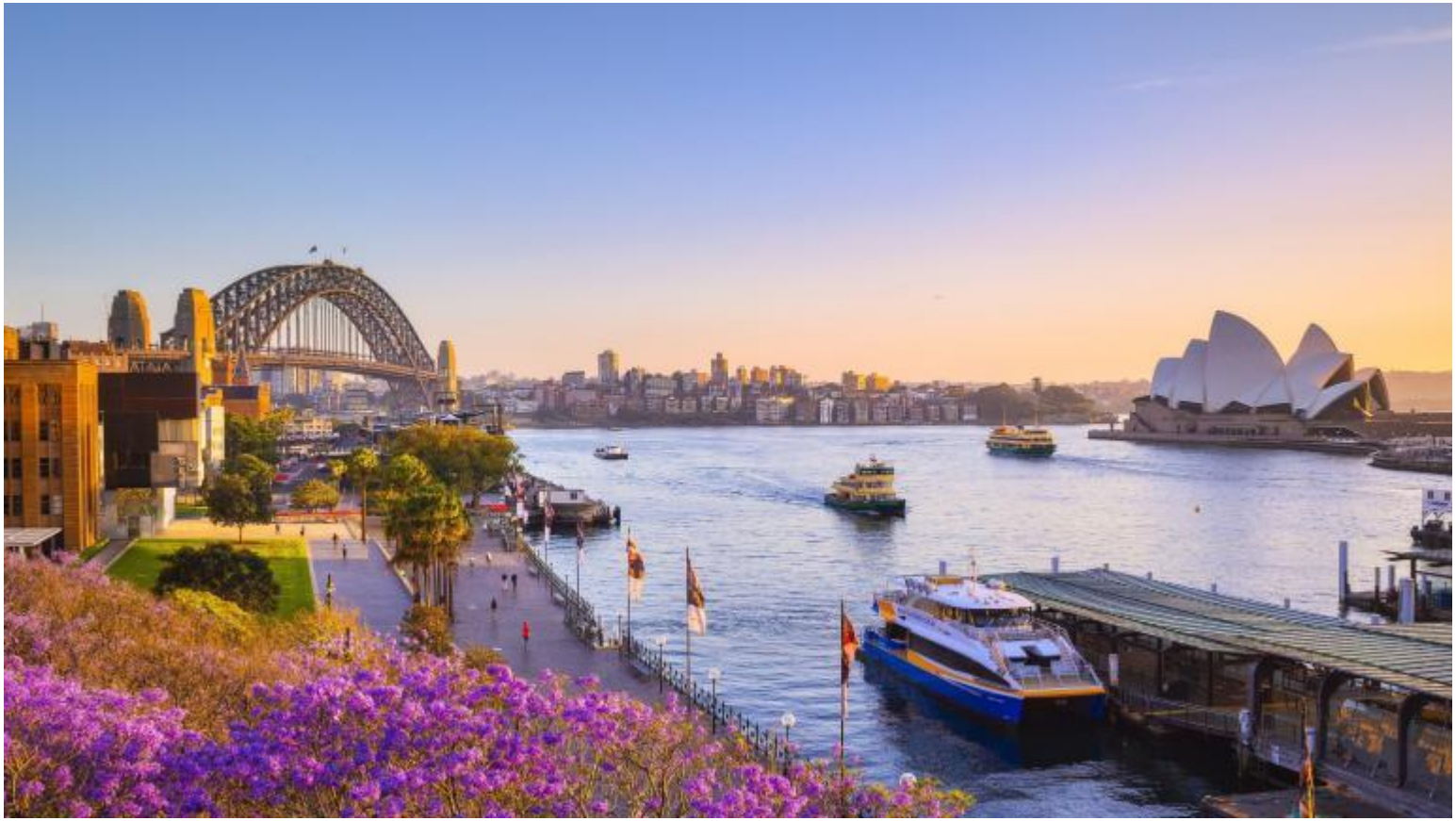
