Clinical Trials and Cohort Studies

The New Environment

- Only $70M in funding
- A lower success rate (~5%)
- Lack of peer review
  - Less able to judge specialised science
  - More based on general approach and well argued case for the non-specialist
- Probably greater emphasis on changes in practice and policy rather than future research (untested)
- Milestones / deliverables will require careful planning and balance
  - To get funds needs a grander vision
  - To deliver the project needs conservative targets

Category Descriptors – Significance (40%)

7	6	5
The proposed clinical trial and/or cohort study: • will comprehensively and convincingly address the objective of this grant opportunity and will deliver against the desired outcomes • is informed by an exemplary analysis or review of existing and ongoing studies in the field • was developed with broad and meaningful involvement of research end-users to ensure it meets their needs • if successful, will have very significant research impacts.	The proposed clinical trial and/or cohort study: • will strongly address the objective of this grant opportunity and will deliver against desired outcomes • is informed by a thorough analysis or review of existing and ongoing studies in the field • was developed with meaningful involvement of research end-users to ensure it meets their needs • if successful, will have significant research impacts.	The proposed clinical trial and/or cohort study: • will address the objective of this grant opportunity with only minor concerns and deliver relevant desired outcomes • is informed by a good analysis or review of relevant existing and ongoing studies in the field, with only minor concerns with respect to the analysis • had research end-user involvement in a number of key aspects of the design • if successful, will have appreciable research impacts.

Significance (Trials)

- High-quality clinical trials that address important gaps in knowledge, leading to relevant and implementable findings for the benefit of human health
- Improvements in health and wellbeing, health care practice or policy, as a result of high-quality clinical trials that provide reliable evidence of the effects of health-related interventions on health outcomes (or appropriate surrogates)
- (Less emphasis on earlier phase trials that inform future research – though still eligible)

Significance – Strong Rationale

- What previous research has occurred? Has the applicant described a systematic review? Do the points of difference between these studies and the proposed research provide a strong justification for the proposed research?
- Does the research question(s) meet the needs of research end-users: consumers, community members, policy makers and clinical practitioners?
- If the research objectives are achieved, would the research have a significant impact on the health issue: including to knowledge, health, economic and social impacts.

Clinical Trials and Cohort Studies

Broad and meaningful involvement of end users

- **Identify the expected end users of the results of the study**
- **Demonstrate the relevance of the proposed question to those end users**
  - Clinicians or other HCPs that would use the results of the study to inform practice
  - Individuals with personal experience (incl consumers or carers)
  - Policy makers - Government / NGOs
  - Guideline developers
- **Consultation in the process of trial design**
  - Relevance of patient-centred outcomes and economic outcomes
  - Consider involving end users in the study's governing body

Davina Ghersi, SPRS, NHMRC

ACTA Super webinar: 11 February 2020
Webinar on a document ACTA has created to guide trialists towards optimising their trials for implementation and implementability.
https://clinicaltrialsalliance.org.au/latest-news/registrations-open-super-webinar/

Category Descriptors – Research Quality (40%)

7	6	5
The proposed clinical trial and/or cohort study: • has a near flawless design and research methodologies appropriate to the research question • is comparable with the best international research in the field • is highly feasible with all of the required techniques and resources established • includes highly appropriate research end-user involvement • includes highly effective milestones and performance indicators.	The proposed clinical trial and/or cohort study: • has a strong, well defined and coherent design and research methodologies appropriate to the research question • is comparable with strong proposals in the field internationally • is feasible with required techniques and resources established • includes appropriate research end-user involvement • includes effective milestones and performance indicators.	The proposed clinical trial and/or cohort study: • is generally clear in its research methodology, logical and appropriate to the research question • raises only very few minor concerns with respect to the study design • is feasible in almost all areas: required techniques and resources established or nearly established • may not be highly competitive with similar research proposals internationally • includes some appropriate research end-user involvement • raises a few very minor concerns about the appropriateness of milestones and performance indicators.

Team Quality and Capability (20%)

7	6	5
Relative to opportunity, the Chief Investigators (CIs): • have a high level of expertise and experience in all aspects of the proposed research • have over the last 5 years, a combined record of research achievement that is outstanding by international standards commensurate with their field of research (research achievement, quality and productivity) • have outstanding national and international reputations in clinical trial or cohort study methodology and relevant research fields • may include junior members who are strong contributors to overall team capability.	Relative to opportunity, the CIs: • have expertise and experience that is highly relevant to the proposed research • have over the last 5 years, a combined record of research achievement that is excellent by international standards commensurate with their field of research (research achievement, quality and productivity) • have excellent national and/or international reputations in clinical trial or cohort study methodology and relevant research fields • may include junior members who contribute to overall team capability.	Relative to opportunity: • there are only minor concerns about the CIs' level of expertise and experience required to undertake the proposed research • the CIs have over the last 5 years, a combined record of research achievement that is well above average by international standards commensurate with their field of research (research achievement, quality and productivity) • the CIs have very good national and/or international reputations in clinical trial or cohort study methodology and relevant research fields • the CIs may include junior members who have the potential to add to the team capability.

