Australian Clinical Trials Alliance

Establishing a CTN: A Facilitated Workshop for Clinicians and Researchers ACTA Summit 2020

ACTA gratefully acknowledges operational funding from the Australian Government's Medical Research Future Fund

Establishing a CTN: A Facilitated Workshop for Clinicians and Researchers

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Australian Clinical Trials Alliance

www.clinicaltrialsalliance.org.au

Australian Clinical Trials Alliance

CTN Establishment Workshop
ACTA Summit 2020

Prof John Zalcberg OAM
ACTA Chair

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What is ACTA?

National peak body supporting and representing investigator-initiated clinical trials sector, including

- Clinical Trial Networks (CTNs)
- Clinical trial Coordinating Centres (CCs)
- Registries

ACTA does not run trials, is not a network

Why a network?

In clinical trials infrastructure is king

Because sample size is king

Small groups can do trials, just won't have impact

Sample size lives in clinical practice

Sites and clinicians are king

No sites = no patients = no trial

Why a network?

Network is not a University

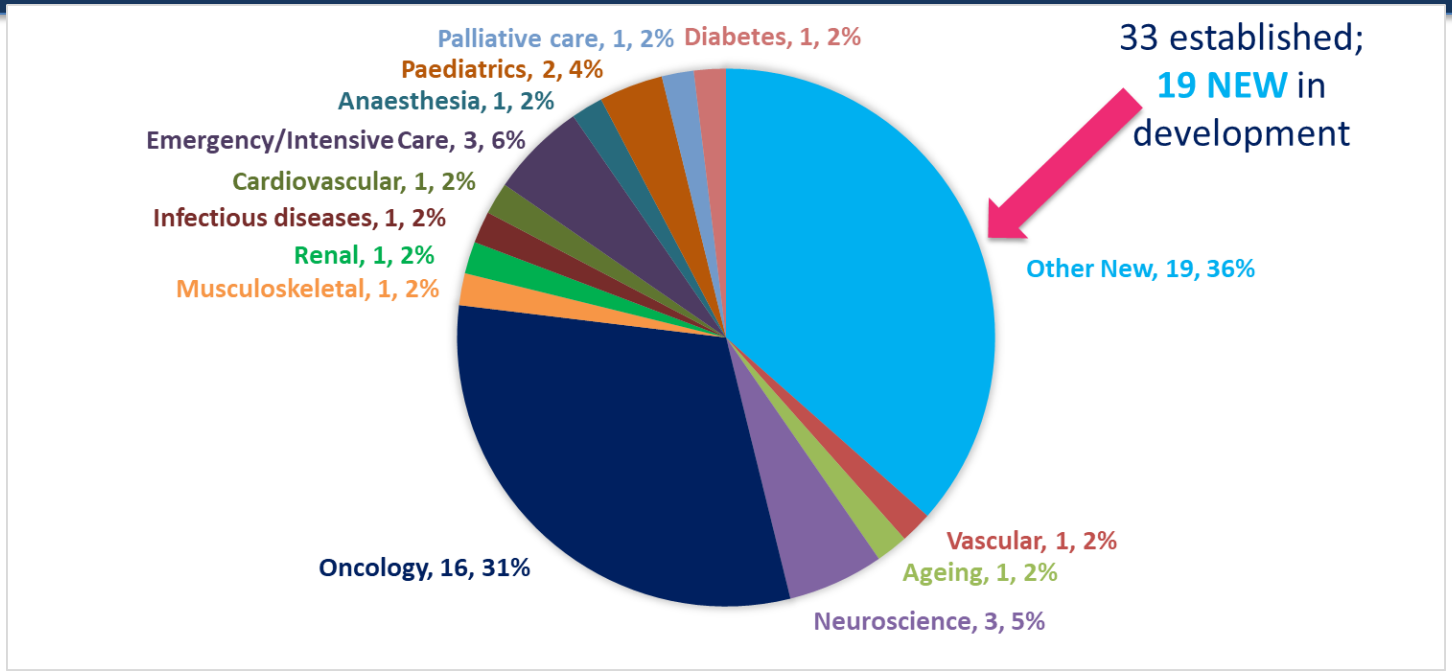
Network is not an Institute

Trial coordinating centre is not a network

Network is the sites and the clinicians who care for patients in those practices

Network is the systems and governance to give control over research to clinicians who care for patients

Clinical Trial Networks in Australia

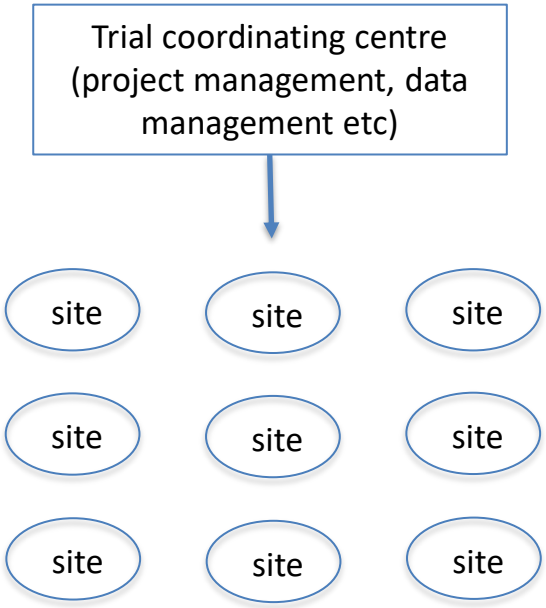


CTNs in Australia

Profiling Networks

- CTNs received **50% of NHMRC budget for trials**

  > $1 million
- Many trials in NEJM, Lancet, JAMA, BMJ, PLOS Med (40,000 citations)
- > 100+ high-impact trials with reported impact on policy/practice


