Breakout Session 4: Track B

Ethical Considerations in the Design and Conduct Clinical Trials of AI: A Qualitative Study of Investigators' Experiences with Autonomous AI for Diabetic Retinopathy

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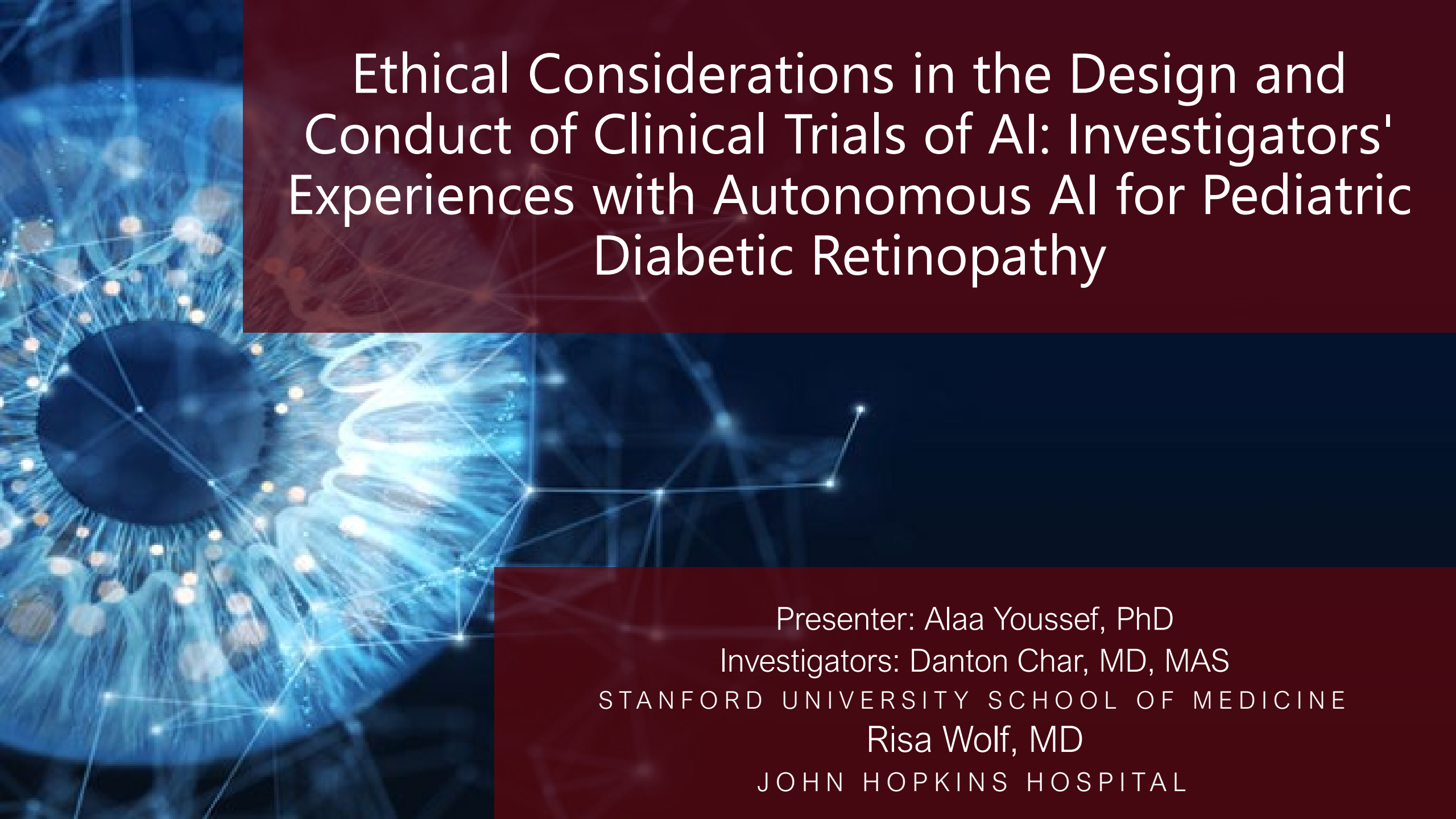

Ethical Considerations in the Design and Conduct of Clinical Trials of AI: Investigators' Experiences with Autonomous AI for Pediatric Diabetic Retinopathy

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Parent Award PI: **Risa Wolf, MD**

