcement"
      - "Parent announcements are broad funding opportunity announcements allowing applicants to submit investigator-initiated applications for specific activity codes."
      - These are typically sponsored by many, but not all Institutes and Centers (ICs). In my case, I applied to the parent version of the R01 Research Project Grant Program Announcement.



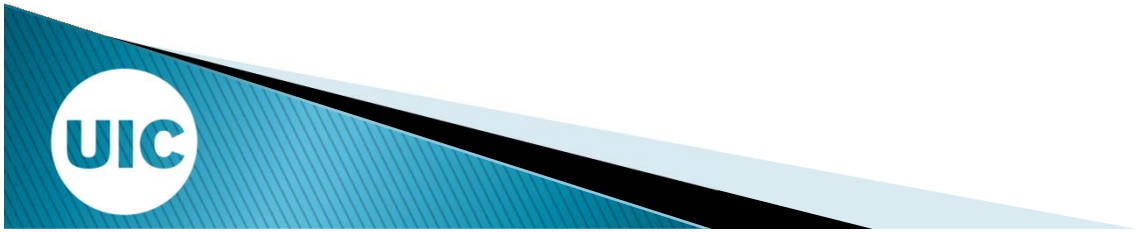
Background

- Essentially need to be selling reviewers and funder on **your idea**
  - topic and aims of research have great social significance
  - your idea and approach to studying it are novel and innovative
  - you have a sure-fire and scientifically (and ethically) sound plan to address the aims
  - you and your team are exceedingly well-qualified to conduct the research
    - you have just the place (environment) in which to do the research with all supporting organizations (e.g., study recruitment sites) fully on-board



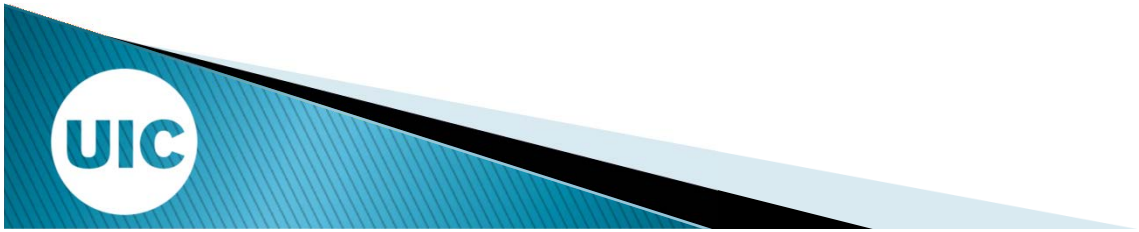
Background

- Obtaining NIH (and other extramural) funding usually requires 3 Ps
  - **P**ractice
    - Researchers who had received R01 awards in FY 15 were found on average to have submitted 5.1 R01 applications in the past 5 years
  - **P**ersistence
    - An application not funded upon the original submission has a much better chance of being funded upon resubmission
      - In 2015, the success rate for original R01 applications was 13.1%, whereas the success rate for resubmission applications was 33.5%.
  - **P**erspicacity
    - Important to be able anticipate reviewer priorities and concerns in preparing application
    - Equally, if not more, critical to be insightful and RESPONSIVE in resubmissions
    - Also, key to know when to "hold 'em" and when to "fold 'em" – that is, does it make sense to further pursue this idea, at least through the current funding mechanism



Background

- NIH proposals typically reviewed anonymously by 3 members of the Review Group (aka Study Section) to which proposal has been obtained
  - My proposal was assigned to the Community-Level Health Promotion study section
  - Reviewers assign "criterion scores" on 1 to 9 scale (lower is better; see next slide) for each of 6 core review areas:
    - **Significance**
    - **Investigator(s)**
    - **Innovation**
    - **Approach** (essentially methodology)
    - **Environment**
    - Written critiques note Strengths and Weaknesses for each area
  - Study Timeline, Protections for Human Subjects, Budget and Period of Support, and various other considerations (e.g., inclusion of women, minorities, and children) as applicable