Trial coordinating centre (project management, data management etc)
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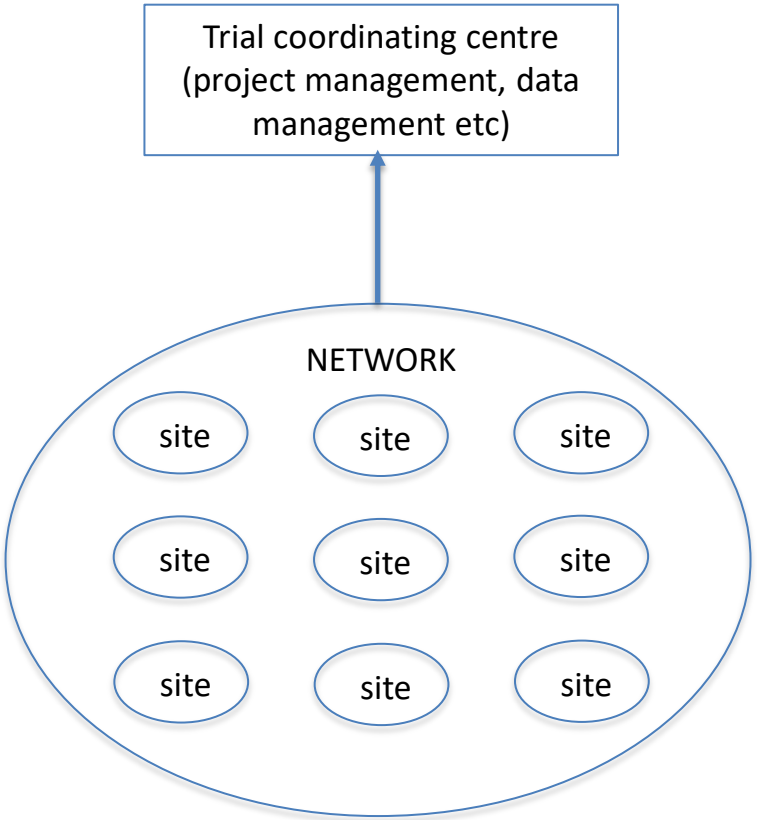
Trial coordinating centre (project management, data management etc)
NETWORK
site
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Other good things happen in a network

Re-usable infrastructure (sites available for multiple trials)

Experience is shared, creates efficiency

Track record of network becomes available to new researchers

Control the research questions and the research agenda

Some things get ‘traded-off’

Network has to manage its reputation

- Can’t do badly designed trials
- Can’t report trials badly

Whole network reputation influenced by everything that is done in the name of the network

Network has to have control of the brand

- Good for quality
- Individual researchers accept some loss of autonomy

Governance

Endorsement of projects

Endorsement of manuscripts

Prioritisation of research questions

Processes for internal peer-review

Rules for authorship

Network relationships

Participation is voluntary, only makes sense to create a network if sufficient relevant stakeholders see it as a 'win-win'

Network leadership must be:

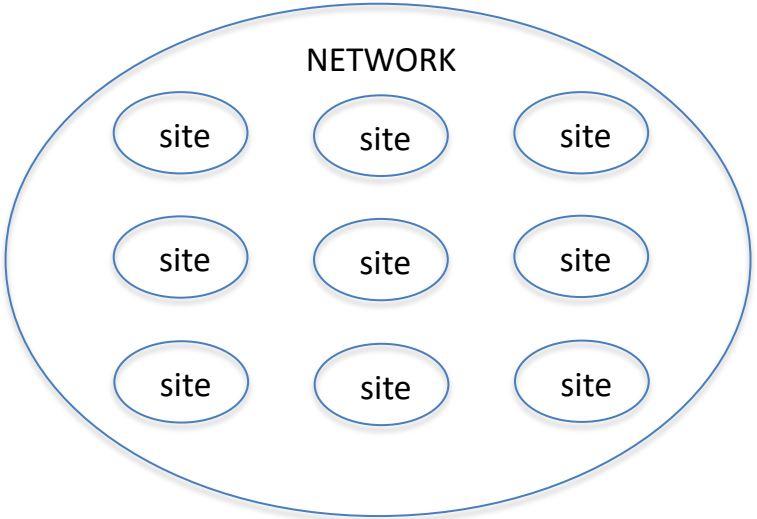
- Representative of member sites
- Responsible to member sites

CTN Establishment- Scope

- **Coordinating/facilitating?**
  - Facilitating
    - Minimal role in direct coordination of trials
    - Not Sponsor
    - Rely on one or more separate trial coordinating centres to run the trials

