Life Cycle of a CREST/RMN Manuscript

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CREST/RMN Partnership

- Started in 2009
- Method for increasing productivity of CREST Scholar graduates and RMN manuscript output
- Secondary analyses of RMN generated data
RMN Trials: Prior Funding Period

- PPCOS II: 1° findings published NEJM
  - Demonstrated increased effectiveness of letrozole over clomiphene in women with PCOS

- AMIGOS: 1° findings published NEJM
  - Demonstrated decreased effectiveness of letrozole compared to clomiphene and HMG for couples with UI

- PhOX: findings presented at ESHRE, Lisbon 2015
  - Advantages of decreased O₂ in cultured human embryos

- Varicocoelectomy trial: stopped 2/2 slow recruitment
Captured a similar baseline dataset of survey questions and demographics

- SF-36, FertiQOL: symptoms and mood
- FSFI and IIEF: sexual function
- Sleep habits: sleep
- Basic medical, surgical, reproductive, medication histories
- Basic demographics, race ethnicity, BMI, insurance status
Data Coordinating Center

- Administrative support
- Data management (CRFs, reports, site monitoring)
- Analytical support
- Website development and maintenance
- Protocol development
  - Development of CRFs and recruitment materials
  - Data entry and support
  - Drug acquisition and blinding
  - Quality control
  - Manuscript preparation
RMN Organization

- **RMN**
  - Steering Committee
    - Site PIs/Co-Is
      - Chairperson - Nanette Santoro, M.D.
        - NICHD Project Scientist *ex officio*
      - NICHD Project Scientist Esther Eisenberg, M.D., MPH
  - Advisory Board
    - NICHD Project Scientist *ex officio*
  - Data and Safety Monitoring Board
    - DCC Heping Zhang, Ph.D, Yale University

Chairperson - Nanette Santoro, M.D.
Secondary analyses

- Planned secondary analyses for each survey instrument used
- Additional secondary analyses proposed in collaboration with CREST Scholars
- Analyses needing new measures done on stored serum, if scientific rationale exists and funding can be found (TSH)
- Analyses follow a specific plan and pattern
New CONFIRM Consortium

- Completely different grant mechanism
- Linked R01 grants
- More independent projects
- Less cross-study standardization
CONFIRM: 3 Main Trials

- NatPRO (Val Baker): Pregnancy outcomes in FET cycles with (natural) and without (programmed) a CL (N=788)
  - 1º outcome = pre-eclampsia

- PREGnant (Hugh Taylor): 60 day elagolix pre treatment of women with endometriosis undergoing IVF (N=816)
  - 1º outcome = cumulative live birth

- FRIEND (Ayman Al-Hendy): Green tea extract in women with fibroids (N=36)
  - Endpoints: safety of epigallocatechin gallate (EGCG), active ingredient in green tea
  - Randomized to EGCG + CC, EGCG + LET and EGCG alone, women with and without fibroids
CONFIRM Progress

COVID
Current CREST Scholar Opportunities

- Remainder of RMN concepts
  - Ideas are getting scarce!
  - ACTorNot, ENDOmarkers, PsyFi

- Additional databases
  - SART, SWAN, WHI, others

- New databases
  - More and more data are being held centrally at NIH
  - Visibility of RMN & CREST makes collaboration attractive

- New sample analyses
  - Requires local funds
Start of a Concept Proposal

- You need an idea
  - Check for possible overlap with existing secondary analysis plans

- You need a partner
  - RMN PIs are available as collaborators
Prepare a Concept Proposal

Format of a CS/AP

- Rationale, hypothesis, outcomes
- Approach to analysis: work with RMN and CREST partners (PI collaborator, Janet Sun, Nanette Santoro, Mary Sammel & Heping Zhang)
- Primary and co-authors
- 3-4 pages
- Can help construct introduction of manuscript
Review for overlap and priority—Nicole Goetz is keeper of CSAPs

If RMN:
- Present to RMN SC (email) for final approval

If CONFIRM:
- Will present at CREST calls
- >50 approved CS/APs
- >30 published or accepted
Presentation of CS/AP

- Used to be done at RMN meetings, now will be done at CREST calls
  - Make sure your PI or a representative will be on the call
  - Make sure your key CREST analyst will be on the call (Janet, sometimes Mary)
  - 10 slides PowerPoint and supply 3-4 page narrative in advance of call to Nicole Goetz
  - Be prepared for discussion, suggestions, modifications
CREST Manuscript Process
After CS/AP Approval

- Manuscript outline and assignments prepared by CREST Scholar with input from Santoro/PI/Writing Group (1st Conference Call)
- Analysis should be done per Analysis Plan from CS/AP
- Review results of analysis with WG (2nd conference call)
- Draft manuscript prepared by WG and circulated to all co-authors—should be fairly complete with all Tables, abstract, formatting done
- Mature manuscript circulated to all co-authors, then submitted
**Time Frame**

- Approximately 2 proposals at a time can be analyzed by DCC (Janet Sun)
- Approximately 2-3 months per proposal
- 12-16 manuscripts per year
RMN-CREST Possibilities

- MOXI: Male Antioxidants and Fertility
- FIT-PLESE: Weight Loss Prior to Fertility
- Psy-Fi: Multiple Pregnancies in ART
- ACTorNOT: treatment options for PUL
- PrISICE: fresh vs cryopreserved embryo transfer
- Similar potential secondary analysis options
- Ability to pool across multiple studies: meta-analysis
Other Databases

- Study of Women’s Health Across the Nation (SWAN; N=3302)
- Women’s Health Initiative (WHI; N=27,347 to 100,000)
- KEEPS (N=738)
- FASTT (N=503)
- FORT-T (N=450)
- ISIS (N=1150)
Using Other Databases

- Discuss at CREST call or in person meeting; assess overall feasibility
- Assure there is no overlap
- Work with MS to develop ‘answerable question’
- Apply for needed database (DASH/other)
Using DASH

NICHD Data and Specimen Hub:
- Log into DASH and create a password
- Register as a SUBSITE under the University of Colorado
  - 2 years of access, with annual reporting requested
  - Data Use Agreement for 3 years