Design and Implementation of a Master Observational Trial: Early Insights from the Cohort Network for Adolescents and Youth with Mental Health Multimorbidity (CALM) study

SOCIETY FOR CLINICAL TRIALS 45TH ANNUAL MEETING

MAY 20, 2024

Session Overview

1. **The use of Master Observational Trials (MOT) to study Mental Health Multimorbidity in Children and Youth**
   – Dr. Peter Szatmari, Centre for Addiction and Mental Health
2. **Statistical Considerations for Master Observational Trials (MOTs)**
   – Dr. Clement Ma, Centre for Addiction and Mental Health
3. **Understanding the Importance of Outcome Selection & Measurement**
   – Dr. Suneeta Monga, Hospital for Sick Children
4. **Youth and family engagement in integrated knowledge translation**
   – Dr. Lisa Hawke, Centre for Addiction and Mental Health
5. **An Embedded Intervention Trial within CALM: Targeting Sleep to Improve Mental Health Outcomes**
   – Dr. Madison Aitken, York University
6. **Q & A**

The use of Master Observational Trials (MOT) to study Mental Health Multimorbidity in Children and Youth

Dr. Peter Szatmari, Director of the Cundill Centre for Child and Youth Depression,

Centre for Addiction and Mental Health,

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Financial Disclosures

- Canadian Institutes of Health Research
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- Centre for Addiction and Mental Health
- Ontario Brain Institute

Outline

- Is there a crisis in child and youth mental health?
- What are some of the issues in the clinical trial literature in child and youth mental health?
- The common occurrence of two or more mental disorders (multimorbidity) represents a significant challenge in child and youth mental health
- The opportunities afforded by a MOT design to meet some of these challenges; give CALM as an example

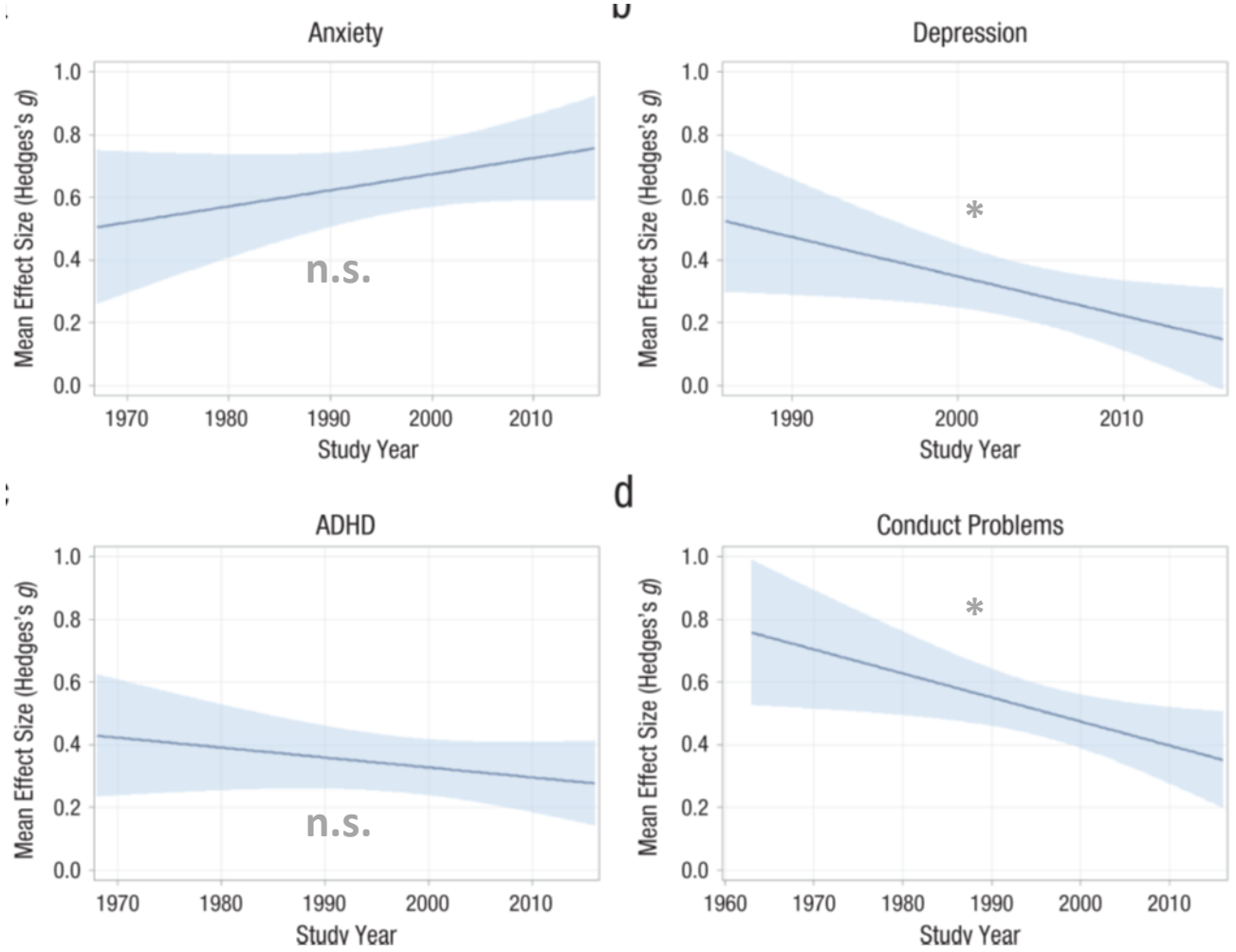
A Crisis in Child and Youth (CY) Mental Health?

- No question CY mental health is a major public health problem
- Recent estimates from the Global Burden of Disease study (Kieling et al 2024)
  - Globally in 2019, 293 million individuals aged 5 to 24 years had at least 1 mental disorder, and 31 million had an SUD.
  - The mean prevalence is 11.63%for mental disorders and 1.22%for SUDs.
  - Mental disorders account for 20.3% of YLDs from all causes in this age group (5-24).
  - Over the entire life course, 24.85% of all YLDs attributable to mental disorders are recorded before age 25 years.
- Clear evidence that prevalence of anxiety and depression have increased post-COVID, as have demand for services (Keyes & Platt Journal of Child Psychology and Psychiatry 65:4 (2024), pp 384–407)
- A pressing need exists for evidence-based interventions that have an important impact

The Current Landscape of Clinical Trials in CY Mental Health

- Systematic reviews of the clinical trials literature in CY mental health
  - More often explanatory than pragmatic (but more pragmatic in recent years)
  - Simple/single intervention vs non-active or waitlist controls
  - Sample sizes too small
  - Multiple outcome domains and OMIs, no defn' of MID
  - Exclusion of individuals with comorbidity
  - Targets a single mental health dimension (ie depression or anxiety)
  - Very little stakeholder engagement
- Lack of a clear framework for development of interventions
- How effective in general are interventions for common mental disorders of children and youth (anxiety, depression, ADHD, conduct)?

No Improvements in child and youth Psychotherapy Effectiveness Over 50 years



Weisz et al. (2018)

k = 453 RCTs

N = 31,933 participants age 4-18

Spanning 53 years

What is the problem? Mental Health Conditions represent a Complex Problem

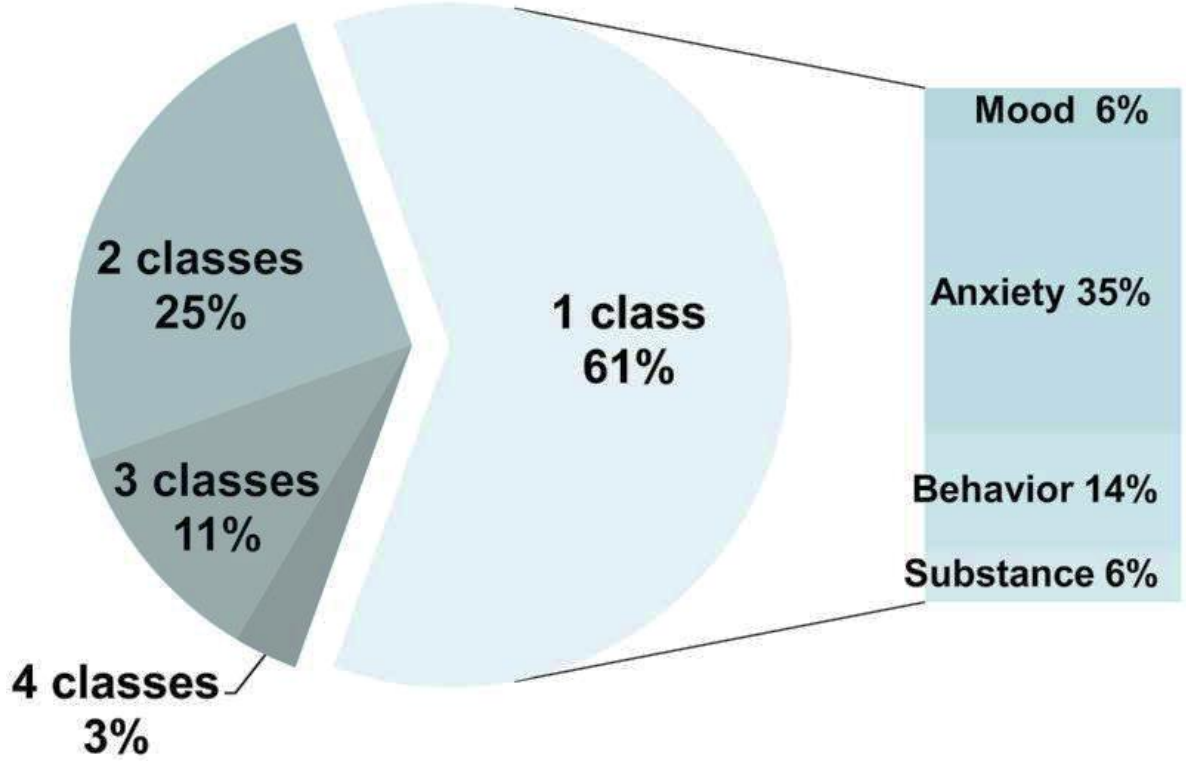
- CY MH disorders characterized by heterogeneity in presentation
  - There are many different combinations of the symptoms that might meet criteria for depression as a disorder

- There is no one to one correspondence between a risk factor and disorder.
  - Different mental disorders share common symptoms/risk factors (multifinality)
    - Disturbed sleep is a symptom of several CY mental disorders (depression, anxiety, ADHD) and may be an important risk factor of depression

  - There are different pathways to the same disorder (equifinality)
    - Depression may be 'caused' by Adverse Childhood Experiences, substance abuse, chronic pain

- MH Comorbidity (or Multimorbidity) is the rule not the exception;
  - At the population level ie in the NCS-A,
  - Within a mental health clinic

MH Multimorbidity in general population: the National Comorbidity Study-Adolescent Supplement (NCS-A)



Distribution of the Major Classes of DSM-IV Disorders Among Adolescents 13 to 18 years old with at Least One Disorder (N=5,163) – Cross sectional data

(Merikangas, 2010)

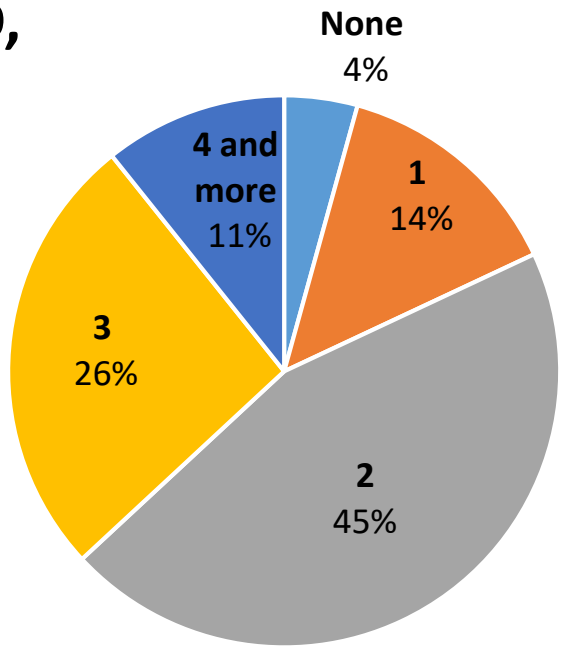
Patterns of MH Multimorbidity in a Clinical Sample of Adolescents (N=233) 14-17 years of age

- **Eligible classes of disorder; any depressive, any anxiety, ADHD, and Behaviour**

- **82% with multiple mental health conditions (2 or more)**

- Anxiety as the most class (9%) that occurs in isolation

- Depression rarely presents in isolation (only 2.6%)



