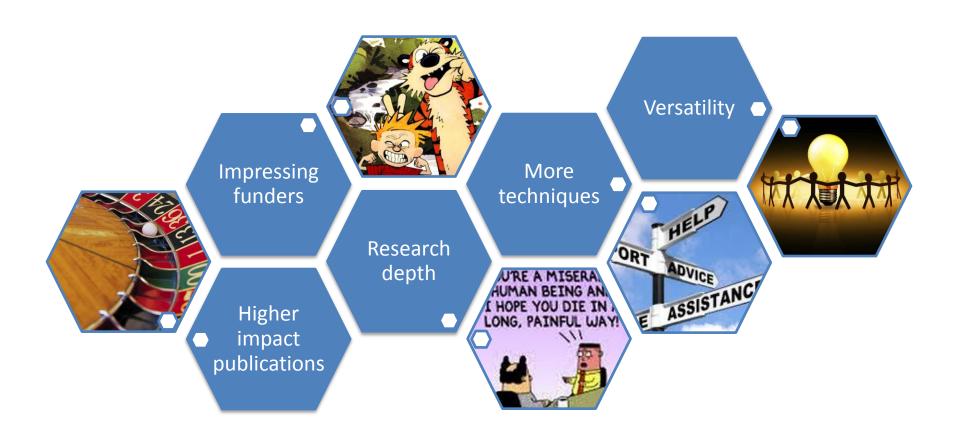


Collaborative ID Research in Singapore

Hsu Li Yang
Director, SIDI
19th March 2015

Why should we collaborate (research)?

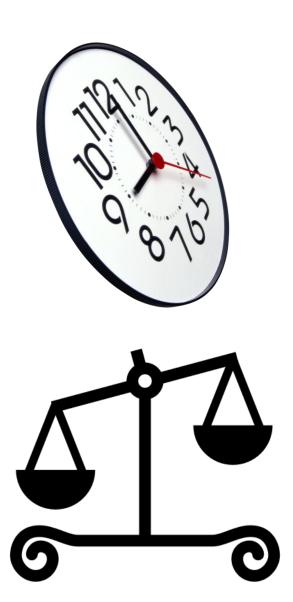


Clinical ID in Singapore

- Small country ID cases relatively fragmented.
 - No central institute like NCC, NSC, SNEC where clinical cases are "concentrated".
 - Difficult to achieve adequate sample size in any one hospital, especially for late-phase clinical trials.
 - Lack of clinical research expertise, especially for clinical trials.

Costs of Collaboration





Singapore ID Initiative (2012-?)







Prof Jeremy Farrar



Prof Peter Horby

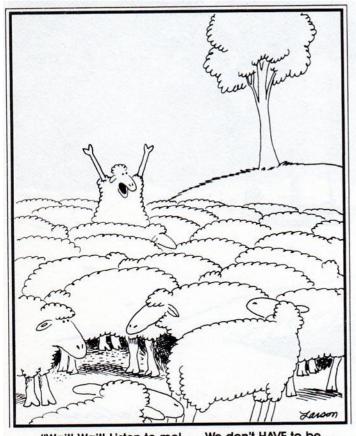
SIDI: Aims

- Non-aligned forum and catalyst to stimulate broad ID community in Singapore.
- Promote interdisciplinary and inter-institutional alliances to facilitate clinical and public health ID research.
- Develop country-wide operational readiness to conduct essential research in response to epidemics/pandemics.
- Enhance ID clinical research community.
- Develop regional linkages and greater international relevance for ID research in Singapore.

SIDI: Culture Change



"What if we don't change at all ... and something magical just happens?"



"Wait! Wait! Listen to me! . . . We don't HAVE to be just sheep!"