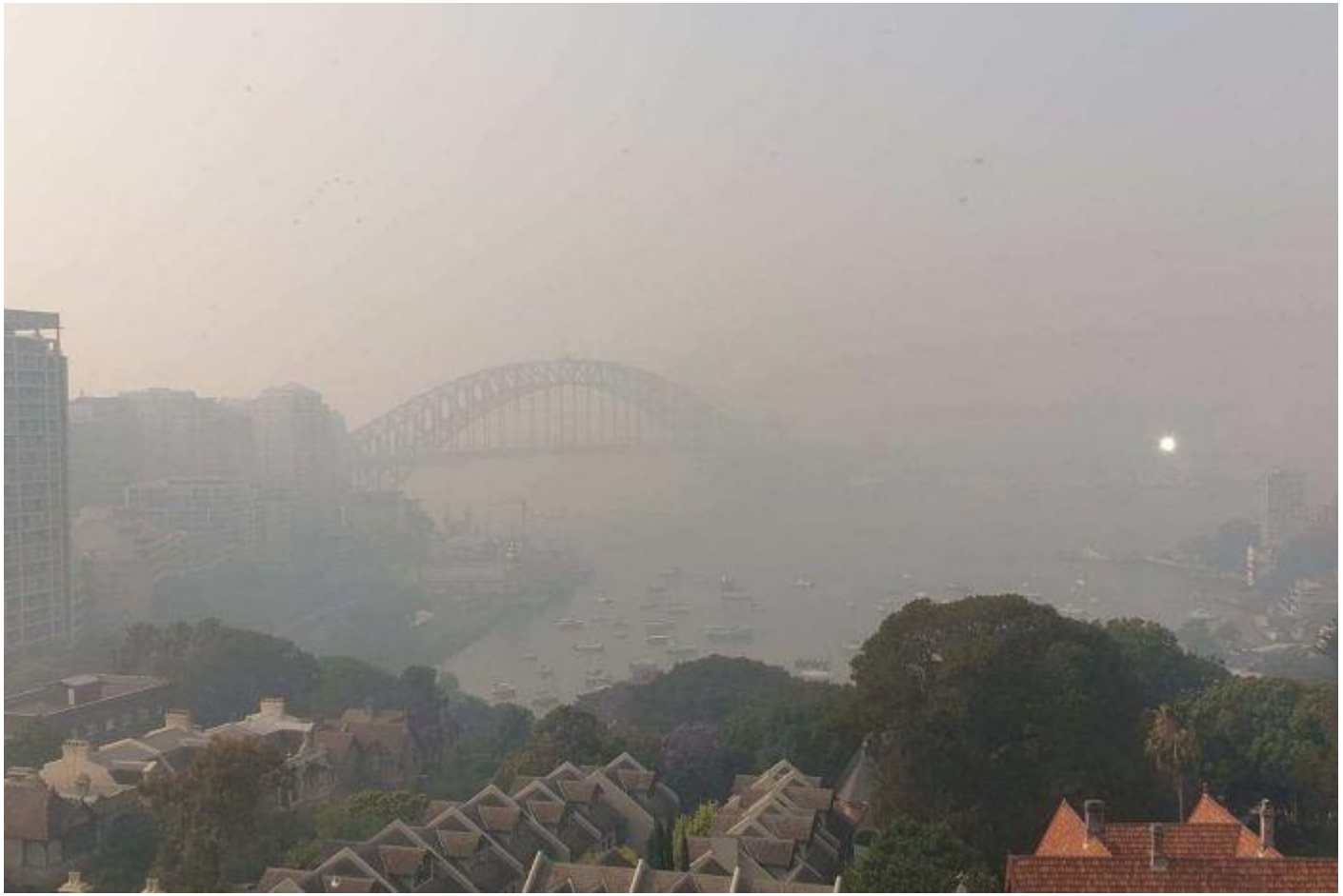
Kirby Institute