Common problems / pitfalls
Previous Large-Scale Trials Scheme

- Treatment effect implausibly large
- Lack of pilot data
- Compliance with treatments overly optimistic
- Insufficient completeness of follow-up
- Incorrect allowance for factors in sample size calculations
- Lack of clinical trial experience
- Budgetary Issues

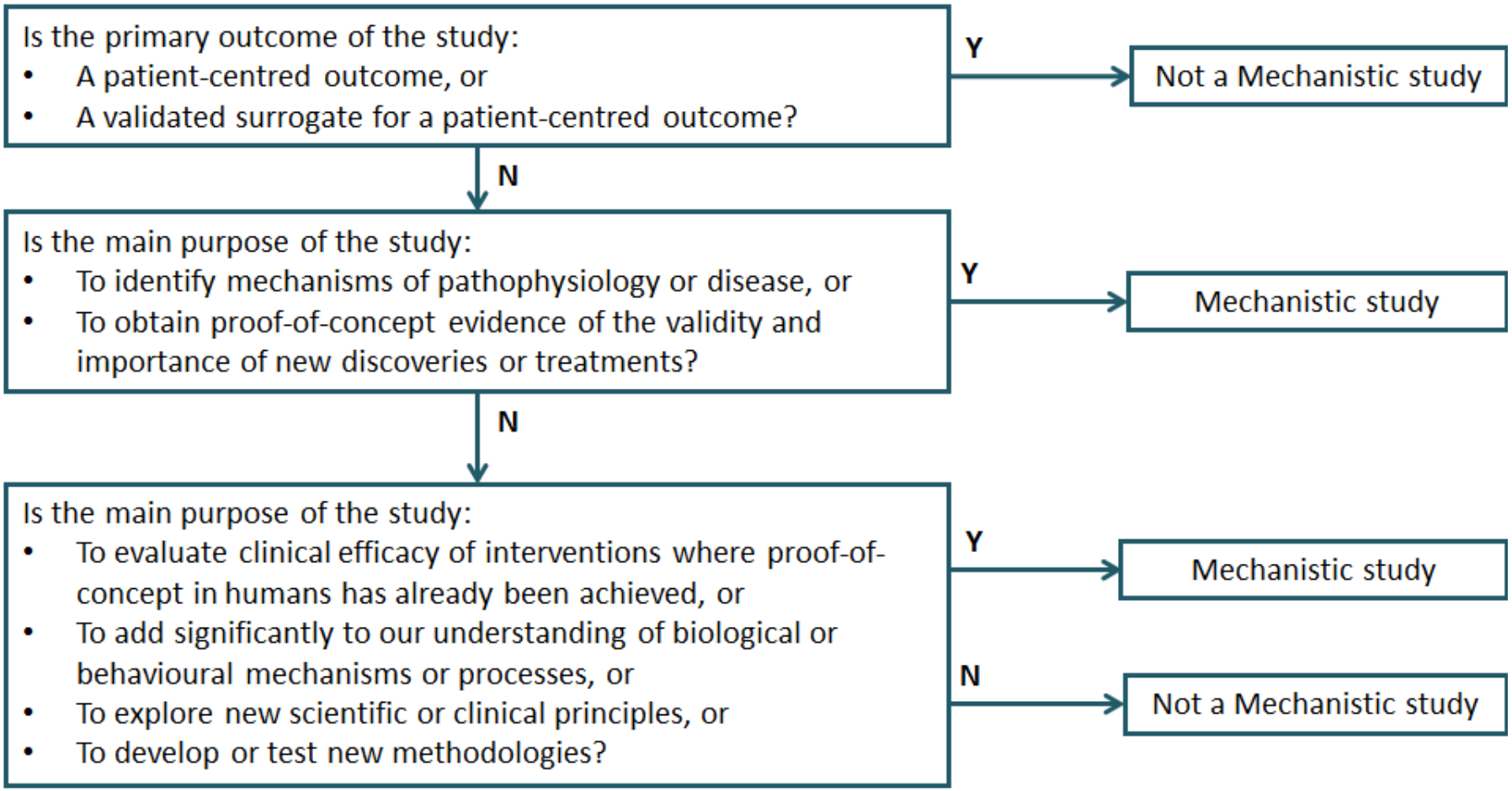
Research Grants 2019

NHMRC Scheme	Amount	Comment
Ideas Grants *	$173M	11.1% success – av. award $822K
Clinical Trials and Cohort Studies	$58.5M (23 Trials)** $16.0M (8 Cohorts)	5.5% success – av. award $2.4M 5.4% success
Investigator Grants	$366M	13.2% success – av award $1.5M
Synergy Grants	$50M	15.6% success – ea. award $5M

*The Ideas Grant scheme is not intended to support research where a clinical trial or cohort study is the primary objective.

** Two cancer clinical trials included in the 23 awarded clinical trials from NHMRC.

If the study is a clinical trial, is it a mechanistic study?



Research Grants 2019

Cancer Australia		
Priority driven research	$8.9M	24 projects mainly basic science (2-4 trials)

Research Grants 2019

Some MRFF schemes	Open / Recently closed	
Ovarian cancer research	$20M	
Rare cancers, rare diseases, unmet need	$15M reproductive ca $5M childhood brain ca $15+M general / earlier rounds	
International clinical trials	$42M over 4 years	$4.2M per cycle about every 4 mos
MRFF Frontiers	$1M → $50M each	Big bold ideas

- **Points for discussion:**
- Low success rate of trials through NHMRC Trials and Cohort Studies Scheme
- Substantial work needed for a successful application (including systematic review of current evidence, pilot work, etc)
- NHMRC trials are likely to be high impact practice changing studies
- Sev trials for Cancer Australia were cut by NFFC by NHMRC
- Low success rate of clinical trials through Cancer Australia – most projects awarded are basic science and/or translational research
- Give consideration of studies linked to clinical trials (biological studies) where the trial is not the primary objective of the grant to be submitted through Ideas Grants (see eligibility ruling up front) – where is it judged on innovation / novelty as much as practice changing

- **Points for discussion:**
- MRFF has been a more successful of funding for cancer clinical trials in recent times
- MRFF requires grants to be already written – in anticipation of funding rounds; recognise these are for niche areas.
- Consideration should also be given for lobbying future MRFF areas of research – eg MRFF is considering calls for research identified by consumer groups; MSAC submissions of current gaps in evidence, etc.