

McCradden LAB



SickKids

Silent trials for health AI: promoting justice, protecting interests

Melissa McCradden, PhD, MHSc

John and Melinda Thompson Director of AI in Medicine

Bioethicist, Associate Scientist The Hospital for Sick Children Genetics & Genome Biology Research Program

Tw: @mmccradden M: @mdmccradden@dair-community.social

Disclosures

• Grant funding:

SickKids

- Canadian Institutes for Health Research
- National Institutes of Health
- National Health Services (UK)
- SickKids Foundation
- No funding to disclose for this talk



RESPONSIBLE ML

CLINICAL TRIALS

POST-INTEGRATION MONITORING







The NEW ENGLAND JOURNAL of MEDICINE				
CORRESPONDENCE				
, Alexandre				
The Clinician and Dataset Shift in Artificial Intelligence				

FDA	U.S. FOOD & DRUG	Health Canada	Santé Canada	Medicines & Healthcare product Regulatory Agency	
Good Machine Learning Practice for Medical Device Development: Guiding Principles					
	C	October 2021			









RESPONSIBLE ML

CLINICAL TRIALS



POST-INTEGRATION MONITORING



Silent trial evaluation



What is a silent trial?

- Mature algorithm is implemented into live clinical environment, run in real-time in 'silent mode' (i.e., predictions are not used clinically)
- Testing a hypothesis: does the model have ecological validity?
 - Protects patients/participants against common AI failures: design or implementation failures, missing safety features (engineering); robustness issues (post-implementation) (Raji et al., 2022)
- Two goals:
 - Empirical: establishing reliable clinical performance characteristics
 - Ethical: clinical equipoise





The silent trial and clinical equipoise

- Healthcare institutions have a positive duty to use evidence to promote and protect patients' interests and wellbeing ←[tension!]→ Healthcare also looks to advance practice to continually improve itself
- Equipoise is the resolution for this state of dissonance
 - If a community of experts holds genuine uncertainty about whether a proposed intervention may be superior to the current standard (Freedman, 1987)
 - When equipoise is met, the ethical justification for initiating a clinical trial is met
 - Promotes interests of patients/participants, prevents research waste



McCradden et al., 2022 AJOB; McCradden, Stephenson, & Anderson, 2020 Nat Med



Empirical goal: distributive justice

- **Distributive justice**: establishing facts about the distribution of benefits and burdens of a given system
- Identify groups on whom subgroup-specific evaluations are relevant
 - Compare the subgroup performance across multiple metrics
 - Reverse prediction to identify potential signal (Banerjee et al, 2021)
- Failure cases
 - Qualitative exploration of failure cases (Rettberg, 2022)
 - Medical algorithmic audit (Liu et al., 2022)
- Empirical foundation for ethical decision-making

Guided by: "Towards a Standard for Identifying and Managing Bias in Artificial Intelligence" NIST Special Publication 1270; "Algorithmic Bias Playbook" The Center for Applied Artificial Intelligence.



Additional opportunities

- Patient, family, community engagement in the implementation and design
- Human factors
- Clinical utility (actionability)
- Visualizations, interface design
- Identify education need(s)







Silent trials and LMICs

- Accountability: conducting a silent trial prior to purchasing or testing an AI system protects patients' interests and guards against AI failure
- Community relevance: silent trial offers a testing period to tailor to the local workflow and user characteristics and values
- Ethics (equity, equality): offers a structure for the empirical foundation for making ethical design decisions to advance the interests of patients experiencing relative disadvantage



SickKids

Some examples from our context

Frontiers | Frontiers in Digital Health

TYPE Original Research PUBLISHED 16 August 2022 DOI 10.3389/fdgth.2022.929508

Check for updates

OPEN ACCESS

EDITED BY David Vidal, Mayo Clinic, United States

REVIEWED BY Aditya U. Kale, University Hospitals Birmingham NHS Foundation Trust, United Kingdom Samar Betmouni, Sheffield Teaching Hospitals NHS Foundation Trust, United Kingdom Jeffry Hogg, Newcastle University, United Kingdom *CORRESPONDENCE Mandy Rickard, mandy.rickardgsickkids.ca

The silent trial - the bridge between bench-to-bedside clinical AI applications

Jethro C. C. Kwong¹²¹, Lauren Erdman^{2,3,41}, Adree Khondker⁵, Marta Skreta³, Anna Goldenberg^{2,3,4}, Melissa D. McCradden^{2,6,7,8}, Armando J. Lorenzo^{1,5} and Mandy Rickard⁵*

¹Division of Urology, Department of Surgery, University of Toronto, Toronto, ON, Canada, ²Temerty Centre for Al Research and Education in Medicine, University of Toronto, Toronto, ON, Canada, ³Centre for Computational Medicine, The Hospital for Sick Children, Toronto, ON, Canada, ⁴Department of Computer Science, University of Toronto, Toronto, Ontario, Canada, ⁵Division of Urology, Department of Surgery, The Hospital for Sick Children, Toronto, ON, Canada, ⁴Department of Biorepy, The Hospital for Sick Children, Toronto, ON, Canada, ⁴Department of Biorepy, The Hospital for Sick Children, Toronto, ON, Canada, ⁴Department of Biorepy, The Hospital for Sick Children, Toronto, ON, Canada, ⁴Genome Biology, Peter Gligan Centre for Research and Learning, Toronto, ON, Canada Proceedings of Machine Learning Research 174:169–182, 2022

Conference on Health, Inference, and Learning (CHIL) 2022

STONEKABONI@CS_TORONTO_EDU

MORGENSH@CS.TORONTO.EDU

AZADEH.ASSADI@SICKKIDS.CA

APOKHREL@CS.TORONTO.EDU

XI.HUANG1@SICKKIDS.CA

ANANDJ@CS.TORONTO.EDU

ROBERT.GREER@SICKKIDS.CA

FANNY@CS.TORONTO.EDU

MJAYE.MAZWI@SICKKIDS.CA

PEKHIMENKO@CS.TORONTO.EDU

MELISSA.MCCRADDEN@SICKKIDS.CA

How to validate Machine Learning Models Prior to Deployment: Silent trial protocol for evaluation of real-time models at ICU

Sana Tonekaboni University of Toronto, Vector Institute, The Hospital for Sick Children

Gabriela Morgenshtern Azadeh Assadi University of Toronto, The Hospital for Sick Children

Aslesha Pokhrel University of Toronto, Vector Institute, The Hospital for Sick Children

Xi Huang Anand Jayarajan University of Toronto, Vector Institute,The Hospital for Sick Children

Robert Greer The Hospital for Sick Children

Gennady Pekhimenko University of Toronto, Vector Institute, The Hospital for Sick Children

Melissa McCradden The Hospital for Sick Children

Fanny Chevalier University of Toronto, Vector Institute

Mjaye Mazwi University of Toronto, The Hospital for Sick Children

Anna Goldenberg ANNA.GOLDENBERG@UTORONTO.CA University of Toronto, Vector Institute, The Hospital for Sick Children







Thank you

@mmccradden

<u>@Mdmccradden@dair-</u> <u>community.social</u>

melissa.mccradden@sickkids.ca

Lab artwork by Stacey McCrady