Distribution of the number of diagnostic classes

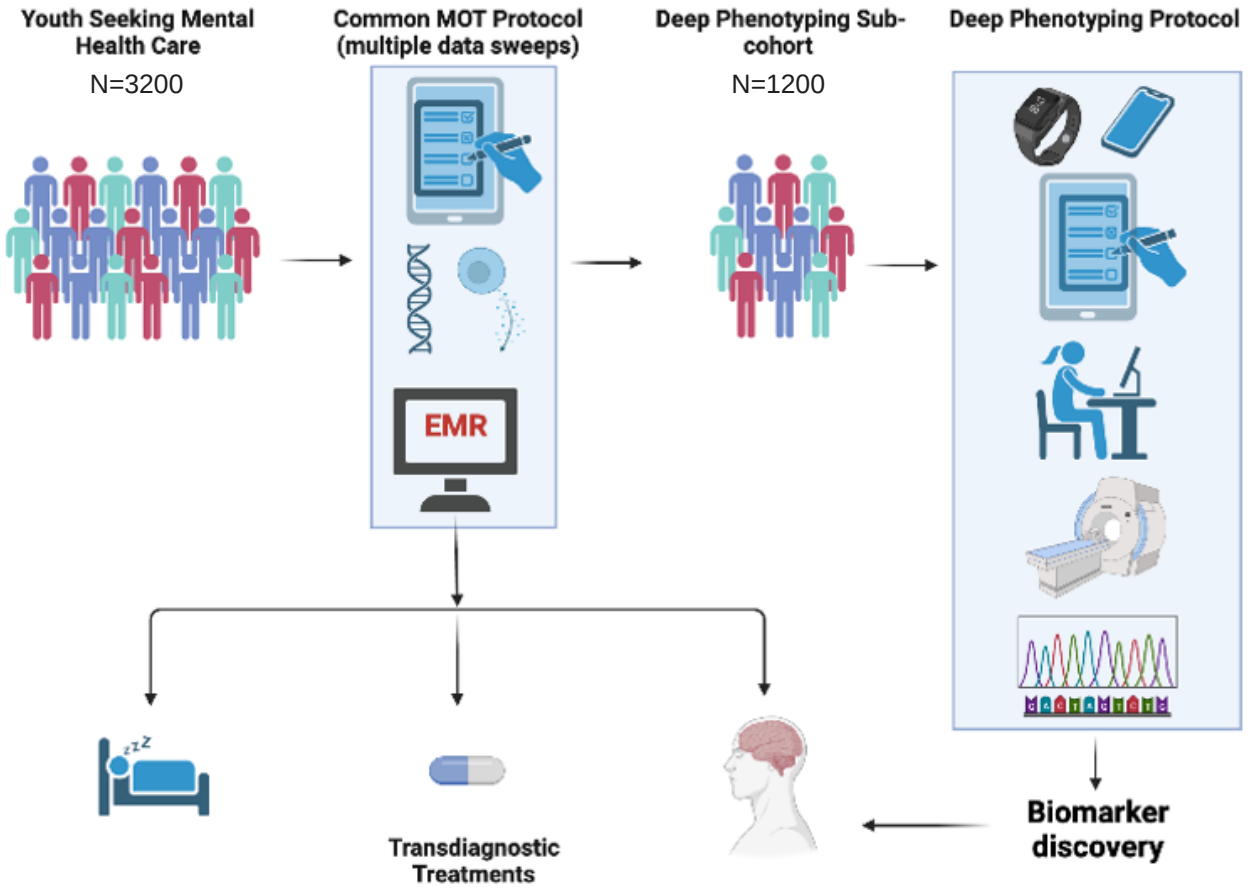
- 16 different combinations (5 diagnostic classes)
- 2 most common patterns of Multimorbidity make up 48% of the sample
  - 35% with anxiety + depression
  - 13% with anxiety + depression + ADHD

Potential Solutions

- Requirements of a new approach
  - MH disorders are complex and so require complex psychosocial interventions (MRC)
  - These interventions have to take account of, and even take advantage of, multifinality and equifinality
  - Interventions need to take into account MH multimorbidity
  - Given the paucity of clinical trials, our field needs conduct more trials within a shorter time frame
- MOT design with embedded clinical trials provides a potential answer to many of these requirements

The Cohort network for Adolescents and Youth with Mental Health Multimorbidity (CALM Study).

- Youth aged 11-24 y. seeking mental health services
- Six participating clinical sites (Ontario & Alberta)
- Master observational prospective cohort trial (MOT)
- + Embedded clinical trials within the cohort



Opportunities Afforded by a MOT Design to Meet Some of These Challenges

- Conduct multiple trials at the same time using a standardized framework
- Targeting a single risk factor may affect multiple outcomes (multifinality and multimorbidity)
- Make use of participants from the cohort study as controls who receive treatment as usual
- Hopefully easier to recruit larger sample size

Statistical considerations for master observational trials (MOTs)

Clement Ma, Ph.D.

Scientific Head, Biostatistics Core Services,
Centre for Addiction and Mental Health (CAMH)

camh

Financial Disclosures

- Canadian Institutes of Health Research
- Ontario Brain Institute
- Canadian Academy of Child and Youth Psychiatry
- Hospital for Sick Children (SickKids)
- Northwestern Mutual Life Insurance Company
- Centre for Addiction and Mental Health Discovery Fund

AGENDA

1 Intro to MOTs

2 Design of CALM MOT

3 Summary

Introduction to master observational trials

Master (interventional) protocols

- Master protocols are trials that “evaluate more than one or two treatments in more than one patient type or disease within the same overall trial structure”

- Types of Master Protocols:

1. Umbrella
2. Basket
3. Platform

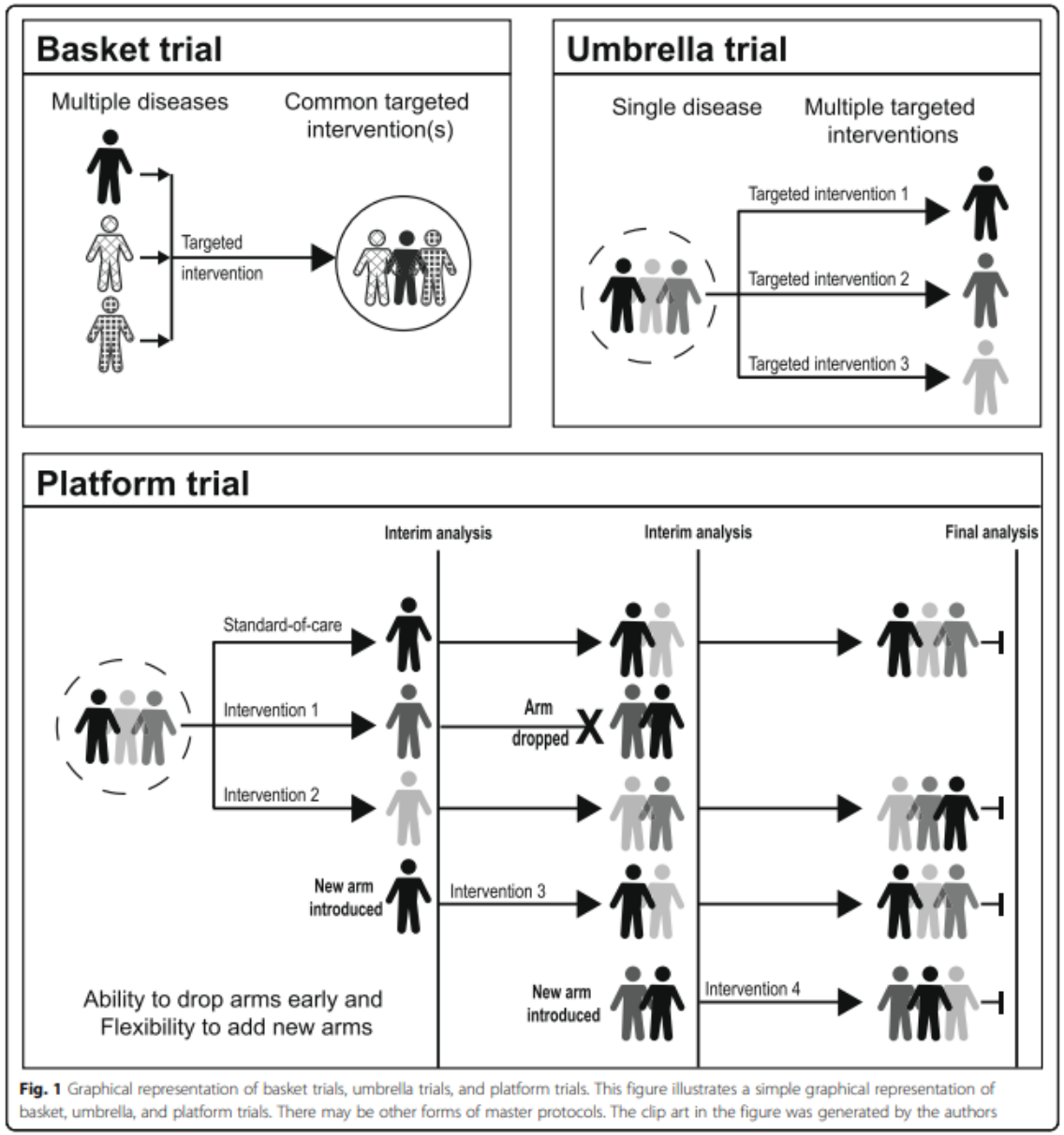


Fig. 1 Graphical representation of basket trials, umbrella trials, and platform trials. This figure illustrates a simple graphical representation of basket, umbrella, and platform trials. There may be other forms of master protocols. The clip art in the figure was generated by the authors

Woodcock & LaVange. *NEJM* 2017 377:62-70. Park et al. Trials. 2019 Sep 18;20(1):572

Advantages and challenges of molecularly-based (master) interventional trials

Advantages

- High quality, focused data collection on one disease, biomarker, and intervention
- Master protocols can improve efficiency for evaluating 1+ diseases and 1+ interventions

Challenges

- Relatively small N
- Interventional trials mitigate bias by fixing as many variables as possible:
  - Restrictive inclusion criteria
  - Selected biomarker with pre-defined thresholds (biomarker negative / positive)
  - Measurement of biomarker at single timepoint
- Unclear how typical trial patient would compare to a patient in the real world

Dickson D, et al. Cell. 2020 Jan 9;180(1):9-14.

Real world data (RWD)

- Real world data (RWD): “the data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources, such as electronic health records (EHRs), claims and billing activities, product and disease registries, patient-generated data from in-home settings, and data from other sources, such as mobile devices”

- RWD can be used to fill knowledge gaps that exist from limited number of trial patients

US Food & Drug Administration. Real world evidence. 2022. https://www.fda.gov/science-research/science-and-research-special-topics/real-world-evidence.

Advantages and challenges of molecularly-based real world data

Advantages

- Large sample sizes
- Broad inclusion criteria
- Diverse set of biomarkers

Challenges

- Retrospective data
- Unstandardized, incomplete, inaccessible, siloed
- Complete biomarker data usually not present
- Biomarkers measured at different labs may not be comparable
- Biomarker data may not be stored in discrete data fields

Dickson D, et al. Cell. 2020 Jan 9;180(1):9-14.

Master observational trials (MOT)

“The MOT is an amalgamation of master interventional trials, prospective observational trials, and a precise method of cataloging molecular data…

The MOT is a prospective, observational trial that broadly accepts patients independent of biomarker signature and collects comprehensive data on each.”

Dickson D, et al. Cell. 2020 Jan 9;180(1):9-14.

Features of master observational trials

- Centralized trial administrative functions
- Traditional interventional trial organization
  - Registered protocol, standardized data collection
- REB approved participant consent and privacy authorization
- Precise molecular testing classification
- Longitudinal data collection
- Seamless integration with interventional trials and RWD

Dickson D, et al. Cell. 2020 Jan 9;180(1):9-14.

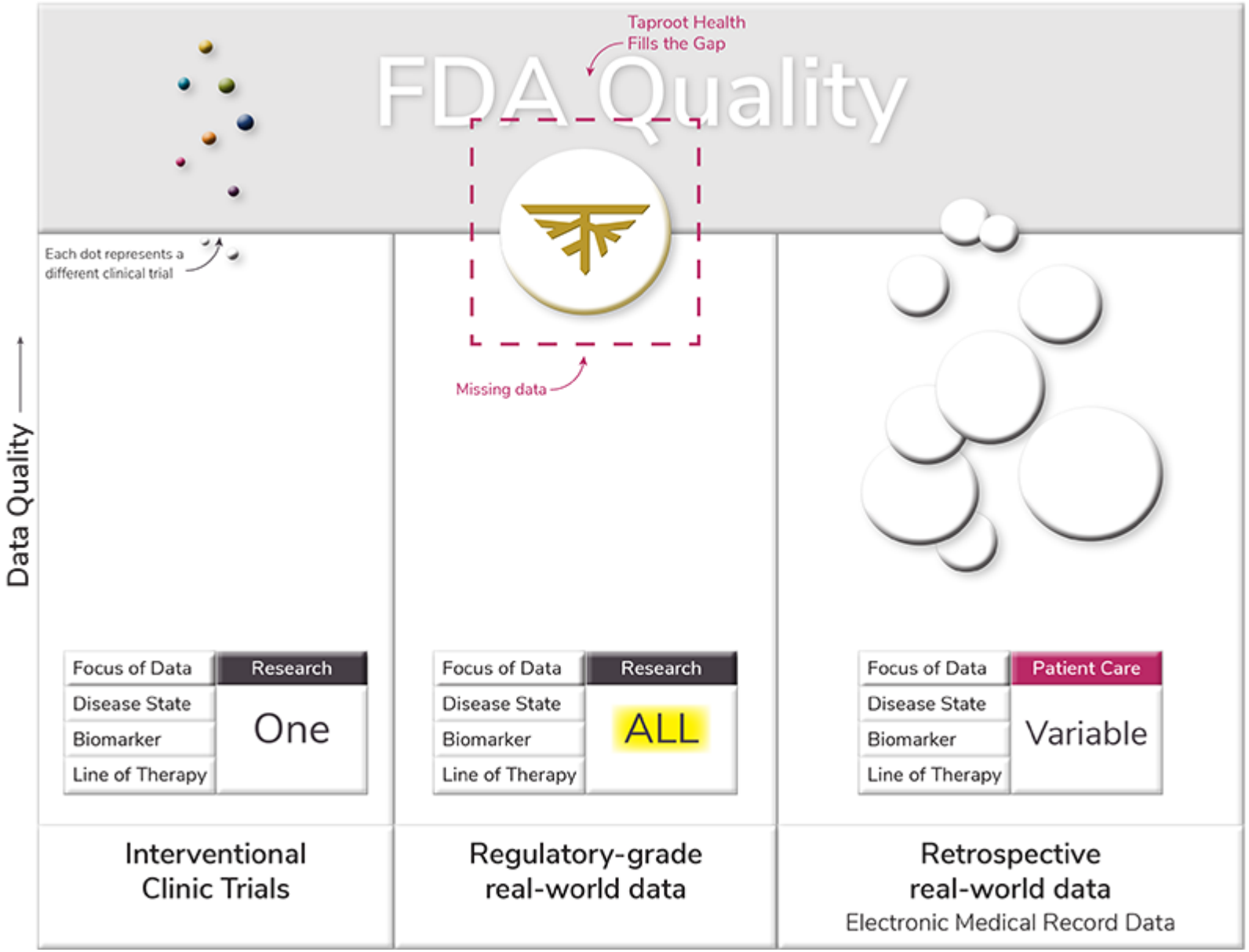
The Registry of Oncology Outcomes Associated With Testing and Treatment (ROOT)

- **Objective:** This study is to collect and validate regulatory-grade real-world data (RWD) in oncology using the novel, Master Observational Trial construct.
- **Population**: Any patient with advanced cancer
- **Treatment:** Standard of care
- **Study Design:** Master observational trial (MOT)
  - **Validation Cohort:** patients enrolled to allow validation of specific data collection, trial processes
  - **Analysis Cohorts:** patients enrolled to determine associations, effects, benefits

