Testing the Safety and Efficacy of a GLP-1 Receptor Agonist for the Treatment of Opioid Use Disorder in Rats and Man

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Disclosures

I have nothing to disclose.

Drugs “hijack” the reward pathway.

(Nesse and Berridge, 1997)

But what about the need pathway?

If addiction hijacks substrates
involved in physiological need . . .,

can opioid seeking and taking
be reduced by treatment with a known
‘satiety’ agent?

Use of a GLP-1 Agonist to Treat Opioid Use Disorder in Rats and Man

HEAL Initiative UG3 DA050325
Start Date: August 1st, 2019

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Pre Clinical Team

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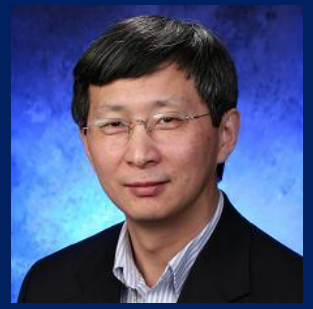

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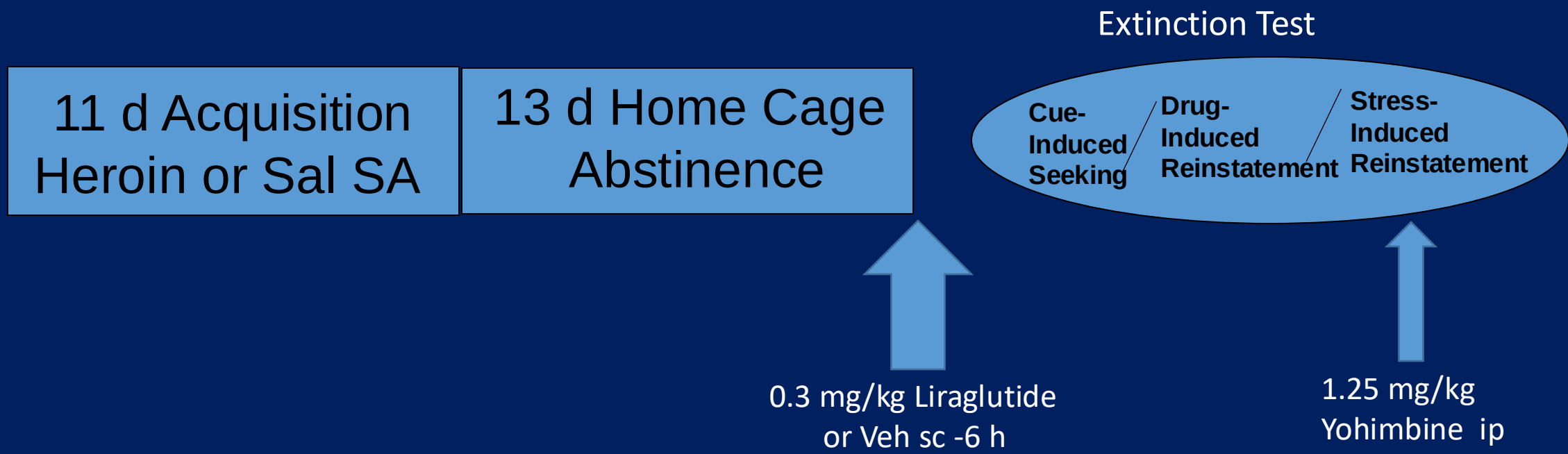
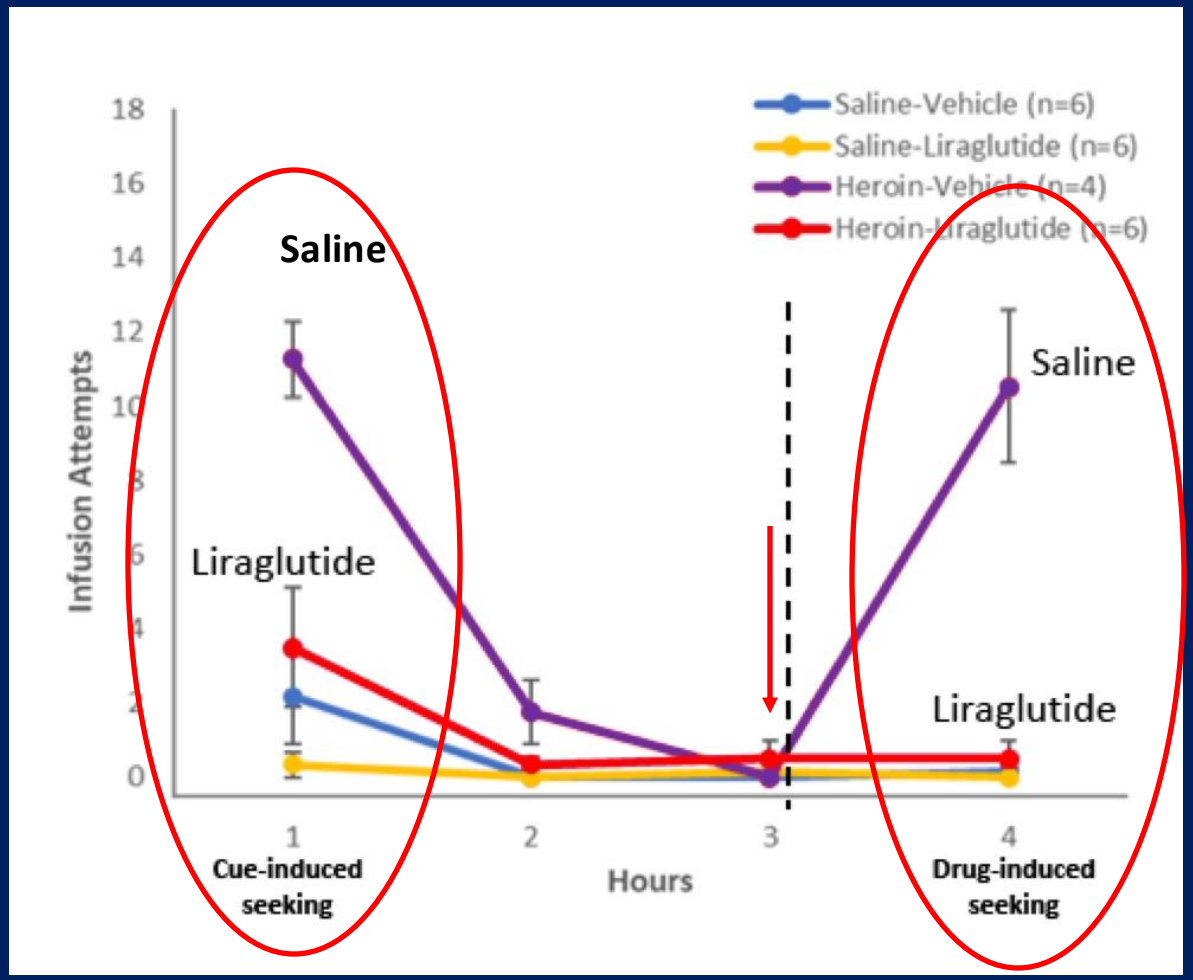
Preclinical Data