Facilitation model

Trial coordinating centre

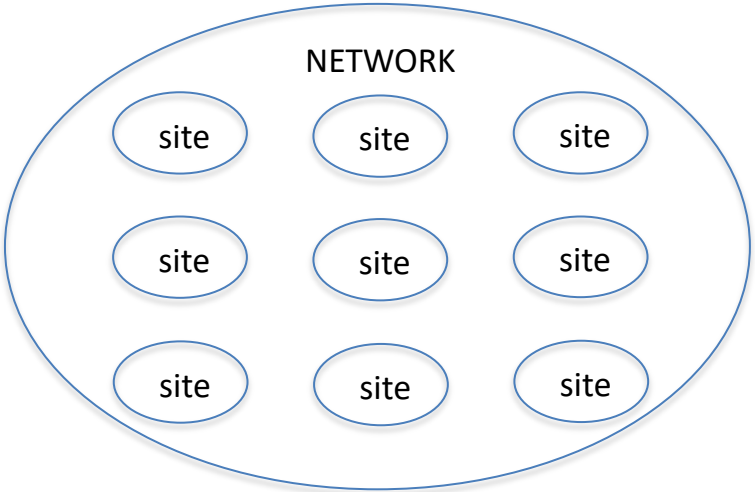


Facilitation model

Trial coordinating centre

Trial coordinating centre

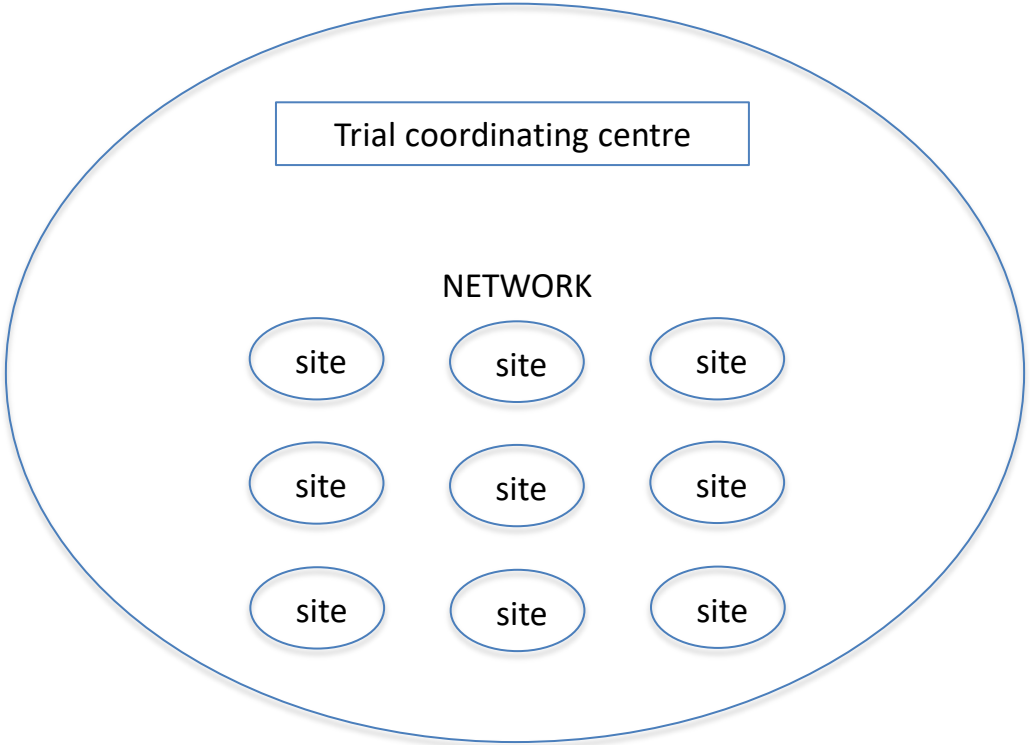
Trial coordinating centre



CTN Establishment- Scope

- **Coordinating/facilitating?**
  - Coordinating
    - Site liaison
    - Direct role in management of trials: recruitment of sites, regulatory compliance, protocol development, coordination, data management, analysis
    - May be Sponsor

Coordinating model



CTN model- coordinating or facilitating?

Potential activities for clinical trial facilitation	Additional activities for clinical trial coordination
Identification of important clinical questions	Direct trial coordination and management by CTN
Collaborative study protocol development	Site management
Peer review and formal endorsement of trials	Data management
Scientific meetings	Recruitment of trial participants
Grant writing	Monitoring
Education/training/mentoring of researchers	Statistical analysis
Advocacy and industry/consumer liaison	Regulatory compliance
Site selection and trial oversight	May or may not act as study Sponsor
Clinical guideline development	

ACTA's role in assisting new networks

- Assisted several new networks (cardiovascular disease, musculoskeletal disease, surgical specialties, endometriosis, drug and alcohol)
- Guidance document
- Template Terms of Reference
- Mentorship

CTN Establishment Process

- **Connect champions and key leaders**
- **Define membership structure**
- **Consider sustainable management**
- **Determine governance structure**
- **Engage stakeholders:**
  - Clinicians, researchers, service delivery
  - Relevant bodies, community health organisations, professional societies, Industry
  - Consumers (including carers), consumer groups and advocacy bodies
- **Consider building a registry**
- Ongoing mentoring, provision of useful docs etc.

- **Needs sustained coordination:** Executive Officer

Acknowledgements

ACTA gratefully acknowledges
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Medical Research Future Fund (MRFF)
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ongoing support from the
Department of Health

Australian Clinical Trials Alliance

Enhancing Primary Care Research: National network of Practice-Based Research Networks (PBRNs)

Phyllis Lau, President

AAAPC
Australasian Association for Academic Primary Care Inc.

ACTA gratefully acknowledges operational funding from the Australian Government's Medical Research Future Fund

Acknowledgement of country – Wurundjeri Land

Australasian Association for Academic Primary Care

Our vision

AAAPC's vision is for a multidisciplinary primary care-oriented health care system founded on patient-centred, primary care principles and developed through evidence and education.

Our mission

To be Australia and New Zealand's leading advocate for high quality multidisciplinary primary care research, education, policy and practice.

AAAPC position on PBRNs

PBRNs plays a critical role in engaging primary health care practitioners in the research process, thereby increasing the relevance of the research conducted to the populations that primary health care practitioners work with and work within.

AAAPC understand the support required to sustain PBRNs. We call for targeted national funding to bring together Australia's primary care PBRNs into a national network.

Australia's current PBRN status

- Approximately 23 PBRNs
- Most are based in general practice and administered through academic institutes
- Examples:
  - ASPREE-XT – Longitudinal, observational follow-up study of ASPirin in Reducing Events in the Elderly (ASPREE) participants
  - NPS Medicine Insights – quality use of medicines
  - SmartVax – vaccine surveillance
  - ASPReN – Australian Sentinel Practices Research Network
  - VicReN – University of Melbourne
  - MonReN – Monash University
  - GoldNet – Bond and Griffith Universities
  - PracNet – Australian National University
  - NRGP – University of Newcastle
  - ISPRN – University of Wollongong

Australia DOES NOT support primary care PBRNs

"Unlike similar countries (eg UK and The Netherlands), Australia no longer has any funding to support the activities of primary-care based PBRNs."

