

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

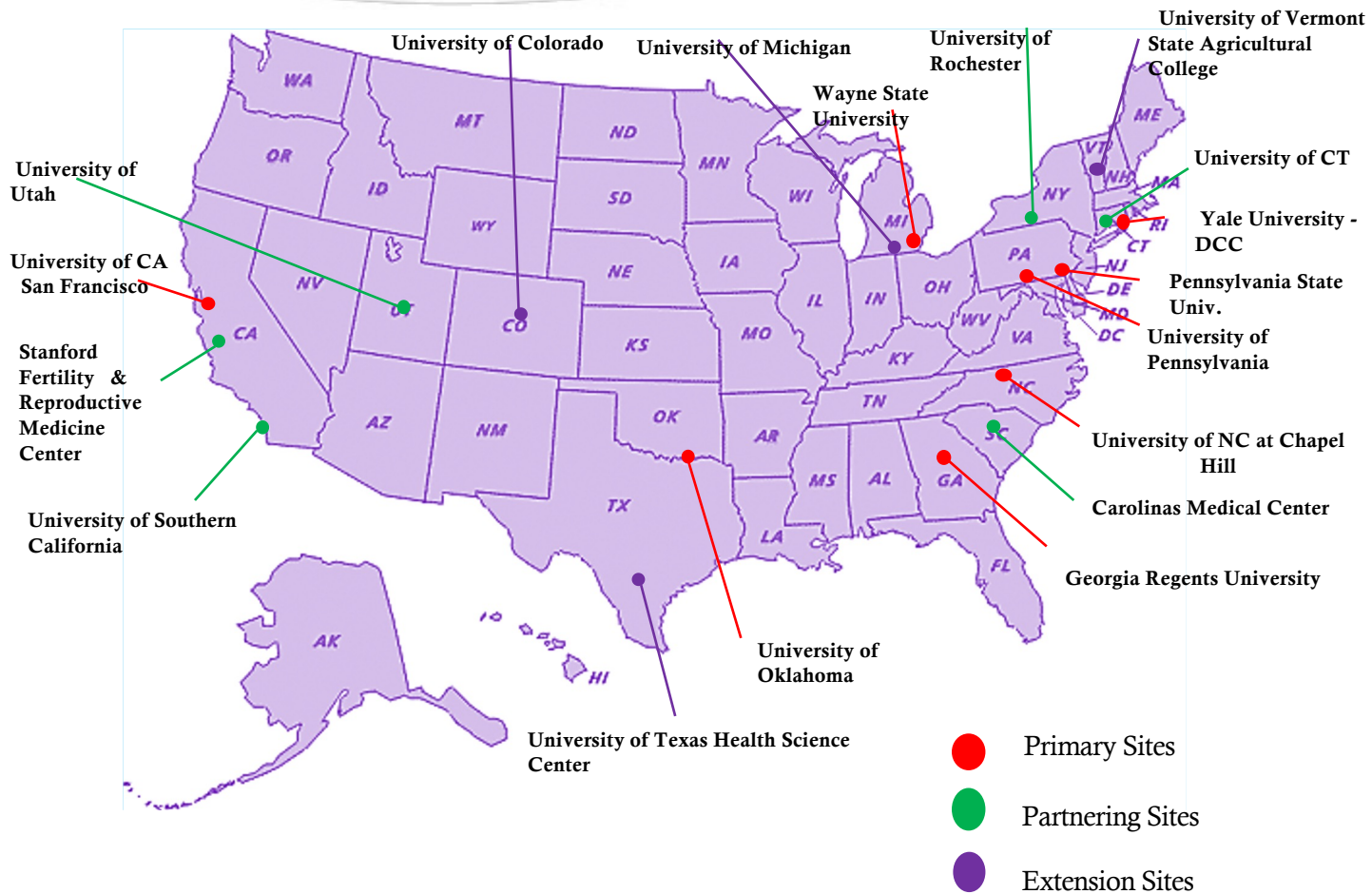
RMN Trials: Prior Funding Period

- ◆ PPCOS II: 1^o findings published NEJM
 - ◆ Demonstrated increased effectiveness of letrozole over clomiphene in women with PCOS
- ◆ AMIGOS: 1^o 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

All RMN Trials

- ◆ 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

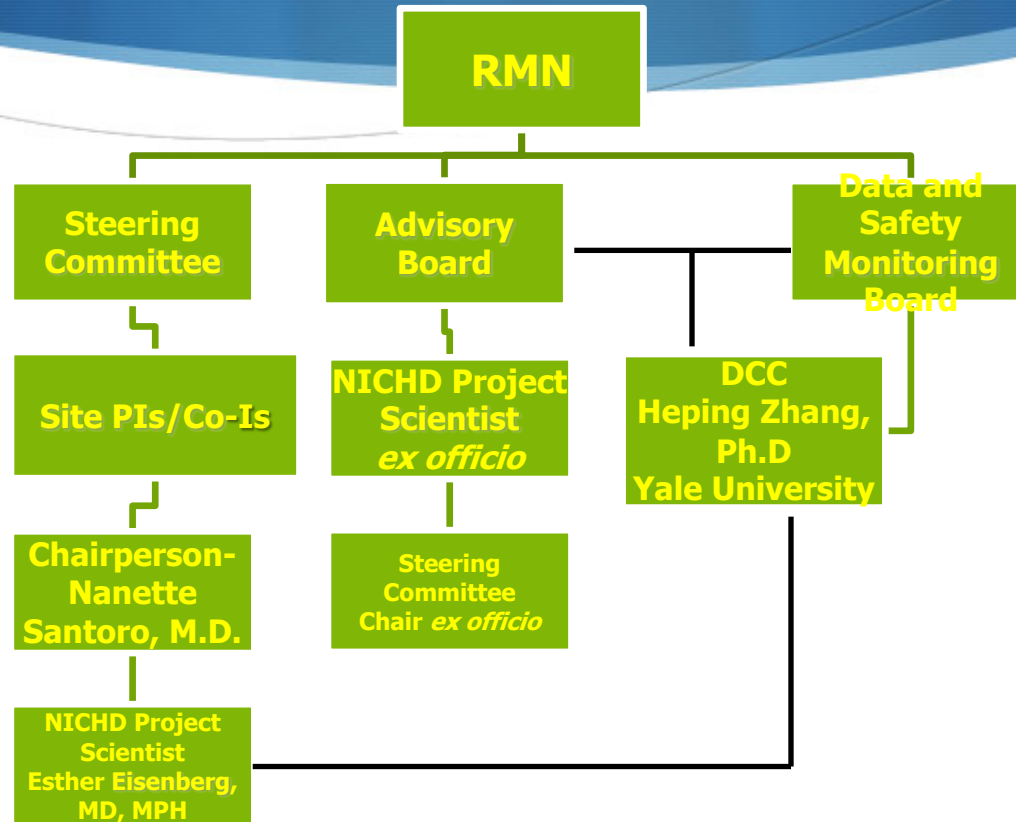
Reproductive Medicine Network Sites 2008-2019



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



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)
 - ◆ 1° outcome=pre-eclampsia
- ◆ PREGnant (Hugh Taylor): 60 day elagolix pre treatment of women with endometriosis undergoing IVF (N=816)
 - ◆ 1° 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

CS/AP (Concept Sheet/Analysis Plan)

- ◆ 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-PLEASE: 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