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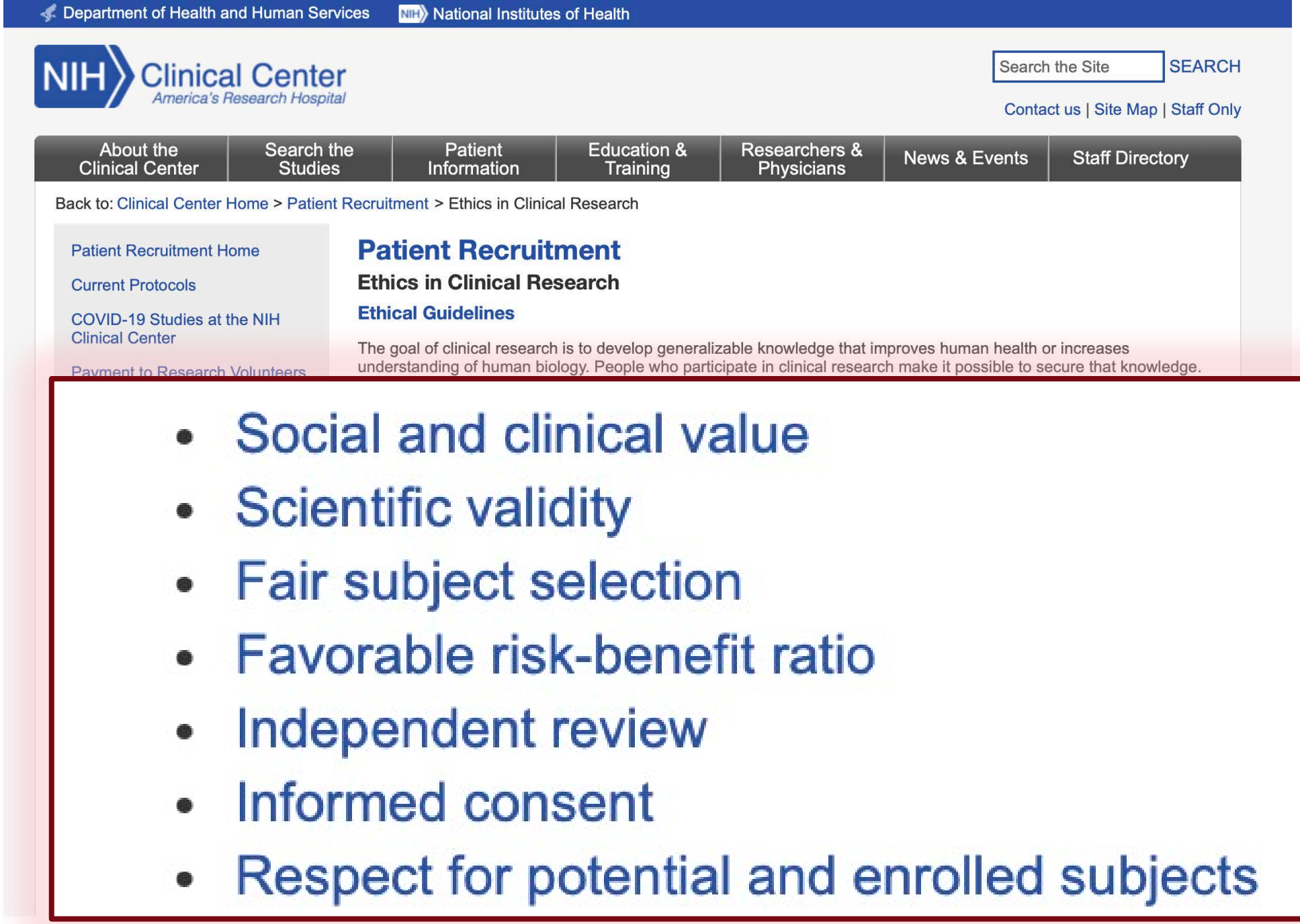

- Social and clinical value
- Scientific validity
- Fair subject selection
- Favorable risk-benefit ratio
- Independent review
- Informed consent
- Respect for potential and enrolled subjects

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PROJECT SUMMARY

Study Objectives

To determine the ethical considerations investigators encountered and negotiated, designing and conducting the first NIH-funded RCT of an autonomous AI and related clinical trials.

Research Question

How do clinical investigators recognize and navigate ethical issues in the design and conduct of clinical trials of AI?

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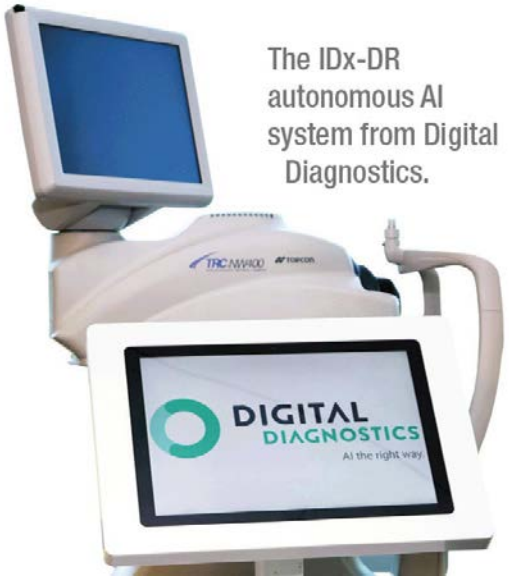
AI for Childrens diabetiC Eye ExamS (ACCESS) Trial

Article | Open access | Published: 11 January 2024

Autonomous artificial intelligence increases screening and follow-up for diabetic retinopathy in youth: the ACCESS randomized control trial

Risa M. Wolf, Roomasa Channa, T. Y. Alvin Liu, Anum Zehra, Lee Bromberger, Dhruva Patel, Ajaykarthik Ananthakrishnan, Elizabeth A. Brown, Laura Prichett, Harold P. Lehmann & Michael D. Abramoff

Nature Communications **15**, Article number: 421 (2024) | Cite this article



Wolf, R.M., *et al.* (2024)

METHODS

Study Design

- Qualitative study using semi-structured interviews with investigators involved in the design and conduct of clinical trials of AI for diabetic retinopathy screening.