Data Safety and Monitoring Boards (DSMB): ethics

Bridget Haire | December 2019





Overview

- **Origin of the DSMB**

NIH : *Every randomized clinical trial must have an independent DSMB*.

- **Roles and responsibilities of a DSMB**
- **My experience as the ethicist on the study CAPRISA 008**
- **Complex ethical issues that can arise**

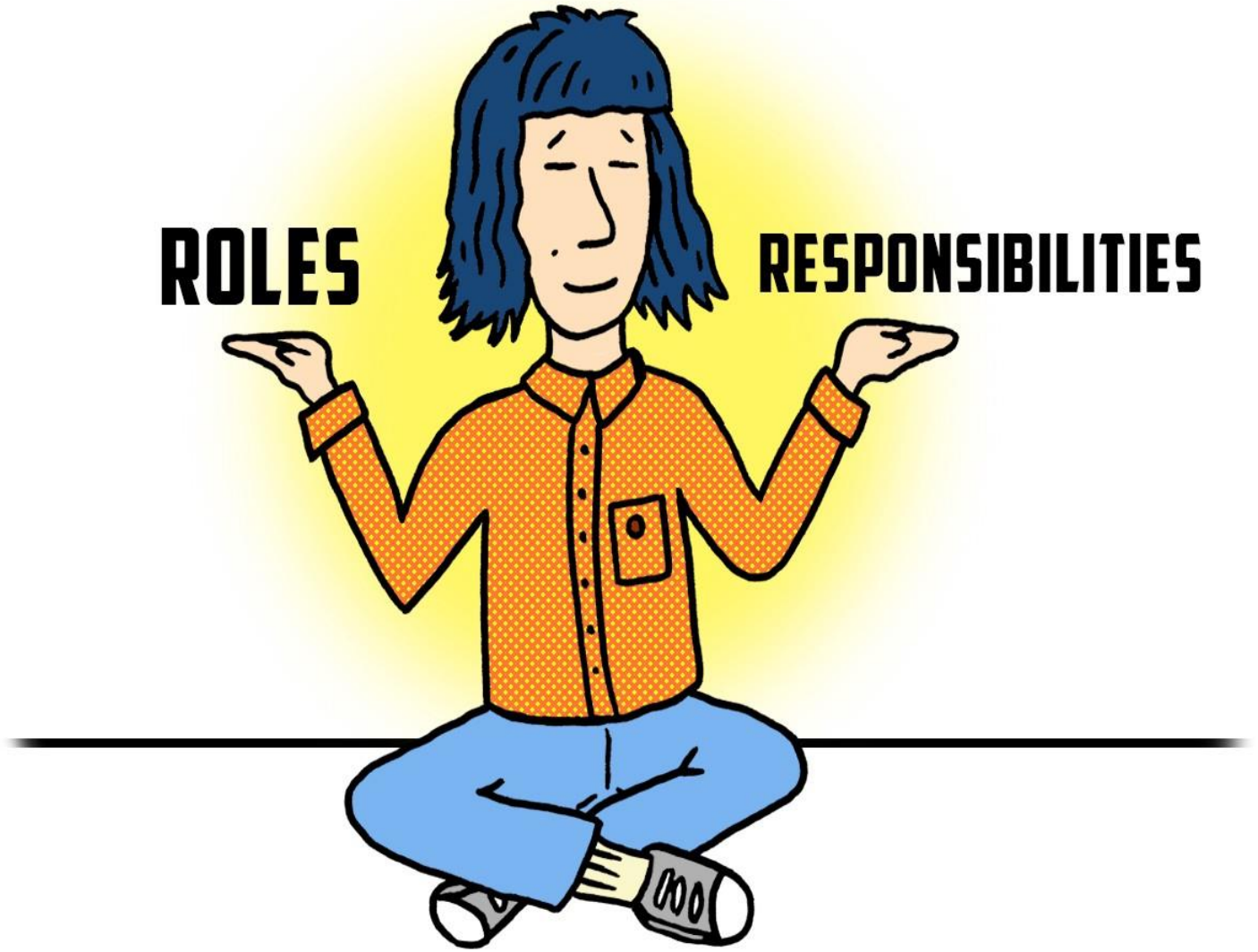
Planning the DSMB (US NIH model)

PI: include data and safety monitoring plan in each new protocol.

HREC: approve the plan, determine what types of safety monitoring processes are required

Convene a DSMB *(responsibility of Institute or Centre)*

PI: Provide all required data to the DSMB, and act on findings of DSMB.


ROLES
RESPONSIBILITIES

Primary role

Key questions:

Is it safe to continue this study?

Is it fair to continue this study?

Powers and responsibilities of a DSMB

What can a DSMB do?

- Scheduled interim analyses, monitoring of trial conduct (normal business), pre-determined ‘stopping rules’
- Can require further (unscheduled) interim analyses
- Can request changes to trial design for statistical, safety or efficacy reasons
- Can unblind data to investigators
- Can stop a trial for a range of reasons, including for reasons relating to new information about the agent under investigation that comes from another trial this is regardless of whether the reason fits with the predetermined stopping rules.
- A DSMB has the responsibility to respond to unanticipated circumstances.