Pirotta M and Temple-Smith M. Practice-based research networks [online]. Australian Family Physician, 2017 Oct;46(10): 793-795. https://search.informit.com.au/documentSummary;dn=139646877615671;res=IELHEA. ISSN: 0300-8495.

Why do we say that?

- Australian Primary Health Care Research Institute (APHCRI) closed in 2015
- Primary Health Care Research and Information Service (PHCRIS) funding ended in 2018
- Contrary to the commitment in Medical Research Future Fund (MRFF) 2018-2021 priorities, there has been no MRFF grant opportunity to “support PBRNs and other collaborations to conduct prioritised primary care research that is led by clinicians, that can permeate daily practice and has potential for scalability”.

Opportunities: time for a national PBRN network

- MRFF has strengthened and sparked initiation of local PBRNs
- COVID-19 has spurred the need for a national primary care PBRN
- Primary care data and linkages
- ACTA
- MRFF Priorities 2020-22 – reiterates commitment to primary care research and elevates its recognition of PBRNs
- Capacity and interest to lead from primary care is high

National PBRN network: challenges and benefits

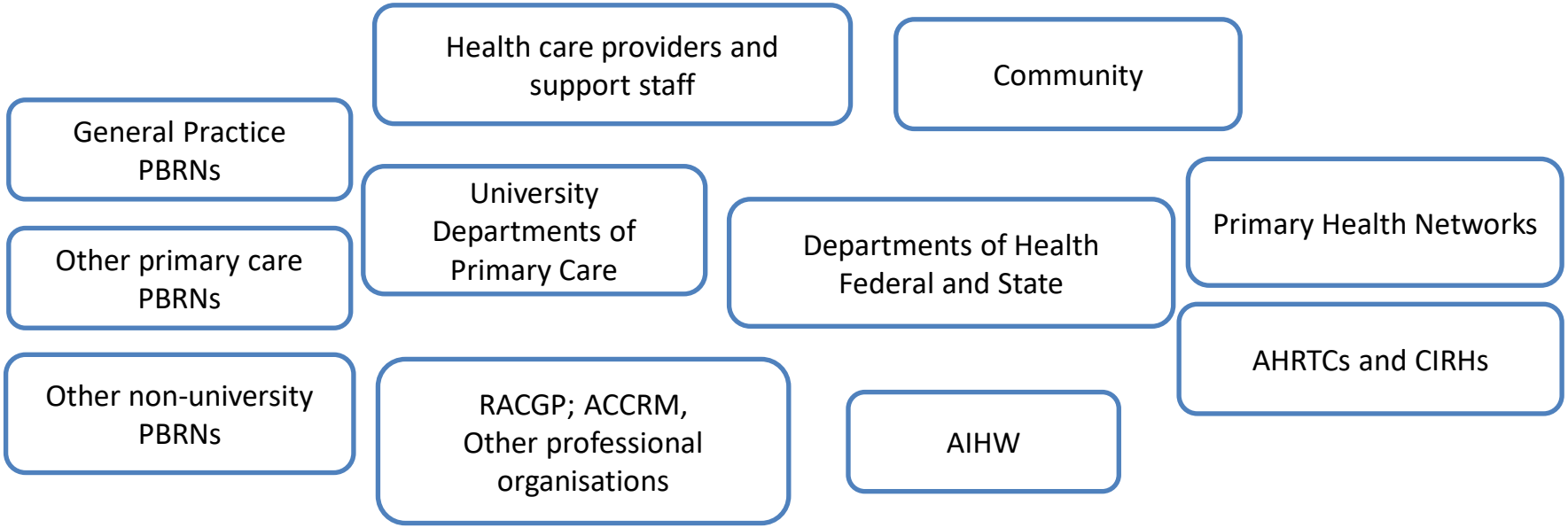
Challenges

- Top-down overpowers bottom-up engagement
- Funding/dominance will belong to a few
- Potentially lose support for local networks
- Crowd out local studies
- General practice becoming a vehicle for other discipline's trials
- ?costly to access
- Complex governance structure required
- ?Tied to certain outcomes alone
- Funding to support/build capacity of clinicians