Cartoons from:

http://www.hrneurope.com/2010/07/apple-pixar-culture-and-decision-science/http://blog.vanillaforums.com/community/dos-donts-making-changes-community/

Phase I Research Projects

| | Title | PI | Sites | Funding | Recruitment |
|---|-----------------|-----------------------|--|-------------------------------|--------------|
| 1 | SARIs Study | Ng Oon Tek | TTSH, NUH, SGH | \$200K | 46 subjects |
| 2 | SHIFT (hep B) | Lee Le Ye | NUH, KKH | \$65K | 103 subjects |
| 3 | SNIP | Limin Wijaya | SGH, TTSH, NUH, Duke-NUS, CGH, KTPH, KKH | \$2,723K + | 61 subjects |
| 4 | HFMD & Seizures | Chong Chia Yin | KKH, NUH | \$5K | N.A. |
| 5 | A-KLASS | Sophia Archuleta | NUH, TTSH, SGH | \$167K Manpower/ SCRN | 56 subjects |
| 6 | MRSA | Shirin Kalimuddin | SGH, NUH, TTSH, SCRI | \$564K + Manpower/SC RN | 11 subjects |
| 7 | CaPES | Kalisvar Marimuthu | TTSH, NUH, SGH, CGH, KTPH, JGH, KKH, NTU, SCRI | \$202K + Manpower/SC RN | 192 subjects |

Phase II Research Projects (Catalyst)

| | Title | PI | Sites | Funding | Recruitment |
|---|------------------|-------------------------|--|---------|-------------|
| 1 | Aedes malayensis | Ian Mendenhall | Duke-NUS, Temasek LS, Hawaii, Rutgers- NJ | \$56K | N.A. |
| 2 | EV71 | October Sessions | Duke-NUS, NUS | \$60K | N.A. |
| 3 | Doxycycline-TB | Catherine Ong | NUH, NUS, Imperial, Southampton | \$60K | 0 subjects |

Phase II Research Projects (Cross-Institution)

| | Title | PI | Sites | Funding | Recruitment |
|---|------------------|-------------|------------------------|---------|--------------|
| 1 | Candidemia Study | Ling Li Min | TTSH, SGH, CGH, NUH | \$200K | 0 subjects |
| 2 | Gonorrhoeae | Martin Chio | NSC, SGH, GIS, WTSI | \$200K | 264 subjects |
| 3 | TB Resistance | Rick Ong | NUS, TTSH, SGH, GIS | \$166K | 0 subjects |

Phase I Infrastructural Grant

- Singapore ID Clinical Research Network (SCRN)
 - PI: Prof Leo Yee Sin -> Dr David Lye
 - Budget: \$1,545K +
 - Based at CDC/IIDE



Singapore ID Clinical Research Network (SCRN)

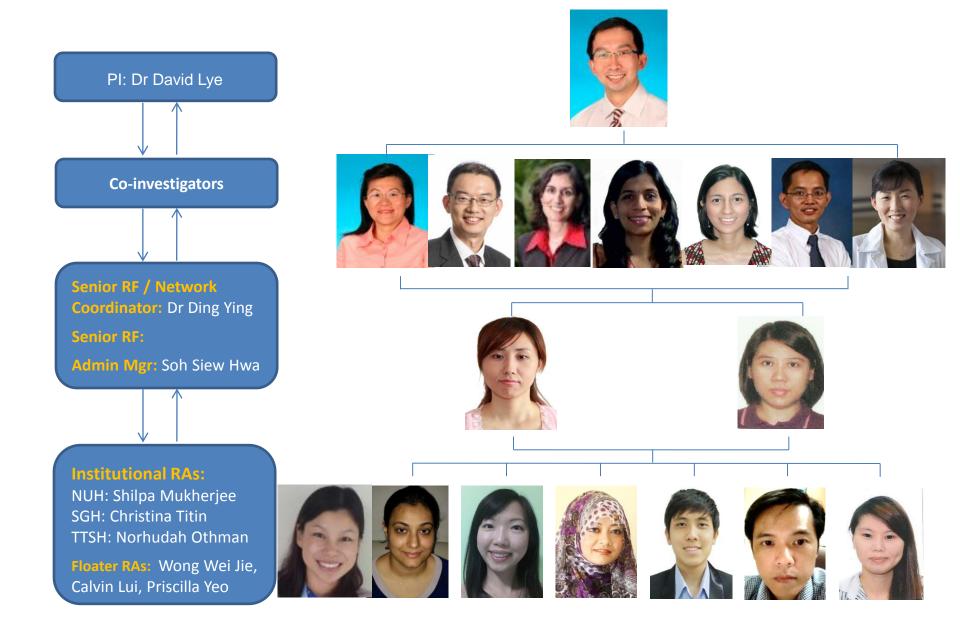
SCRN established to enable multicentre randomised clinical trials and prospective observational studies in infectious diseases in Singapore.