(1) Dickson D, et al. Cell. 2020 Jan 9;180(1):9-14. (2) https://clinicaltrials.gov/study/NCT04028479

ROOT

- Proposed ROOT MOT “fills in” the missing regulatory-grade RWD between interventional trials and retrospective RWD

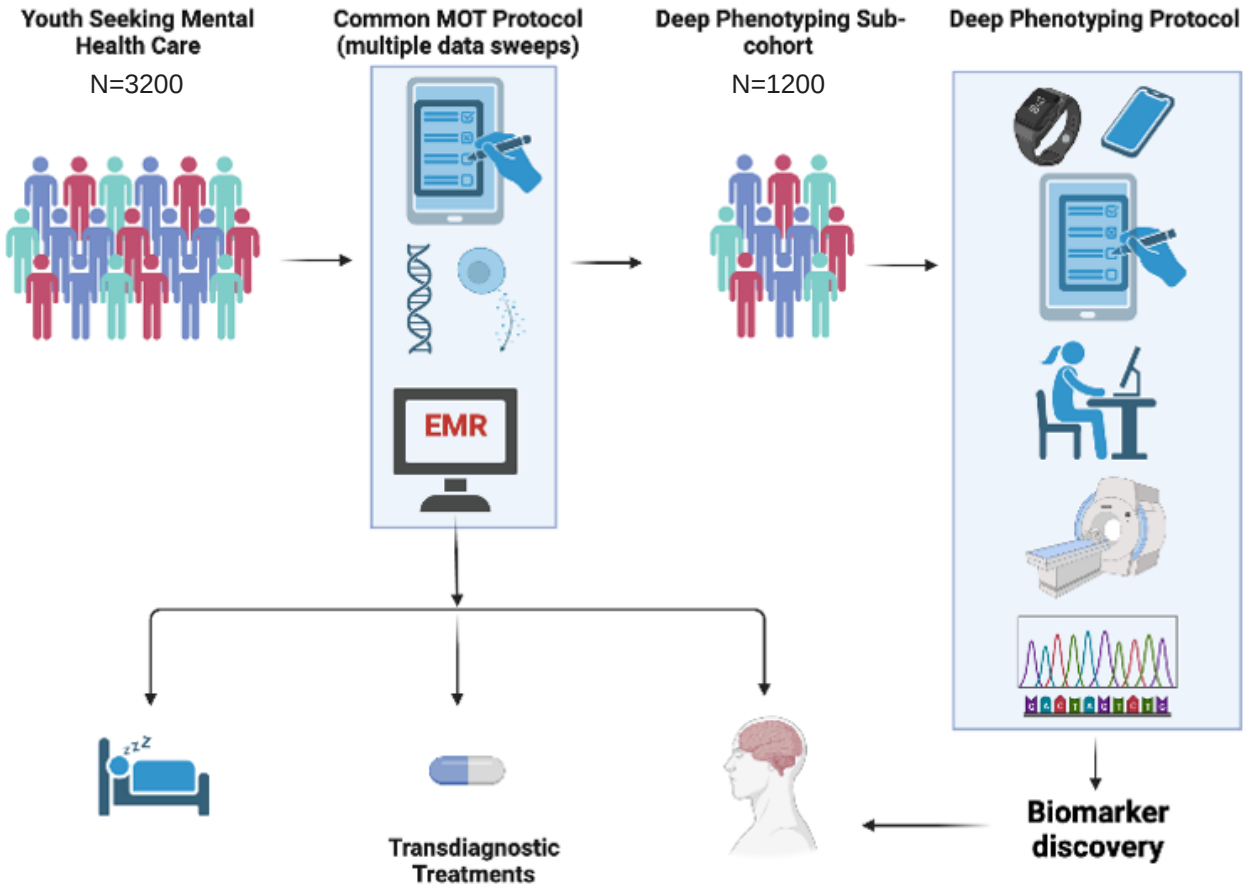


https://taprootco.com/root/

Design of the CALM MOT

The Cohort network for Adolescents and Youth with Mental Health Multimorbidity (CALM Study).

- Youth aged 11-24 y. seeking mental health services
- Six participating clinical sites (Ontario & Alberta)
- Master observational prospective cohort trial (MOT)
- + Embedded clinical trials within the cohort



Overall Goal:
To improve clinical care for youth with mental health disorders with a focus on multiple mental health conditions (MMHC).

Research objectives

1. To define and characterize MMHC in youth aged 11-24 years

2. To evaluate the association of increased MMHC with longitudinal clinical and functional outcomes, response to treatment, and healthcare utilization

3. To evaluate trans-diagnostic interventions (e.g. treatments for sleep disorder, self-harm) that target shared symptoms for internalizing disorders in improving functioning in youth with MMHC

Broad eligibility criteria

Inclusion Criteria

Light Phenotype

1. Sign informed consent
2. Aged 11-24 years old
3. Accessing mental health services at any of the 6 CALM sites
4. Are able to complete assessments in English

Deep Phenotype

1. Must enroll in CALM light phenotype cohort
2. Sign deep phenotyping informed consent
3. Stated willingness to comply with deep phenotyping procedures

Exclusion Criteria

Light Phenotype:

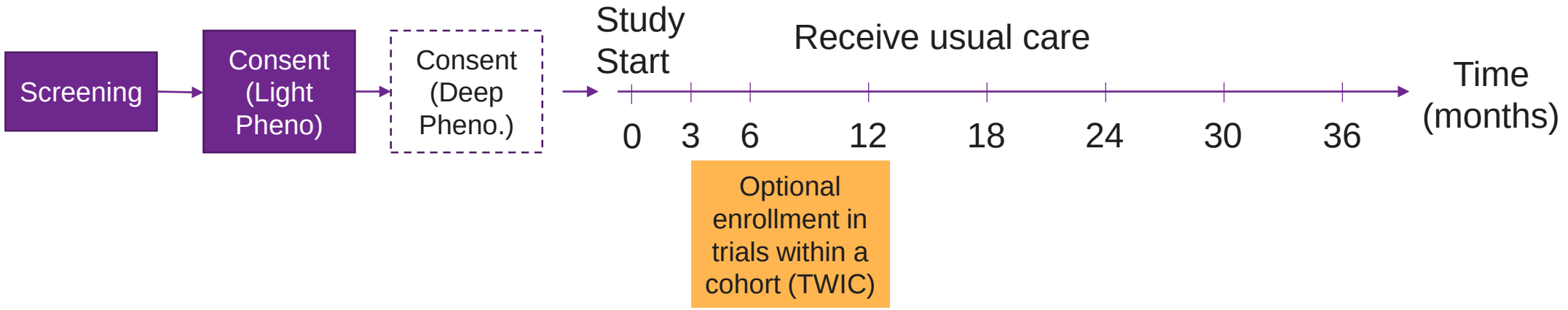
1. Does not provide informed consent or assent

Deep Phenotype:

1. Those unable to complete MRI can still take part in other aspects of the deep phenotyping protocol
2. Unable to participate in deep phenotyping protocol apart from MRI (e.g., uncorrected vision or hearing impairments, unwillingness to complete assessments)

Study design

- CALM MOT is a longitudinal cohort study with light and deep phenotyping cohorts
- Participants receive usual care as directed by healthcare provider
- **Decision Point:** All participants consented to light phenotype cohort will be offered to enroll in deep phenotype cohort



Data collection

- **Light phenotype cohort**: demographic data, psychopathology, adaptive functioning, cognition and educational attainment, physical health, social media use patterns, social and family factors and health services utilization

- **Deep phenotype cohort:** additional clinical, behavioural, developmental and functional outcomes, neuroimaging, cognition

Sample size considerations

- Power is determined based on the primary objective to define and characterize MMHC
- Dziak et al. (2014) proposed a Monte Carlo simulation approach to estimate power for the bootstrap likelihood ratio test (BLRT) in Latent Class Analysis to compare the fit of a (K-1)-class versus a K-class model
- N=**3,200** participants achieves >80% power (α=5%) for the BLRT, assuming a small effect size of Cohen's w=0.11 and a model with 10 items, and 6 or fewer classes (Cohen, Erlbaum, 1988).

Embedded TWICs within an MOT

- A key benefit for MOTs is to leverage the existing trial infrastructure to test novel interventions in prospective “trials within a cohort” (TWIC)

- TWICs may use different designs:
  - Non-randomized pilot / feasibility
  - Randomized pilot / feasibility
  - Randomized confirmatory
  - Master (interventional) protocols (e.g. basket design)

Planned TWICs in CALM to date

TWIC # 1 — Pilot RCT for personalized sleep intervention

- **Population**: N=30 youth (age: 13-18) with an internalizing disorder and initial insomnia / delayed sleep
- **Aim**: To evaluate the feasibility of a personalized behavioural sleep intervention vs. usual care

TWIC # 2 — Pilot RCT for specialty care for youth with complex mental illness (SCY-WELL)

- **Population**: N=24 youth (age: 14-24) with multiple, complex mental illness
- **Aim**: To evaluate the feasibility of the NAVIGATE model of coordinated specialty care vs. usual care

TWIC # 3 — Randomized basket trial for stigma intervention (NECT-Y)

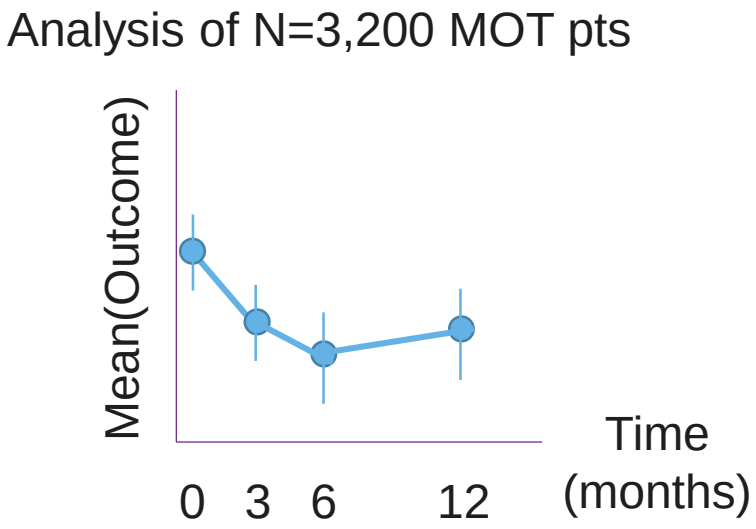
- **Population**: (Basket 1) youth with bipolar disorder; (Basket 2) youth with MMHC
- **Aim**: To evaluate the efficacy of Narrative Enhancement and Cognitive Therapy - Youth (NECT-Y) vs. usual care in improving self-stigma
-

Analytical challenges for embedded TWICs

- Participants in CALM MOT receive usual care as directed by their healthcare providers
- Analysis of longitudinal outcomes in CALM MOT represents an average usual care in youth with MMHC

CALM MOT

N=3,200 Usual Care (UC)



Analytical challenges for embedded TWICs

- A subset of participants will also enroll in 1+ TWICs and receive novel interventions
- Suppose these interventions affect mean outcomes over time
- How to best account for the effect of novel treatments on the analysis of longitudinal outcomes in the MOT?

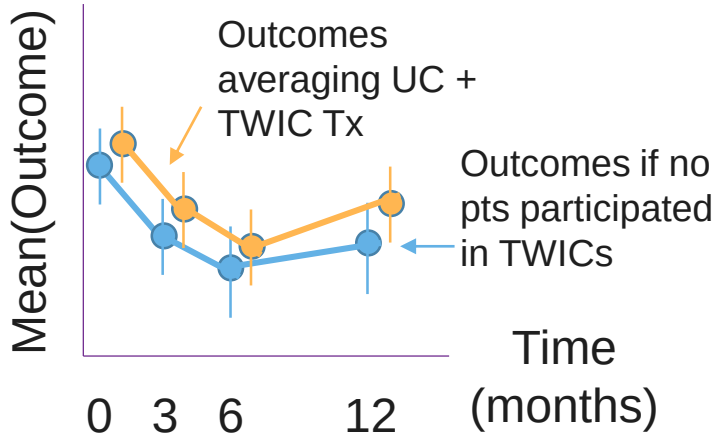
Participate in 1+ TWICs

UC + Novel Tx (N=500)

CALM MOT

N=2,700 Usual Care (UC) ONLY

Analysis of N=3,200 MOT pts

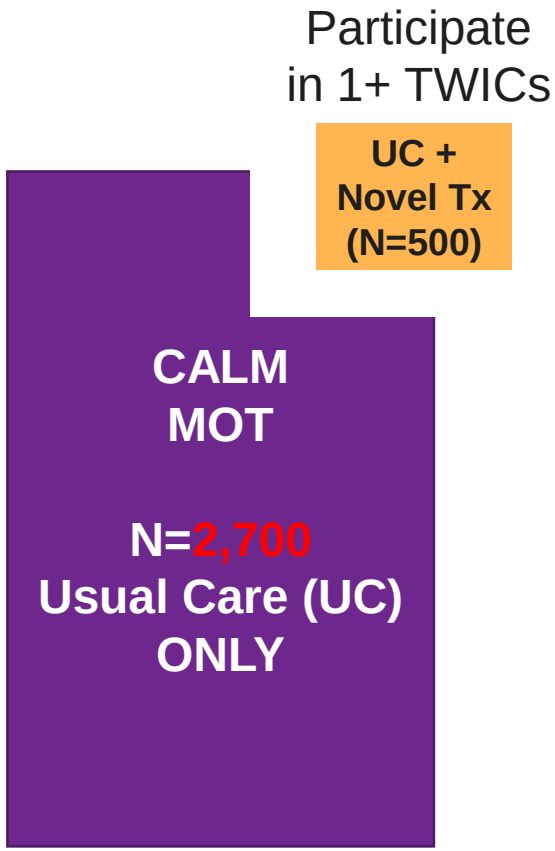


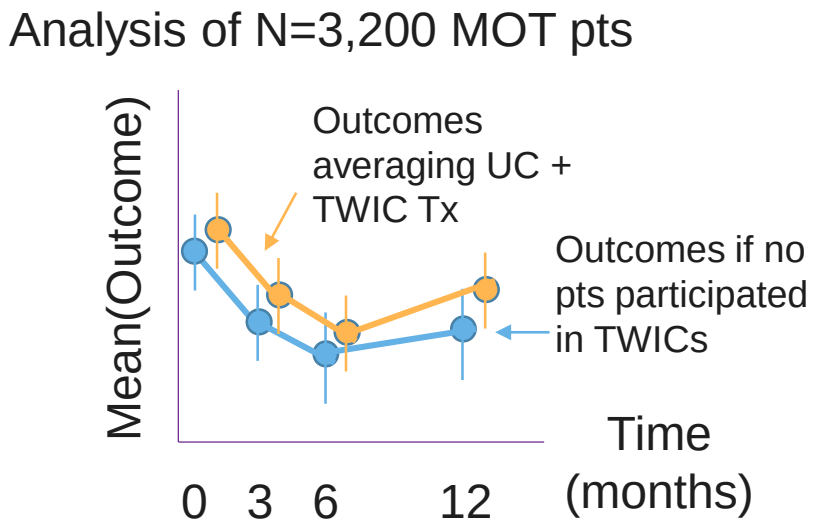
Analytical challenges for embedded TWICs