Benefits

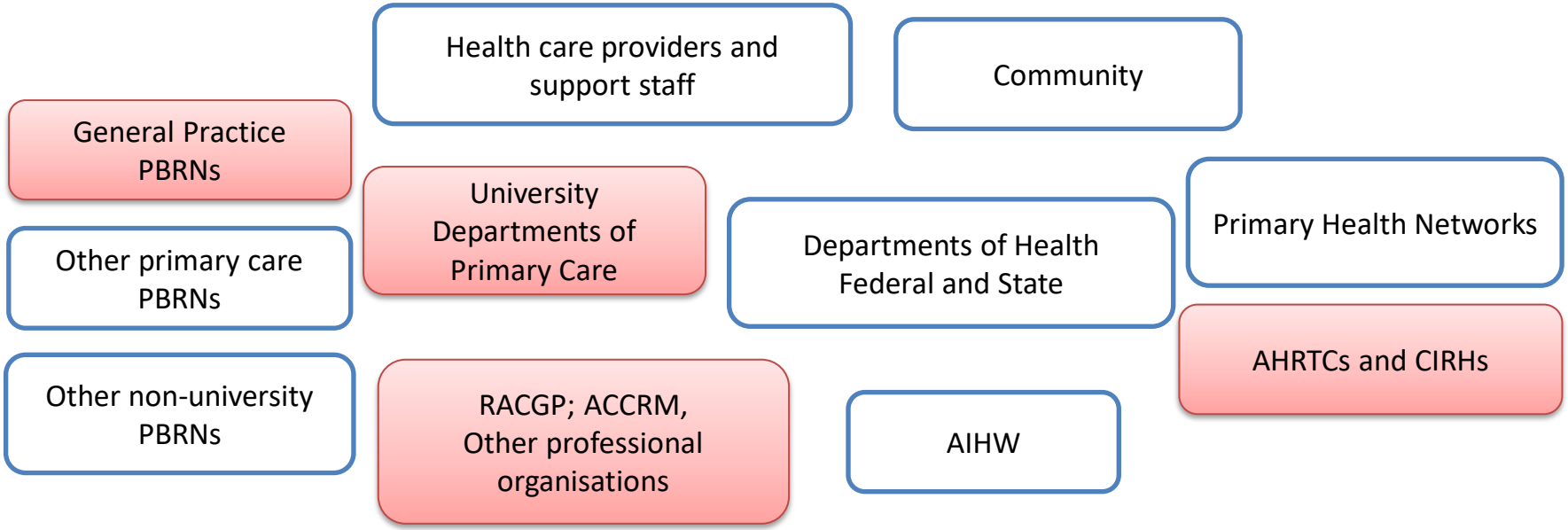
- Enables high quality impactful trials on issues that matter to advancing primary care
- Gives more voice and role to primary care in national policy responses
- More competitive for category 1 funding
- Enables efficient and effective international and national collaboration
- Enables greater participation from a greater number of practices (?reduces overburden on same practices)
- Potentially enhances local PBRN support and engagement
- Primary care Led
- Contributes to practice capabilities with research and research training

PBRN Stakeholders



1st AAAPC PBRN Stakeholder Roundtable (next week)

To call for targeted MRFF funding for a national PBRN network



Moving forward

- Proposal to MRFF for a national network of PBRNs
- Increase advocacy to Health Department
- Update national audit of primary care PBRNs (UoM)
- Agree on an appropriate governance and operation model
- Continue links with RACGP, ACCRM, APNA, PHNs, etc
- Develop links with professional groups of other primary care disciplines
- Increase collaborations with AHRTCs and CIRHs
- Develop links with ACTA
- Engage with clinicians, practice staff and the community

"I can't understand why men make all this fuss about Everest — it's only a mountain."
Junko Tabei, first woman to climb Everest

plau@unimelb.edu.au

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Surgical trainees and students clinical trials and audits

Lessons and opportunities from the Sunrrise Trial and COVIDSurg projects

Dr Peter Pockney

Clinical Trials Network Australia and New Zealand

Royal Australasian College of Surgeons

ACTA gratefully acknowledges operational funding from the Australian Government's Medical Research Future Fund

Declarations of Interest

- For the trials and studies I will mention today
- I am CIA for Sunrrise Australia RCT, funded by the MRFF
- No other studies have received direct funding from any agency
- I have no personal financial interests to declare

Scope of this talk – Surgical Collaborative Research

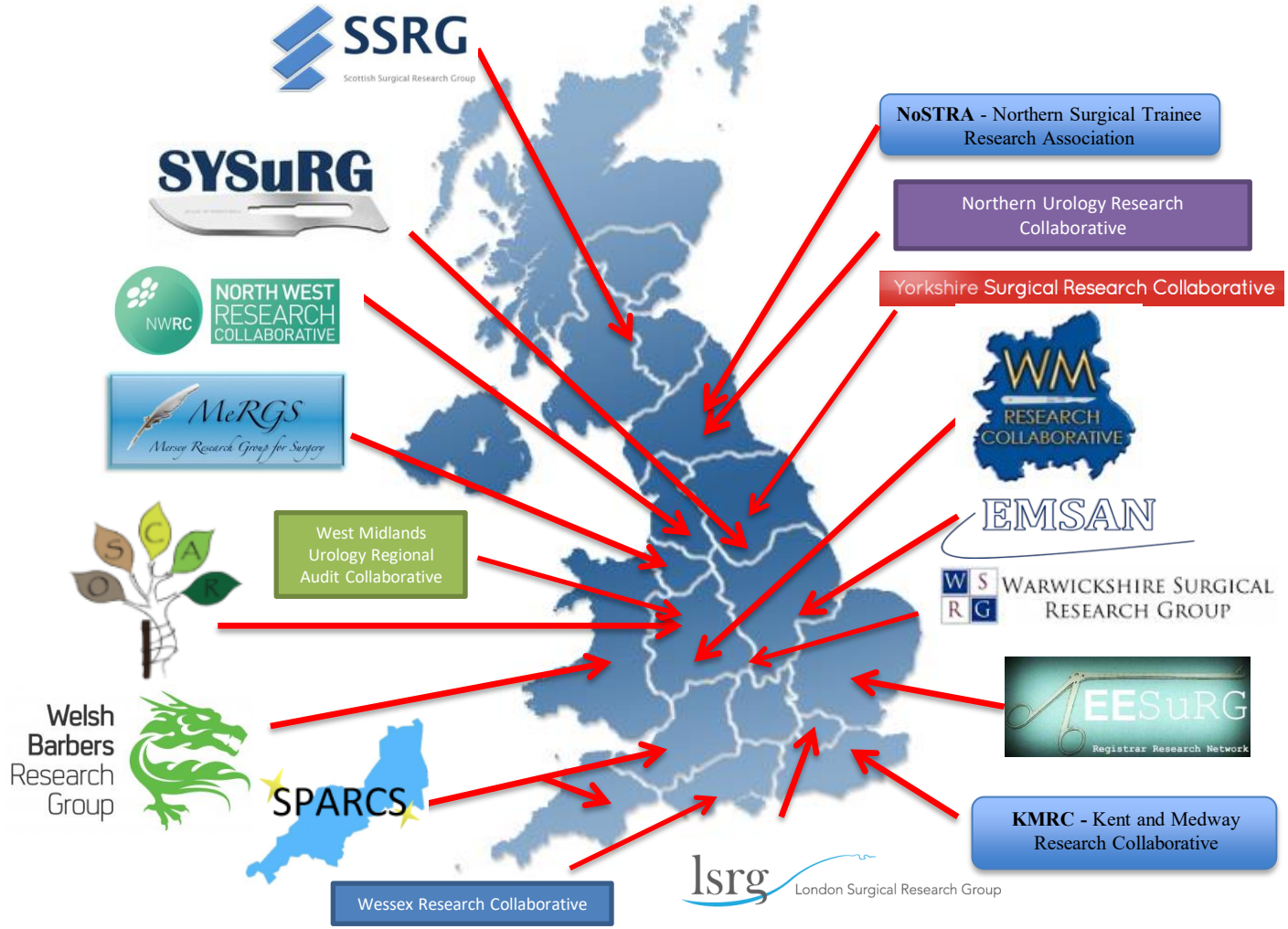
- Where we have come from
- 2020
- Obstacles and opportunities

