The CDP: Looking Back 50 Years Contributions of CDP to the Role and Function of Coordinating Centers

Society for Clinical Trials

Jim Neaton

May 20, 2019

Outline

- In the beginning there was the CDP
- Recollections of visit to CDP coordinating center
- Evolution of models over time
- Looking forward 50 years
- Summary

In the beginning there was the CDP (actually the UGDP)

- CDP funded by NHLBI in April 1965
- "The UGDP begot the Coronary Drug Project and after that there were other begots". (Meinert CL, The Trials and Tribulations of the University Group Diabetes Program, 2015).
  - About 5 years of experience as a coordinating center when CDP was funded.

Some of the Begots of the CDP
(Canner P, Cont Clin Trials, 1983)

- CDP Aspirin Study (CDPA)
- AMIS (Aspirin Myocardial Infarction Study [AMIS])
- Persantine-Aspirin Reinfarction Study (PARIS)
- Diabetic Retinopathy Study (DRS)
- Early Treatment Diabetic Retinopathy Study (ETDRS)
- International Mexiletine and Placebo Antiarrythmic Coronary Trial (IMPACT)
- Many more since 1983!

Some of the Begots in the Early 1970's Coordinated By Other Universities

- Hypertension Detection and Follow-up Program (HDFP) (University of Texas)
- Lipid Research Clinical (LRC) Program – Coronary Primary Prevention Trial (CPPT) (University of North Carolina)
- Multiple Risk Factor Intervention Trial (MRFIT) (University of Minnesota)
- Many more!

Recollection of Visit to University of Maryland in Early 70's

- Fear of what was to come (we had a long ways to go!)
- Importance of coo rship
- Caricatures of my tamler
- Much learned
  - Staffing requiremer
  - Case report forms a
  - Appointment remin
  - Patient profiles
  - Laboratory quality c
  - "DSMB" reports
  - Analysis files

And all of this without:
- Word processing
- Internet
- Email
- SAS/R
- PCs
- Powerpoint
- Teleconferences

Leadership

- Greenberg BG (American Statistician, 1959)
  – "To the statistical consultant, the cooperative endeavor offers new and stimulating challenges…not the least is learning to work with several principal investigators."
- Greenberg Report (May 1967, published in Cont Clin Trials in 1988)
  – "The Coordinating Center is a key point in a cooperative study".
- Meinert CL (Cont Clin Trials 1983)
  – "The organizers of the trial (CDP) recognized the importance of the strong leadership role for the Coordinating Center from the outset. It was seen that a passive service role for the Center would not meet the needs of the study."

Some References on Role and Operation of Coordinating Centers Still Relevant Today

- Coronary Drug Project. Methods and Lessons of Multicenter Clinical Trial (Cont Clin Trial 1983, Volume 4, Number 4)

- Meinert CL. Organization of Multicenter Clinical Trials. (Cont Clin Trials, 1981; 1:305-312)
  - "Consideration should be given to a phased approach to initiating trials in the future…".

- The Coronary Drug Project Research Group. Practical Aspects of Decision Making in Clinical Trials: The Coronary Drug Project as a Case Study (Cont Clin Trials, 1981; 1:363-376).
  - "…no single statistical decision rule or procedure can take the place of the well-reasoned consideration of all aspects of the data by a group of concerned, competent, and experienced persons with a wide range of scientific backgrounds and points of view."

" Not all centers of education in the relevant disciplines have faculties with first hand experience in the design and conduct of such studies. Most of the knowledge about design and maintenance of long-term studies is translated by on-the-job training and other informal methods rather than the usual academic routes."

Grizzle J, The case for management research for large field trials, J Chronic Dis, 1977.

" This monograph deals primarily with methodology of and experiences gained from the Coronary Drug Project (CDP). However, certain experiences in other studies are referenced as well. T ts of more recent studies t , opinions, represent r vances beyond the CDP."