Impact	Impact/Priority Score	Descriptor	Additional Guidance on Strengths/Weaknesses
High	1	Exceptional	Exceptionally strong with essentially no weaknesses
	2	Outstanding	Extremely strong with negligible weaknesses
	3	Excellent	Very strong with only some minor weaknesses
Moderate	4	Very Good	Strong but with numerous minor weaknesses
	5	Good	Strong but with at least one moderate weakness
	6	Satisfactory	Some strengths but also some moderate weaknesses
Low	7	Fair	Some strengths but with at least one major weakness
	8	Marginal	A few strengths and a few major weaknesses
	9	Poor	Very few strengths and numerous major weaknesses

Definitions

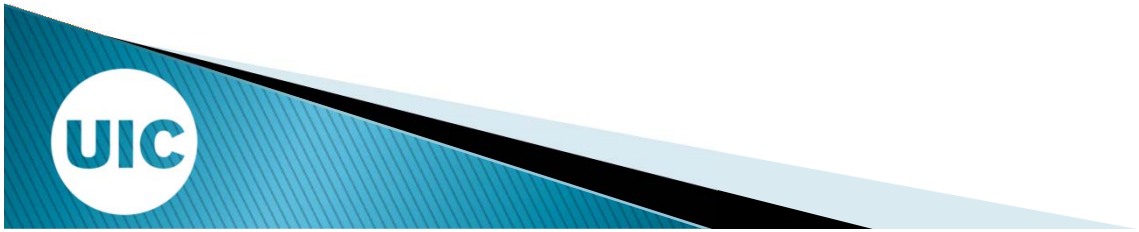
Minor: easily addressable weakness that does not substantially lessen the impact of the project.
Moderate: weakness that lessens the impact of the project.
Major: weakness that severely limits the impact of the project.

Background

- Preliminary "Overall Impact" score on same 1-9 scale also assigned by each reviewer along with explanatory paragraph
  - Reflects "their assessment of the likelihood for the project to exert a sustained, powerful influence on the research field(s) involved, in consideration of the following five core review criteria, and additional review criteria (as applicable for the project proposed)."
  - If the average of the overall impact scores places the application in ~lower half of applications reviewed by that study section in its last 3 meetings, then…
    - Application will **not be discussed** by the study section when it meets
    - You receive written critiques of the reviewers and their criterion score ratings, but not their preliminary overall impact scores for your application

Background

- NIH guidance on not discussed applications
  - "This issue should be considered on a case-by-case basis. Read the summary statement carefully and note weaknesses that you could address in a reasonable length of time. Discuss the critiques with your collaborators, colleagues, and/or senior researchers/mentors to get their suggestions. The PO also can discuss your options going forward. ***It is possible for an application that carefully addresses the reviewers' comments to go from being "not-discussed" to receiving outstanding scores upon resubmission***."



Background

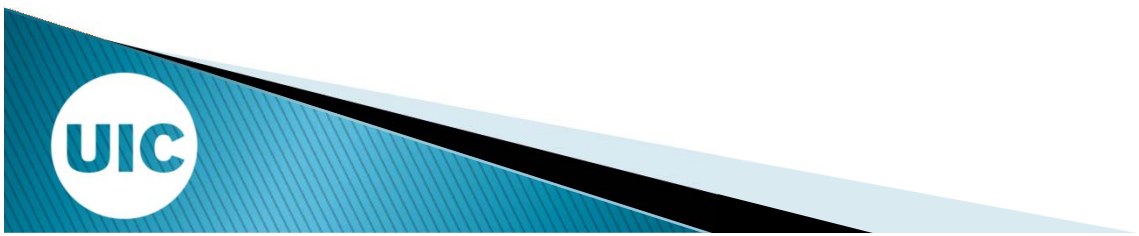
- Proof of Concept
  - I am co-I on an R01looking at mentoring in relation to cardiovascular health for urban, low-income youth
    - Initial submission was not discussed
    - Resubmission scored 20th percentile (39 impact)
    - New submission (required as can only resubmit once) to a new study section scored 23rd percentile (37 impact)
    - Resubmission was funded!