Where we have come from

- New model of collaborative research in Surgery – UK and Europe 2009
- ROSSINI RCT 2009 – Surgical Trainees West Midland Circuit
  - Simple concept – you recruit for my study in your hospital, I recruit for yours
  - When we rotate hospitals (annually) – you carry on recruiting, I carry on recruiting
  - Studies recruited ahead of schedule, larger numbers, better (quality) results
  - Collaborators share recognition – ‘authorship’ in journals

Where we have come from

- New organisations developed – Collaborative Research Networks
- Specialty, Regional and Training grade based
  - Neurosurgery, General Surgery etc
  - By Training Region (big specialties) and
  - By Specialty (smaller specialties national networks)
  - By Grade – Registrars, JMO & Student, specialist societies (consultants!)


SSRG
Scottish Surgical Research Group
SYSuRG
NWRC
NORTH WEST RESEARCH COLLABORATIVE
MeRGS
Mersey Research Group for Surgery
SCAR
West Midlands Urology Regional Audit Collaborative
Welsh Barbers Research Group
SPARCS
Wessex Research Collaborative
NoSTRA - Northern Surgical Trainee Research Association
Northern Urology Research Collaborative
Yorkshire Surgical Research Collaborative
WM RESEARCH COLLABORATIVE
EMSAN
WSRG WARWICKSHIRE SURGICAL RESEARCH GROUP
MEESuRG
Registrar Research Network
KMRC - Kent and Medway Research Collaborative
lsrg London Surgical Research Group

Impact of trainee research collaboratives in the UK

Individual surgical trainees link together in research collaboratives, working together to deliver multi-centre research

GI surgery trainee collaboratives have run studies across 99% of the 241 GI surgical units in the UK

CUMULATIVE PARTICIPATION OF UK GI SURGICAL CENTRES IN TRAINEE COLLABORATIVE STUDIES

National Surgical Research Collaborative. *Lancet Gastroenterology & Hepatology 2017*

Where we have come from

- GlobalSurg

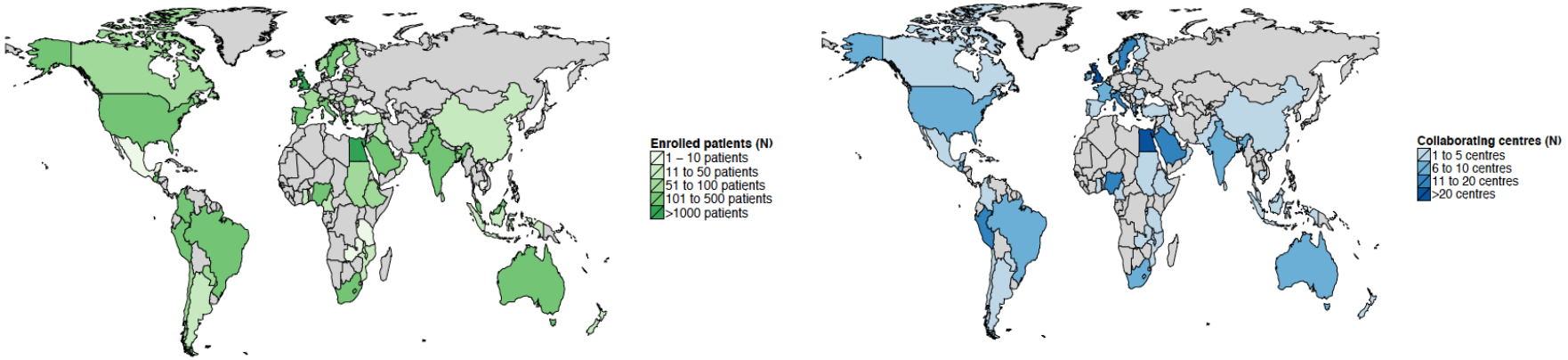
Globalsurg to 2017

2013 -> frontline clinicians

> 2000 collaborators

> 100+ countries (50% LMIC)

> data on 27,000 patients (undergoing abdominal surgery)



Durable, Flexible and Responsive Model

- SARS- CoV-2 PANDEMIC February 2020
  - COVIDSurg Projects
    - GLOBALSurg Network – 1st discussions 2nd week March 2020