The trial for which I was DSMB member

CAPRISA
CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA

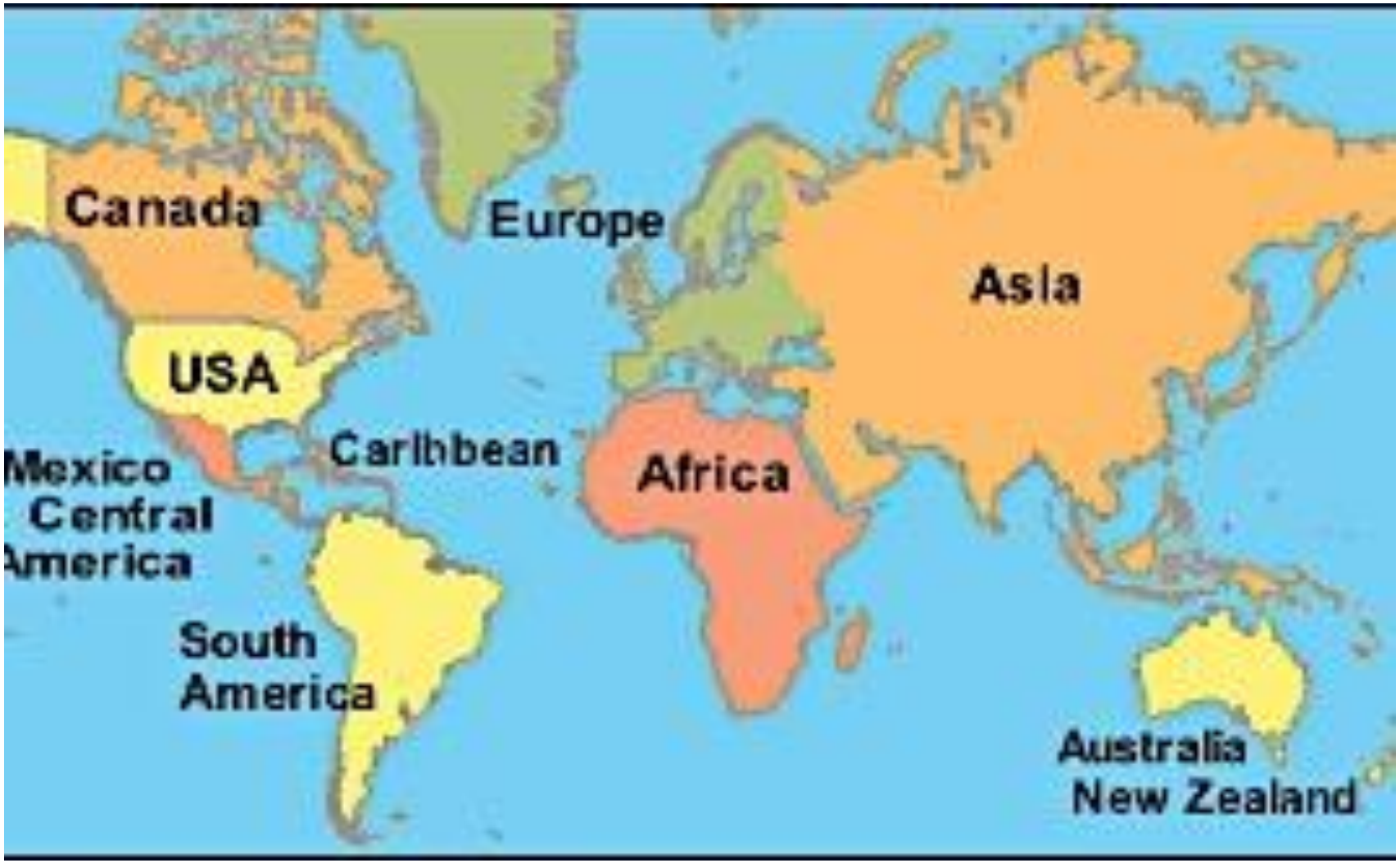
UNAIDS
CAPRISA is the UNAIDS Collaborating Centre for HIV Research and Policy

CAPRISA 008
Tenofovir Gel Implementation Trial

Good Adherence in Trial of Topical Pre-Exposure Prophylaxis Integrated into Family Planning Services

Dr Leila E Mansoor (PhD) *
Co-Principal Investigator
* on behalf of the CAPRISA 008 team

AIDS 2016 – Durban, South Africa – 22 July 2016


Canada
Europe
Asia
USA
Carlhbean
Africa
Mexico
Central
America
South
America
Australia
New Zealand

What are the ethical issues that can arise for a DSMB?

Issues around modifying the trial schedule in response to data

- Issue/s about safety or emerging efficacy or futility from within the trial (could result in requesting unscheduled analyses)
- New data impacting on whether or not continuation of the research is warranted or feasible (could result in requesting changes to trial design as a result of data generated inside or outside the trial
- Unblinding trial data (to investigators or to another DSMB)
- Stopping the trial

Thinking about stopping rules

When should a trial be stopped?

- Safety.
- If pre-determined conditions for stopping are reached.
- Efficacy?
- Futility?
- Commercial reasons?

Ethical concerns about stopping a trial early

Participants have volunteered on the basis of potential benefits of the research to themselves, their communities, and humanity

Overview

When should unblinded data be shared outside a DSMB?

To avoid introducing bias, sharing data may occur in exceptional circumstances:

Safety issues

- serious adverse events in a treatment group
- Serious adverse events in a related trial

Issues related to trial feasibility

- If early trial cessation is recommended by DSMB
- Need for further statistical advice?
- If trial completion is threatened, perhaps due to release of data from a related trial, but there is still equipoise

Summary and conclusion

- The DSMB role is the stewardship of the trial
- Participant safety is the primary and overriding responsibility
- DSMBs can require a ranges of changes to the trial if seemed necessary for safety and monitoring purposes
- To avoid introducing bias, unblinded data should be available only to the DSMB
- The exception to the above is where there is a compelling reason related to safety or trial feasibility that cannot be managed without unblinding.


THANK YOU!