My Undiscussed Proposal

- *Evaluating a Volunteer-Delivered Community-Based Mentoring Model to Reduce Mental Health Treatment Disparities for Low-Income Youth*
  - Co-PI: Dr. Carla Herrera
  - Community partner: Great Life Mentoring (GLM), located in Vancouver, WA/Portland, OR area; program founder/director, Elizabeth Higley
  - See handout for Abstract, which includes specific aims

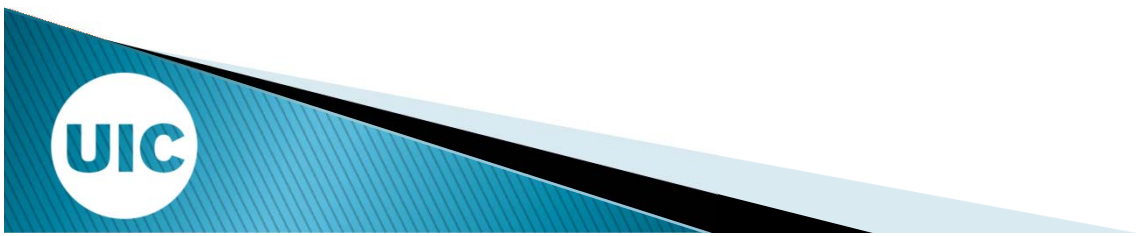
My Undiscussed Proposal

- Significance
  - Criterion Scores: 2, 2, 1
  - Strengths:
    - Reviewers tracked and agreed with our arguments for:
      - importance of problem (mental health disparities among low SES youth)
      - scientific premise (mentoring promising adjunct to standard MH care for low SES youth, but rigorous tests of effectiveness lacking; GLM provides a promising opportunity for taking next step)



My Undiscussed Proposal

- Significance (cont'd)
  - Weaknesses:
    - Rev. 2 wanted more specificity – which particular mental health disorders
    - Rev. 2 also wanted more consideration of cultural and contextual factors
  - Lessons Learned
    - **Be specific and focused in your arguments** – in this case, build a case for a couple of particular MH disorders (e.g., those most prevalent, likely to be impacted by non-specific social support of mentor)
    - **Make best case possible for broad impact** – in this case, how representative is setting of study of those in which low SES youth reside (e.g., urban areas?) and similarly for the youth served (e.g., racial/ethnic minority group representation) and where limitations exist acknowledge those proactively

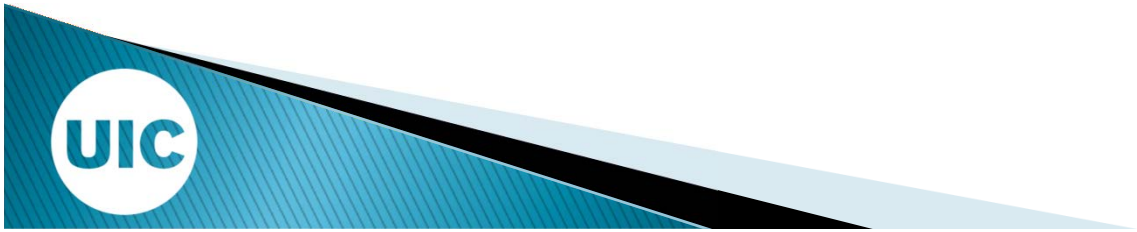


My Undiscussed Proposal

- Investigators
  - Criterion Scores: 4, 2, 1
  - Strengths:
    - History of collaboration between PIs and with community partner
    - Strong backgrounds of PIs for conducting similar research
    - Filling out team with complementary expertise (e.g., biostatistician)