Possible strategies:

1. No adjustment
2. Adjust participation in TWIC in model
3. Sensitivity analysis using UC only group

Decision point:
Restrict participants from enrolling in multiple TWICs simultaneously





Summary

Summary

- MOTs combine the strengths of master (interventional) protocols with the benefits of longitudinal observational cohorts
- The CALM MOT provides a platform to evaluate outcomes to improve the care of youth with MMHC
- Embedded TWICs leverage the MOT infrastructure to efficiently and flexibly evaluate novel treatments
- Future work will address novel analytical challenges in MOTs and TWICs

Thank You

camh

Understanding the Importance of Outcome Selection & Measurement

Suneeta Monga, MD, FRCPC
Professor, Temerty Faculty of Medicine, University of Toronto

SickKids

UNIVERSITY of TORONTO

Disclosures

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3. Ontario Brain Institute (OBI) – grant funding
4. TD Bank Financial Group Chair in Child & Adolescent Psychiatry
5. Royalties from Springer Publishing for the book Assessment and Treatment of Anxiety Disorders in Young Children

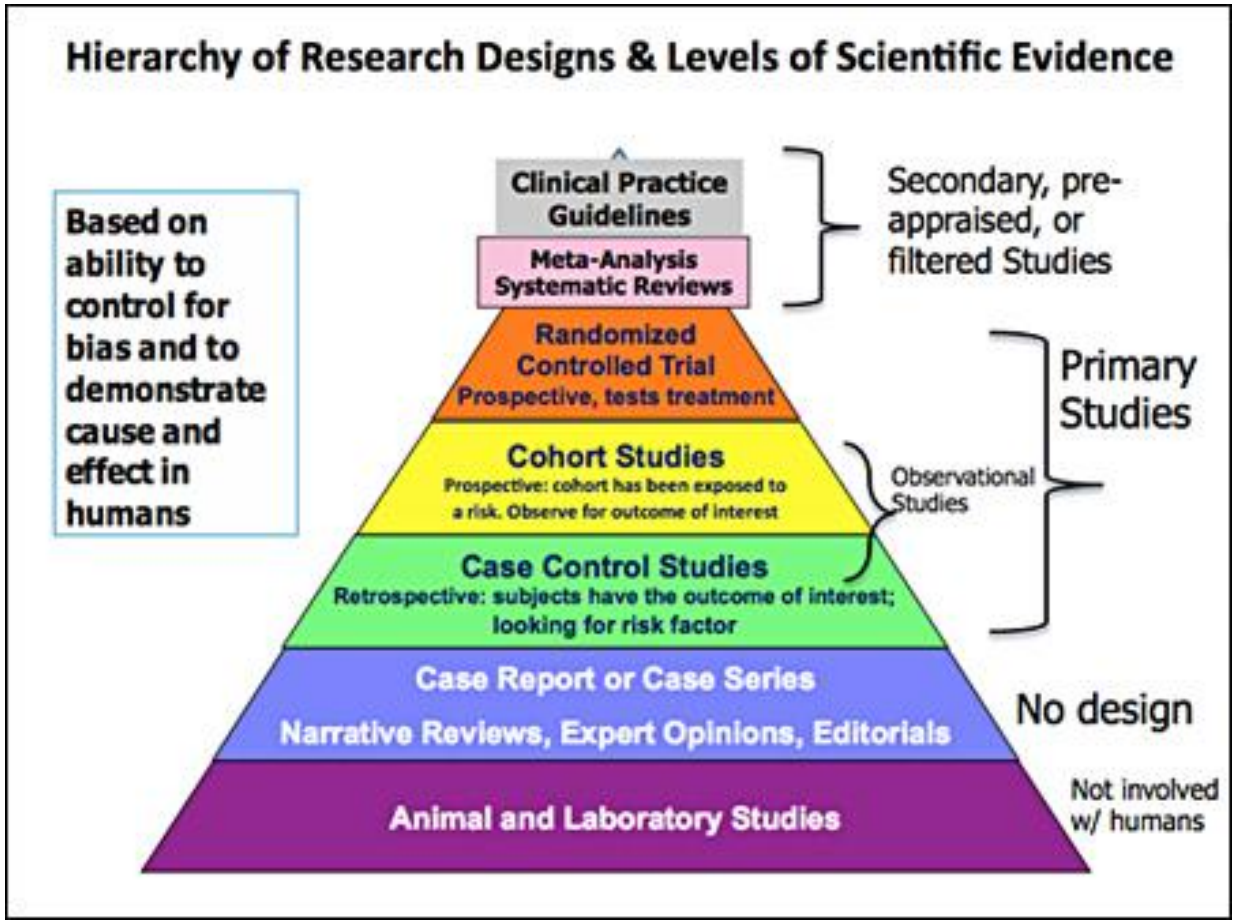
Learning Objectives for this presentation:

1. Understand the impact of outcome and outcome measurement instrument heterogeneity in trials
2. Describe what a Core Outcome Set is
3. Appreciate the need for ongoing work in outcome selection and measurement in mental health trials

Why are health outcomes important?

- **Outcomes or endpoints of a trial are:**
  - what are measured in a trial (on participants) to examine the effect of exposure to a health intervention

- The synthesis of evidence across outcomes, across trials, provides the evidence that drives clinical and policy decision-making



Outcome Heterogeneity in Adolescent Depression Trials

- Scoping Review of adolescent depression trials between 2008 and 2017
- Across 32 unique trials – 86 unique outcomes were measured using 118 different outcome measurement instruments (OMIs)
- Nearly half (45%) of outcomes reported in only a single trial
- **Depression symptom severity** (most common outcome) was measured using 19 different OMIs

ELSEVIER

Check for updates

Journal of Clinical Epidemiology 126 (2020) 71–79

Journal of Clinical Epidemiology

REVIEW

Systematic scoping review identifies heterogeneity in outcomes measured in adolescent depression clinical trials

Emma J. Mew[a], Andrea Monsour[a], Leena Saeed[a], Lucia Santos[a], Sagar Patel[a], Darren B. Courtney[b,c], Priya N. Watson[b,c], Peter Szatmari[b,c,d], Martin Offringa[a,e,f,*], Suneeta Monga[c,d], Nancy J. Butcher[a,*]

Nancy J. Butcher, PhD

Anxiety Disorders Scoping Review

- Clinical trials in pediatric anxiety disorders between 2010 to 2023 were systematically evaluated
- Across 189 unique trials - **97 unique outcome** were measured using **265 different outcome measurement instruments (OMIs)**
- Out of the 265 unique OMIs, 44 were non-standardized outcome measures designed by the investigator themselves
- **Anxiety symptom severity**, the most commonly reported outcome, was measured using 29 different outcome measurement instruments

What is a Core Outcome Set (COS)?

A core outcome set (COS) is a standardized ***minimum*** set of outcomes that should be measured and reported in all clinical trials in specific areas of health or health care, **while not precluding** the inclusion of other outcomes.

- **Development of a COS involves consensus building amongst experts** including people with lived experience (patients and caregivers), clinical care providers, researchers, people who make decisions about care (health policy-makers), journal editors, funders, etc.
- **Most pediatric COS have had 6 to 9 outcomes**

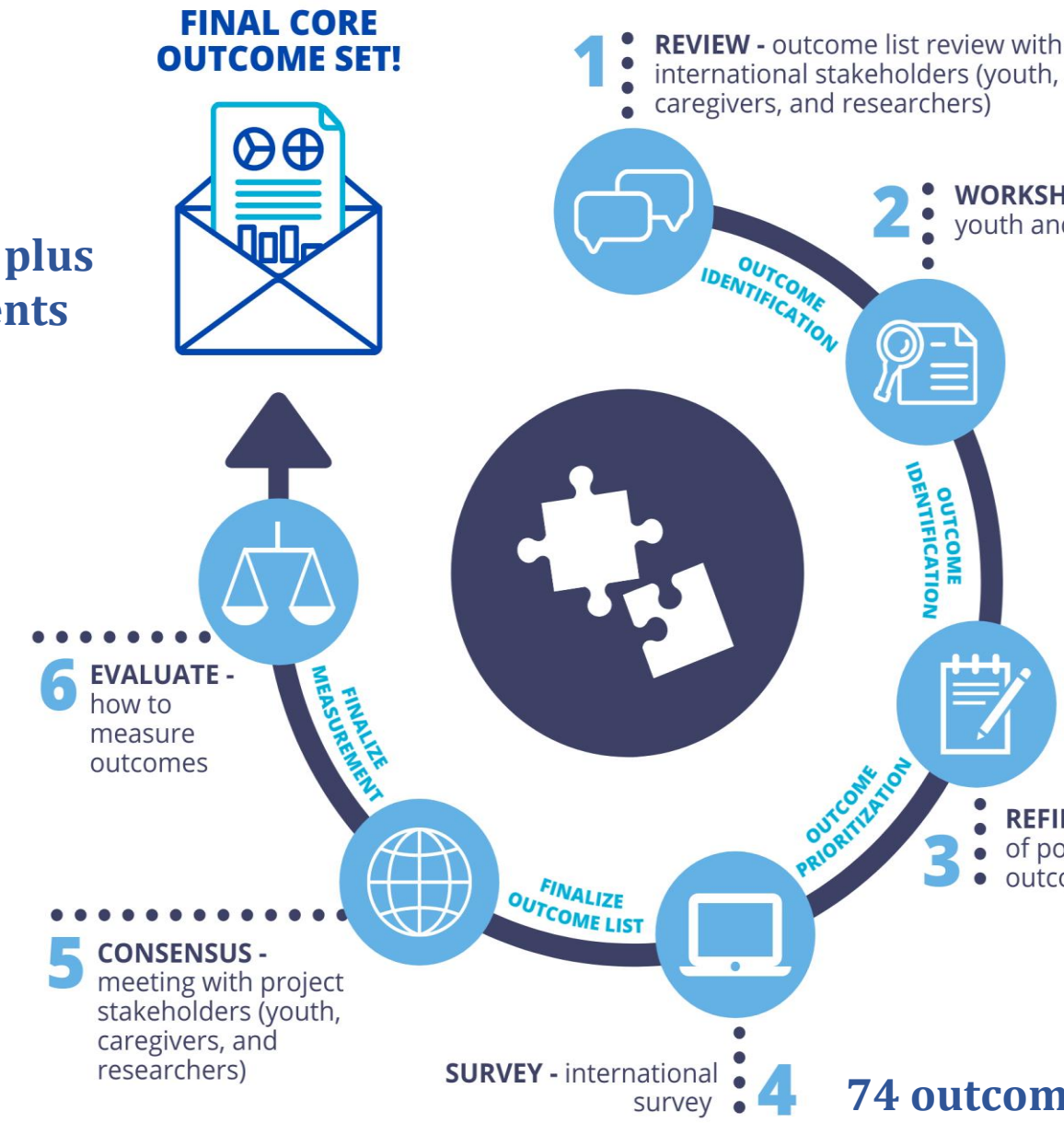
COMET INITIATIVE Core Outcome Measures in Effectiveness Trials Initiative

Core Outcome Measures in Effectiveness Trials Initiative

- COMET Initiative houses a database of all Core Outcome Sets that have been developed or are in development

- In other areas of medicine, a COS has allowed for:
  1. **Increased consistency** across trials;
  2. Maximized potential for a trial to contribute to **systematic reviews** of key outcomes;
  3. Increased measurement of outcomes **important to stakeholders**; and
  4. **Reduced selective outcome reporting** (which leads to biased estimates of treatment effects).