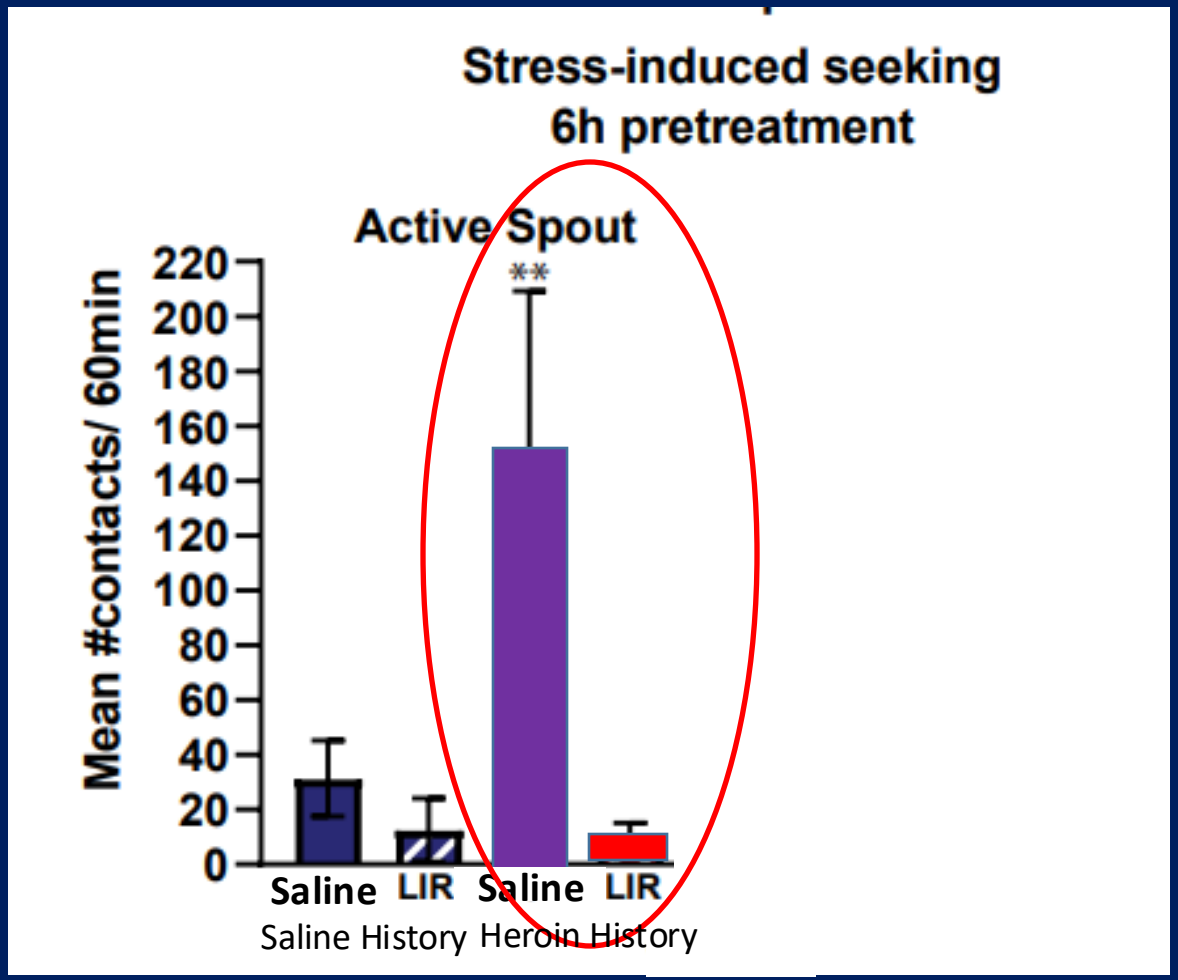
Acute Liraglutide and Heroin Seeking



Acute liraglutide reduces cue-, drug-, and stress-induced heroin seeking

Cue- **Drug-** **Stress-**





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Douton et al. (2022)
Beh Pharm 33: 364-378

Acute LIR fentanyl seeking (Male): Urbanik et al. 2022. Brain Res Bull 189: 155-162

Acute LIR fentanyl seeking (Female): Urbanik et al. Submitted

Chronic LIR heroin seeking: Evans et al. 2022. Brain Res Bull 189: 155-162

Chronic LIR fentanyl seeking: Urbanik et al. Submitted

What about people?

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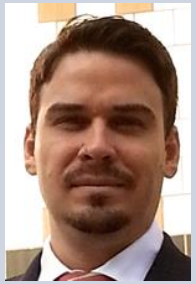

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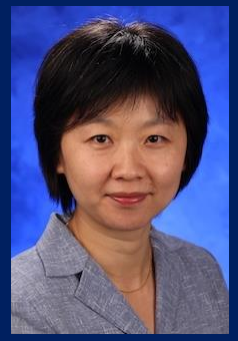