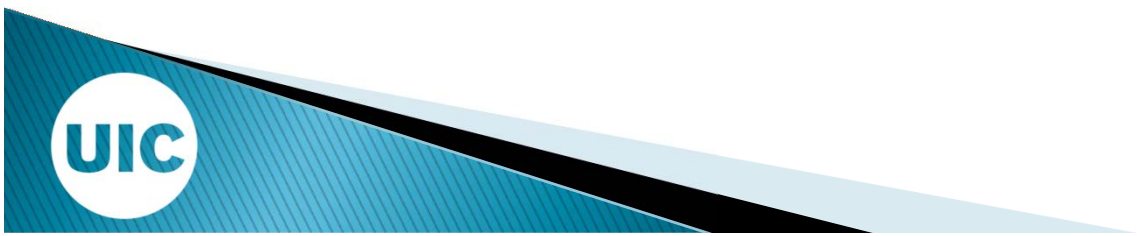
My Undiscussed Proposal

- Investigators (cont'd)
  - Weaknesses:
    - Geographic separation of PIs from each other and **PIs from study site**
    - Community partner included only as consultant
    - No biosketches for consultants
    - Not enough qual and mixed methods expertise
  - Lessons Learned
    - **Practicality matters** – need to make a strong case for feasibility of project management when research setting is remote; also consider bringing on a co-I who is closer to study site (e.g., UW researcher who conducted pilot evaluation of GLM)
    - **It takes a "study team" ….**
      - **Introduce the entire team** – even though biosketches optional for consultants, should include
      - Use co-I designation for major components of proposed research rather than consultant
        - include qual/mixed methods consultant a co-I
        - also consider community partner as co-I, but need more guidance on this given potential concerns this could introduce with independence of the evaluation



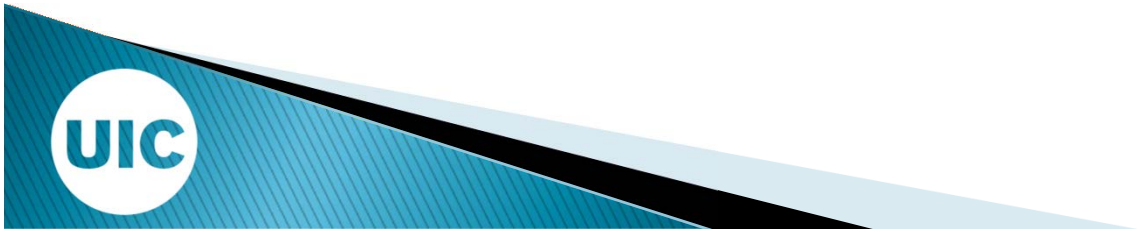
My Undiscussed Proposal

- Innovation
  - Criterion Scores: 4, 3, 2
  - Strengths:
    - Addition of community-based mentoring to traditional MH care to compensate for limitations of latter for meeting needs of low SES youth seen as novel
    - Incorporation of dyadic data
      - "Understanding the unique and potential divergent/convergent perspectives of the mentor and mentee is considered to be a highly innovative strength of this application" (Rev. 1)