IN-ROADS



86 outcomes pruned by IAG

New Outcomes added by youth & caregivers

FYPAC collated outcomes as coming from the literature or from workshops or from both

74 outcomes inputted into Delphi

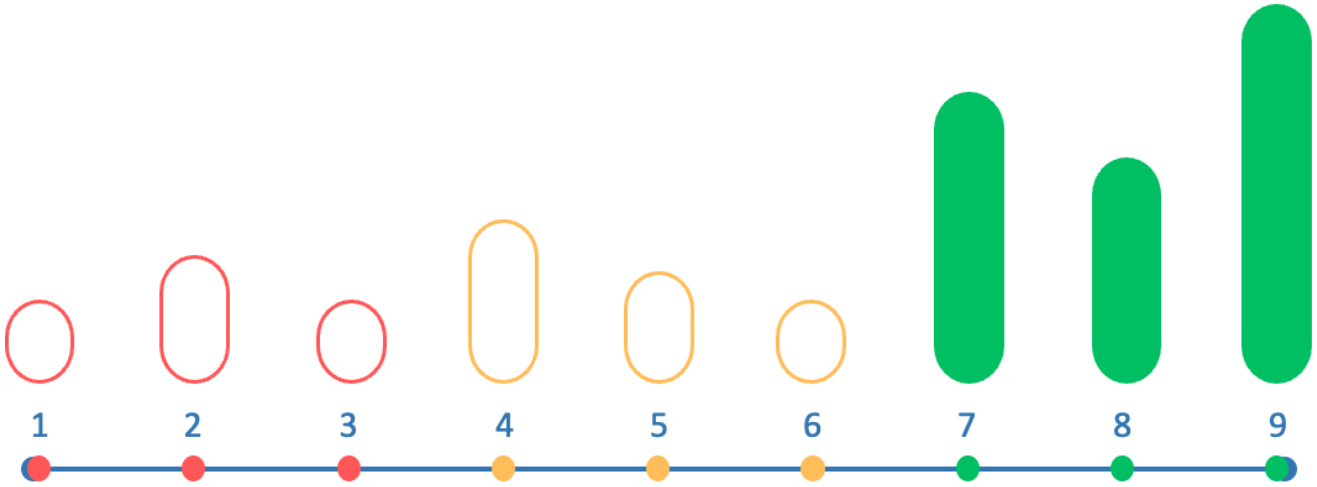
Consensus meeting members voted on 25 outcomes

5 outcomes plus adverse events

Delphi Survey– October 2022 to January 2023

	ROUND 1	ROUND 2	ROUND 3
Survey invitations	Distributed broadly and internationally to: • Youth • Parents/caregivers • Researchers • Clinicians • Other Stakeholders (journal editors, funders, regulators)	Round 1 participants and new participants	ONLY Round 1 and/or Round 2 participants
Survey task	Evaluation (rating) of 74 outcomes on importance of including in a COS Suggestion of additional outcomes	Re-evaluation (rating) of 70 Round 1 outcomes Overall mean ratings and individual ratings from Round 1 provided	Re-evaluation (rating) of 70 Round 2 outcomes Overall mean ratings and individual ratings from Round 2 provided

Rating Criteria

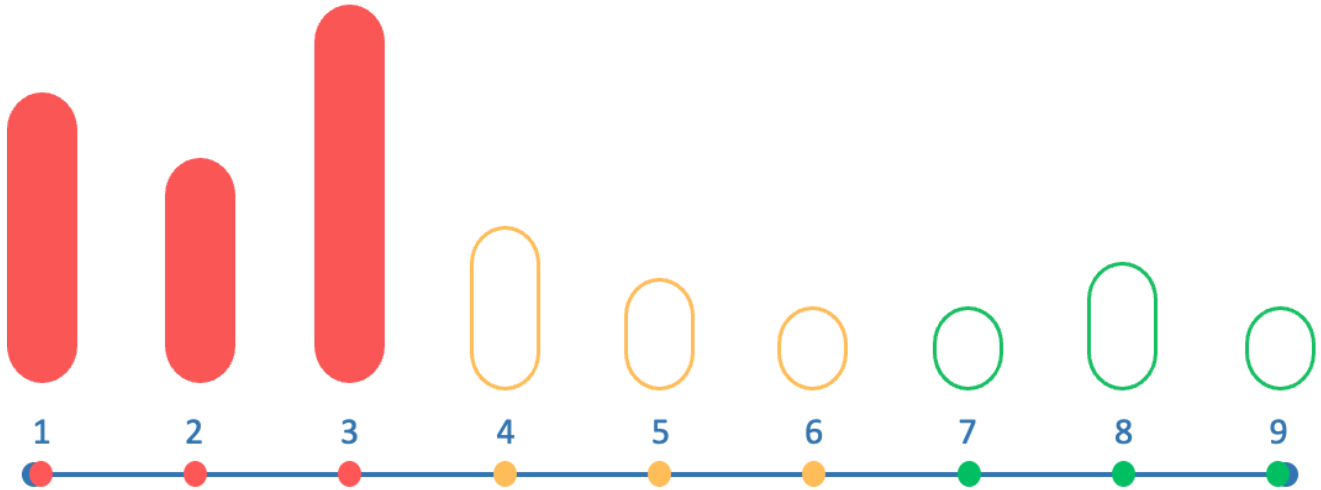


“Consensus in”

(At least 70% of participants voted the outcome as 7, 8, or 9)

“Consensus out”

(At least 70% of participants voted the outcome as 1, 2, or 3)



Top 10 Outcome Rankings

All Respondents Top 10 Rankings (N=81)	Youth and Caregiver Top 10 Rankings (N=19)	Researchers, Clinicians and Other Stakeholders Top 10 Rankings (N=62)
1. Depression Symptom Severity	1. Depression Symptom Severity	1. Depression Symptom Severity
2. Suicidal Ideation	2. Suicidal Ideation	2. Suicidal Ideation
3. Overall Functioning	3. Overall Functioning	3. Overall Functioning
4. Self-Harm Behaviours	4. Self-Harm Behaviours	4. Self-Harm Behaviours
5. Anhedonia	5. Psychological Distress	5. Anhedonia
6. Quality of Life	6. Sense of Control	6. Quality of Life
7. Psychological Distress	7. Anhedonia	7. Anxiety Symptoms
8. Anxiety Symptoms	8. Hopelessness	8. Psychological Distress
9. Accomplishing Activities of Daily Living	9. Quality of Care Received	9. Sleep Disturbance
10. Sleep Disturbance	10. Quality of Life	10. Accomplishing Activities of Daily Living

Remaining candidate outcomes: Adverse events, School functioning, Irritability, Frequency of substance use for self-medication, Isolation, Loneliness, Therapeutic Alliance, Fatigue, Depression Remission, Emotional Regulation, Substance Use Impacts, Self-esteem

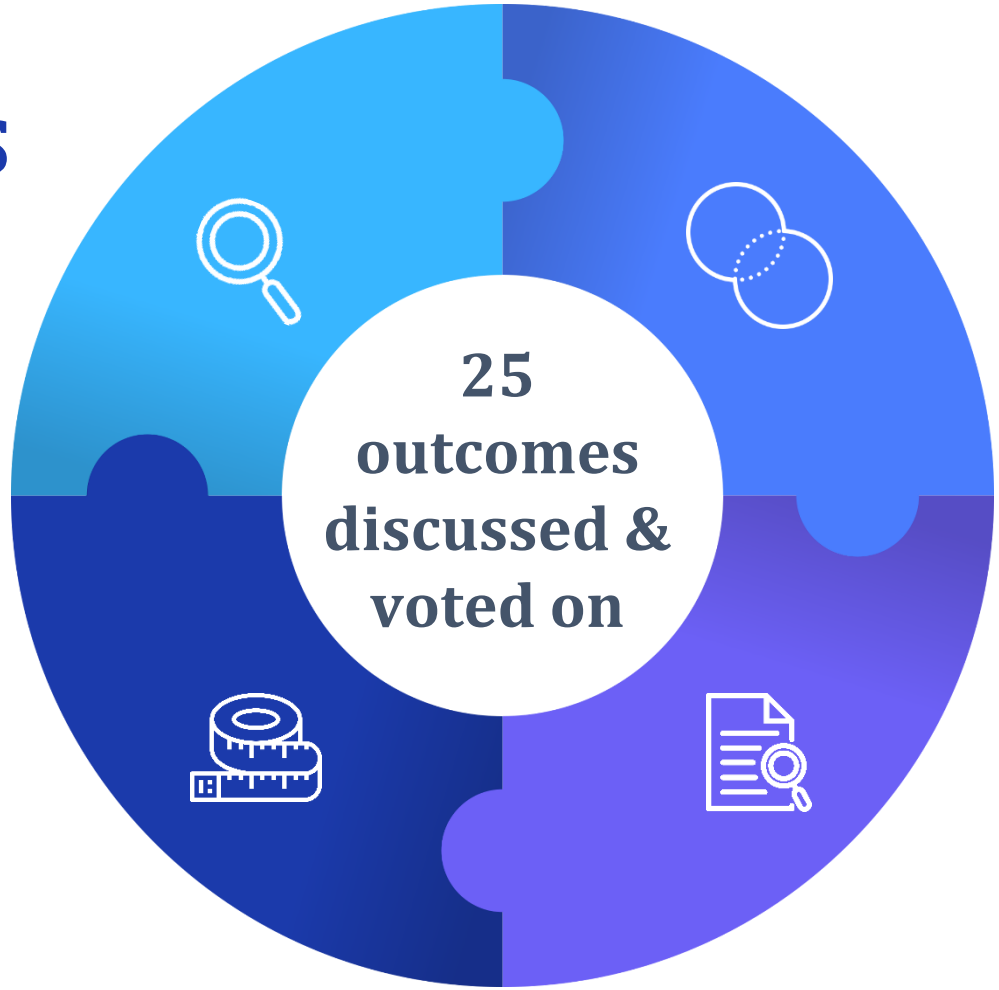
Consensus Meeting Voting – Things to Consider

SURVEY RESULTS

How did each stakeholder group rate it?

OVERLAP

How similar is it to other outcomes?



MEASURABLE

How easy or difficult is it to measure?

APPLICABLE

Is it relevant to all types of trials?

Final Core Outcome Set for Adolescent Depression Trials

1. Depression Symptom Severity
2. Suicidal Ideation
3. Overall Functioning
4. Self-harm Behaviors
5. Quality of Life
6. As a plus one – Adverse Events

Measurement of Patient Reported Outcome Measurement Instruments (PROMS)

Find the right tool

COSMIN

COnsensus-based Standards for the selection of health Measurement INstruments

COSMIN is an initiative of an international multidisciplinary team of researchers with a background in epidemiology, psychometrics, medicine, qualitative research, and health care, who have expertise in the development and evaluation of outcome measurement instruments.

> *We call for standardization of outcomes and outcome measurement instrument selection by developing core outcome sets (COS) and universally applicable IRT-based instruments.*

COSMIN Framework

- Systematic review of each of 10 measurement properties (e.g., content validity, structural validity, internal consistency, reliability, etc.) across each study of a specific instrument along with a systematic review of each measurement property across studies and a review of the quality of evidence for each evaluated measurement property across studies
- This results in categorization into 3 categories
  - Can be recommended for use and measurement properties can be trusted
  - Potential to be recommended but require more evaluative work
  - Should not be recommended for use
- The work done to date highlights the need for more evaluative work in measurement for mental health

Summary

- COS across youth mental health trials should allow for greater synthesis of evidence across multiple trials allowing for greater translation of research results into evidence-based clinical care
- The COS developed within this adjunct work will be implemented in trials initiated as part of the CALM Network
- Measurement of core outcomes remains a major concern within the field of mental health
- Our aim is to leverage work done through the CALM Network to enhance the evidence around measurement

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3. Eiko Fried (Leiden University, Netherlands)
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Questions & Answers
Thank you!

Youth and family engagement in integrated knowledge translation

Lisa D. Hawke, Centre for Addiction and Mental Health

& The CALM Engagement and Knowledge Translation Working Group

Disclosures

Centre for Addiction and Mental Health
Canadian Institutes of Health Research
University of Toronto
Ontario Brain Institute

camh
mental health is health

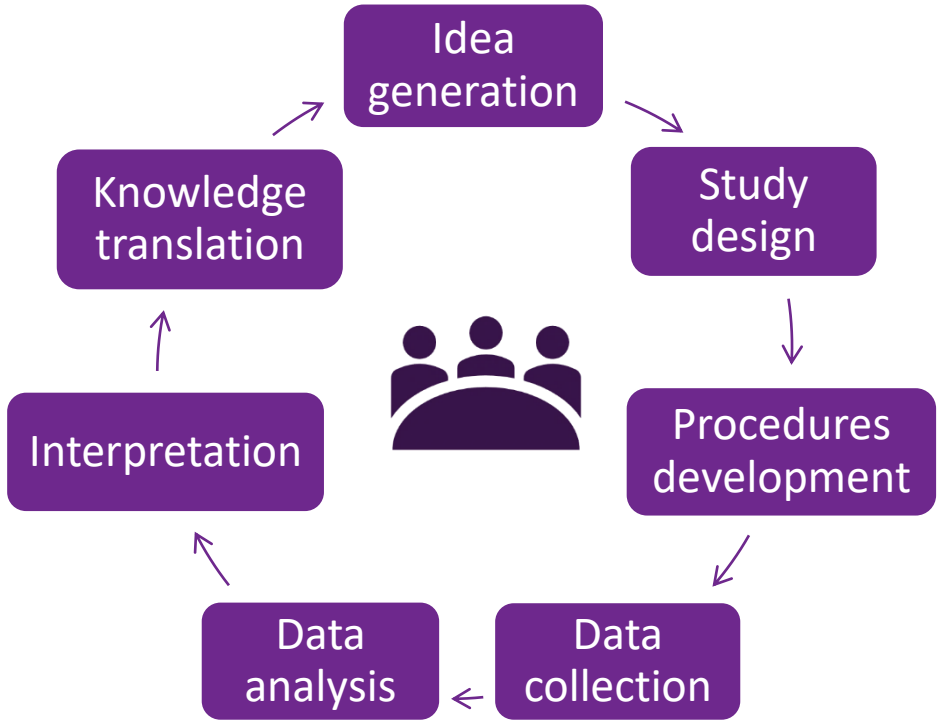
CIHR IRSC
Canadian Institutes of Health Research | Instituts de recherche en santé du Canada