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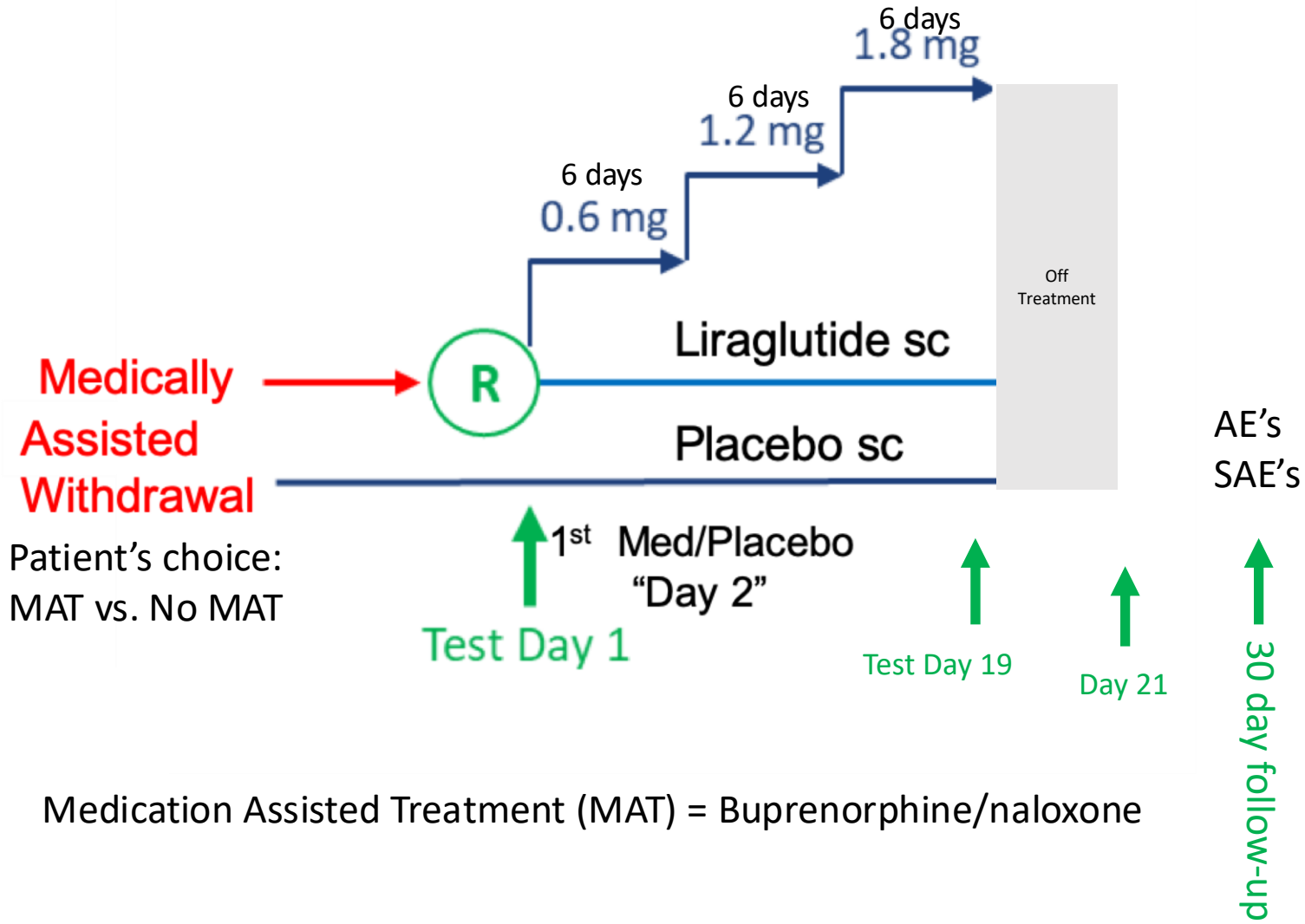
Study Design



Medication Assisted Treatment (MAT) = Buprenorphine/naloxone

Recruitment

UG3 – Phase 2 Clinical Trial

- Approached: Total: n=100+
- Declined: n≈75. Reasons:
  - need to focus on treatment
  - not interested in research, study burden
  - on too many medications already
- Randomized : Total n=25
- Valid EMA Data: Total n=20

UG3 – Phase 2 Clinical Trial
Ecological Momentary Assessment (EMA)

- Participants (n=20)
- Completers (n=9)
- 84% male; 92% Caucasian
- Groups
    - No MAT – Placebo (n=4)
    - No MAT – Liraglutide (n=3)
    - MAT – Placebo (n=6)
    - MAT – Liraglutide (n=7)

Medication Assisted Treatment (MAT) = Buprenorphine/naloxone

Safety

The GLP-1R agonist, liraglutide, had no adverse effect on body weight, blood glucose, or the cardiovascular system.