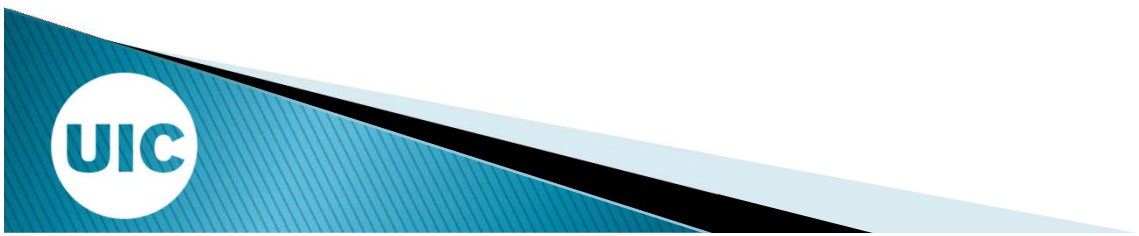
My Undiscussed Proposal

- Innovation (cont'd)
  - Weaknesses:
    - Concern that program already widely adopted in WA and that there are other mentoring programs focused on serving youth with MH needs
    - "Not clear how proposal will 'reduce disparity'. In what specifically and how?"
    - 'Population specific tailoring' is rudimentary
  - Lessons Learned
    - **Need to make tight argument for unique features of intervention approach/model – what's NEW & NOVEL -- and remember that for NIH reviewers at least its wider implementation and interest in similar models may not be seen as a positive (e.g., indication of feasibility/adoption potential) –**
      - Do more to underscore how GLM stands alone in having features expected to be key to effectiveness for this population (e.g., amount and intensity of mentor training provided, use of community settings, integration of mentor into treatment team) and are otherwise novel and could be key to not only effectiveness but scalability (e.g., use of community volunteers as mentors)
      - Clarify that GLM actually is NOT widely adopted in WA
    - **Spell out logic for assertions that are at the core of your proposal no matter how self-evident you think they may be** – MH disparities will be reduced because X, Y, and Z; consider whether you need to build a test of assumptions for your argument into study design (e.g., in this case, comparative test of efficacy for low SES and non-low SES youth or even perhaps a "weak" comparison like bench marking results against existing data?)
    - **Anticipate what could be conceived of as concerns with unconventional aspects of intervention proactively and educate reviewers, making them an innovative strength wherever possible** – in this case, we could have (and could in resubmission) make the argument that the tailoring is in fact extreme in that individualized and non-scripted nature of mentoring goes beyond population to be fluidly responsive to the unique and changing circumstance of each individual youth!



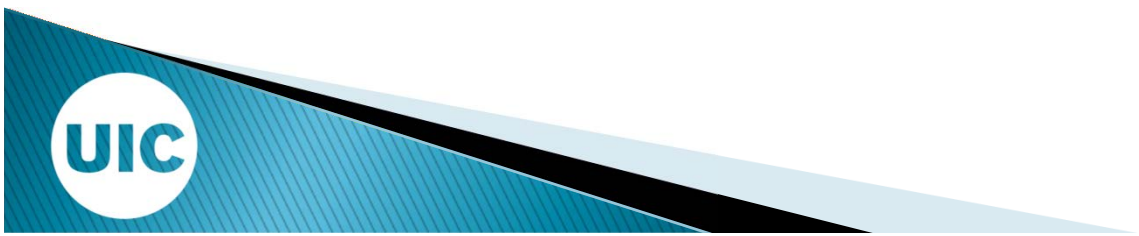
My Undiscussed Proposal

- Approach
  - Criterion Scores: 6, 5, 5
  - Strengths:
    - Tight experimental design isolating effects of mentoring (GLM) as supplement to traditional MH care
    - Preliminary evidence of effectiveness for GLM
    - In-depth investigation of intervention, including dyadic data analyses
    - Solid measures mapped to conceptual model
    - Strong statistical analysis plan



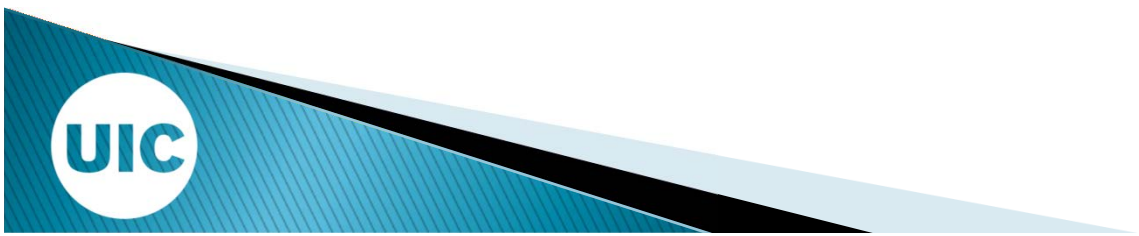
My Undiscussed Proposal

- Approach (cont'd)
  - Weaknesses:
    - Conceptual model under-developed
      - Generality with respect to MH disorders
      - "lack of clarity in how GLM will systematically engage youth in mental health treatment and improve outcomes"
    - Ethical concerns with potentially coercive nature of design b/c opt-outs will need to wait 2 years (2 reviewers) and potential harm to control youth of being referred to GLM and then not able to participate in it