UNIVERSITY OF TORONTO

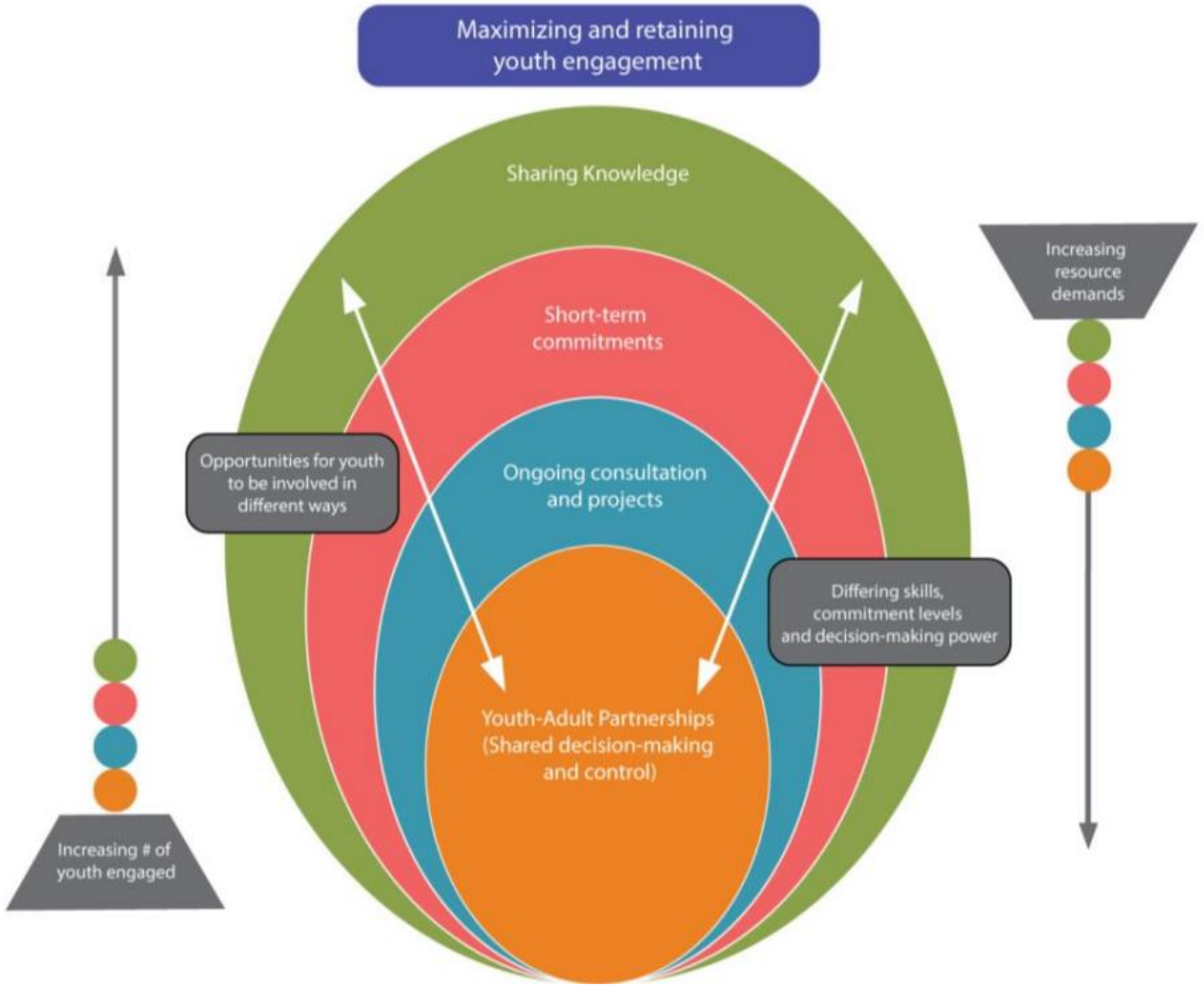
ONTARIO BRAIN INSTITUTE

Lived experience engagement in research

- Patient-oriented research, patient engagement in research, youth engagement, patient and public involvement
- Partners, co-researchers, advisors
- Important across health
- Ethical imperative in mental health given inequities



McCain Model of Youth Engagement



Heffernan, O., Herzog, T., Schiralli, J., Hawke, L.D., Chaim, G. Henderson, J. (2017). Implementation of a youth-adult partnership model in youth mental health systems research: challenges and successes, Health Expectations, 20(6), 1183–1188.

Family/caregiver engagement

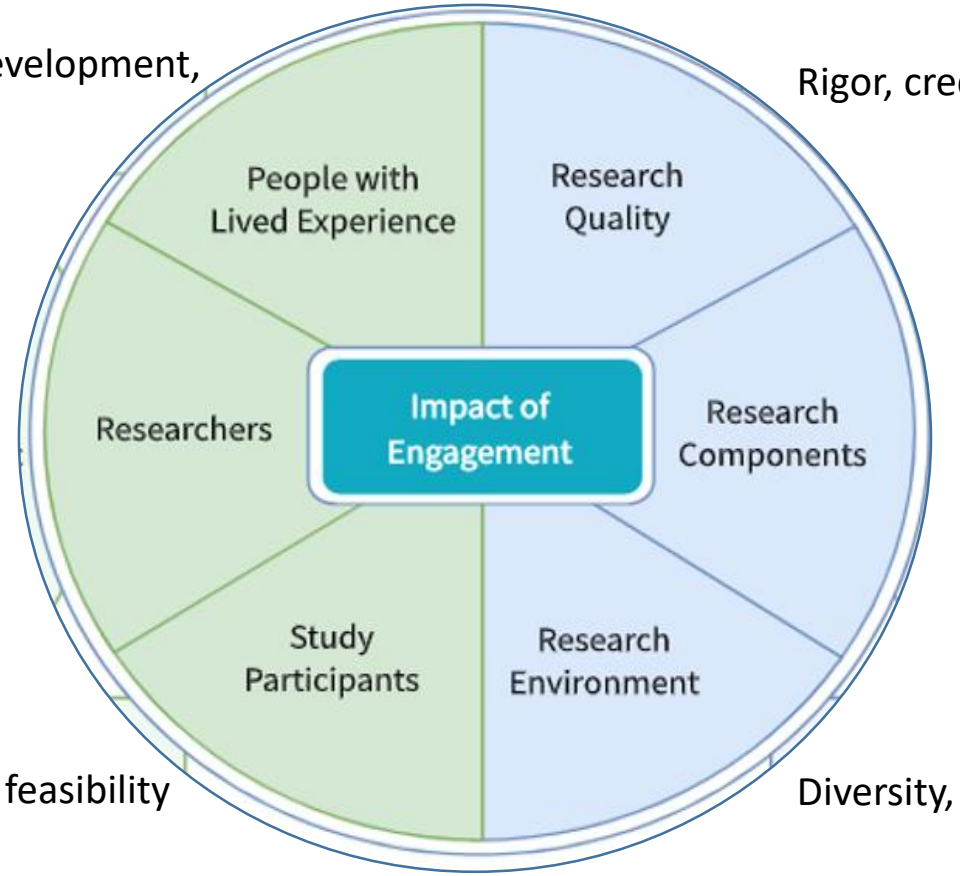
- Balance between direct lived experience and family insights
- Consider engaging families when
  - ✓ Research is about family perspectives
  - ✓ PWLE are unable to fully represent themselves
  - ✓ Researchers recognize the value of family contributions
  - ✓ Researchers have specific questions for family members
  - ✓ PWLE engaged support family engagement in the project

Hawke, L.D., Putterman, C., Dawthorne, N., Pascoe, S., Pind, S. (2023). The elephant in the room: Family engagement in mental health and substance use research, Health Expectations, 26, 1789–1792.

Impacts of engagement

Mental health & recovery, skill development, social connection, confidence

Rigor, credibility, validity, relevance



New perspectives, rewarding, strengthened commitment

Priorities, recruitment, dissemination, impacts

Retention, accessibility, feasibility

Diversity, shifts power, destigmatization

Sheikhan, N.Y., Kuluski, K., Hubert, M., McKee, S., Hawke, L.D., (2023) Exploring the impact of engagement in mental health and substance use research: a scoping review and thematic analysis. Health Expectations, 26, 1806–1819.

Youth & Family Engagement in CALM

Youth engagement in CALM

.5 day/week

1 Youth Coordinator (Lead)

2 Youth Engagement Specialists

15h/week each

(3h/month)

12 Youth Advisors

Paid roles

Family engagement in CALM

(3.5h/m)

1 Family Coordinator (Lead)

6-member Family Advisory

(1.5h/m)

(1h/m)

1 Advisor

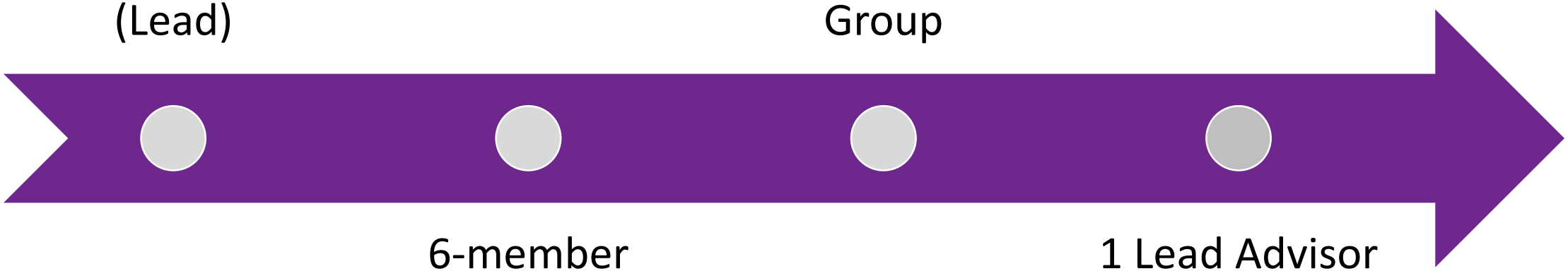
KT Working Group

1 Lead Advisor

(+ other components)

(3.5h/m)

Paid roles



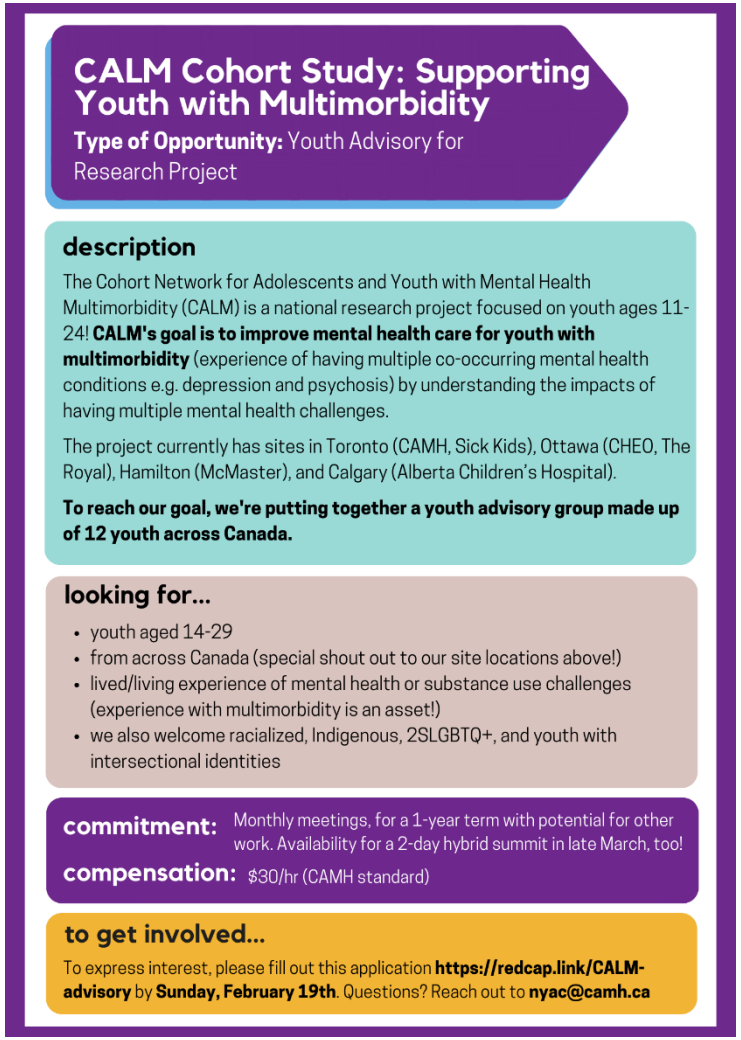
Contributions to Date

Launching engagement

Co-developing engagement plan and engagement recruitment plans

Co-developing youth & family summit

- Aims:
  - Meet & greet between researchers and youth/family partners, build rapport
  - Orientation, present substudies, begin active discussions
  - Provide engagement training
- Contribution: Conceptualization, agenda setting, recruitment, scheduling, training, co-design materials



CALM Cohort Study: Supporting Youth with Multimorbidity

Type of Opportunity: Youth Advisory for Research Project

description

The Cohort Network for Adolescents and Youth with Mental Health Multimorbidity (CALM) is a national research project focused on youth ages 11-24! **CALM's goal is to improve mental health care for youth with multimorbidity** (experience of having multiple co-occurring mental health conditions e.g. depression and psychosis) by understanding the impacts of having multiple mental health challenges.

The project currently has sites in Toronto (CAMH, Sick Kids), Ottawa (CHEO, The Royal), Hamilton (McMaster), and Calgary (Alberta Children's Hospital).

To reach our goal, we're putting together a youth advisory group made up of 12 youth across Canada.

looking for...

- youth aged 14-29
- from across Canada (special shout out to our site locations above!)
- lived/living experience of mental health or substance use challenges (experience with multimorbidity is an asset!)
- we also welcome racialized, Indigenous, 2SLGBTQ+, and youth with intersectional identities

commitment: Monthly meetings, for a 1-year term with potential for other work. Availability for a 2-day hybrid summit in late March, too!

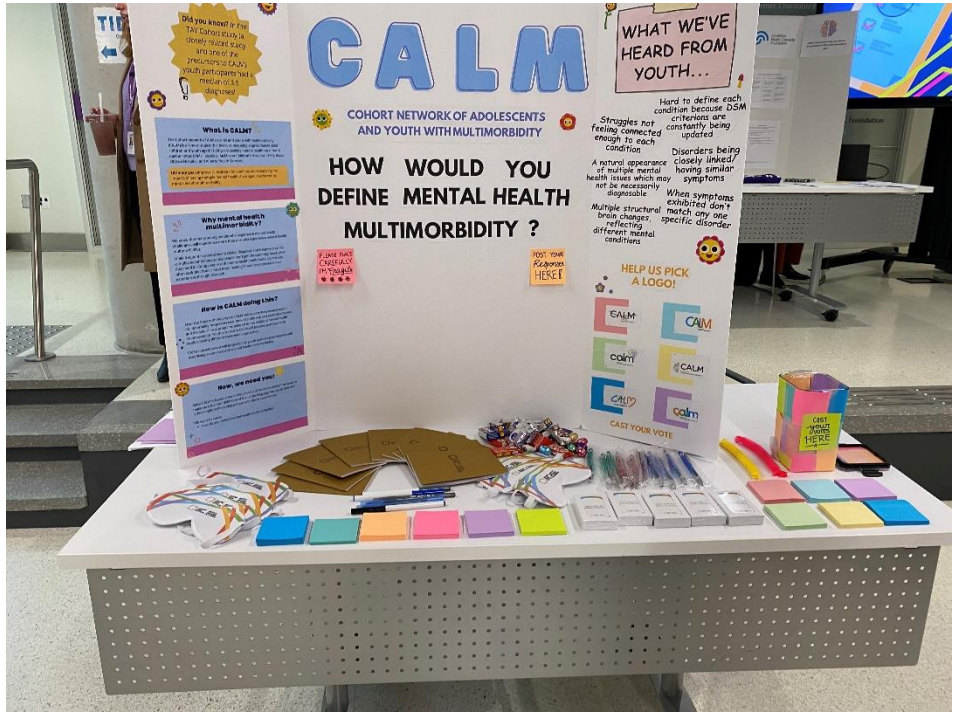
compensation: $30/hr (CAMH standard)

to get involved...