Efficacy

EMA Desire for Drugs Scale

Score = mean of three items, each scored on 5-pt Likert scale:

[0 = 'strongly disagree' . . . . . 4='strongly agree']

Drug intru ”

Missing dr

Drug satis

Scale relia
converger

With EMA:
N= 596 data points
across 202 person days

Love, James, & Willner (1998). *Addiction*, *93*, 1091–1102.

Cleveland, H.H., Knapp, K.S., Brick, T.R., . . . & Bunce, S.C. (2021). *Substance Use and Misuse*, 1-11.

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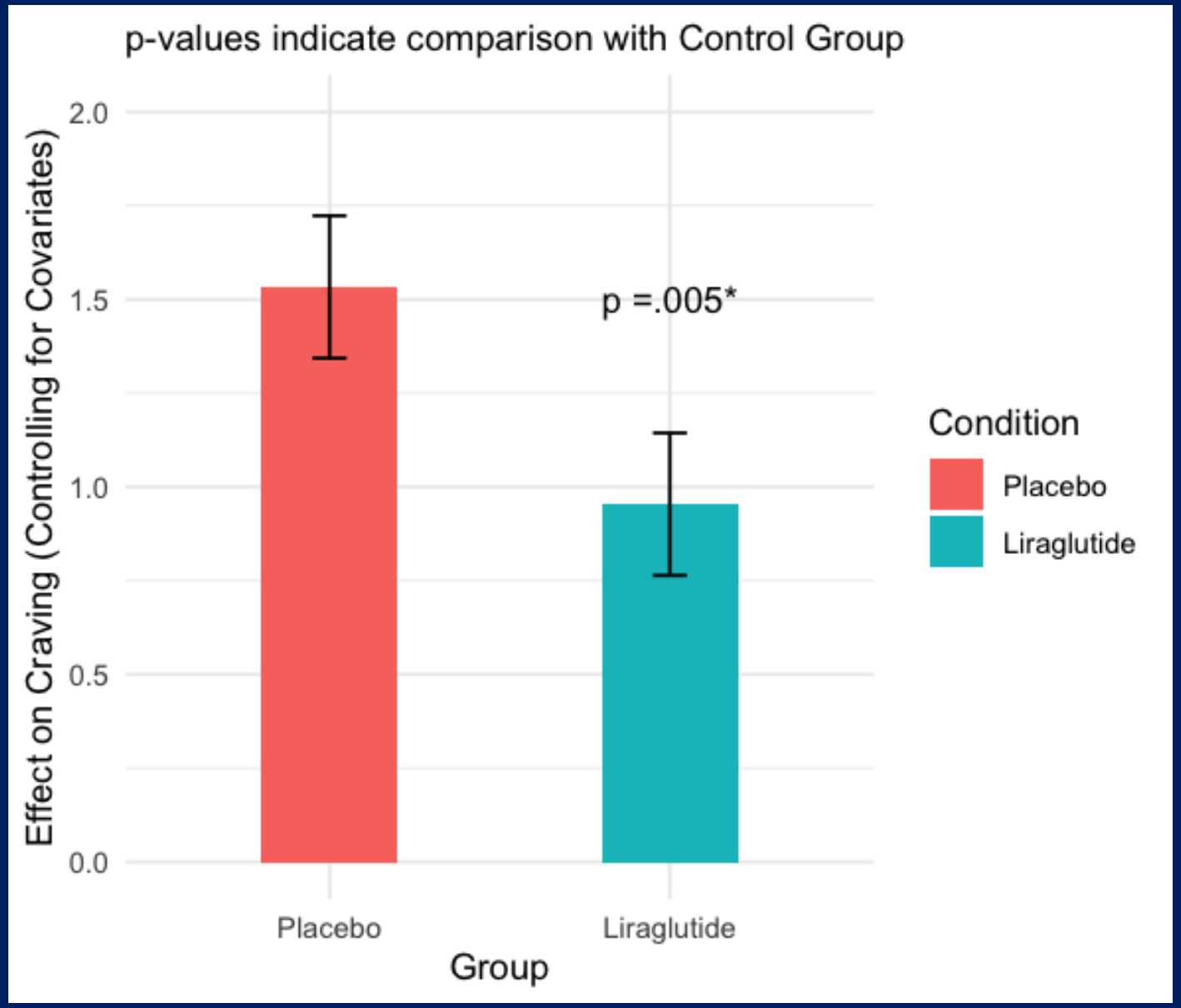
So, what did we find?