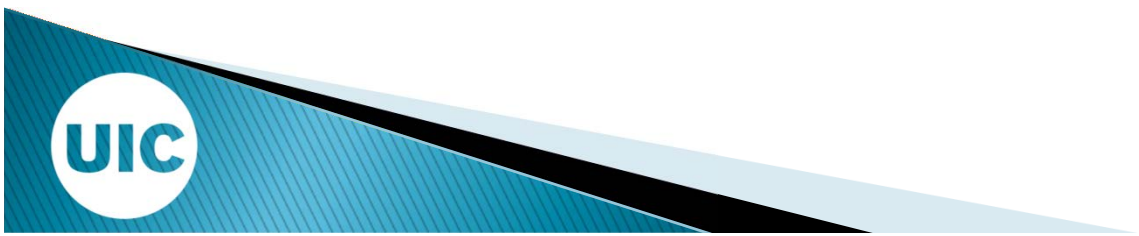
My Undiscussed Proposal

- Approach (cont'd)
  - Weaknesses (cont'd – sigh):
    - Concerns relating to statistical power
      - Rationale for expected medium effect size – needs to be developed for specific outcome(s)
      - Ability to meet enrollment goal
        - Lack of evidence of ability to secure high consent rates from all relevant parties (parents/youth, mentors, therapists)
        - Program already operating at capacity at two targeted sites – how will additional participants be added?
        - Need to account for attrition
      - Need to take into account dyadic nature of data



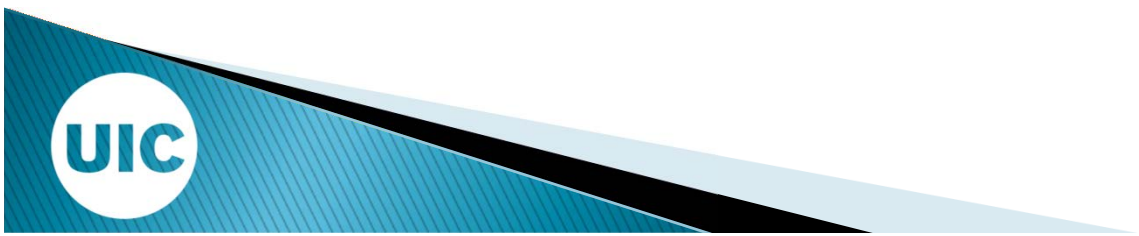
My Undiscussed Proposal

- Approach (cont'd)
  - Weaknesses (cont'd – double sigh):
    - Aim 3 (mentoring relationship processes) under-developed and not mapped to conceptual framework
      - "there's no description of quantitative data that would be collected for SEM analyses"
      - Not clear how qual data will be used
      - Important processes under-attended to – goodness of fit between mentor and mentee, mentor integration into treatment team/mentor-therapist collaboration (2 reviewers)
    - Qual component under-developed
      - Rev. 2: "What are the core themes/questions being proposed? What is the added benefit of collecting this data beyond understanding potential mediators and moderators?"
    - Under-developed rationale for including parent as data source
    - Generalizability to other settings, particularly due to cultural and contextual factors (e.g., urban vs. rural) not attended to