To express interest, please fill out this application **https://redcap.link/CALM-advisory** by **Sunday, February 19th**. Questions? Reach out to **nyac@camh.ca**

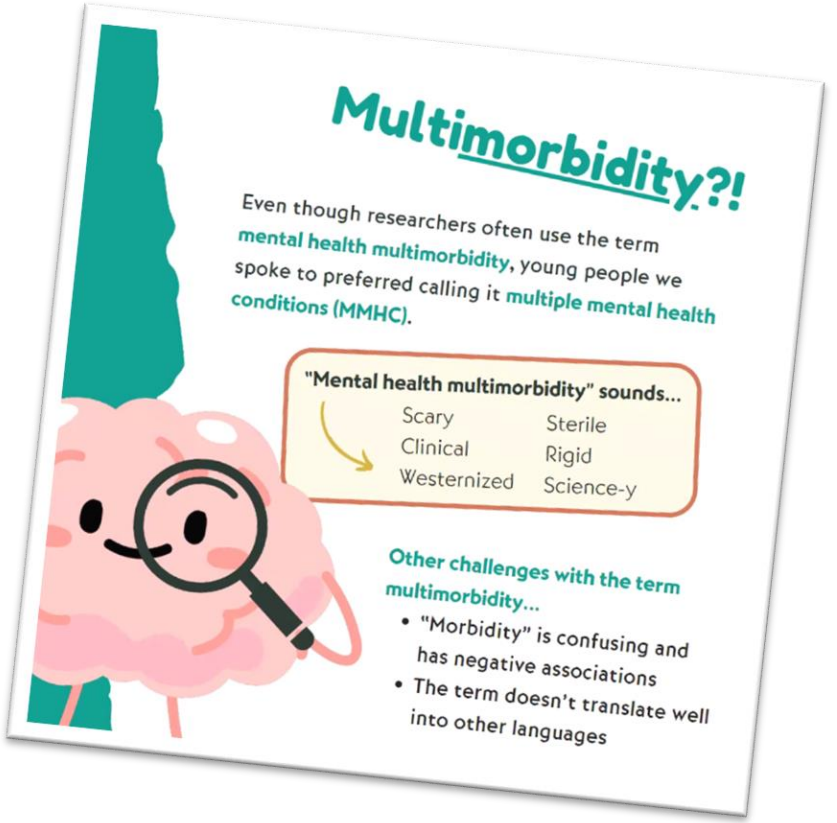
Youth Research Expo

- CAMH Youth Mental Health Expo designed to acknowledge and celebrate youth and family engagement in research
- Hosted a booth, engaged with visitors & raised awareness of CALM
- Explored the definition of ‘multimorbidity’ with visitors
- Supported CALM presentation development



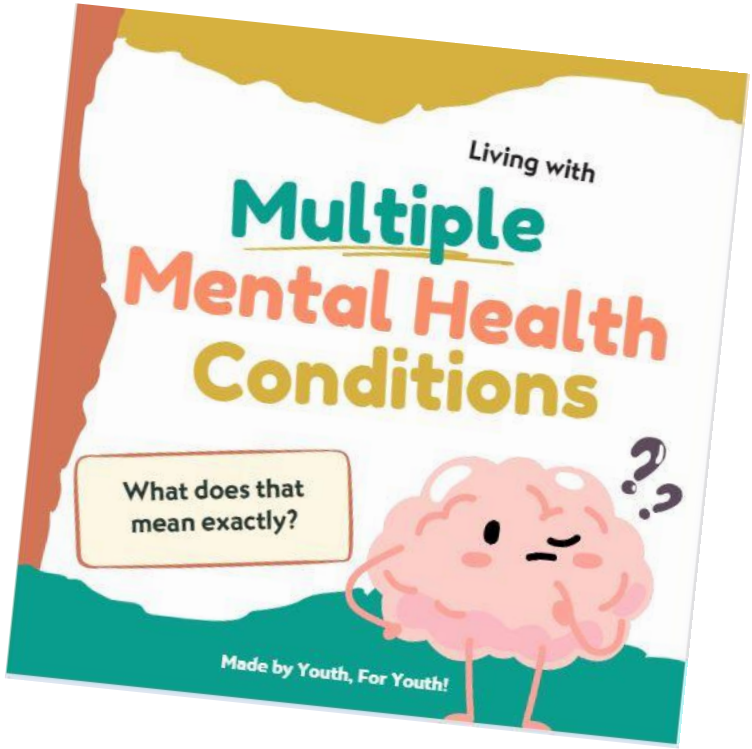
Defining multimorbidity

- Formal and informal consultations with youth advisors, family, study team, engagement leads, etc.
  - Youth: Scary, clinical, sterile, scary, scientific, inaccessible
  - Family members: Highly stigmatizing
  - Recommendation: “Multiple mental health conditions”



KT Product

- Early CALM deliverable
- Break down the concept of multiple mental health challenges
- Highlight youth thoughts and concerns
- Start the conversation with youth, highlight areas of future work
- Audience: youth with multiple mental health challenges, families, clinicians, people working with youth
- To be shared via social media



MOT design

- Review overall design
- Review measures, contribute to selection
- Review consent forms, youth-friendly language
- Discuss role and design of biosampling component

Subprojects

- Youth AI Insights qualitative study & scoping review
  - Two Youth Engagement Specialists
- Clinical trials
  - Sleep intervention trial
  - Basket trial of a self-stigma reduction intervention
  - Other clinical trials in development
- Grant support

Future contributions

- Recruitment, retention
- Data analysis, interpretation
- Subproject development
- Knowledge translation
  - Paper co-authorship
  - Conference co-presentations
  - Web/website

Lessons Learned

- Complexity of alignment & cohesion with such a large project
  - Importance of communication across groups and subgroups
- Balancing youth and family engagement
  - Being explicit about the role and importance of each
- Geographical diversity vs. pragmatic scheduling
  - Time zones, travel
- Volume of work vs. advisor capacity
  - McCain Model of Youth engagement

Key takeaway

- Engagement leads to important contributions across the study.
- It ensures study relevance to youth and families.
- It keeps us authentic.

Thank you!

An Embedded Intervention Trial within CALM: Targeting Sleep to Improve Mental Health Outcomes

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Disclosures

Research Funding:

- Canadian Institutes of Health Research
- Cundill Centre for Child and Youth Depression
- Ontario Brain Institute
- Social Sciences and Humanities Research Council

Objectives

1. Describe an example of a pilot intervention trial embedded in a master observational trial (MOT)
2. Highlight important decision points
3. Discuss strengths and limitations of an embedded trial

Brief Background: Sleep and Mental Health

Sleep problems in youth with mental health disorders are:

- Common: up to 90% (Reynolds et al., 2020)
- A risk factor for worsening mental health (Alvaro et al., 2013; Marino et al., 2022)
- A predictor of poor treatment outcomes (Curry et al., 2011; Manglick et al., 2012)
- Responsive to behavioural treatments (Blake et al., 2017; Reddy et al., 2023)
- An example of multifinality = good fit with MOT

Treatments for youth sleep problems are:

- Rarely offered in clinical practice (providing clinical equipoise)
- Multi-component (Blake et al., 2017)
- Poorly adhered to (Micic et al., 2019)

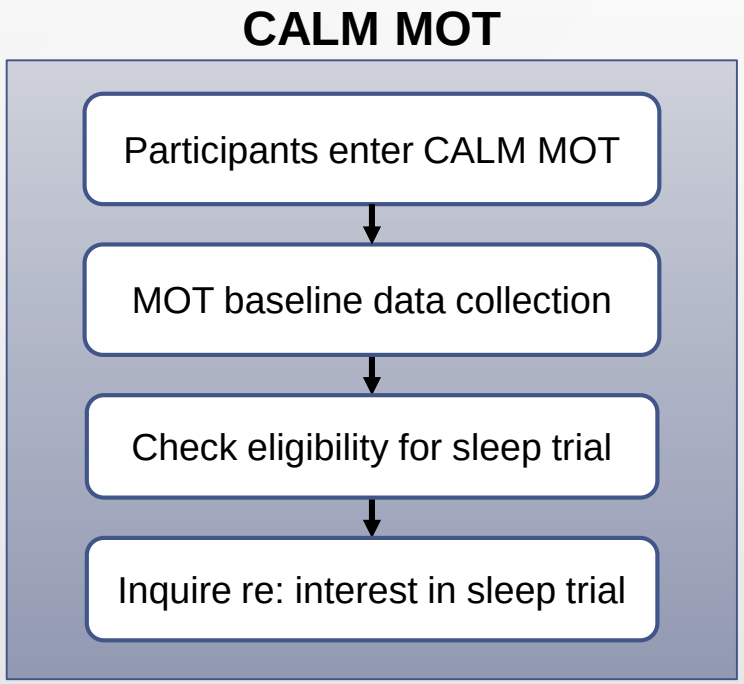
Pilot RCT Overview

Primary Research Question

Is a RCT of a personalized behavioural sleep intervention incorporating shared decision-making feasible in adolescents with multiple mental health conditions?

- **P** *N* = 30 youth age 13-18 with an internalizing disorder and initial insomnia/delayed sleep
- **I** Personalized behavioural sleep intervention based on shared decision-making and pre-treatment EMA and actigraphy
- **C** Usual care
- **O** Subjective sleep; drop-out/retention; shared decision-making; anxiety; depression; quality of life
- **T** 3 months post-randomization

Integration with CALM MOT



Two Protocol Versions:

1. Deep phenotype
2. Light phenotype

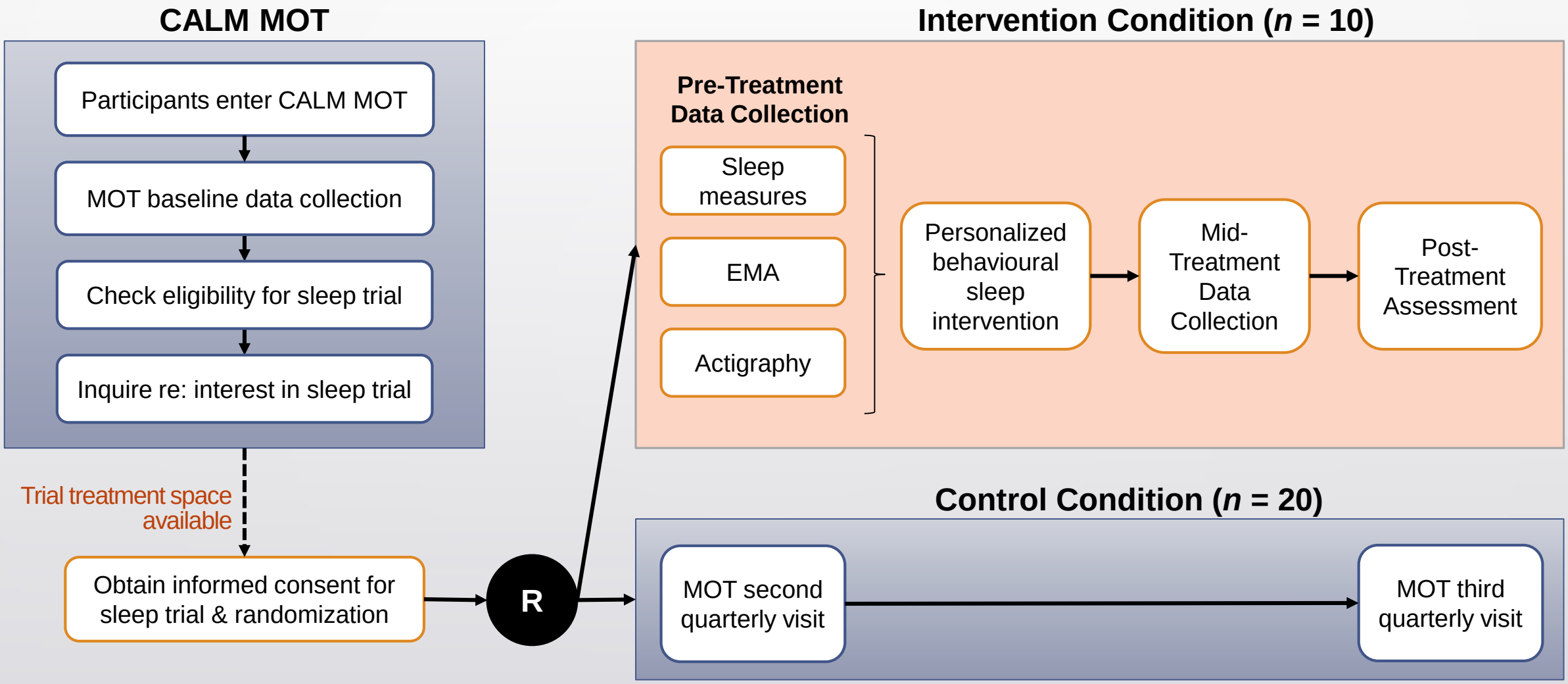
Inclusion Criteria:

- Self-reported sleep disturbance
- Meet diagnostic criteria for an anxiety or depressive disorder