Effect of Liraglutide on daily Desire for Drugs



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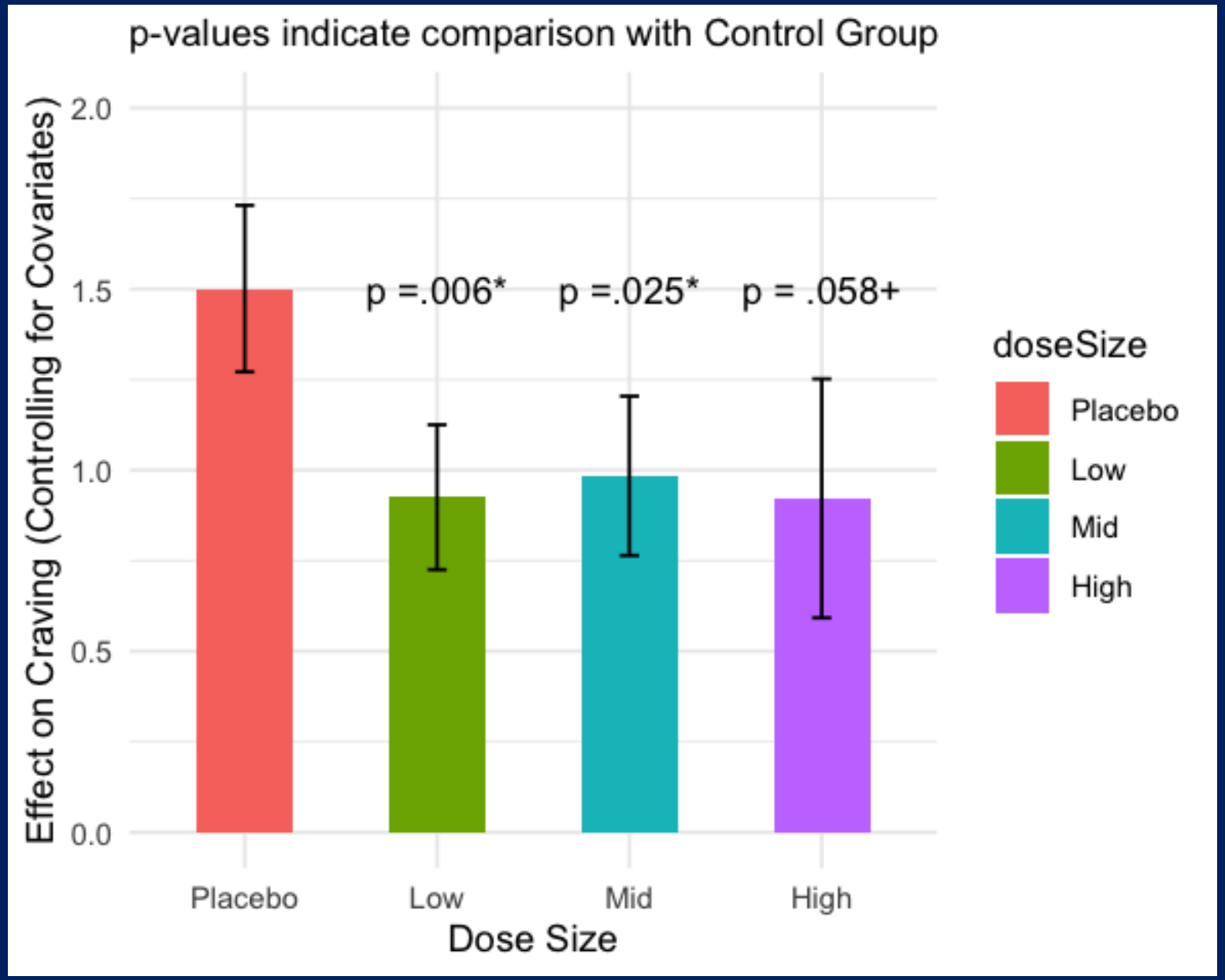
Effect of Liraglutide on Desire for Drugs across dose