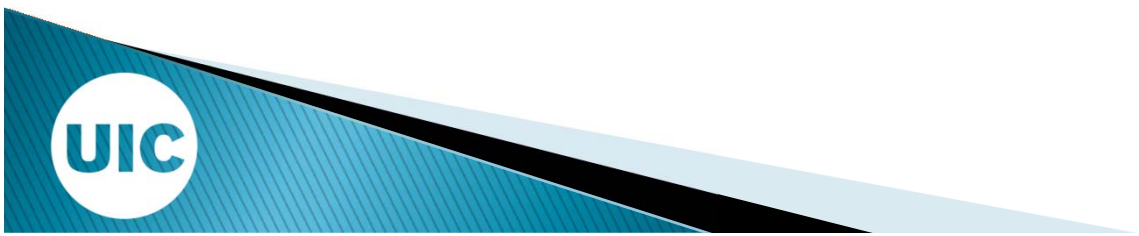
My Undiscussed Proposal

- Approach (cont'd)
  - Weaknesses (cont'd – double sigh):
    - Aim 3 (mentoring relationship processes) under-developed and not mapped to conceptual framework
      - "there's no description of quantitative data that would be collected for SEM analyses"
      - Not clear how qual data will be used
      - Important processes under-attended to – goodness of fit between mentor and mentee, mentor integration into treatment team/mentor-therapist collaboration (2 reviewers)
    - Qual component under-developed
      - Rev. 2: "What are the core themes/questions being proposed? What is the added benefit of collecting this data beyond understanding potential mediators and moderators?"
    - Under-developed rationale for including parent as data source
    - Generalizability to other settings, particularly due to cultural and contextual factors (e.g., urban vs. rural) not attended to



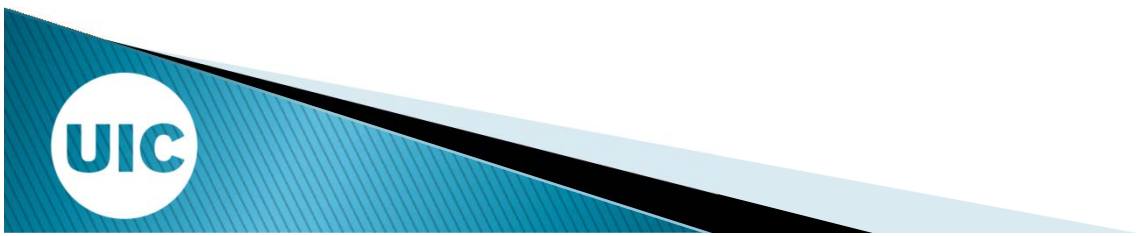
My Undiscussed Proposal

- Approach (cont'd)
  - Lessons Learned:
    - **Depth over breadth -- keep study scope manageable and focused on key priorities (avoid too many "moving parts")**
      - Perhaps re-cast proposal to focused on:
        - overall program efficacy for 2 to 3 specific MH problems with current "mediators" proposed instead as "secondary outcomes" and moderators examined only in exploratory manner
        - mentoring relationships and mentor/treatment team relationships – deep dive on those with better explication



My Undiscussed Proposal

- Approach (cont'd)
  - Lessons Learned (cont'd):
    - **Don't leave room for doubt about critical features of study design (e.g., power), especially practical considerations that will be outside your control (e.g., consent rates, sample accrual)**
      - Survey therapists and existing GLM mentors and parents/youth to gauge prospective consent rates
      - Look into recruiting a third recruitment site to provide more buffer for attrition, provide power for a smaller (and arguably more realistic) effect size – program would need resources, however, to serve greater number of youth (e.g., seek funding from county MH funder that is very supportive of the program and research?)



My Undiscussed Proposal

- Approach (cont'd)
  - Lessons Learned (cont'd):
    - **Anticipate potential human subjects concerns, keeping in mind that to reviewers limiting access to even unproven programs that are already in operation may be seen as unacceptable, especially if prospect of program participation is presented**
      - Make clear that study would affect which youth receive program during study period but not the number (i.e., still will serve youth at capacity)
      - Consider having the sites incorporate standardized mental health measures into standard assessments so that random assignment could occur without needing to engage participants
        - Challenges, however, including how to collect outcomes data after leaving care (continuity of mentoring – "after care" – is an important part of the GLM program)

Next Steps

- Huddle with co-PI and community partner to further develop potential responses to reviewer concerns
- Consult with NIMHD program officer
- Consult with senior researchers/mentors with track records of NIH success for guidance (e.g., Robin Mermelstein)
- Make a call on whether to re-submit and, if yes, seek more pre-review support and consultation from above and make use of SPH grants consultant and pre-review service