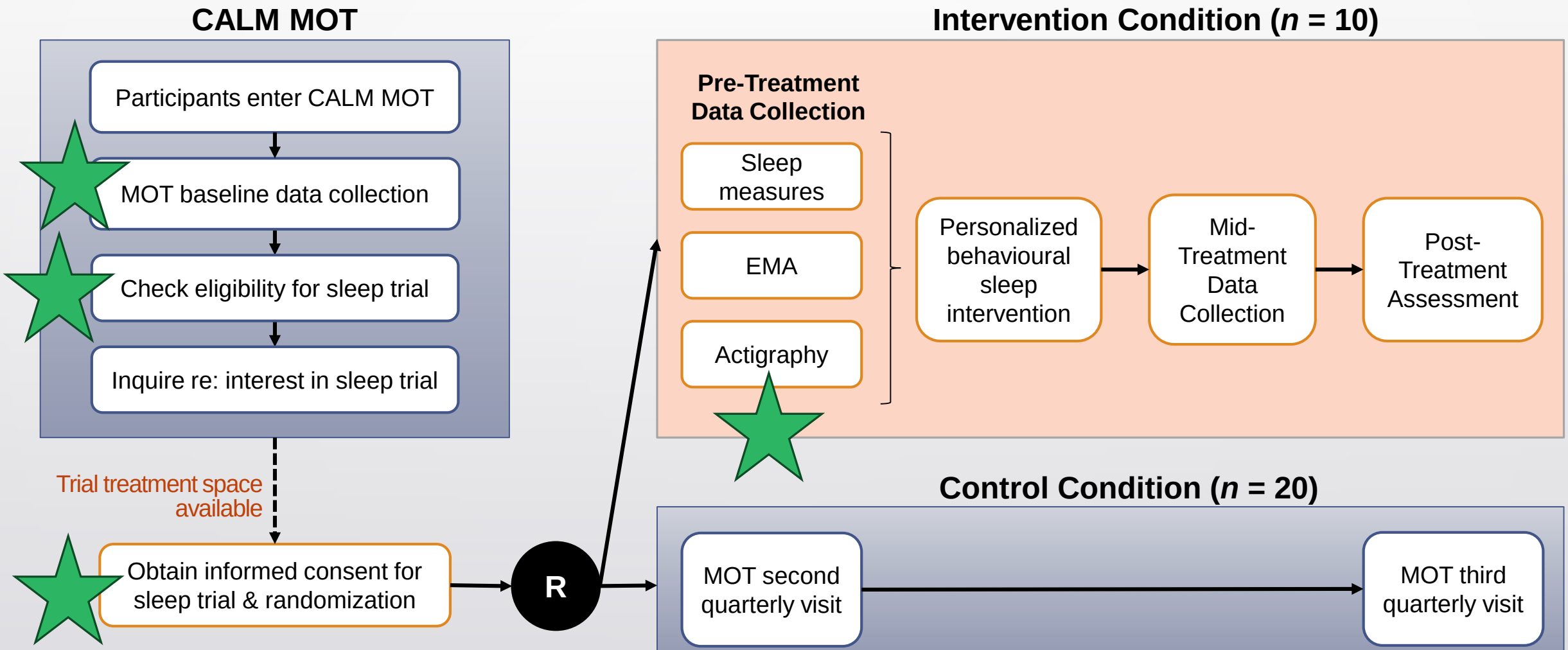
Exclusion Criteria:

- Intellectual disability
- Acute suicide risk
- Current manic/hypomanic episode
- Autism spectrum disorder
- Psychosis not well managed
- Stimulant use
- Severe substance use disorder
- Medical issues that may affect sleep
- Participating in another trial

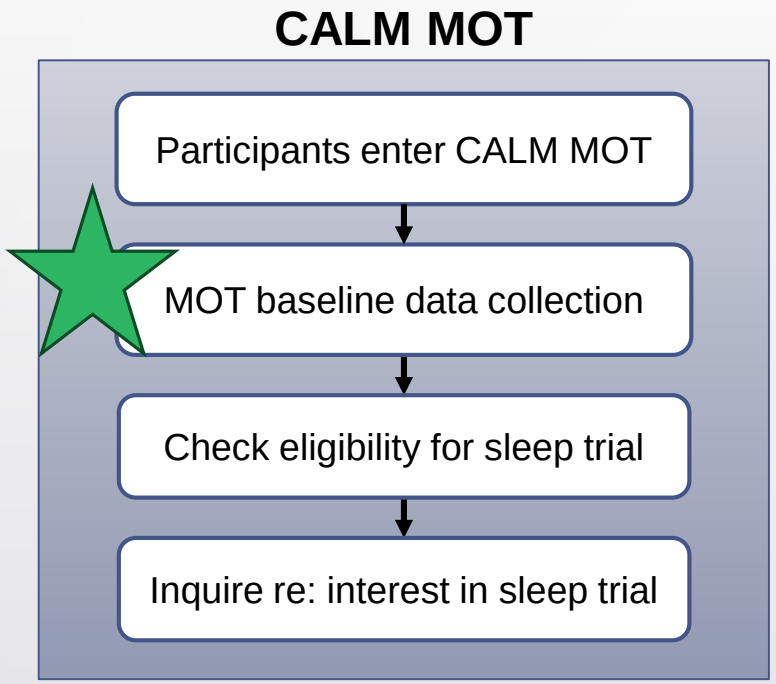
Integration with CALM MOT



Integration with CALM MOT



Key Decision Points



Decision Point #1: Include participants in the deep or light version of the MOT protocol

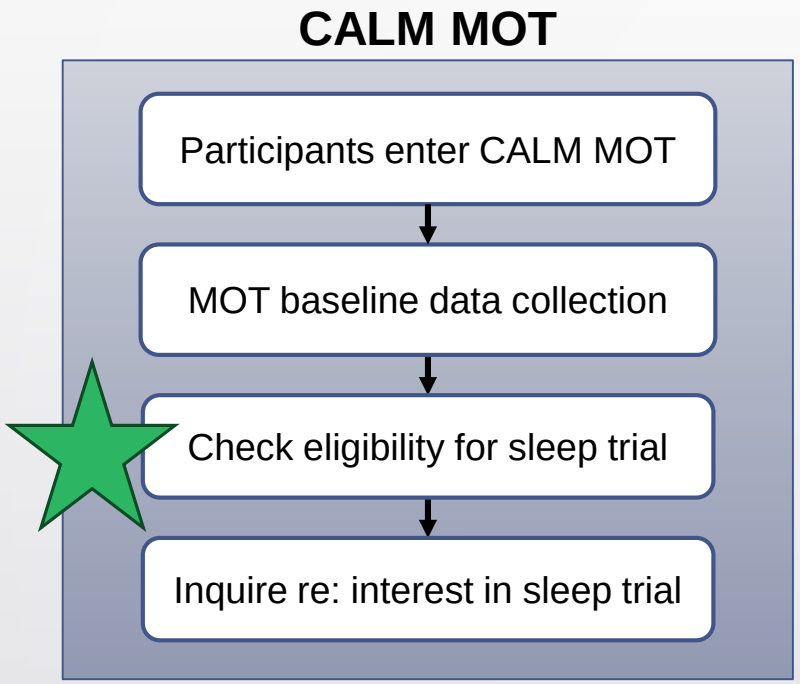
Rationale:

- Increase external validity of results
- Increase pool of potential participants

Trade-Offs:

- Limited options for outcome measures

Key Decision Points



Decision Point #2: Use existing measures in MOT for screening

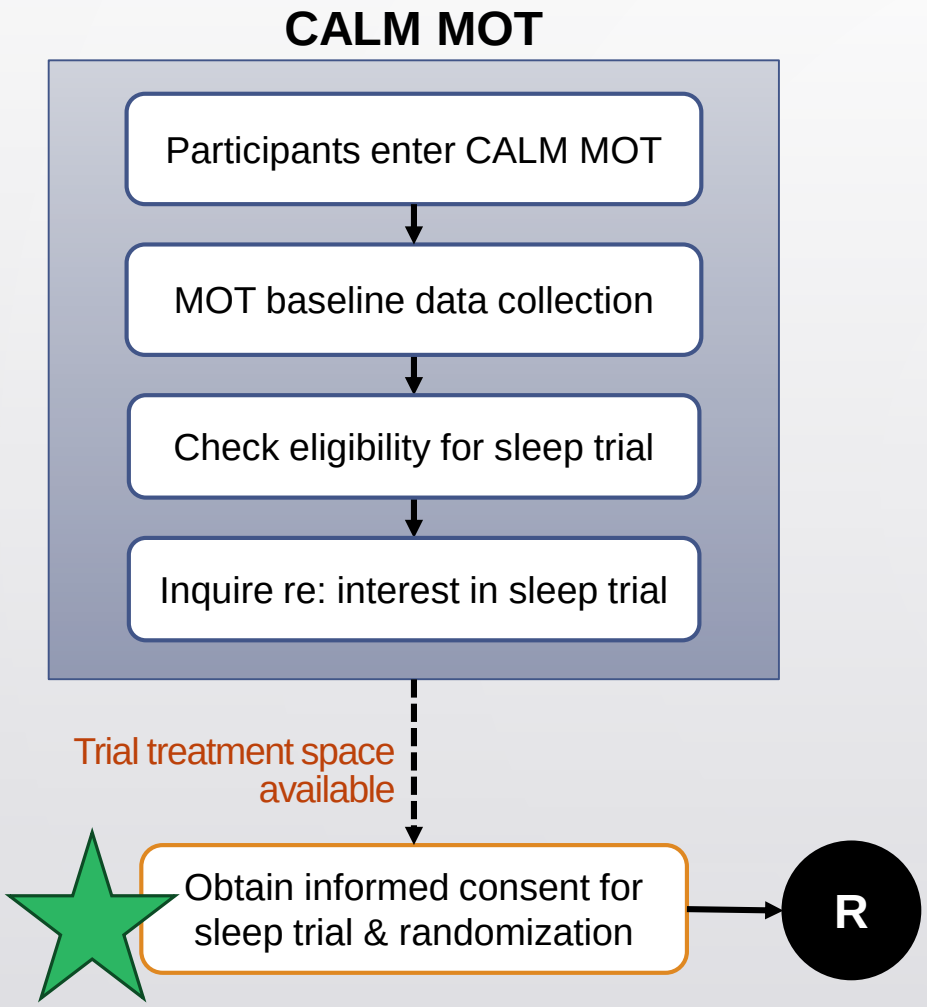
Rationale:

- Leverages benefits of the MOT infrastructure
- Pragmatic approach

Trade-Offs:

- Limited measurement of exclusion criteria (e.g., restless legs syndrome)

Key Decision Points



Decision Point #3: Obtain consent from all participants, including those in the control arm

Rationale:

- Increase similarity between control and intervention participants
- Decrease bias (e.g., retention & measure completion)

Trade-Offs:

- Does not fully address bias in retention & measure completion (controls > intervention)

Key Decision Points

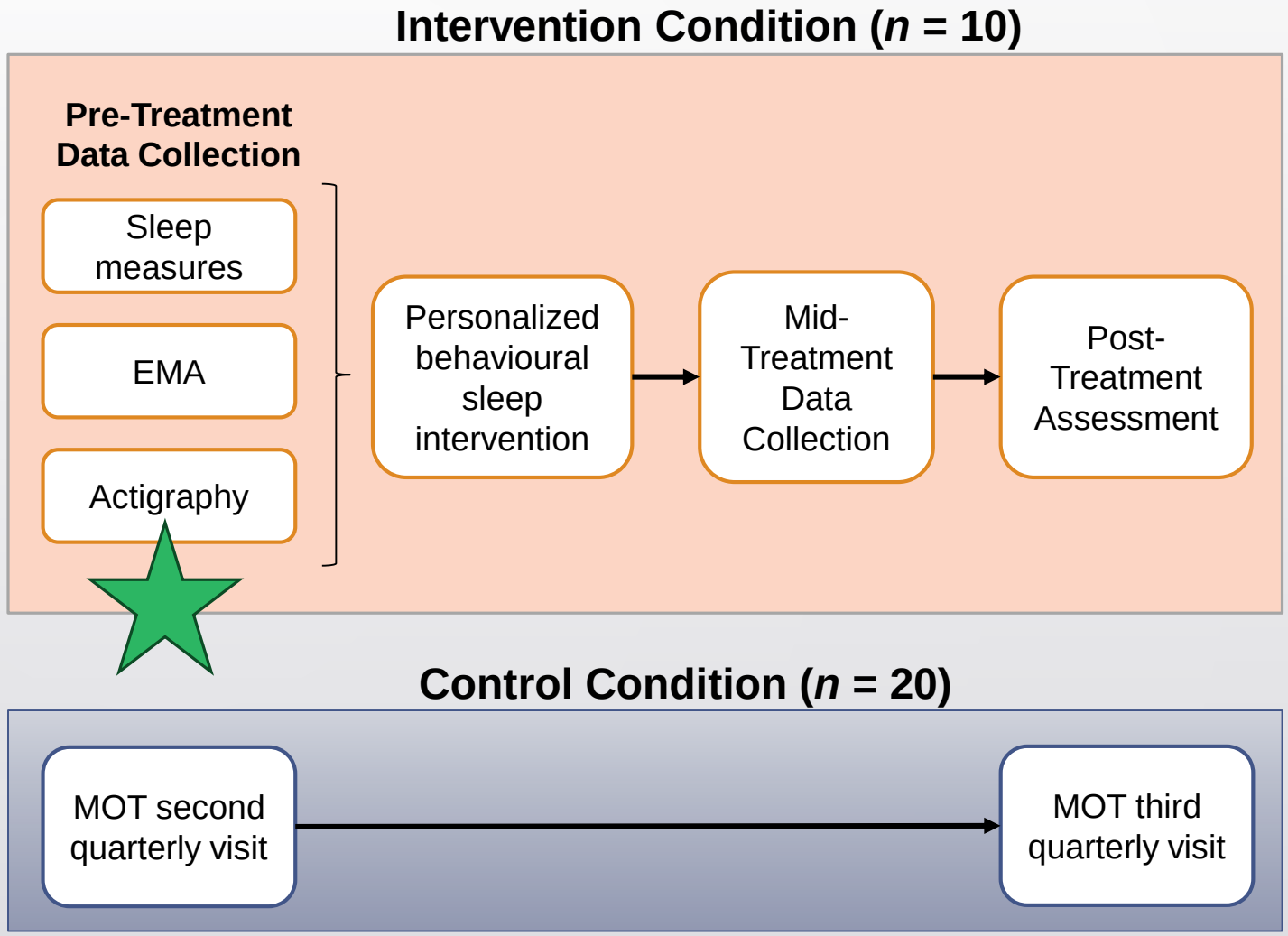
Decision Point #4: Only MOT measures for control participants

Rationale:

- Leverages MOT infrastructure
- Essential outcomes measured in MOT
- Additional measures are part of the intervention
- Cost savings = increased sample size

Trade-Offs:

- Limited outcome measurement
- No measurement of mediators in control group



Considering Embedded Trials

Limitations

- Working with existing measures for inclusion/exclusion
- Working with existing measures and time points for outcomes
- Potential participant fatigue

Strengths

- Relevant measures already being collected
- Infrastructure
- Cost savings = larger sample
- Facilitate recruitment

Diversity, Equity, and Inclusion

- Aspects of the trial that will increase sample diversity:
  - Publicly funded, single-payer hospital in a diverse city
  - Youth input on methods and recruitment

Acknowledgements

Team Members

Peter Szatmari

Louise Gallagher

Clement Ma

Darren Courtney

Gary Goldfield

Mahalia Dixon

Lisa Hawke

Martin Offringa

CALM Clinical Trials Working Group

CALM Project Team

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camh | Cundill Centre for Child and Youth Depression