Durable, Flexible and Responsive Model

- COVIDSurg Collaborative
  - 3 rounds of focussed hospital system and patient outcomes data collection
    - Impact on Workforce and Planned Surgery
    - Impact on Cancer Surgery outcomes
    - Outcomes of all surgery – when is it safe to operate on a COVID +ve patient?
  - Currently, data on >200,000 patients globally, >5,000 Australia
  - >500 collaborators in Australia, c100 in NZ, >120 countries around the world, >15,000 collaborators globally

Durable, Flexible and Responsive Model

- SARS- CoV-2 PANDEMIC February 2020
  - >10 publications (Incl Lancet, Journal of Clinical Oncology)
  - >850 citations,
  - Impact on delivery of surgery across globe
    - Clinical Pathways
    - Restoring surgical services

Durable, Flexible and Responsive Model

- Sunrrise Australia RCT
  - Australian arm of trainee led RCT in emergency abdominal surgery
  - MRFF Funded in Australia, NIHR in UK, target 840 patients
  - Opened first sites in UK December 2018, Australia Jan 2020
  - By March 2020 – 413 pts in UK, 30 in Australia
  - COVID halted non-pandemic clinical research in UK

Durable, Flexible and Responsive Model

- Sunrrise Australia RCT
  - Australia opened 13 sites in 5 states by Sept 2020
  - Recruited local target (210) by end July
  - Extended recruitment (no extra cost) to 300 by Dec 2020
  - UK recruitment restarting Sept – Dec
- Multi national, multi site model has been durable to the pandemic

Obstacles

- There are significant obstacles to clinical research of this kind in Australia
  - Ethics and Governance
  - Infrastructure

Obstacles

- Ethics and Governance
  - Lack of consistency between HRECs
  - Lack of actual NMA
  - “Research” attitude to Audit
  - Bureaucratic obstacles to student doctors taking part in research/audit

Obstacles

- Infrastructure
  - Professional research staff who know how to do ethics/governance (SSA)
  - Professional clinical research staff (usually, not always, research nurses)
    - Cannot be maintained on ad hoc, project at a time, employment basis
  - Professional Clinical Trials and Cohort Studies Coordinating staff
    - Clinical Trial Centre – surgery is different, surgeons are different!
- Continual ‘rebuilding’ or ‘reinforcing’ trainees research skills and knowledge

Opportunities 2021 ⟶

- POSTVenTT Audit
  - Students and JMOs auditing iron and anaemia treatment after surgery
- POSTVenTT RCT
  - Trainee delivered multi-national RCT of iron vs none in post op patients
- ROSSINI 2 ANZ
  - Trainee delivered multi-national RCT of interventions to reduce SSI
- TASMAN, Regional and Specialty Groups, and CTANZ….

Thank You

- peter.pockney@newcastle.edu.au
- @ppockney

Australian Clinical Trials Alliance

Mental Health Australia General Clinical Trials Network (MAGNET)

Steering Group:

Professor Michael Berk (Deakin)
Professor Susan Rossell (Swinburne)
Professor Paul Fitzgerald (Monash)
Dr Krys Mossop (Deakin)
Dr Carthur Wan (Consultant)
Bern Spinks (Consultant)
Dr Anthony Fillipis (NSV)

ACTA gratefully acknowledges operational funding from the Australian Government's Medical Research Future Fund

The History

- Recognised need experts in the field
  - Agreed significant improvements required to strengthen trial quality, impact and efficiency in mental health
- Discussions NSV Science Council
- Formed small steering committee
- Canvassed community:
  - Experts nationally working in mental health
  - Lived experience / First Nations / CALD
  - ACTA
- Call from MRFF (Million Minds)

Construction of MAGNET

- Guided by:
  - Other successful CTNs e.g. musculoskeletal, ICU
  - Mental health community (clinicians/researchers/lived experience/First Nations/CALD
  - ACTA
  - RANZCP, APS
  - MRFF guidelines
- Two components to the applications
  - Network platforms
  - Signature trials

MAGNET platforms

Data Management: Comprises data management systems and infrastructure, and data science (biostatistics, artificial intelligence (AI), bioinformatics) expertise. This ensures CTs generate meaningful, translatable outcomes, and facilitates novel cutting-edge trial designs. Centralised (clinical, phenotypic, genetic) data and biospecimen management services for both existing and future CTs will form a valuable research asset for MAGNET collaborations.

Health Economics and Knowledge Translation: Support will embed cost assessment and feasibility as an essential outcome measure in CTs. This expertise will lead to faster approval, translation, and adoption into clinical practice of interventions with positive clinical outcomes.

Assessment: Standardised training and resources will build consistency in CT assessment (e.g. battery selection, data collection, interrater reliability) and enhance ongoing sector capacity and quality. CTs incur considerable start-up time and associated costs. Assessment standards and guidance will accelerate trial site establishment markedly reducing this sector inefficiency.

Governance and Policy: Harmonised support for CT governance (ethics, Good Clinical Practice (GCP), regulatory requirements, consent processes, Data Monitoring Committees) to reduce the resource burden of conducting CTs & ensure network trials have the utmost scientific rigour & ethical standards

MAGNET signature trials

- 4 signature trials
- Reviewed, rated and consolidated by 50 CIs
- **The Kite Study** will definitively explore ketamine as a potential novel BD therapeutic.
- **Hearts and Minds 1 (HM1)** will be the first definitive evaluation of a comprehensive lifestyle program against established psycho-therapeutics.
- **Hearts and Minds 2 (HM2)** will be the first randomised placebo-controlled clinical trial (RCT) to definitively evaluate if statins and metformin can help people struggling to find effective treatment for their MDD to improve both their both mental and physical health.
- **The HeLiPaD Study** will examine an interactive online intervention aimed at increasing help seeking behaviours compared against psychoeducation.