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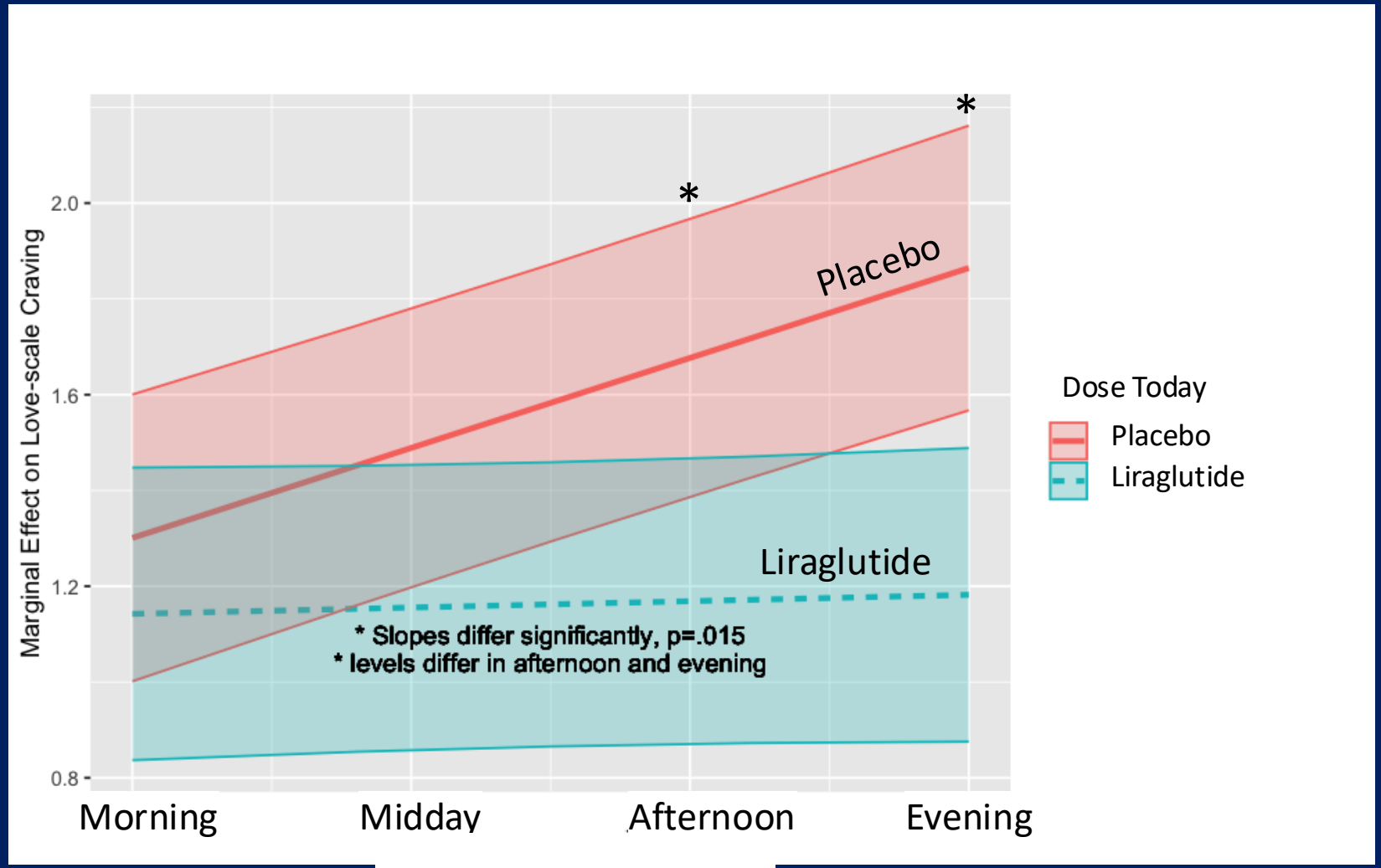
Effect of Liraglutide + MAT on Desire for Drugs across the day