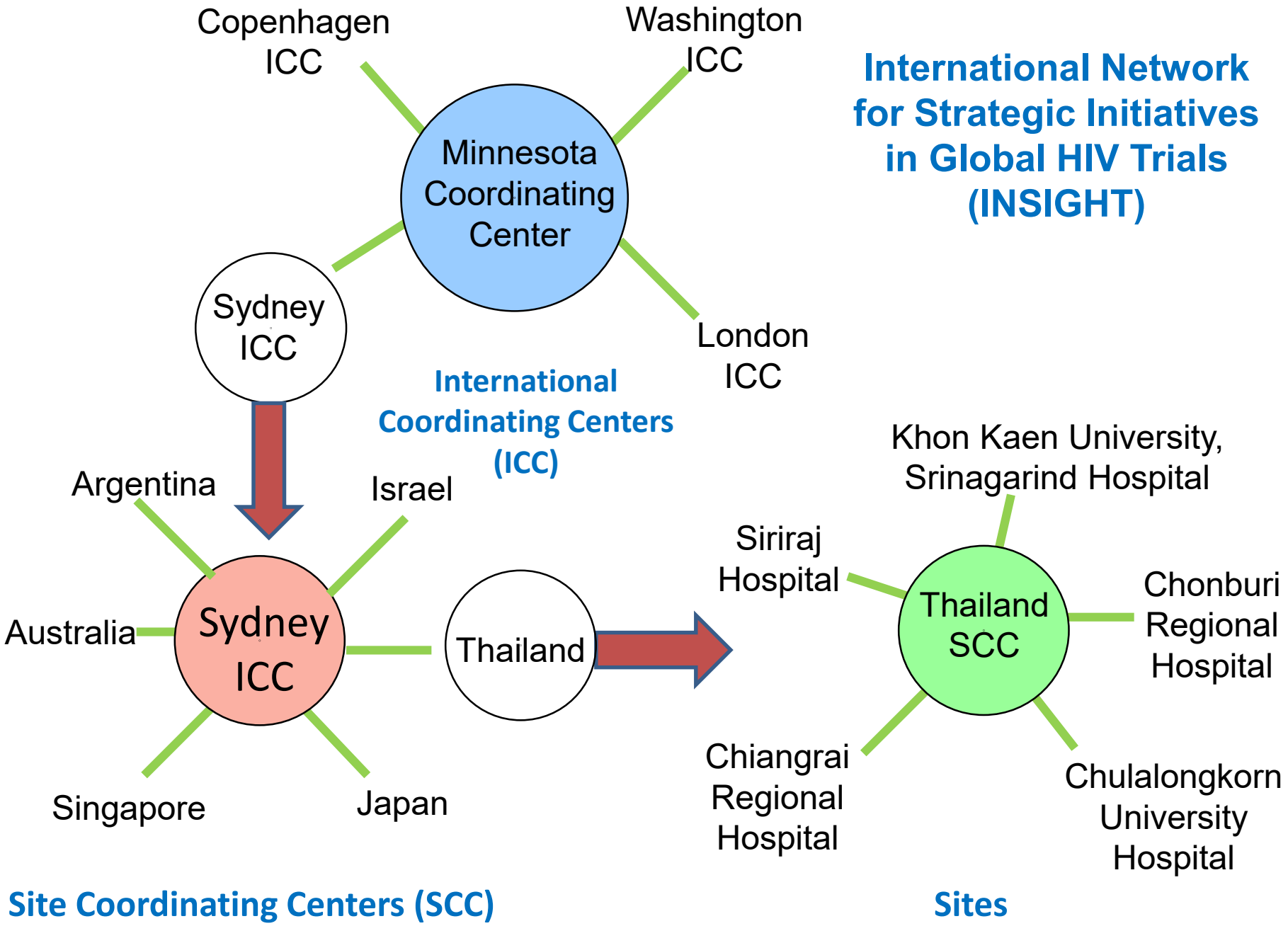
And **still** without:

- WORD
- Internet
- Email
- SAS (as we know it)/R
- PCs
- Powerpoint
- Webinars

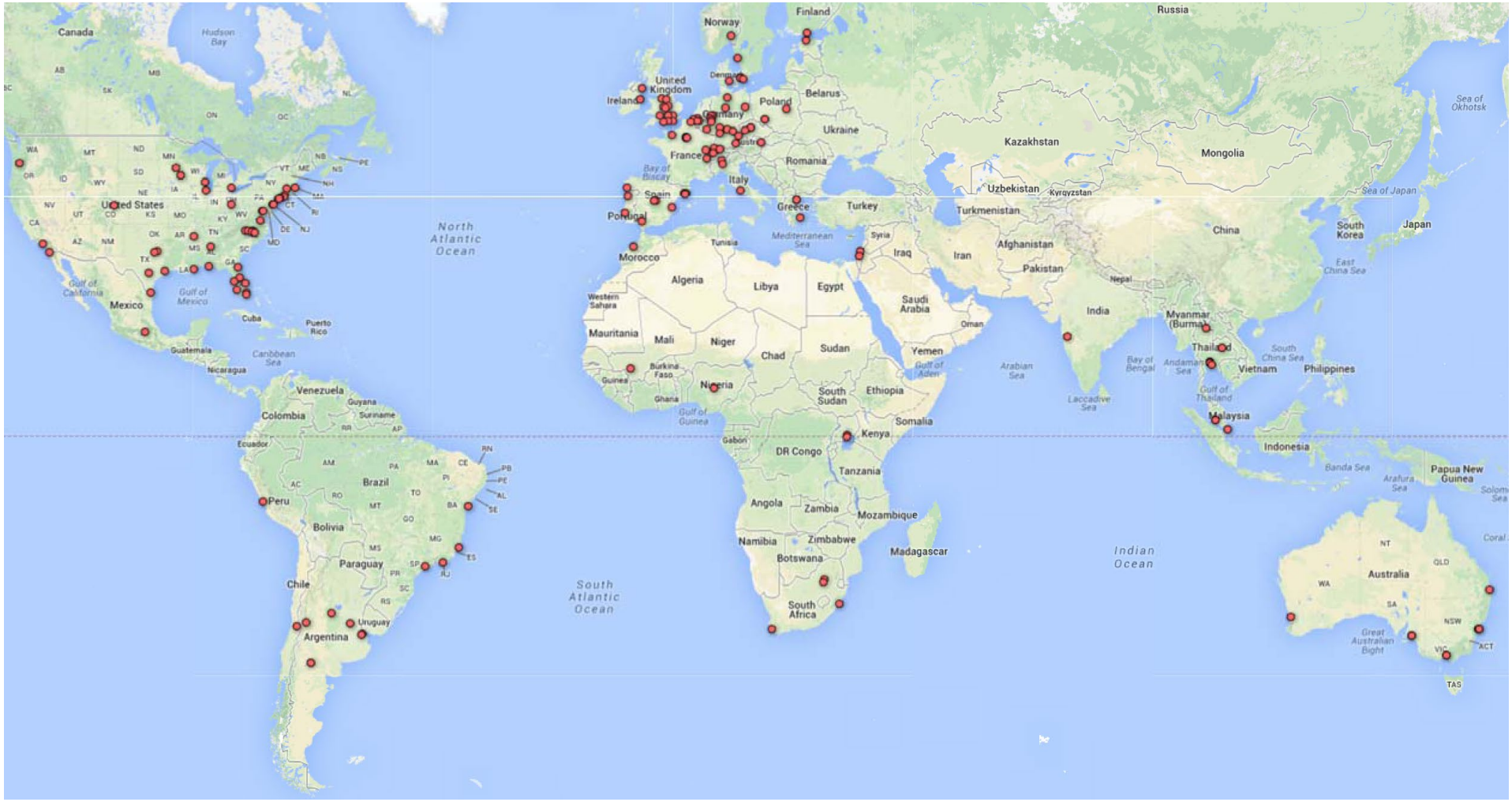
Canner P. Chapter 1 of the 1983 Monograph on CDP Methods and Lessons Learned, Cont Clin Trial 1983; 4:273-280.