Objectives/Aims

- Establish long-term research collaboration between clinical infectious diseases and microbiology departments
- Facilitate the pooling of patients with infections of interests, with numbers that may suffice for rigorous clinical studies that cannot otherwise be attained on an individual institutional level
- Provide support to clinician-investigators, permit these investigators to perform clinically relevant and practice-oriented research that addresses local controversies in treatment
- As a supporting infrastructural network to free busy clinician from having to deal with the minutiae and bureaucracy of research
- Function as an immediately available capacity for clinical research in the event of an outbreak

Slide courtesy of Dr. David Lye and the SCRN team

Singapore ID Clinical Research Network (SCRN)



Slide courtesy of Dr. David Lye and the SCRN team

Framework

- Central core of investigators from each site → executive committee
- Up to 3 clinical projects (1 from each site)
- Central administrative core (based at IIDE) for
 - Hiring and payment of research staff
 - Processing of research reports
 - Ethics approval and update
 - Establishment of DSMB
 - Liaison with SCRI
 - Storage of microbiological and clinical samples
- Publications involve all active investigators
 - All data jointly shared and accessible to each participating institution

Type of projects

- Clinical condition/problem:
 - Common to all sites
 - Recruitment and follow-up within clinical workflow (i.e. registrars and consultants)
 - Culture-based (microbiological laboratories able to identify pathogen of interest)
 - Simple binary trial design
 - Potential for further studies













Slide courtesy of Dr. David Lye and the SCRN team

Projects facilitated by SCRN

8 clinical studies

- 6 RCT (including 1 pharma-sponsored trial)
- 1 Prospective observational study (active recruitment)
- 1 PK PD Study (planning for study initiation)

Local participating sites & academic institutions

- TTSH, NUH, SGH, JGH, KTPH, CGH & Private Hospitals
- NUS and NTU

Overseas collaboration

 Australasian Society for Infectious Diseases Clinical Research Network (ASID CRN)

SIDI: Training & Development

Research time funding – Dr Limin Wijaya (40% protected time to 31 May 2015).

- OUCRU Ho Chi Minh City visit
 - SNIP and SCRN staff.
 - 13th-17th Oct 2014.

- SIDI Overseas Research Training Fellowship.
 - Leong Wei Yee Sri Lanka.

SIDI Phase 2 Aims

 Foster a culture of collaborative research on clinically relevant ID issues in Singapore and the region.

 Lower the barriers for collaborative clinical ID research in Singapore so as to increase the volume, breadth and depth of such research locally.

Infrastructure Building

- Continued support for SCRN:
 - Clinical manpower.
 - Administrative expertise.
- Genomic database Shared access model.
- Microbe Bank Two-tiered hybrid model (central site + branches).
- Clinical Databases.

Barriers & Hurdles

Ethics Approval.

Research Agreements.

Research staff support.

Cross-institutional support.

Aborted Study

Multicenter Phase IIB open-label randomized controlled trial on the efficacy of combination antibiotic therapy for serious infections caused by extensively drug-resistant Gram-negative bacteria (XDR-GNB).

PI: Dr David Lye, TTSH

Participating Institutions: TTSH, SGH, CGH, NUHS, SCRI

This study was terminated because of protracted issues with ethics approval (but largely scientific queries rather than ethical issues).

The Humble Research Assistant

- Central to successful clinical research, especially for clinical trials.
- Lowly paid in the public sector.
- No career progression.
- No real job stability.



- Often no intrinsic motivation after a while.
- Likely overworked...

Conclusion

- Collaborative clinical ID research has come a long way since 2003.
- Costs of collaboration high but potential gains are greater.
- Failure of collaborative projects can often be the seeds of new and better research.
- Singapore in the foreseeable future has an ideal structure and human resources for great ID clinical & research collaboration.
- Real issues in terms of:
 - Costs.
 - Administrative barriers to research.
 - Failure of talent development.