MAGNET members

Australian Clinical Trials Alliance

www.clinicaltrialsalliance.org.au

MAGNET governance and management

Steering Committee (SC): A 7-9 member committee, with at least 1 (preferably >1) consumer and carer leaders. Remaining membership will comprise a subset of CIs, and leaders from auspicing/ supporting organisations.
Leadership Committee (LC): All MAGNET CIs, as well as leaders from relevant stakeholder groups, will form the LC.
Secretariat: A small team will be recruited (Executive Officer, Platform and Program Manager, Lived Experience and First Nations Engagement Officers, Business Development Manager and Trial Monitoring Officer.)
Lived Experience Advisory Panels (LEAPs): LEAPs will serve as vehicles for building lived experience (LE) leadership and engagement both at the Network level and in CT design, delivery and translation.
Trial Steering Groups (TSG): Each MAGNET trial will have a TSG comprising CI(s) leading the trials, other clinical/methodological researchers, and relevant people with LE either from LEAPs or appropriate consumer/carer groups and/or peak bodies.

MAGNET summary

- Submission 9th Dec
- Any questions?

Australian Clinical Trials Alliance

Multi-centre clinical trials research for eye disease through an Eye Trial Research Network

Marios Constantinou
Clinical Trials Research Centre Manager

CENTRE FOR Eye Research Australia

ACTA gratefully acknowledges operational funding from the Australian Government's Medical Research Future Fund

Who are we?

- Established in 1996 by Professor Hugh Taylor
- Affiliated with the University of Melbourne Department of Ophthalmology
- Co-located at the Royal Victorian Eye and Ear Hospital

Mission

To conduct eye research with real-life impact.
We are unravelling the causes of diseases, preventing blindness through earlier diagnosis and better treatments, and restoring sight

How are we doing?

World University Rankings

1. University College London
2. Harvard University
3. Johns Hopkins University
4. University of Melbourne
5. National University of Singapore

Clinical Trials Research Centre (CTRC)

- Head of CTRC: Assoc/Prof Lyndell Lim
- CERA has over 20 years experience in ophthalmic clinical trials
  - phase 1 to 4
  - extensive expertise in leading clinical research
  - dedicated Clinical Trials Research Centre (CTRC)
- CTRC conducted >100 IIT/Sponsored trials
  - >20 trials progressing
  - passed 3 industry audits
  - delivered ICH TransCelerate-accredited GCP courses
- Multi-centre trials delivered with external partners

Rationale of the CERA Eye Trial Research Network (ETRN)

- The top three causes of irreversible blindness in Australia are age-related macular degeneration (AMD), glaucoma and diabetic retinopathy
- Increasing age is the major risk factor for AMD and glaucoma. A major challenge in all three diseases is to find better treatments to prevent and ideally to cure blindness

- ETRN
  - Increase and broaden access and delivery of novel treatments available in commercial and investigator-initiated ophthalmic clinical trials (IITs) through a common, standardised, ICH-GCP compliant framework and data platforms
  - Increase efficiency, speed, data quality and professional engagement as well as provide educational and research opportunities
  - IIT collaboration / generate research hypotheses

Network Model: Hub and Spoke

- ETRN will be an unincorporated network of member organisations
- CERA's CTRC as the "hub"
- the "hub" will provide the founding expertise, oversight and central support for the other research sites ('spokes")
- spokes can include private eye clinics and public hospitals as well as optometry
- scope of clinical studies extends from early and preventative treatment measures in the primary care setting, through to Phase 1-4 interventional studies for advanced disease
- ETRN vehicle for initiating and completing collaborative Investigator- Initiated Trials (IITs) and implementing industry-sponsored trials

ETRN ‘Hub and Spoke’ Roles

CERA ‘Hub’

- Central support (tailored to need) and training provided from the pre-study to study close out period across all phase trials

- ETRN oversight through CERA Clinical Research Manager or Senior Study Coordinator (SSC), pre-study start up, study start up, study coordination and study close-out

Network Site Roles (‘Spoke’)

- Masked and Unmasked Investigators (dependent on study protocols)
- Equipment requirements (imaging, laboratory and pharmacy)

Current and Next Steps

- Engaged first ophthalmology clinic ('spoke') site in Victoria late 2018
  - currently conducting 3 clinical trials with a further 6 more in 2021
- Recently added another Victorian private ophthalmology site
- Discussions held with other sites. Victorian ETRN can be limited
- Growth of ETRN by expanding interstate
  - include not only researchers from Ophthalmology, but also academic Optometrists, basic scientists who work in vision/vision related fields, plus patient advocacy groups like Vision 2020, Vision Australia, Macular Degeneration Foundation, Fred Hollows Foundation, Guide Dogs
  - national start up meeting was to be established by approaching the above groups
    - map out the aims/purposes of this network through representatives from all groups

Pro and Cons of National ETRN

Pro and Cons of National ETRN

Pros

- United we stand…
  - Australia is too small to support duplicate trials/research groups/registries
- One identity & one voice for:
  - Funding
  - Lobbying/Advocacy
- Power in patient numbers
  - Meaningful clinical trials/registries through collaboration
- Our size/number lends well to the ability to agree on research direction/design by committee- i.e. not to few, not too many

Cons

- Planning to fail & Failure to plan…
  - Who's going to lead this?
  - Where do we start?
  - Does anyone know what they're doing?
- We are/I am doing just fine, I don't need to collaborate
  - What do I stand to lose by joining?
- Who's going to pay? This will be expensive just to set up…
- This will be as fun as herding wild cats…

CENTRE FOR
Eye Research
Australia

Hope in sight™

the royal victorian
eye and ear
hospital

THE UNIVERSITY OF
MELBOURNE

CERA gratefully acknowledges the support of its affiliates, the University of Melbourne and the Royal Victorian Eye & Ear Hospital