Participants

- We employed purposeful sampling to engage investigators from the ACCESS study.
- We used snowball sampling for additional insights from those involved in related trials of autonomous AI.

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RESULTS

- We interviewed a total of eleven participants.
- Six were from the NIH-funded ACCESS RCT, including investigators, regulators, biostatistician.
- Three investigators from an RCT in a developing country.
- Two investigators from the private sector.

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KEY THEMES

There were unresolved ethical questions for all seven principles. These issues included:

- Measuring social value
- Establishing scientific validity
- Ensuring fair subject selection
- Determining risk-benefit ratios
- Obtaining informed consent

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Social Value

What are social values of AI that should guide design of study outcomes, and how could these outcomes be measured?

- Difficulty in defining and agreeing on the social value AI adds to clinical trials.
- Challenges in designing study outcomes that effectively measure the social value of AI.

"I think we should see what [social value] is from the patient's perspective that would be beneficial and then identify and measure that potentially with a quantitative metric." (008)

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Scientific Validity

What do you compare the AI to, to ensure that the trial is scientifically valid?

- The challenge of integrating AI model outputs into existing clinical workflows adds complexity to trials.
- Difficulty in finding an appropriate benchmark for AI, unlike more straightforward comparisons in drug trials

"I think — you know — there are some issues with AI around [scientific validity] because it's more of a systems intervention…it's hard to see whether individual randomization really makes sense." (001)

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Fair Subject Selection

How do you select trial participants fairly, when current access to care (and gold standard validations) is already disparate?

- Fair subject selection emerged as a critical focus area.
- Challenges in using AI tools to expand screening access due to existing health disparities and socioeconomic factors.

"It's tricky to ensure equitable access to AI screening, especially for those less likely to receive regular diabetes care. Monitoring the prevalence of diabetic retinopathy post-AI implementation and understanding the reasons behind disparities in screening rates and follow-up care are crucial." (002)

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Informed Consent

What are important barriers to informed consent in clinical trials of AI?

- Key barriers include privacy concerns and the challenge of explaining AI's technical aspects for informed decisions.
- Difficulty in ensuring understanding of privacy and confidentiality with AI tools.
- Transparency in participants' data use for AI development.

"The short answer is… that the informed consent that we've been using for a very long time, and really not suitable for digital health and not suitable for AI for many, many reasons. And IRB committees in general don't understand AI, so the whole system needs to be reconsidered." (009)

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CONCLUSION

This study highlights practical ethical challenges investigators need to consider and negotiate in conducting clinical trials of AI, exemplified by the diabetic retinopathy screening use-case.

FUTURE WORK

- Expand empirical research to understand ethical challenges in diverse clinical settings.
- Develop comprehensive ethical frameworks tailored to AI's unique attributes in clinical research.
- Strengthen normative guidelines to safeguard patient safety in AI trials.

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REFERENCES

- Youssef, A., Nichol, A., Martinez, N., Larson, D.B., Abramoff, M., Wolf, R., Char, D. Ethical Considerations in the Design and Conduct Clinical Trials of AI : A Qualitative Study of Investigators' Experiences with Autonomous AI for Diabetic Retinopathy. (In Submission)
- Wolf, R.M., Channa, R., Liu, T.Y.A. *et al.* Autonomous artificial intelligence increases screening and follow-up for diabetic retinopathy in youth: the ACCESS randomized control trial. *Nat Commun* **15**, 421 (2024). https://doi.org/10.1038/s41467-023-44676-z
- Abràmoff MD, Tobey D, Char DS. Lessons Learned About Autonomous AI: Finding a Safe, Efficacious, and Ethical Path Through the Development Process. Am J Ophthalmol. 2020 Jun;214:134-142. doi: 10.1016/j.ajo.2020.02.022.
- Alaa Youssef, Michael Abramoff & Danton Char (2023) Is the Algorithm Good in a Bad World, or Has It Learned to be Bad? The Ethical Challenges of "Locked" Versus "Continuously Learning" and "Autonomous" Versus "Assistive" AI Tools in Healthcare, The American Journal of Bioethics, 23:5, 43-45, DOI: 10.1080/15265161.2023.2191052
- Emanuel EJ, Wendler D, Grady C. What Makes Clinical Research Ethical? *JAMA*. 2000;283(20):2701–2711. doi:10.1001/jama.283.20.2701

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