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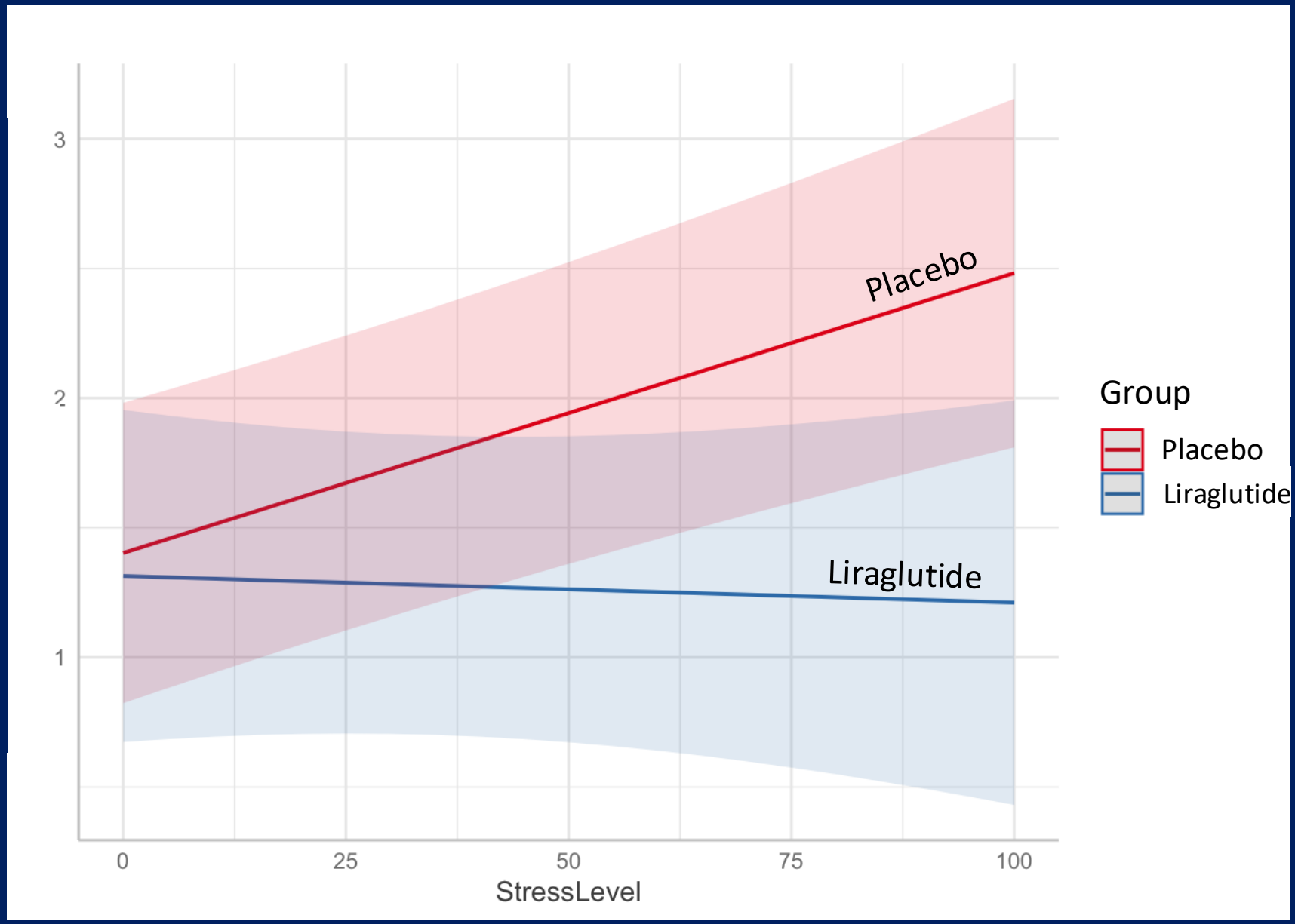
Effect of Liraglutide + MAT on stress reactivity



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Summary: UG3 Phase of Testing

Limitations

- Sample size was low (n=10 placebo; n=10 liraglutide)
- Population mostly male and mostly Caucasian
- Population residential

Findings: What did we learn?

- With EMA, liraglutide reduced craving relative to placebo treated controls
- Liraglutide was effective beginning with the lowest dose of the drug
- Liraglutide was effective when administered with MAT (buprenorphine/naloxone)
- Liraglutide was effective during times of high risk (i.e., in the afternoon and evening)
- Liraglutide blocked the facilitating effect of stress on craving

Future Considerations

- What is the ideal drug, drug formulation, dose, treatment regimen, treatment length, concomitant treatments, medical oversight?

Acknowledgements

UG3 TEAM

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