Evolution of Coordinating Center Models

- Clinical trial networks
- Data and clinical coordinating centers
- Regional centers for coordinating recruitment
- International coordinating centers


International Network for Strategic Initiatives in Global HIV Trials (INSIGHT)
Copenhagen ICC
Washington ICC
Minnesota Coordinating Center
Sydney ICC
London ICC
International Coordinating Centers (ICC)
Argentina
Israel
Australia
Sydney ICC
Thailand
Singapore
Japan
Khon Kaen University, Srinagarind Hospital
Siriraj Hospital
Thailand SCC
Chonburi Regional Hospital
Chiangrai Regional Hospital
Chulalongkorn University Hospital
Site Coordinating Centers (SCC)
Sites

INSIGHT: Clinical Sites in 37 Countries on 6 Continents



An Early Prediction on Evolution

- "Suppose you are suddenly cast in the role of organizing a large-scale multicenter trial" (Meinert CL, Cont Clin Trials, 1981)
  - "…there are separations of responsibilities where two or more centers together may assume the overall coordination role". (reference to industry-sponsored international trial with 2 coordinating centers, one in France and one in the U.S.)

In the 50 Years Following CDP

- A society was formed: Society for Clinical Trials in 1978.
- Journals were started: *Controlled Clinical Trials* (now *Clinical Trials*) in 1980
- Text books on clinical trials were written
- Clinical trial courses were developed as part of biostatistics graduate programs
- The recognition of biostatistical science as a critical discipline (Zelen, *Stat Med* 2006).

Looking Forward 50 Years…

Graduate programs in biostatistics and the establishment of coordinating centers in research poor settings

Six Reasons for Conducting Randomized Trials in Developing Countries

- Over 80% of global burden of all diseases occurs there.
- Diseases that contribute to disability adjusted life years are different in developing countries.
- Even for similar diseases, environmental factors may vary so that findings in developed countries are not applicable.
- Differences in ethnicity may influence drug metabolism and side effects.
- Preventive and treatment strategies should be targeted to diseases common in those countries.
- More people are involved in randomized trials, stimulates critical thinking and creates a group of clinicians that will practice evidence-based medicine.

Yusuf S. Stat Med 2002; 21:2859-2867.

“… the best way to train a new generation of African scientists is by teaching them on the job…”

- A New Vision for Clinical Trials in Africa, PloS Medicine 2004 - an editorial announcing the formation of the European and Developing Countries Partnership (EDCTP)

Good Clinical Trial Biostatistician =

Graduate Training

+

On-the-Job Experience

Needs in Resource Poor Settings

- Programs to motivate undergraduates to pursue graduate training and careers in biostatistics/clinical trials (e.g., like Summer Institutes for Biostatistics).
- More graduate programs in biostatistics.
- Coordinating centers for on-the-job training.

Summary

- CDP – a study with a pioneering group of investigators – we owe them much.
- Methods for designing and conducting trials continue to improve due to meetings like this.
- An important lesson for the future: take what we have learned to resource poor settings where the needs are great.